THE ANATOMY OF THE FOETAL PLACENTAL CIRCULATION.

by

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PREFACE.

In the preparation of this thesis the author was assisted by many people. He would like particularly to record his indebtedness to the following.

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INTRODUCTION

The human placenta is neither an easy structure to understand or to investigate. It is rather ironic that so little is known about this organ on which the continuity of mankind is utterly dependent. As late as 1950 it was stated by Hamilton and Boyd that our knowledge of the intimate structure and growth of the placenta is still only a first approximation.

The external appearance of the placenta is familiar to all who practice obstetrics and has been described by many authors. The internal anatomy is however still a matter for discussion and there is a wide divergence of opinion. It may be asked why so little is known about the anatomy of the placenta when other organs of the body, and seemingly more complicated, have had their structure demonstrated. The explanation of this anomaly lies in the innate structure of the placenta. It is not easy to dissect the placenta. The foetal vessels present, as the dissection is continued, an ever increasing network of divisions and ultimately dissection must be abandoned or becomes so inaccurate that it is of little value.

Dissection has, of course, been attempted and Bumm in 1893 published an account of placental anatomy based on many years of patient dissection. He visualised the placenta being composed of tree-like fronds or villi extending from the foetal chorion to the maternal decidua. Some of these fronds were attached to the decidua but the majority floated free in the maternal blood. This was a simple arrangement and easy to understand. It is possible to understand how widely this conception was accepted and it remained an accepted fact until Spanner in 1935 proposed a completely new idea of placental anatomy. After Bumm the method of injecting the placental vessels with dyes or 'fillers' such as gelatine or celloidin came to be used and various papers were published on the findings obtained by such methods. For example, in 1924, Kellog, Davis and Amolsch published photographs of the placental vessels, obtained by filling these vessels, through the umbilical cord, with bismuth and taking x-ray photographs. Their results were a great advance in so far as they showed the mode of division of the placental arteries and veins.

Also the penetration of bismuth was sufficient to demonstrate the terminal arterioles and venules. This gave an appearance at the end of the placental vessels of a "basket-like" arrangement. These workers also used celloidin to fill the placental vessels, and when the material had hardened the placental tissue was corroded away with a suitable acid, leaving a cast of the placental vessels which could be handled and dissected. This injection-corrosion technique was a great advance. Not only could the mode of division of the placental vessels be seen, but the cast was in three dimensions and the relationship of the vessels to each other could be appreciated. By this time it was appreciated that the umbilical arteries when they entered on the foetal surface of the placenta underwent a series of dichotomous divisions over the surface of the foetal chorion. At each of these divisions a proportion of the arteries would perforate the chorion and enter the substance of the placenta. These perforating branches would form the arterial blood supply of the villi. It was appreciated too that these vessels formed the villi and ended in a maze of small branches which were located at the periphery of the maternal surface of the placenta. The foetal veins were observed to accompany the arteries more or less regularly. Kellog, Davis and Amolsch were unable to demonstrate any arterial anastomosis after the primary anastomosis of the umbilical arteries immediately before the insertion of the cord. They believed however that an arterio-venous anastomosis was present in the substance of each of the villi. The objections to the injection-corrosion technique can be stated at this point and they are quite formidable. In the first place the placental vessels must be washed out with normal saline solution to get rid of foetal blood. This can produce vessel rupture and subsequent leakage. Thereafter, as a preliminary to the actual injection of the chosen 'filler' the foetal vessels must be washed out once again with acetone to prevent premature hardening of the filler and ensure its farthest possible penetration. Acetone denatures vessel walls and makes them still more liable to rupture. The fillers usually employed have a certain viscosity and considerable pressure is necessary to force the filler along the vessel lumen. As a result of this and the preliminary treatment the filler usually leaks and the cast is often distorted. Artefact is an ever present possibility and since the foetal vessels are removed by the subsequent corrosion there is no way of checking the accuracy of the cast.

In 1935 Spanner after ten years investigation, both of delivered placentae and placentae in situ, published an account of the foetal placental circulation. His views have been widely adopted and are still the basis of standard teaching in most countries. He used mostly liquid latex as the filler and studied not only corrosion casts but also injected placentae in situ. His results were excellent and no one has obtained better preparations with this technique. He described the placental vessels perforating the foetal chorion and entering the villus. The villus then passed down to the maternal decidua where the most peripheral branches entered the decidua and after an interval re-emerged and passed up into the placenta. The "downwards and upwards" course of the vessels of the villi has been compared to the branches of an old-fashioned chandelier in their arrangement. Stieve, rather derisively perhaps, called them "weeping willow trees" (Wie

Trauerweiden). The extent of penetration into the smallest vessels, obtained by Spanner, was excellent and even terminal capillaries were entered. He described villi giving off long terminal capillaries which, of course, were in intimate contact with the maternal blood. Spanner also described the presence of sphincters in the foetal veins of the villi. It is a tribute to the excellence of his work and opinions that even today most workers in this field still accept Spanner's conclusions more or less completely. At this point it is perhaps worth explaining that the term "villus" has been used more or less synonomously for cotyledon or lobe. Subsequently Stieve, a fellow German, disagreed in his published works with Spanner's findings. In particular he objected to the chandelier arrangement of villi and believed it to be quite untrue. Also, he objected to Spanner's contention that the terminal portions of the villus float freely in maternal blood. This would constitute a "villous" type of placenta such as is found in the lower orders of mammals. This, he urged, is not borne out by histological examination. The terminal villi in histological section are seen to be mostly adherent and Stieve inferred that the terminal villi formed a labyrinth and would suggest that the human placenta is fundamentally "labyrinthine" in nature. He urged that all the villi should be regarded as adherent and without free terminal villi. The labyrinth of villi was described by him as a three dimensional lattice work or fringe (Gitterzotten) and analagous to a sponge, the maternal blood being present in the interstices of the fringe rather than free in the form of a lake. He also believed that not only fusion of syncytium took place but also capillaries passed from one villus to another. Hamilton agreed with Stieve that fusion of syncytium between terminal villi certainly occurred, especially in the latter half of pregnancy. He doubted however whether all terminal villi should be regarded as fixed and also whether sharing of blood vessels took place except perhaps occasionally. Since Stieve's last paper in 1948 two more investigations concerning the foetal placental circulation have been published. In 1951, Romney and Reid carried out a series of injection-corrosion studies using a plastic, vinyl acetate, as a filler. This investigation was concerned mostly with the capillary bed of the placenta but an adequate account was given of the gross anatomy of the foetal placental circulation. The casts obtained were excellent. The capillaries were entered and could be shown, at least in part. The general arrangement of the larger vessels was described. They claimed to have observed anastomosis between adjacent arteries on the foetal chorionic surface at the periphery of the placenta. In addition they noted that the placenta possessed a very extensive capillary bed which was most dense nearest to the decidua. They could not confirm Spanner's 'chandelier' arrangement of vessels and could find no evidence of sphincters. They believed that the capillaries of the terminal villi, whilst extremely numerous were relatively short. The casts of the capillary vessels which were obtained led them to believe that the capillaries under the chorion differed from those at the decidua and concluded that they had perhaps a different function from each other. The latest work on the placenta was published in 1954 by Watkin. He also used injection-corrosion technique. He described the villus or cotyledon as being drum shaped with vessels around the periphery and hollow in the centre. The base of the villus had a gap which he termed the crown (couronne). In addition he supported Spanner's chandelier arrangement of the villous vessels.

The history of the investigation of placental anatomy related so far has given some idea of the difficulties inherent in this particular subject. The divergence of opinion has made it difficult to form a clear picture of placental anatomy. It is quite impossible to be even reasonably sure which view is the correct one and this indicates the urgent need for a fresh investigation of the whole subject. If possible a new technique would be desirable. It has been pointed out previously the ever present risk of artefacts with injection-corrosion techniques and this may well explain the diversity of views expressed.

The need for an accurate picture of placental anatomy is not just an academic quest. An understanding of placental anatomy would permit in turn, an understanding of the pathological lesions observed in the placenta, an understanding of clinical results particularly in relation to foetal death or survival and last but by no means least, an understanding of placental growth.

The precise way in which the placenta grows is quite unknown. There is a popular impression.

that the placenta grows in size by spreading over the surface of the uterus like a fungus. In the process of growth it is presumed to establish connections with new maternal vessels and so ensure a continuity of maternal blood for the whole placenta. It manifestly increases in size, weight and thickness, throughout pregnancy. The actual method by which these increases are brought about has not been the subject of any scientific scrutiny. This has not indicated a lack of desire but indicated rather the technical difficulties in the way of such an investigation. Spanner did not believe that the placenta grew in circumferential area during the second half of pregnancy but only increased in thickness. Stieve took the opposite view. He believed that circumferential growth took place in the latter half of pregnancy but no increase in thickness. It has been pointed out by Barcroft that the oxygen needs of the foetus as it grows are continually expanding. This increase has to be met by placental growth and the foetus is continually threatening to outstrip its oxygen supply. There would seem to be a series of oxygen crises in utero during pregnancy and as term approaches the placental growth does not keep pace with foetal growth. As pointed out by Walker, this may have serious consequences in labour and especially in post-mature labours, producing foetal anoxia and even death, in utero or in the neo-natal period.

These problems, clinical and anatomical, emphasise the need for a re-investigation of the foetal placental circulation using a fresh technique. In the next part of the thesis a technique will be described which is free from most of the objections which beset the injection-corrosion techniques and allows a more complete demonstration of placental anatomy than has been possible so far.

PART 1.

The Technique of Digestion.

Rationale of Technique.

In the early stages of this study of the foetal placental circulation the method used was the injection-corrosion technique. Both latex and vinyl acetate were used as fillers. In the performance of this method the difficulties which have been alluded to previously became obvious. The placental vessels are filled with foetal blood and this must be removed by washing before injection of filler is possible. As a preliminary to washing it was found that deep-freezing the placenta for 24 hours previously produced haemolysis of the foetal blood and made the subsequent washing out easier. Even so it was not easy to wash out the whole placenta and leakage from the vessels which commonly occurred made the washing out much less efficient. It was necessary afterwards to wash out the placental vessels with acetone and this denatured the vessels and made subsequent rupture more certain. The actual filling with latex or vinyl acetate was alwaysincomplete and rupture somewhere almost always took place. Thus with the spilling of filler artefacts were always likely and since the placental vessels were corroded away there was no method of checking the accuracy of the cast. The likelihood of artefact, it was felt, certainly helped to explain the extremely contrary views expressed by previous workers. At this point in the investigation it was felt that a new approach by a new technique was necessary. In particular a technique which would avoid the creation of artefacts.

In histo-chemistry it is the practice to use trypsin for the identification of protein. The material to be studied is digested with trypsin in an alkaline medium suitably buffered. Thereafter it is processed in the usual way and if a certain tissue component has disappeared it is certain that it was protein in nature. Also, in pathology where areas of tissue necrosis are present parenchymatous tissue disappears before connective tissue and blood vessels and this disappearance is related presumably to proteolytic digestion. In this fashion the idea was conceived of digesting the placenta and removing parenchymatous tissue whilst preserving connective tissue such as blood vessels. Since proteolytic enzymes are the most important trypsin was finally selected, after some experimentation, as the most likely enzyme to employ. Before proceeding to the actual method of digestion various points were gone into with regard to the conditions under which enzyme activity takes place. It is well known that for the continued action of an enzyme a buffered environment is necessary, trypsin for example requiring a medium with a pH of 8. In a complex structure such as the placenta which contains maternal and foetal blood, maternal and foetal tissues it was felt that any attempt to maintain a constant pH would be extremely difficult or impossible. It was therefore decided to adopt a simpler technique and to renew the enzyme solution whenever it was necessary to obtain more complete digestion of the placental structures.

In practice it has been found that parenchymatous tissue is easily digested whereas connective tissue resists the action of the enzyme for a considerable time. It is possible therefore by controlled digestion to remove the parenchyma and leave structures such as blood vessels, intact. Preliminary experiments showed that it was possible to remove decidua, chorionic epithelium and mesoderm leaving behind the foetal vessels, chorion and umbilical cord. Subsequent work, however, has shown that the technique must be modified according to the type of vessel it is desired to study, and the duration of digestion watched carefully. If the main structure of the vascular tree is to be studied, digestion may be allowed to proceed unchecked, but removal of all support from the vessels in this manner renders them liable to damage and it is difficult to demonstrate the finer ramifications of the vessels. This is particularly so in relation to the terminal capillaries. These are extremely fragile and if not already attacked by the enzyme may easily be swept away in any subsequent washing or handling unless extreme care is exercised. It has even been found possible to limit the digestion to the decidual layer leaving the villi complete with their covering of chorionic epithelium. This has greatly facilitated the study of the villus and its constituent capillary. Following digestion with trypsin the placental vessels may be injected with a coloured gelatin solution and subsequently hardened and preserved in formalin.

When digestion and injection are completed the placenta is a permanent preparation and can be handled and dissected without difficulty.

Materials.

Placentae. Only fresh placentae were used and were digested usually within a very few hours of delivery. If any delay was anticipated the placenta was refrigerated until required. The object of using fresh material was to guard against any possibility of artefact by decomposition. Since the start of this investigation of the foetal placental circulation more than 100 placentae have been examined. In addition five specimens of placentae "in situ" have been obtained and digested while still attached to the parent uterus. Round glass jars sufficiently big to accommodate the whole placenta and allow it to lie flat without distortion were employed. For digesting single lobes or smaller pieces smaller vessels were used; the important point being to adjust the size of the vessel to the size of specimen and so keep all of the enzyme in contact with the tissue.

For injection of the specimens following digestion, polythene catheters were employed, of a diameter small enough to enter the umbilical vein and arteries. It is of advantage to cut the catheters straight across and not to a point. The vessel walls are thin and can be penetrated easily.

A large hypodermic syringe, of at least 50 ml. capacity, was used for the actual injection.

A one per cent. solution of a water soluble opaque dye made by Imperial Chemical Industries was found to be most satisfactory, "Monolite" for green, yellow and red; "Monastral" for blue. The arteries and veins may be injected with red and blue dyes respectively. These dyes can be used alone or dissolved in fifteen per cent. gelatine solution.

The digest solution. This consists of a one per cent. solution of sodium carbonate, and is used to immerse the whole placenta or a lobe as required. Then to the alkaline solution is added sufficient trypsin powder (B.D.H.) or liquor trypsin compound, (Allen and Hanbury), to produce a one per cent. solution of digest.

The Method of Digestion.

(a) The Placenta.

A fresh placenta is washed carefully in cold running water to remove blood clot, and the foetal membranes pared off around the placental edge. The cord is cut short but should not be less than three to four inches in length. The placenta is placed in a glass container, maternal surface downwards and covered completely with the solution of digest. The container is covered with a lid and the placenta incubated at 37°C for periods varying according to the structure to be examined. It is of advantage to inspect the rate of digestion frequently during the digestion period. It has been found that the activity of commercial trypsin varies and digestion may proceed more rapidly than anticipated with a loss of specimens. A fume chamber, in which the incubator can be placed, is of immense advantage. At the end of digestion the odour is offensive.

When digestion is complete the placenta in its container is placed in a larger vessel into which a gentle stream of cold water is led. It is important that the water should not run directly on to the placenta. After a few hours the digested material will have been washed away. If it is considered that further digestion is necessary the placenta can easily be replaced in the incubator with fresh digest solution and

and the digestion continued. When digestion is complete the placenta consists only of umbilical cord, chorion, and cotyledonary vessels.

The specimen is next immersed in 10 per cent. formol saline for approximately 1 hour. This hardens the tissue somewhat without producing distortion. Thereafter the specimen is immersed in warm water. The umbilical vein and arteries are catheterised gently and gelatin solution, suitably coloured blue or red, injected into the vein and arteries. The gelatine should be at a temperature of fifty degrees centigrade or more to ensure the fullest penetration of the solution. An ordinary 50 ml. hypodermic syringe is quite suitable and gentle finger pressure sufficient. Excessive pressure should be avoided. About 100 ml. are required for each artery and vein, and the quantity should be too little rather than too much. Injection should be carried out rapidly and when completed the placenta is placed in a cold solution of 10 per cent. formol saline for at least another hour before being handled.

(b) The capillary vessels.

A rather different technique is necessary to demonstrate the capillaries of the villi.

The placenta is washed as before in cold water and a suitable lobe selected. The main artery and vein supplying this lobe are injected with a one per cent. solution of red and blue dye respectively with the addition of a small amount of one per cent. solution of sodium carbonate. The alkali appears to favour penetration of the dye. A fine hypodermic needle is used and the vessels entered directly in the usual way as for a venepuncture. About 20 ml. are sufficient in each case.

The lobe is now cut out of the placenta and placed in a small glass jar or container with the maternal surface uppermost. This is most important. It allows the vessels to float freely in the digestion solution and permits examination without disturbing the specimen unduly. Digestion solution is added and the lobe incubated for not more than twenty four hours at 37°C.

At the end of this time the container is opened and with great care the digest solution is siphoned from it and replaced with ten per cent. formol-saline. Formol-saline hardens the capillary vessels and makes them more amenable to dissection. The specimen can be examined at once but storage in a refrigerator for considerable periods does no harm provided the lobe is kept moist with formol-saline.

By sharp dissection very small pieces of tissue are cut from the surface of the lobe and placed on a glass slide which has been moistened with water. After digestion pieces may be dissected from a cotyledon at any level from the chorion outwards, thus allowing a complete picture of capillary distribution to be built up. Before proceeding with the mounting of the specimen, it should be examined with a low power objective to ensure that the area is well coloured, both red and blue. Glycerine jelly is dropped on the specimen and a glass cover slip placed over it. Gentle pressure with the point of a fine hypodermic needle is now exerted over the area of tissue under the cover slip. The material will be seen to flatten and gradually spread out. Pressure is continued until it is apparent that no further spreading will take place and also until the jelly is sufficiently hardened to keep the material in its present position. The preparation is now ready for examination. This pressure method of mounting has been found to be much easier and more satisfactory than dissection under direct vision.

The placental capillaries are, in life, closely enmeshed with each other and the difficulty in their examination has been to devise a simple method of separating them without causing damage. Pressure does this in a satisfactory fashion and allows individual capillary vessels to be seen in their entire course. The digestion can be controlled in such a manner that only the maternal decidua and fibrinoid layer is affected thus permitting the retention of the syncytial membrane around the capillary. This gives a satisfying picture of the capillary vessel.

(c) Placenta in situ.

Five placentae have been digested while still in situ. The method employed has been the same as for ordinary placentae with the exception that a larger container was needed to accommodate the uterus. The uterine vessels and placental vessels were injected with filler before digestion instead of afterwards as is the usual practice. After digestion the uterus is soft and the arteries and veins most difficult to identify and catheterise. By using placentae in situ it was hoped that the foetal vessels nearest to the decidua could be studied intact and the extent of their penetration into the maternal decidua, if any, determined. Stieve has pointed out that to study only placentae delivered per vaginam is quite wrong. The most terminal branches are often missing and any study made of them is bound to be incomplete and fallacious.

Part II.

The Gross Anatomy of the Foetal Placental Circulation.

It is proposed to describe the anatomy of the placental circulation under three headings.

First - The Umbilical Cord.

Second - The Foetal Surface of the Placenta, describing arteries and veins separately.

Third - The Maternal Surface of the Placenta.

The Umbilical Cord.

The chorionic covering of the cord is relatively resistant to the digestive power of trypsin. At the end of digestion the umbilical vessels are intact and can be catheterised readily with a suitable polythene catheter. The warm gelatine solution will flow easily into the foetal vessels almost under its own pressure. At the same time, owing to the resistance of the connective tissue to tryptic digestion, rupture of vessels practically never occurs.

There are usually two arteries and one vein, but a single artery is occasionally found. If two arteries are present they communicate by a very short branch just before the insertion of the cord into the placenta. In many cases this communication is in the nature of an artery to artery anastomosis without any intervening branch.

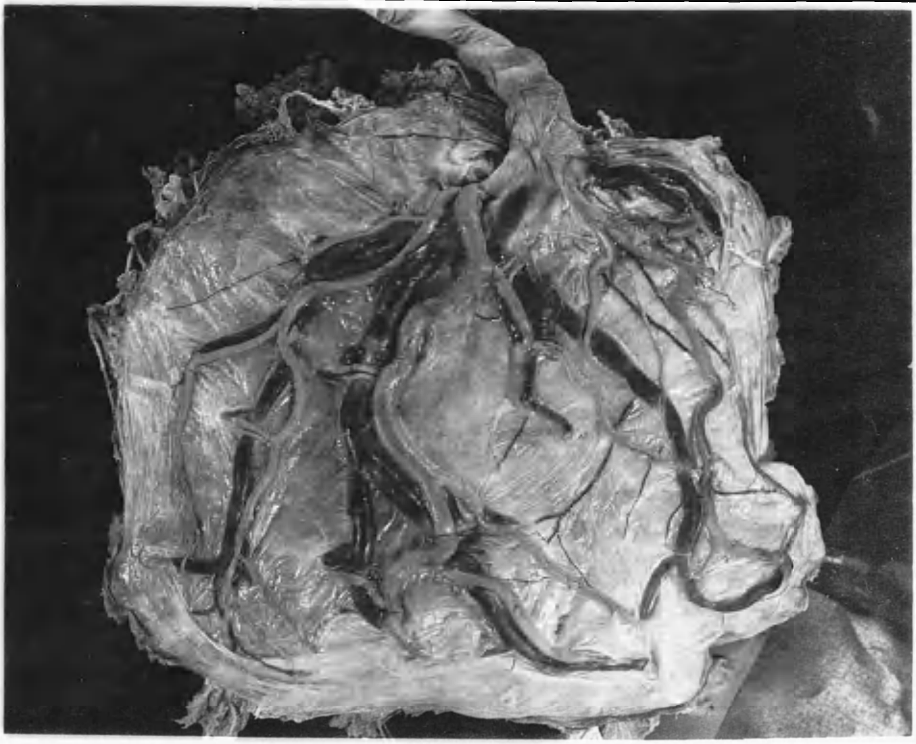

Figure 1.

This photograph shows a placenta which has been digested and thereafter the vessels filled with coloured gelatine. The arteries appear light, and the veins dark, in colour. The large size of the vessels is apparent and bears testimony to the great volume of blood circulating through the placenta at any instant.

Immediately after this anastomosis the arteries divide into their primary divisions and pass forwards onto the foetal surface of the placenta.

The Foetal Surface of the Placenta.

The chorion over the foetal surface of the placenta is also resistant to trypsin and, unless excessive digestion has taken place, will be intact, providing a firm framework for the placental vessels. When the placenta is ready for examination it is seen to consist only of umbilical cord, chorion and the vessels with their related cotyledons. The main vessels run between two layers of chorion and are most firmly secured in place. It is necessary to employ sharp dissection to free a main trunk from the chorion.

Each umbilical artery begins to divide before the placenta is reached and the divisions are usually of unequal size. The main trunk divides as a rule into several primary divisions. Two or three of these in each half of the placenta, course forward over the chorionic surface. It will be shown later that there are more primary divisions but they cannot as yet be seen.

The fate of each of these primary divisions

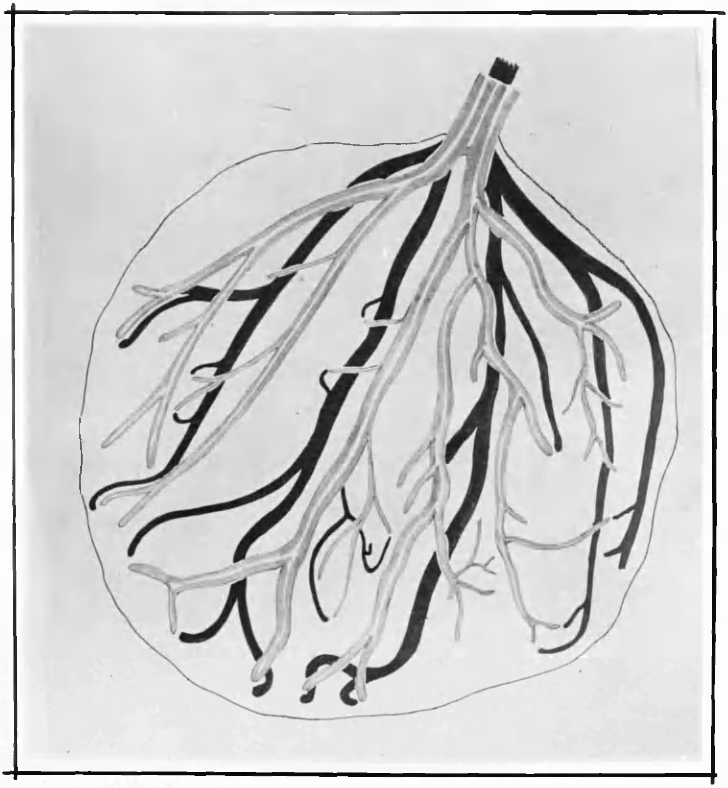

Figure 2.

This drawing is intended to illustrate the manner in which both arteries and veins undergo division on the chorion before penetrating it and entering the interior of the placenta.

is subject to variation in individual placentae. It is quite usual for one division to end at once and enter a cotyledon, leaving the other primary divisions to continue their course. These vessels undergo further division into secondary branches. A proportion of these secondary divisions end in cotyledons and leave the remaining divisions to continue towards the periphery of the placenta. Division again takes place and a proportion of the tertiary divisions will again end in cotyledons. The remainder are now approaching the periphery and a final division into cotyledonary arteries takes place at the limits of the chorion. In other words at each division of the main vessel a number of the branches plunge immediately through the chorion to end in cotyledons while others continue their course in the chorion towards the periphery. This provides for a roughly concentric distribution of cotyledons.

From the level of the main artery down to the level of the last division lateral branches of varying size, some extremely small, arise directly from the parent vessel and end after an interval in a cotyledon or sub-divide and the sub-divisions end in cotyledons. In general these vessels are much smaller than the main divisions of the umbilical arteries and the size of the corresponding cotyledons is in direct proportion to the vessel.

Two aspects of the arterial circulation are of note. First, in all the placentae examined there was no evidence of collateral circulation, after the primary anastomosis, between the branches derived from the same parent artery or between the branches derived from either umbilical artery. Second, all of the arterial divisions, large or small, ended ultimately in cotyledons. A diligent search has been made for branches which might be concerned in the nutrition of the chorion but these, so far, have not been seen, but this point will have to be investigated in greater detail before a definite conclusion is reached. By the time that the terminal sub-divisions have taken place each half of the chorion is occupied by a network of dividing and sub-dividing vessels and these, as already mentioned, do not communicate with each other or with the branches in the other half. In some placentae where one umbilical artery is larger

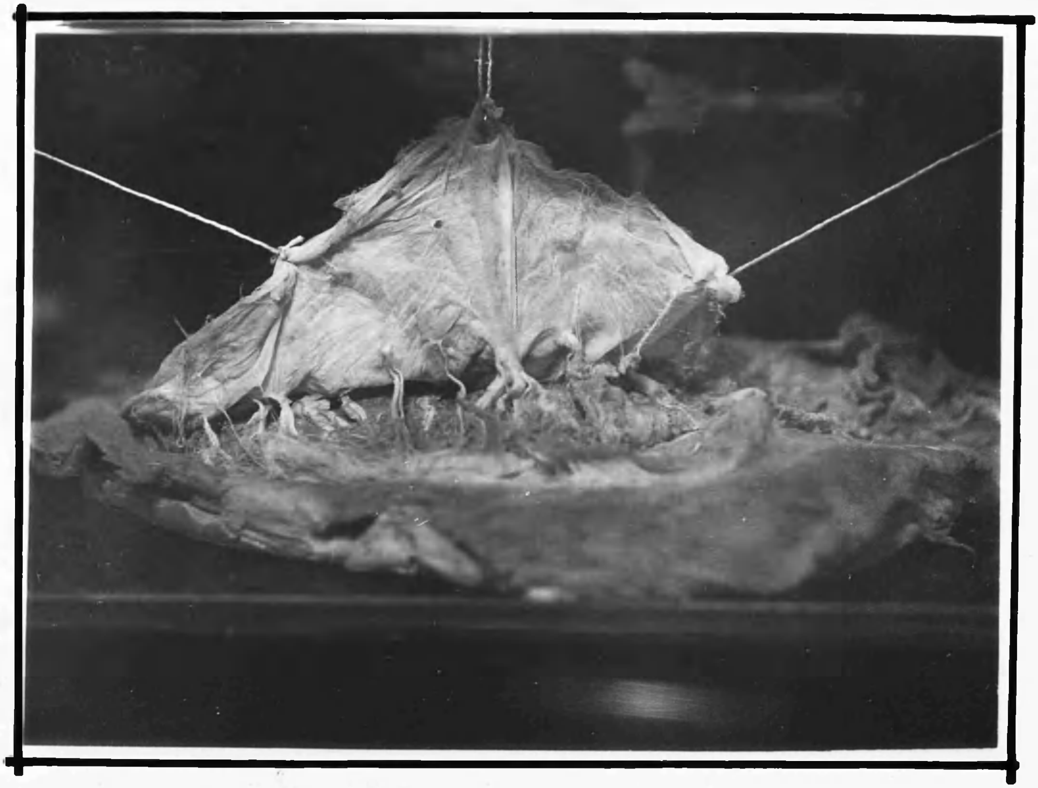

Figure 3.

In this photograph the placenta remains attached to the uterus and the chorion has been reflected upwards. The vessels to the cotyledons can be seen emerging through the chorion. The bare areas of chorion on the maternal aspect, between the vessels, is also apparent.

than the other, it may occupy more than half of the chorion with its system of branches.

An arterial branch may enter a cotyledon in one of two ways. The artery may leave the chorion quite suddenly by turning through a right angle, perforating the chorion and passing straight down to the cotyledon. In this variety the artery is joined at the moment of perforation by the accompanying vein and the vessels enter the cotyledon side by side. The chorion accompanies these branches and binds them firmly together.

On the other hand the artery may leave the chorionic surface more gradually and proceed obliquely down to the cotyledon. The vein will join it along this course and the cotyledon is entered by the artery and vein together invested with chorion. Usually, arterial branches lie superior to veins on the chorionic surface.

The umbilical vein is formed by the union of sub-divisions and divisions of veins much in the same way as the umbilical artery is distributed. The veins in the main accompany the corresponding arterial branches, and the size of the vein matches the artery. Many of the veins show lateral branches which accompany and begin

Figure 4.

This photograph illustrates a placenta which has been digested and thereafter its vessels filled with coloured gelatine. The arteries appear lighter than the veins which are not easily seen as they lie almost entirely inferior to the arteries on the chorion: The placenta has been dissected to demonstrate the general distribution of its main vessels and their branches. To facilitate dissection the chorion has been largely removed. The largest cotyledons appear as end terminations of the largest vessels. Smaller cotyledons can be seen, in the bottom left hand corner, originating from the deep surface of the main vessels as they lie on the chorion. Even smaller vessels also derived from the main branches, run laterally in the chorion before perforating the chorion and ending in small cotyledons.

with the small lateral arterial branches already described. These small veins may travel a considerable distance from the accompanying arterial branch before reaching the parent trunk and some of them describe a curved pathway to do so.

None of the veins which were examined show evidence of sphincters. In some of the veins, however, there are constrictions at right angles to their course but these appear to be constrictions by the investing chorion rather than actual sphincters.

The Maternal Surface of the Placenta.

The cotyledons in this state are readily separated from each other and their structure easily examined. They vary greatly in size and complexity and as previously stated the calibre of the vessels supplying them is in direct proportion to the size of the individual cotyledon. It will also be seen that quite considerable areas of bare chorion separate the perforating vessels supplying the cotyledons.

The cotyledons are formed in two separate ways. It has already been mentioned that the total number of primary divisions of the umbilical

Figure 5.

The maternal aspect of a digested placenta is shown in this photograph. The large number of cotyledons present is most apparent. In addition the bare areas of chorion between the cotyledonary vessels are most striking.

artery is not immediately obvious from scrutiny of the foetal chorionic surface. Subsequent examination of the digested specimen reveals that there are deep branches springing from the under surface of the parent vessels and passing directly through the chorion to form cotyledons. Such deep vessels may arise at the stage of primary or secondary division of the main arteries. They are joined on the way as before by the related vein. Some of these branches may be quite large and themselves constitute primary or secondary divisions.

In the second way cotyledons are formed by the arterial branches perforating the chorion as already described in company with their veins and entering a cotyledon together. The vessels supplying the largest cotyledons may be of considerable size and sometimes remain intact for 2-3 cms. before branching to form the cotyledon.

In the case of the largest vessels division may occur after perforation of the chorion, into two or more branches, usually of unequal size. The method of branching is rather different from that occurring on the chorionic surface. In the latter case branching is in the form of a repeated dichotomy, whereas beneath the surface of the chorion the vessels tend to give off lateral branches while holding to their main course. Both the main stem and these lateral branches give rise to cotyledons, the size varying with the vessel. That supplied by the main stem is usually the largest.

The artery and vein supplying a cotyledon have been described as running side by side but occasionally the vein in order to reach the cotyledon may describe a simple spiral over the artery which is running straight or the artery may describe a simple spiral over the vein. This spiral is essentially simple, consisting of one or two turns, and not comparable to the spiralling of endometrial vessels.

In all of the placentae examined there was no evidence of a collateral circulation; each cotyledon has its own separate blood supply.

The Diameter of the Placental Vessels.

1. Arteries.

Primary division:	0.7 cm.
Secondary division:	0.5 cm.
Tertiary division:	0.4 cm.
Cotyledonary vessel:	0.2 cm. or less.

2. Veins.

Primary division:	0.8 cm.
Secondary division:	0.7 cm.
Tertiary division:	0.5 cm.
Cotyledonary vessel:	0.3 cm. or less.

Figures 1 to 5 illustrate some of the anatomical features described in Part II.

PART III.

The Anatomy of the Cotyledon.

The Method of Description.

The structure of a cotyledon is not easy to describe: in part because it is complicated, and in part because it is a three dimensional structure, and its relationship to neighbouring cotyledons must also be described at the same time in order that a complete picture of placental anatomy is presented. The method adopted tries to overcome the above difficulties by describing a cotyledon as if it had already been separated from its neighbours, dissected completely and, its constituent structures laid bare. When the cotyledon has been described, its constituents will be assembled and considered as a whole and integrated structure.

The Origin of the Cotyledon.

A cotyledon can be defined as that portion of the foetal placental circulation which will bear at the termination of its smallest vessels, the capillaries.

Apart from the investing chorion around the larger vessels, and the mesoderm and covering syncytium which is present peripherally, the cotyledon is composed of a system of dividing and sub-dividing arteries and veins. The divisions become more complicated and numerous as the periphery is reached.

A cotyledon can be formed in a number of ways. The most obvious method is for a branch of the superficial arterial vessels on the foetal chorion to perforate the chorion and pass downwards into the placenta. This perforation may occur quite suddenly when the artery turns through a right angle and passes through the chorion. In some cases the artery descends more gradually into the placenta. The accompanying vein, as a rule, leaves the chorionic surface with the artery. The cotyledons formed in this manner are usually large, but it has already been shown that small superficial arterial branches arise laterally from the major superficial vessels and accompanied by veins perforate the chorion and form small cotyledons. Again, deep branches arise directly from the maternal surface of these major vessels and pass down, at once, into the placenta. The cotyledons so formed are usually of middle size but they can be almost as large as any formed from the major vessels. Finally, small cotyledons arise from the main cotyledonary vessels either before they divide or from the subsequent divisions.

These small cotyledons are presumably analogous to the small cotyledons which are derived superficially and are very numerous.

It will be seen that cotyledons are in three sizes. The least numerous are the very large cotyledons, the next in order are the medium sized cotyledons, and the most numerous, are the small cotyledons.

The small cotyledons continue to be formed even after the divisions of the cotyledonary vessels have begun, and it is uncertain whether to regard them as separate cotyledons or just part of the general branching effect. These formed initially are usually separate from the main cotyledon by an appreciable interval and have been regarded as separate cotyledons. The author has counted more than 200 separate cotyledons without feeling that the count was exhaustive. Of this number 50 could be regarded as large and perhaps 10 of these really large. The greatest concentration of cotyledons appears to be in the peripheral and mid-zones of the placenta. In the central region the cotyledons tend to be mainly of the larger variety but this is only a question of degree. Cotyledons of all sizes may be found in all parts.

A feature of the artery and vein supplying cotyledons is the manner in which an artery or vein will describe simple spirals over one another in order to run side by side. The spiral is simple consisting of one or two turns. The spiralling is not by any means general and most arteries and veins run side by side in characteristic fashion.

The Structure of the Cotyledon.

A large cotyledon will be described in detail and thereafter compared with a small cotyledon.

The large cotyledon extends to the maternal decidua and takes part in the fixation of the placenta.

The artery and vein running to the cotyledon may be 2-3 cm. in length and usually lie side by side and are firmly invested in chorion. Sometimes, the spiralling effect, already described may be seen. Before and after the primary division small arterial and venous branches arise and pass to small independent cotyledons.

The main vessels now divide into two or more primary divisions and arteries and veins divide simultaneously. This division and the subsequent

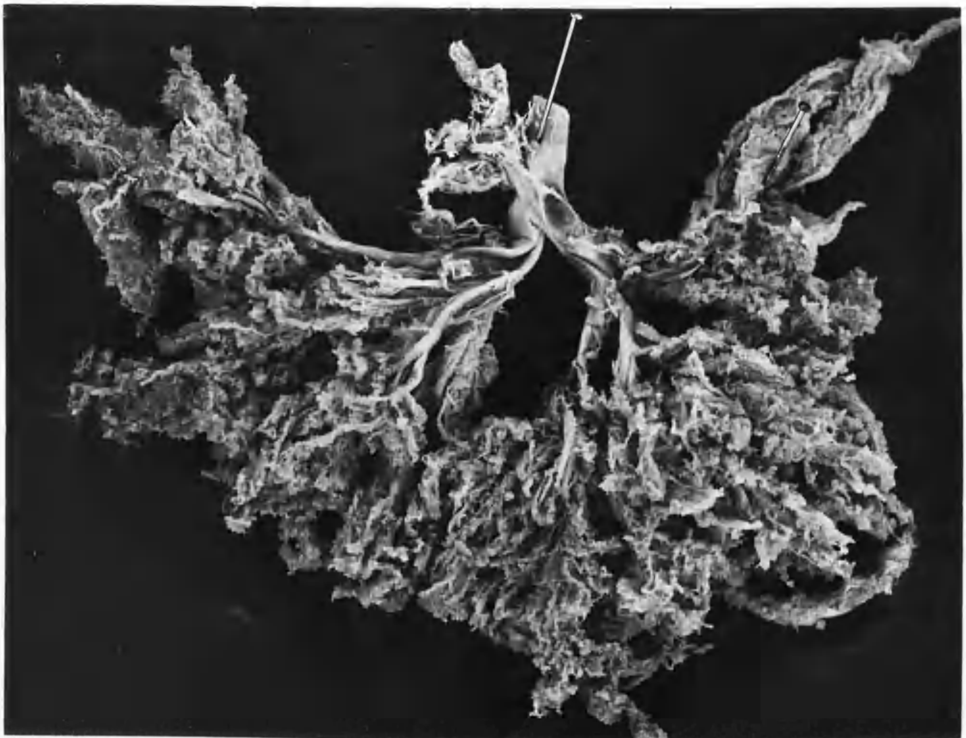

Figure 6.

This shows a large cotyledon which has been dissected into its constituent sub-cotyledons after digestion. It will be apparent that the bulk of the small vessels are borne in the distal half of the cotyledon leaving the proximal half comparatively free of small vessels and of course, villi.

ones occur as a regular dichotomy. Small branches, supplying cotyledons, arise laterally at all levels but they do not obscure the pattern of a regular and repeated series of divisions. The primary divisions pursue independent courses outwards and have the effect of partitioning the cotyledon into a series of sub-cotyledons. This effect is intensified when the primary divisions become secondary divisions and again tertiary divisions. The whole cotyledon is now of considerable size and clearly partitioned into a number of sub-cotyledons. The veins and arteries run side by side as before and divide simultaneously. The vessels have now the calibre of arterioles and venules and these bear as lateral projections the capillary loops. Each capillary loop, in life, being enclosed in its villus.

During the dissection of the cotyledon it is apparent that although the sub-cotyledons are separate structures there is considerable adhesion between them and small branches can be seen intermingling at their common related surfaces. These adhesions can be readily separated by blunt pressure and there is no evidence of vascular connection between such branches. The sub-cotyledons are related to each other in rather a complicated fashion and this will be described later. The nature of the 'adhesion' has not been subjected to detailed study, but appears to be both an intermingling of the smallest vessels and syncytial adhesion.

A cotyledon, in saggital section, is seen to have a triangular form. The apex is at the chorion and the broad base against the decidua. The bulk of the capillaries are borne at the base and along the two sides. The vessels of the sub-cotyledon are comparatively free from villi until these basal and lateral areas are reached. Viewed from above a cotyledon could be regarded as a cone with the apex towards the chorion. The sub-cotyledons number at least four in the average cotyledon, and usually more than four. They also show an intermingling of their own smaller and terminal branches. By careful dissection these branches can be separated and are without suggestion of any vascular connection between them.

The bulk of the cotyledon is increased by projections of adjacent sub-cotyledons into its substance, and these may penetrate quite deeply. The projections can be separated from the cotyledon but there are obviously adhesions due to intermingling of smaller villi at the common and related surfaces. The initial task of separating cotyledons is essentially the separation of these projections from the main cotyledon.

In contrast the small cotyledon never reaches the decidua. As already described it is much more numerous and whether derived superficially or from the cotyledonary vessels within the placenta shows a much simpler structure. The main vessels divide into sub-cotyledon, as before, but usually arterioles and venules are produced after one or two divisions. The entire cotyledon is quite small and may measure as little as 1 cm. in length. The terminal vessels intermingle with each other, with adjacent small cotyledons and with the sub-cotyledons of adjacent large cotyledons. In addition, since they are so near to the chorion, many of these small cotyledons show a firm adhesion to this structure.

It is evident that in life the placenta, both in depth and width, is filled with the vessels of the cotyledons. The small cotyledons are by far the most numerous, but in terms of actual bulk the large and very large cotyledons will occupy most of the space within the placenta. These large cotyledons, in contrast to the smaller ones, reach the decidua and it has been shown that the bulk of the small vessels bearing villi are present at the periphery of the cotyledon. That is, at the decidua and along the external surface of the cotyledon. This implies that the concentration of villi diminishes away from the decidua and will be least under the chorion. There is no empty space within the placenta as can be seen by examining a fresh placenta but in terms of actual concentration of villi the number will be least below the chorion. The bare areas of chorion on the maternal aspect after digestion are primarily due to the separation of the smaller cotyledons from the chorion but their existence does underline the fact that the concentration of vessels is less below the chorion than elsewhere.

The Plan of the Cotyledon.

The cotyledon has already been described as a triangle in saggital section or cone-shaped if viewed from above, but these descriptions are rather superficial because the plan of the cotyledon is essentially one of three dimensions.

Figure 7.

This photograph illustrates a cotyledon which has been divided in the sagittal plane. The sub-cotyledons composing the cotyledon are distinctly separate but small vessels can be seen in the gaps between. The drawing shown in Figure 8 is intended to make the anatomy clear.

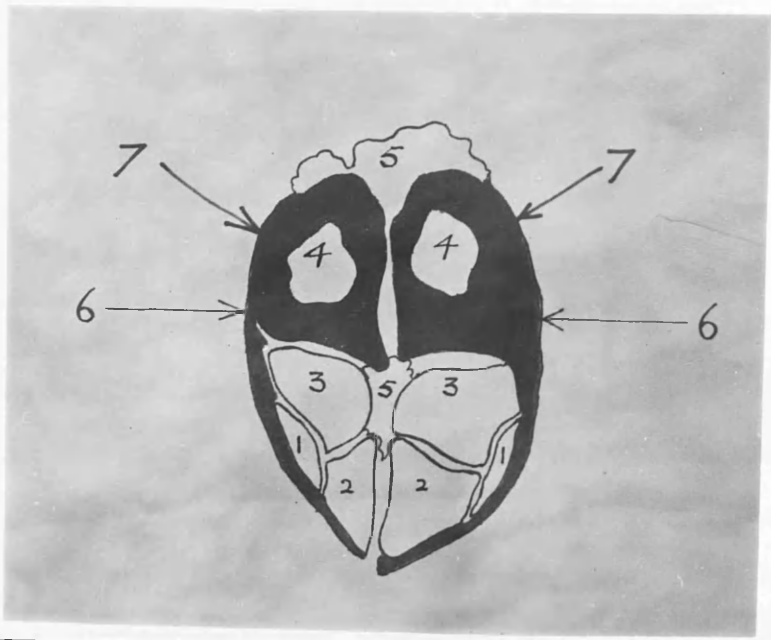

Figure 8.

In this drawing are shown the matching halves of a cotyledon.

Numbers 1, 2, 3 and 7 are the matching halves of the sub-cotyledons. Number 4 is a protrusion from a neighbouring cotyledon.

Number 5 represents the small vessels, derived from adjacent sub-cotyledons, which are present in the gaps between them.

Number 6 is the decidual covering still present over the maternal surface of the cotyledon.

The sub-cotyledons which compose this plan are usually more than four in number and are arranged, in section, in a mosaic like arrangement with relation to each other and, of course, the projections of adjacent cotyledons also share and complicate this pattern. The elements of the mosaic are the relationship of the sub-cotyledons with each other and on section this may produce a complicated pattern of areas of sub-cotyledons which, while being distinct from their immediate neighbours, show projections into each other, and at their common related surfaces an intermingling of their smaller villi. The complications of this arrangement can be appreciated when a cotyledon is dissected and the sub-cotyledons traced back to their common parent vessels. It is not unusual for areas of sub-cotyledons which are quite distinct and separated from each other by intervening sub-cotyledons to be shown to possess the same parent vessels.

The Fixation of the Cotyledon.

It has been shown previously that the large cotyledons reach the decidua and take part in the fixation of the placenta. When a cotyledon, in situ, is separated carefully, it is apparent that

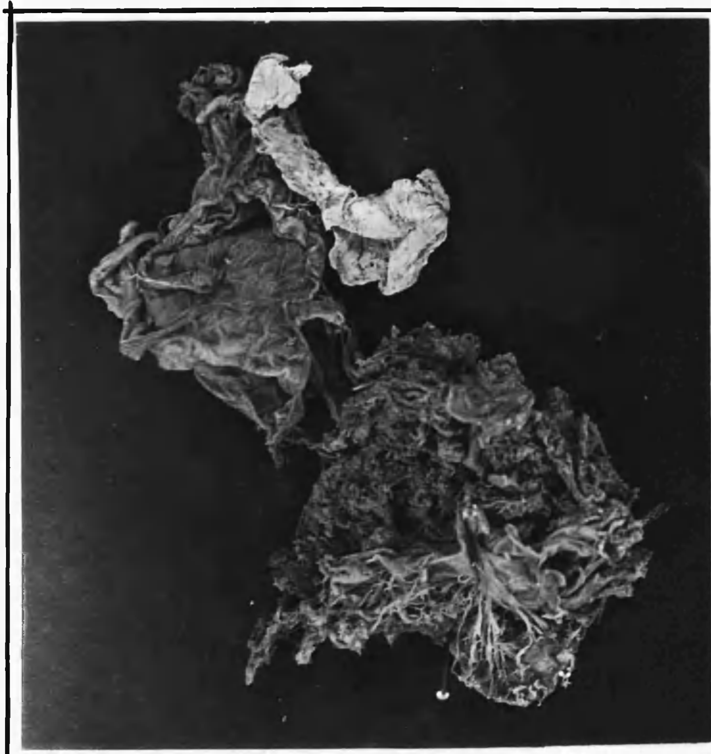

Figure 9.

This photograph shows a cotyledon removed from the uterus after digestion and with decidua still adhering to its maternal aspect. In the bottom of the photograph are seen the fixing vessels ending by firmly anchoring themselves to the decidua. They contrast with the dark coloured or functional portion of the cotyledon lying above. The light colour is, as explained in the text, due to the inability of the fixing vessels to fill with coloured gelatine.

The structure in the upper part of the photograph represents the chorion which has been reflected upwards.

although the whole area of cotyledon which reaches the decidua takes part in its fixation there is one area where fixation is particularly intimate. This fact is more clearly shown by dividing a cotyledon while still attached to the uterus and examining the sub-cotyledons. There will be seen to be a sub-cotyledon which is more dependent than the others and it is this sub-cotyledon which fixes itself most firmly to the decidua. In one view it will appear to be centrally placed in the cotyledon but a view of a saggital section at right angles may reveal it to be more peripherally placed. In a saggital section this sub-cotyledon is usually quite apparent. In addition to being the most dependent it always colours badly with filler especially in its area nearest to the decidua. The pale area stands out in contrast to the well coloured areas around it and, naked eye at least, is obviously different from its neighbours. The sub-cotyledon concerned with fixation may colour with filler in its upper part but as its branches near the decidua they show no colouring and the number of villi borne by it diminish considerably. In some cases there may be only a single vascular trunk without any side

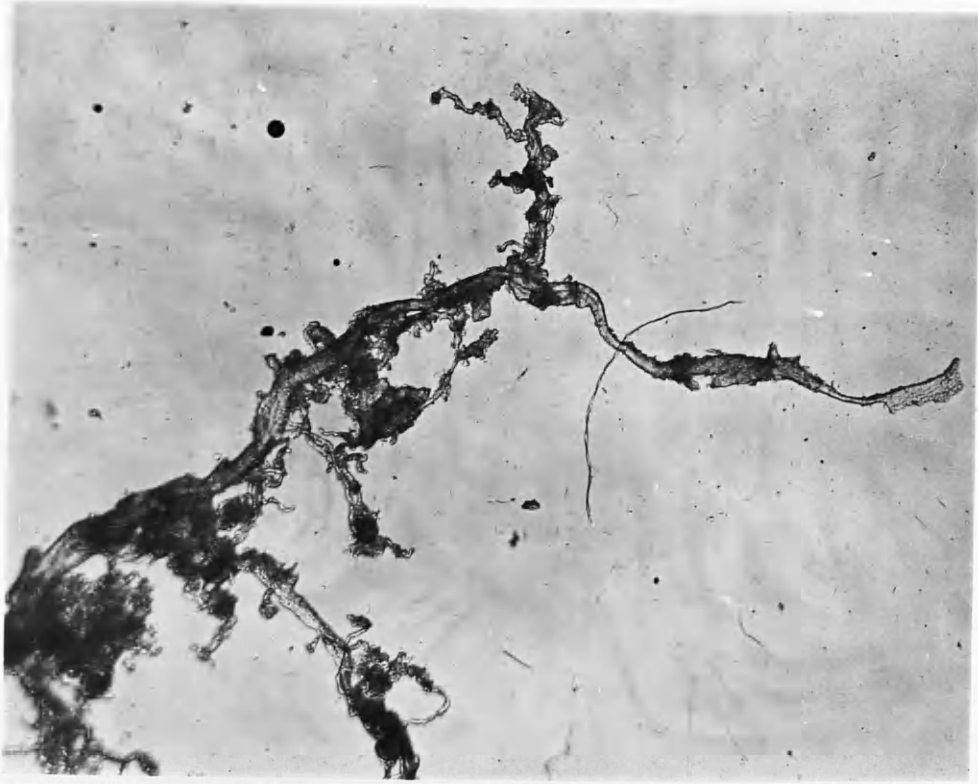

Figure 10.

X 20. This shows a fixing vessel dissected from a large cotyledon. The paucity of branching and the normal fringe of capillaries around the vessels is noteworthy. The dark areas at the ends of the vessels represent decidual tissue into which the fixing vessels are inserted ultimately.

Figure 11.

X 350. This is a microphotograph of a fixing vessel in transverse section. The bulk of the trunk, and the small calibre of the vessels in relation to this bulk, is a striking feature. The vessels shown appear to be almost occluded by an endarteritic process occurring within the lumen.

Figure 12.

This photograph shows the peripheral regions of a placenta still attached to the uterus. The peripheral fixing vessels can be seen perforating the chorion and passing to the periphery where they appear to be inserted into the superior aspects of the larger cotyledons.

vessels at all. In these fixing trunks artery and vein are, of course, still present but they appear small in relation to the total volume of the trunk. The trunk passes into the substance of the decidua either singly or divides into several finger-like processes, each of which is separately inserted. The terminal part of the fixing villus as it lies in the decidua is apparently solid and without vessels. If small side branches, bearing villi, are given off before insertion they are derived from the upper or free surface of the trunk. Some of the trunks as they lie in the decidua appear to fuse one with another.

All around the fixing villi are the well coloured areas bearing numerous villi and they stand out in contrast.

At the periphery of the placenta many of the cotyledons are small and appear to be completely transformed into fixing structures. The main vessels arise from the chorion in the usual fashion, and are observed to be simple in arrangement. The main cotyledonary vessels show the usual branching but hardly any smaller branches are borne and in consequence there are few villi present. The insertion of these peripheral cotyledons into the

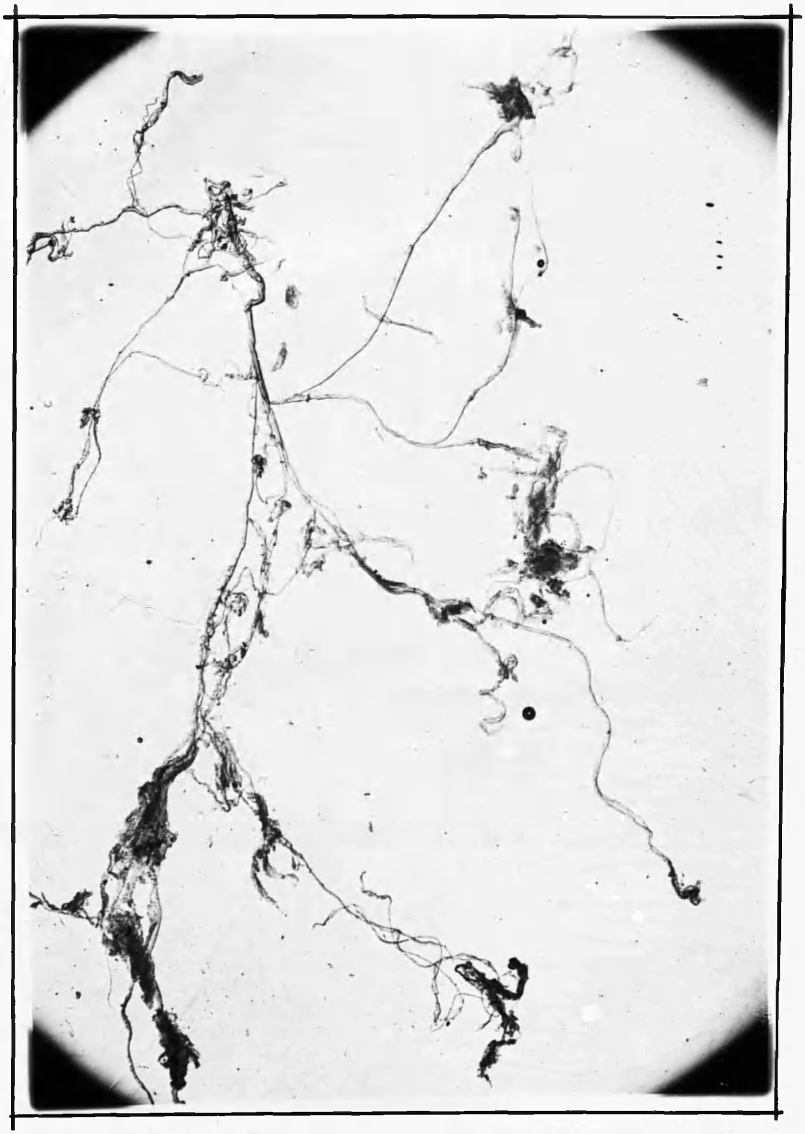

Figure 13.

A fixing vessel from the periphery of the placenta is shown. It shows, in its course from above downwards, a number of branches and there is a complete absence of the normal fringe of small vessels around them. The dark areas at the ends of the branches are decidua, into which they are inserted ultimately.

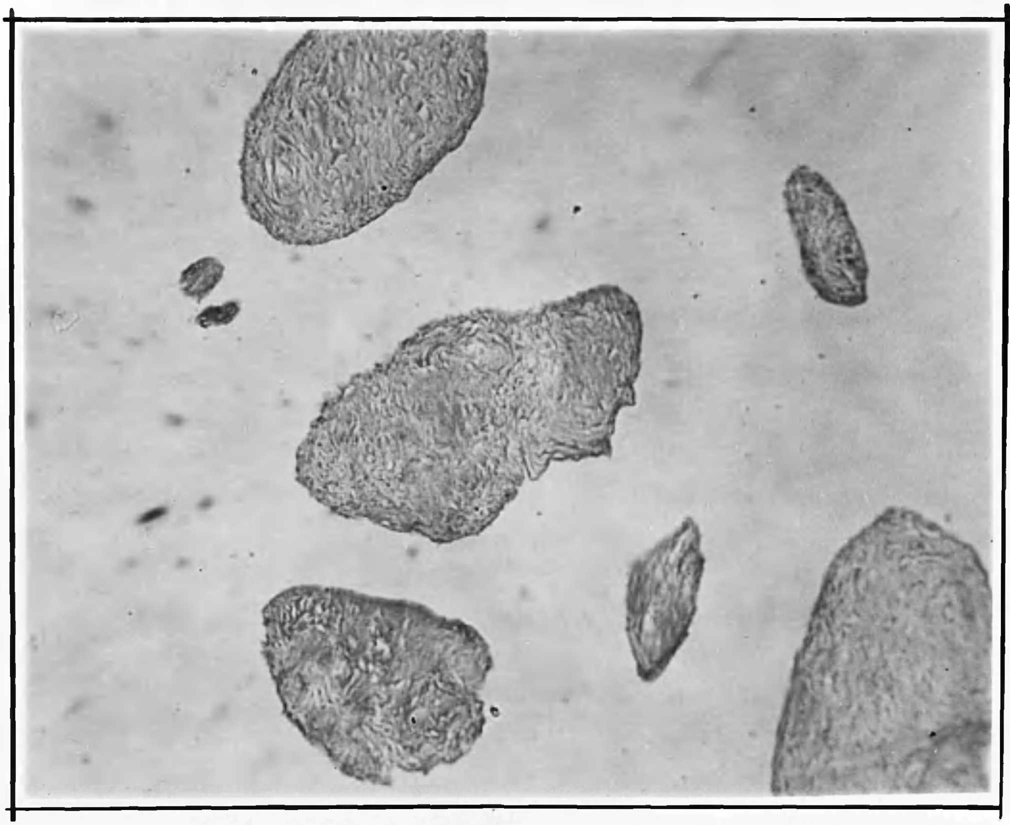

Figure 14.

X 350. This microphotograph shows a peripheral fixing vessel in transverse section. The trunks are quite solid and without evidence of any vessels within them.

maternal decidua is also of characteristic type. Decidual plates or sleeves are seen to envelope the cotyledonary structures of the placenta, forming the large so-called cotyledons, 15-20 in number, which are apparent to the naked-eye on examining the fresh organ. The small fixing cotyledons form an almost continuous ring around the outermost limit of the placenta. The most peripheral of the decidual envelopments involves the outer ring of functioning cotyledons. In this way a decidual barrier is apparently raised between these functioning cotyledons and the final ring of small fixing cotyledons. These latter structures are then implanted into the decidua over the lateral and superior aspects of the larger bodies.

In all the placentae examined the fixing cotyledons at the periphery were derived from vessels which had perforated the chorion. None of them were derived from cotyledonary vessels which had already entered into the placenta.

The vascular trunk of the fixing cotyledon at the periphery may enter into the decidua without division but usually it divides into a number of finger-like processes which enter into the decidua. These trunks or processes may run

Figure 15.

In contrast the trunk of a non-fixing or functional vessel is shown. It can be seen to enter the decidua and thereafter pass upwards again (into the placenta) where it ends in a number of branches each with its capillary fringe. The very dark area at the top represents the decidua through which the trunk runs before emerging and re-entering the placenta.

for a considerable distance in the decidua beyond the limits of the placenta. The trunks, before insertion, contain, in each case, an artery and accompanying vein but they appear, as before, rather small in relation to the bulk of the trunk. After insertion some appear quite solid and devoid of vessels, and some are solid before insertion.

It has been pointed out previously that considerable areas of chorion on the maternal aspect are quite bare and free of cotyledons. These free spaces do not exist in life as can be seen in inspecting a fresh placenta. These free spaces do not exist in life as can be seen in inspecting a fresh placenta. These areas are filled by cotyledonary divisions some of which are firmly adherent to the chorion. It can be assumed, with reason, that these bare areas are in life occupied by the numerous small independent cotyledons previously described, which adhere to both chorion and related and adjacent cotyledons.

At the periphery of the placenta the trunks of the main fixing cotyledons are inserted without any particular arrangement of the decidua. Elsewhere the decidua may appear thickened. In some instances the decidua is raised into ridges, often quite small, but sometimes ascending into the cotyledon between its sub-cotyledons for considerable distances. The trunks of the fixing vessels of the sub-cotyldeon often appear to be inserted into the decidua where these ridges or thickenings occur.

The anatomical features described in Part III are illustrated by Figures 6 to 15.

PART IV.

The Anatomy of the Villus and its Capillary Structure.

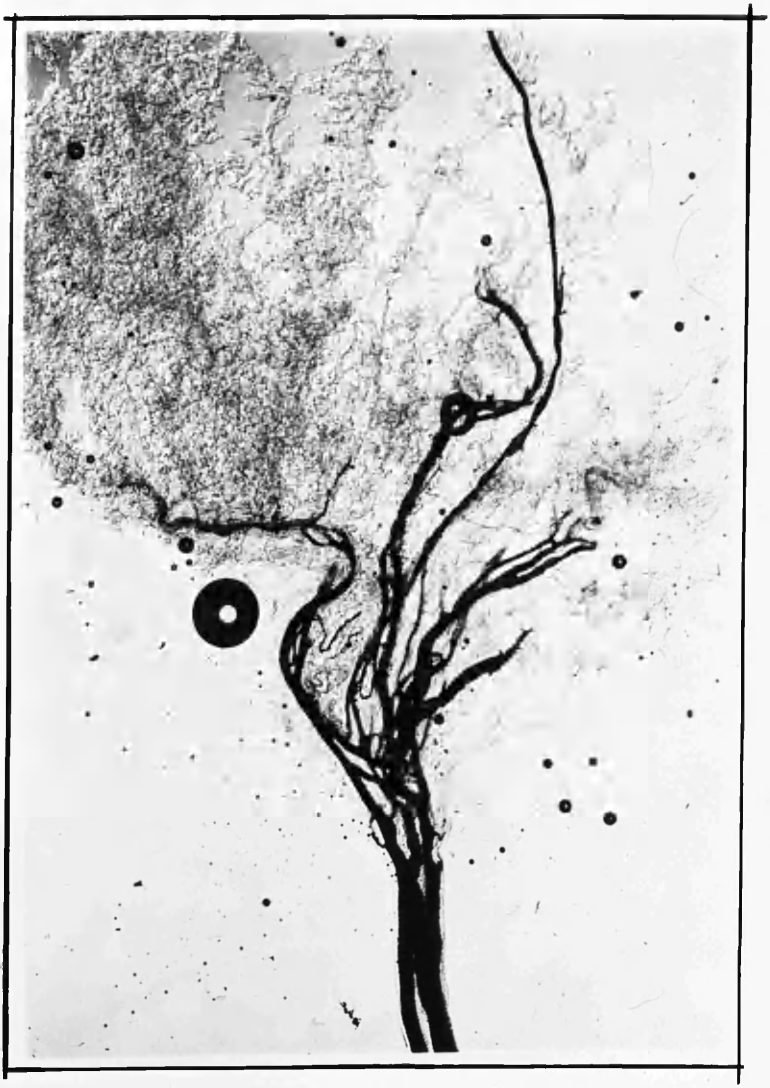

Figure 16.

X 20. This shows the terminal vessels in a cotyledon. The artery and vein are proceeding side by side and end in a 'fringe' composed of the terminal arterioles and venules and their capillaries. The dye has not penetrated into the fringe and separate vessels are not seen in consequence.

Figure 17.

X 200. This is the 'fringe' area in higher magnification with the arterioles and venules proceeding upwards side by side and giving origin laterally to the capillary vessels. The parent arteriole and venule end finally in a capillary.

Figure 18.

X 300. This photograph shows capillary vessels at the periphery of the 'fringe'. The covering syncytium is plainly seen and the most distal capillaries are obviously very convoluted.

The Anatomy of the Capillary Vessel.

It has been shown previously that the main vessels of the cotyledon divide and sub-divide until very small vessels of the calibre of arterioles and venules are produced at the periphery. These vessels can be formed at any level of division but are produced in greatest numbers at the periphery and form the "fringe" of the cotyledon. The arterioles and venules now produce the capillary vessels as side branches while they pass onwards and themselves end in capillaries. The use of dyes at this stage is absolutely essential, because, without them, the vessels appear as a maze in which no separate structures can be distinguished with any clarity.

The size, number and complexity of the capillary vessels vary greatly. As a rule the capillaries given off at first by the parent arteriole and venule are small and simple. The later ones become progressively larger and more complex, and the final ones, in which the parent vessels end, are large and complex structures. In these structures the capillary shows many convolutions which are not easy to follow. The preservation of the syncytial membrane has greatly

Figure 19.

X 800-900. This microphotograph shows a capillary vessel of comparatively simple arrangement. The covering of syncytium is clearly visible and separate nuclei can be distinguished. At the base of the capillary loop a vessel can be seen passing from the arterial to the venous end of the loop. This type of vessel is seen fairly frequently and would appear to constitute a type of vascular 'shunt'. This question is discussed in the text.

assisted in their study. The capillary vessel begins as a lateral branch from its parent arteriole and enters the villus. Thereafter it descibres a course which varies in its complexity and length. It will be seen that along its course it describes small loops or spirals and these are reproduced by the enveloping villus which shows corresponding projections. This spiralling and projections of villus are continued in the venous side of the loop in exactly the same way until the capillary ends by leaving the villus and entering the parent venule. The calibre of the capillary appears to be the same throughout its course although the blue dye on the venous side, being denser, may make that side look larger. The penetration of the red and blue dye follows no set pattern. Some loops are filled with red dye and others with blue. In other vessels the colours meet halfway. It would appear to be a matter of chance.

The varieties of capillary vessels which have been described should not be considered as clear cut and constant in position. All varieties may be seen arising at any level, from the parent arteriole and venule, but generally speaking, the

Figure 20.

X 850. A more convoluted type of capillary vessel is shown. It will be apparent that the syncytium closely reproduces the convolutions and forms lobules where the looping of the capillary is sufficiently exaggerated.

most convoluted vessels are given off nearest to the periphery.

It will be apparent from what has been described that the capillary vessel in its convoluted course is a multi-dimensional structure and it not confined to a single plane.

The Anatomy of the Villus.

The simplest type of villus seen is found in conjunction with the simplest capillary. The villus, even here, shows projections along its course which correspond to the convolutions in the capillary vessels. When the capillary loop is more complex and has many convolutions the villus projections are correspondingly more numerous and large enough to be regarded as lobules. The villus will therefore have the shape of a multilobulated structure. It is apparent that the conception of a villus as a simple 'glove' requires modification. The villus is a three dimensional structure presenting numerous lobules on its surface and having within it a capillary vessel of very considerable length.

The Disposition of the Capillary Bed.

The anatomy of the peripheral or 'fringe' area of the placenta, which has been presented will

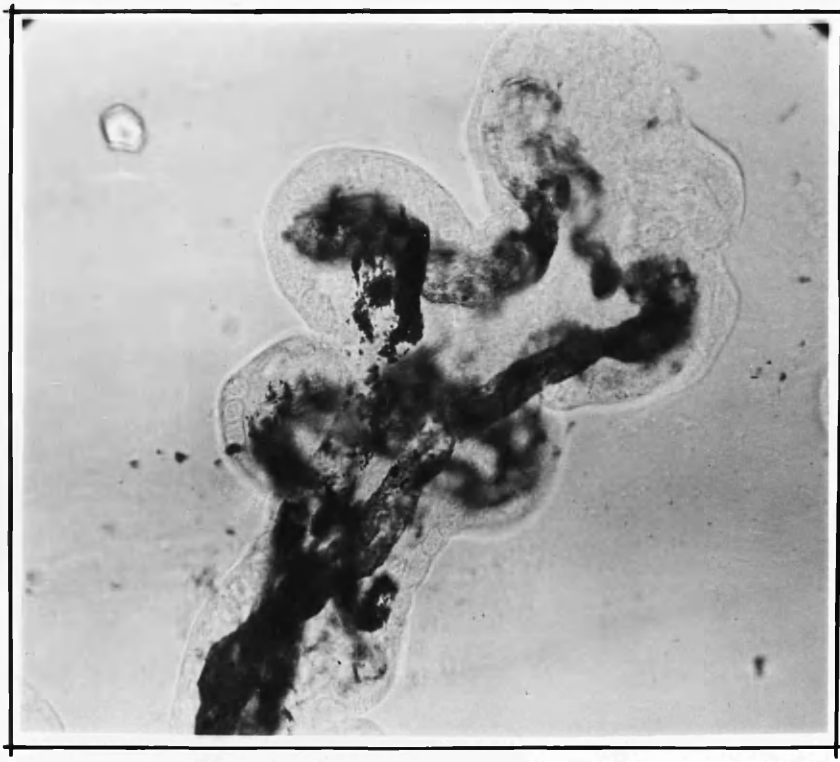

Figure 21.

X 850. This photograph illustrates the lobulation of a villus and demonstrates that the villus is a multilobulated structure in three dimensions.

provide some realisation of the magnitude of the capillary bed. The multitide of capillaries which are present will also give an indication of the immensity of oxygen exchange and metabolic activity which is taking place at any moment within the placenta. In this connection the disposition of the capillary bed is of some interest. From what has been described already it is apparent that the greatest concentration of capillaries is found nearest to the decidua and diminishes in degree as the chorion is approached. The least concentration of vessels would appear to be within the centre of the cotyledon, and thereafter immediately below the chorion. It follows, from these concentrations of capillaries, that the greatest metabolic activity and oxygen exchange will be nearest to the decidua, less under the chorion, and least within the cotyledon. This must be related to the problem of maternal blood flow within the placenta, and although this present investigation has been concerned with the foetal circulation, it is not unreasonable to make certain deductions. The dense enmeshment of capillaries in the 'fringe' areas at the decidua must offer considerable resistance to the flow of

Figure 22.

X 850. This type of villus is most often seen at the extremity of the fringe and the convolutions of the capillary vessel are reminiscent of a renal glomerulus.

maternal blood but would certainly ensure time for oxygen exchange and other metabolic activities. Beyond this fringe however, around the main stems of villus and cotyledon and under the chorion, obstruction to maternal blood flow will be considerably reduced.

It is also apparent that many of the villi which are seen in ordinary histological preparations will be derived from the same parent villus. Also a proportion of the syncytial adhesion which is observed so commonly between villi may simply indicate, in part at least, a common origin from a villus. The "villi" seen in histological preparations would therefore often represent the 'lobules' of the villus as described earlier and the extent of the "adhesions" depending on the vagaries of direction of the histological sections.

Arterio-venous Anastomosis.

The possibility of an arterio-venous anastomosis is considered at this point with some reluctance. The observed evidence for such an anastomosis is confused and uncertain.

In the 'fringe' area at the level of the arterioles and venules, the vessels are very numerous and in close proximity to each other. In some of the preparations, which have been examined, branches are seen running laterally suggesting that communication exists between adjacent arterioles and venules. These lateral branches are difficult to follow because of the many vessels which are present. In areas where the density of vessels is less, the lateral branches can often be shown to be ordinary arterioles or venules which have been broken off during the preparation of the specimen, and lie across intact vessels producing the effect of anastomotic vessels. In other areas no such distinction can be made with certainty, and the possibility of anastomosis remains.

In a similar fashion within the villus, near its base, or even during the course of the capillary vessel, extra vessels can be seen. These vessels appear quite separate from the loops of the capillary and appear to travel directly from the arterial to the venous end of the capillary. These extra vessels, if they do exist, would represent a vascular shunt with the ability to exclude blood from the foetal villus. Many intact villi have been examined and no firm conclusion has been reached. In some villi the extra vessels clearly represent a convolution of the capillary vessel in a different plane or a convolution which has become detached. In other villi the extra vessels are capillary vessels supplying separate villi and produced as an artefact by the pressure exerted with mounting. It must be said however that other extra vessels within villi cannot be explained in these ways and the possibility of an intra-villus vascular shunt remains. Further work will have to be carried out to determine the true anatomy of these vessels. The point is of some importance in view of the possible part they may play in relation to placental lesions.

The anatomy of the arteriole, venule, capillary and villus is presented in Figures 16 to 22.

PART V.

The Maternal Aspect of the Placenta.

Figure 23.

This photograph shows the maternal surface of the placenta. The lobes are well seen and separated from each other by deep and shallow fissures. In this specimen the deep fissures penetrate into the centre of the placenta. It will be appreciated that the lobes are not all clearly delineated. Where deep fissures are present the lobes are clearly separate but elsewhere there is either no separation or an imperfect separation by shallow fissures. Over the convexity of the lobes and around the periphery are seen very numerous white areas of calcification. These areas, as explained in the text, mark the insertion of the fixing vessels.

Introduction.

The external anatomy of the placenta will be considered in this part. The foetal surface of the placenta has already been discussed in Part II and will not be described any further at this point. Instead, it is the intention to describe the maternal surface of the placenta and correlate its appearance with the structure of the placenta which has been previously described.

The Maternal Placental Surface.

The naked-eye appearance of the placenta after delivery is familiar to all. It shows a number of convex or flattened structures described variously as 'lobes' or 'cotyledons'. These lobes vary greatly in number and are separated in varying degrees of completeness by fissures which are so much a characteristic feature of the placenta. The lobes vary in number and can be as few as three or more than thirty. There is obviously a considerable variation in this respect. In most placentae it is usually difficult to be certain just how many lobes are actually present because the degree of separation from each other by fissures is subject to variation. One part of a lobe may be well separated from its neighbour and

Figure 24.

This is the maternal surface of a placenta after digestion and before the dissection of the lobes has begun. Two of the deep fissures have been sufficiently separated to show their extent. In the bottom fissure are seen a number of oval decidual openings which are so constantly present in these areas.

yet elsewhere the fissure is shallow and frequently absent and the lobe appears to be no longer a separate structure. The lobes are covered in varying degrees of completeness by the maternal decidua. In some placentae the decidual covering is remarkably complete whereas in others it may be virtually absent and only found in the fissures. The decidual covering is usually well seen in the deepest fissures between lobes where it forms a close investment to the lobes and separates them quite effectively. The decidua does not stop at the margin of the placenta. Instead it can be traced on to the foetal membranes where it fuses with them. The deepest fissures are seen most often in the peripheral and middle zones of the placenta but they can only be present in the central area. The decidual covering, if sufficiently complete, shows in certain areas oval openings which are clearly not artefacts but may represent the openings of maternal blood-vessels. The largest ones are present in the deeper fissures and are best seen in those areas. At the periphery of the placenta the same oval openings are also present but not continuously. Their formation is quite striking in this situation

Figure 25.

The photograph shows a digested placenta in which the lobes have been separated by blunt dissection.

and some authors have referred to them as part of the "marginal sinus" of the placenta. Over the convexity of the lobes and around the shallow fissures small oval openings are also present but they are not so prominent and must be looked for quite closely.

In mature placentae small white areas are present at intervals over the surface. These are frequently hard or gritty and are usually referred to as "areas of calcification". In less mature placentae they are not a prominent feature. The calcified areas are present over the lobes in an irregular fashion and are often more prominent at the margins of the deep fissures.

The Anatomy of the Lobe.

The digested placenta is very suitable for studying the structure of the lobe and it is an advantage to fill the foetal vessels with coloured gelatine before beginning the dissection. The filled foetal vessels are much more obvious and easier to trace back to their parent stems.

In order to give a clear understanding of the anatomy of the lobe it will be described as if it had already been separated into its constituent structures. Thereafter it can be reassembled and

Figure 26.

A large lobe is shown which has been dissected partially into its constituent cotyledons. On the left the cotyledons are completely separated but on the right about half of the lobe has been left intact. The bare areas of chorion are clearly seen between cotyledons with arteries and veins running on the foetal surface of the chorion. The cotyledons are, of course, derived from these vessels. The large numbers of cotyledons present in a lobe of this size will be readily appreciated.

a complete picture presented. A lobe consists of an aggregation of cotyledons and the number present depends entirely on the size of the lobe. A small lobe may contain only one or two large cotyledons, the remainder of the structure being composed of several medium cotyledons and numerous small cotyledons. A large lobe, on the other hand, may contain many large, medium and small cotyledons. All of the cotyledons are in origin, of course, quite separate but they tend to arrange themselves into clumps or groups which constitutes the lobe. The cotyledons intermingle with each other by sending projections of branches into each other substance. There is therefore a continuity of cotyledonary vessels throughout the length and depth of the placenta. The form and size of the lobe as seen externally is determined by the number and shape of the cotyledons or sub-cotyledons which reach the decidua. The grouping of the cotyledons into lobes is determined by the number of vessels, perforating the chorion and entering the placenta, in any area. Contiguous vessels and their cotyledons tend to become associated with each other in this area. The shallow fissures mark the boundary between

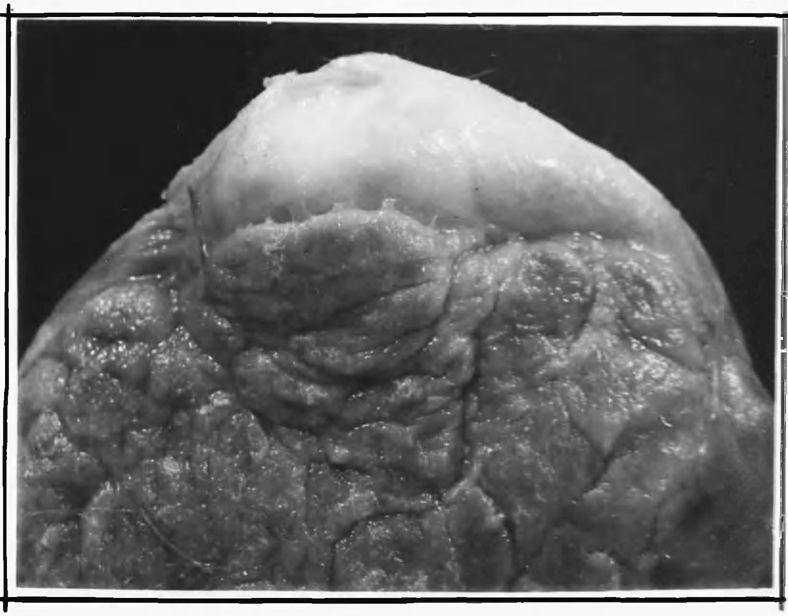

Figure 27.

The periphery of a fresh placenta is shown with the chorion and foetal membranes pulled out to show oval openings in the decidua. There, as indicated in the text, are considered to be analogous to the oval openings present in the deep fissures and to serve the same function of venous drainage from the placenta.

adjacent cotyledons or sub-cotyledons. The cotyledons are separated more clearly in the deep fissures, and such a fissure may penetrate quite deeply into the placental substance. The fissure is lined by decidua and it is only above this that continuity of cotyledonary vessels is once again established. It will be evident from the foregoing that the lobes of the placenta are really only a naked-eye appearance, and do not in any way indicate the numbers of cotyledons which are present. From the functional point of view the cotyledons represent a continuous structure throughout the placenta.

The Placental Fissures.

The disposition and variety of the placental fissures have been already indicated and it will suffice to summarise what has been said previously. The deeper fissures mark, most clearly, the boundaries between the lobes. They are present more often peripherally rather than centrally and may penetrate quite deeply into the placental substance. These deep fissures contain the oval openings in the decidua which clearly represent the position of maternal vessels. The oval openings grouped around the periphery are of the

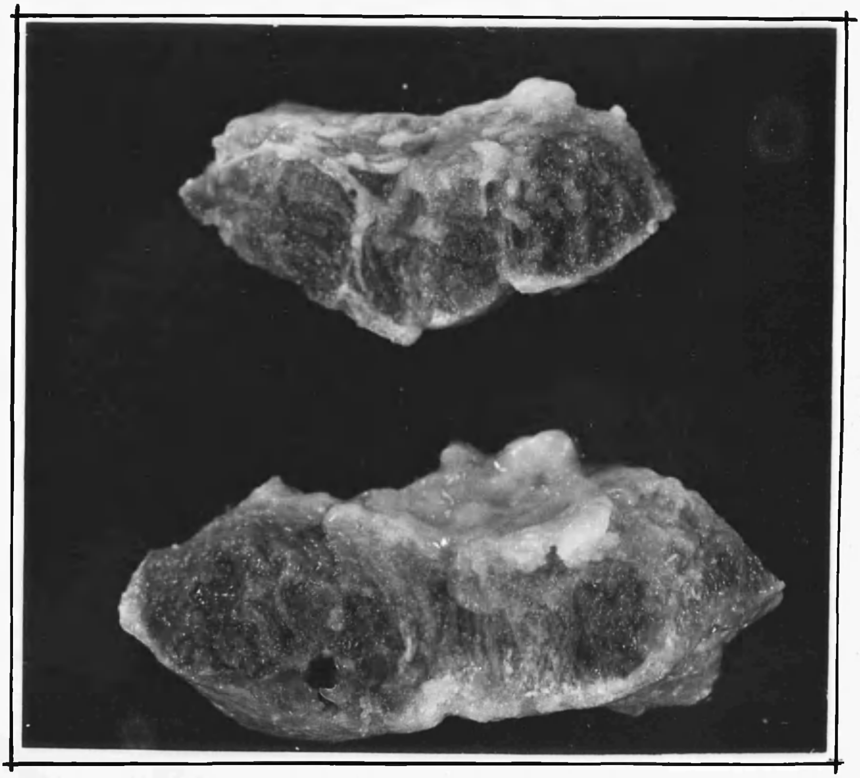

Figure 28.

In this photograph two portions of placenta are seen which have been cut through where calcified areas are present. These calcified areas are seen as a white thickening along the base of each portion.

same variety and by dissection it can be shown that they lead into the same deeper vessels in the decidua. The shallow fissures may be seen anywhere over the placental surface. As a rule they are denoted by condensations in the decidua which bridge over them rather than lines them. These shallow grooves mark the boundaries between adjacent cotyledons. Over the surface of the lobes smaller oval openings are usually present in the decidua but they are not so obvious and must be searched for carefully.

The Calcified Areas of the Placenta.

The calcified areas on the placental surface are white in colour and often hard or gritty. They vary in number and are seen best in placentae at or near term rather than less mature placentae. The numbers and distribution vary. They are present over the surface of the lobes in an irregular fashion. Often they have a characteristic relation to the edges of the deeper fissures. If these white areas are examined they can be shown to have a definite relation to the foetal vessels. It has been shown previously that one part of a cotyledon which reaches the decidua is particularly concerned with fixation. The vascular trunk ends

Figure 29.

The portion of the placenta has been partially digested and the white area, now along the top of the specimen, is beginning to be seen more clearly and contrasting very clearly with the dark areas of placenta around it.

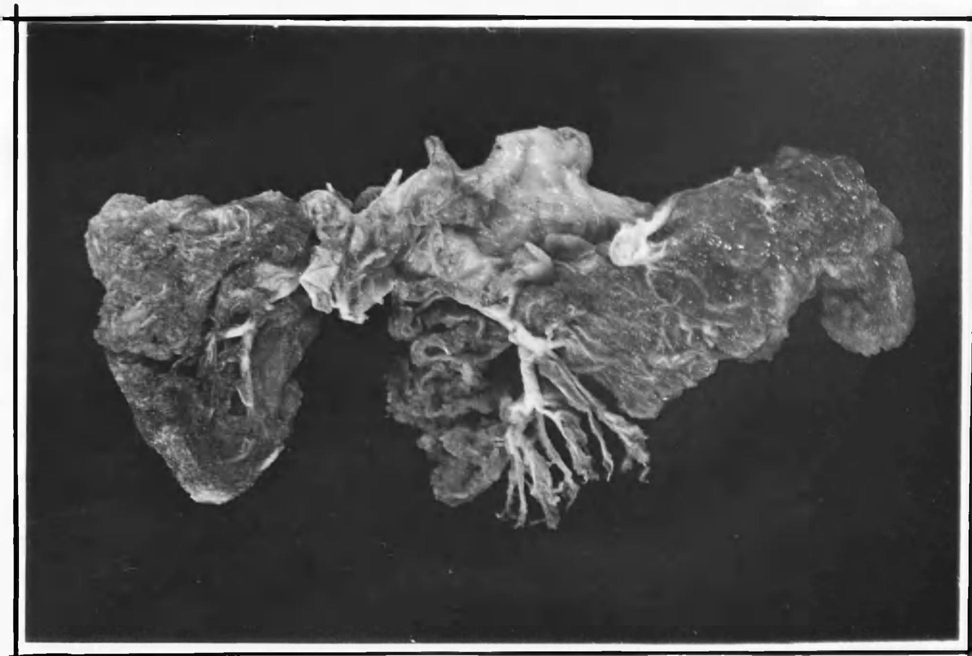

Figure 30.

The white area and the vessels related to it have been dissected out after digestion. The terminal vascular trunks are seen to be comparatively free of the normal fringe of small vessels and capillaries. Around these vessels are seen dark areas of placenta with the usual profusion of capillary vessels.

in the decidua which is thickened around it and white in colour. The vascular trunk may contain vessels showing endarteritis, and others are of small size in relation to the bulk of the trunk. In some instances no vessels may be seen at all. The inference to be drawn from these findings would suggest that this area of cotyledon is more concerned with fixation than oxygen exchange and the other placental functions. The foetal vessels supplying this region are usually paler in colour and fill poorly with filler. They contrast with the surrounding areas whose vessels are well coloured with filler.

It would appear therefore that the calcified areas in the more mature placenta really mark the insertion of the fixing vessels of the cotyledon. Indirectly too they must be an indication of the degree of endarteritis present in the related foetal vessels. It can also be assumed with some reason that the fixing trunks represent functional trunks which have become modified by the development of an endarteritis of the vessels within them.

These fibrous or calcified foetal vessels are not the only ones to enter the decidua. If the vascular trunks in the well coloured areas

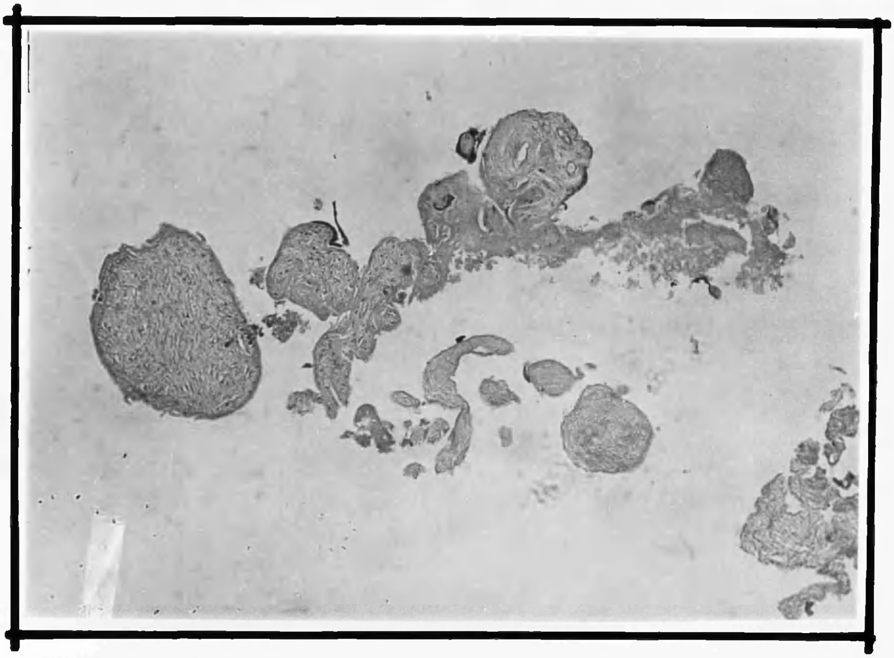

Figure 31.

X 350. This microphotograph shows a transverse section through the vessel trunks shown in Figure 30. Very few vessels can be seen in the trunks and indeed most of them appear quite solid and avascular.

are examined many of those nearest to the decidua enter and after a variable distance leave again and pass upwards into the substance of the cotyledon. The course of these trunks is most characteristic, and the smaller terminal branches show the normal capillary fringe, and are obviously functional in nature. This contrasts with the fixing trunks described previously.

The anatomical details discussed in this part are illustrated by Figures 23 to 31.

PART VI.

The Growth of the Definitive Placenta.

Introduction.

The placenta has completed its initial development by the end of the twelfth week of pregnancy. It may then be termed the definitive placenta. It has the characteristic shape and appearance of the mature placenta but is, of course, much smaller. Thereafter it continues its growth and manifestly increases in diameter, weight and thickness. The mode of growth is quite unknown, and this lack of knowledge indicates quite effectively the technical difficulties in the path of any such investigation. The object of the investigation in this part of the thesis has been to describe the growth characteristics of the placenta. For this purpose the digested placenta has been employed and has proven to be most suitable. This investigation has more than an academic value. An understanding of placental growth would greatly assist in the understanding of the many clinical problems connected with foetal death and placental insufficiency.

The Mode of Investigation.

The Rationale of Investigation.

It has been shown previously (Part II) that all of the placental vessels end in cotyledons. This fact has been utilised in this investigation. If the cotyledons are counted after digestion it is reasonably certain that all of the vessels derived from the chorion have been accounted for, and the number of cotyledons will represent fairly accurately the total number produced. Further, by counting cotyledons in placentae at varying stages of development, weighing them and measuring them individually, it is possible to have an accurate method of demonstrating placental development.

Materials.

Twenty placentae were examined with maturities ranging from the twelfth week of pregnancy until term. They were not in any selected, apart from discarding any which appeared incomplete or exhibited gross pathological changes. In all cases the placentae had been delivered per vaginam and the maturity was calculated from the date of the last menstrual period as given by the patient.

Method.

Method.

Each placenta was washed free from blood clot by a gentle stream of water. Thereafter it was digested for at least 24 hours and washed free from digested material in a gentle stream of water. In the more mature placentae the umbilical vessels were catheterised and the vessels filled with coloured gelatine. This was dispensed with in the smaller placentae because the umbilical vessels are small and not readily catheterised.

The placenta was now ready for examination. As a first step it was weighed after excess fluid had been removed by pressure between layers of absorbent lint. Excessive drying was avoided as it promotes distortion of the tissues. The weight obtained was not strictly accurate since the placenta was not completely dry but as each placenta was treated in the same fashion, the weights are comparable. The diameter of the placenta was next measured and care was taken to avoid excessive measurement.

The maternal surface of the placenta was exposed and the cotyledons separated from their neighbours by careful blunt dissection. The larger cotyledons were easily identified and separated from each other but the small cotyledons presented a more difficult task. They are very numerous, small and difficult to isolate. The total counts for small cotyledons should be regarded as low in most of the placentae. In turn the large, medium and small cotyledons were counted and the totals in each case noted. From each of the three sizes a typical representative was selected and its length measured. The large and medium cotyledons were then weighed. The small cotyledon was not weighed since it was very small and its weight of little significance.

In turn, the placentae used in this study were investigated in the manner described above. Each placenta was investigated in exactly the same way in order to make the results strictly comparable.

The Results of the Investigation.

Placentae.

The total number of placentae was twenty and distributed in the following maturities.

Maturity.	Number.
12 weeks	One
16 weeks	Four
20 weeks	Two
24 weeks	Three
28 weeks	Two
30 weeks	One
32 weeks	Three
34 weeks	One
36 weeks	One
40 weeks	Two
Total	Twenty

Individual Results.

The individual results of the investigation are set forth in Figure 34. They will be examined in detail and commented upon.

The Diameter of the Placenta.

It will be seen that the placenta undergoes a gradual increase in diameter and by full term has doubled its original diameter of 9 cms. at twelve weeks. The placenta has a characteristic round or oval shape and this implies that increase in diameter is accomplished by a uniform enlargement of the placenta either peripherally or centrally or both and not by any localised portion. The diameter of a placenta is not a reliable index of its size since they vary so much both in width and thickness. A reliable index of growth is required and this is given by the weight.

The Weight of the Placenta.

After digestion and washing the placenta consists only of cord, chorion and foetal vessels. The contained maternal and foetal blood have been removed with the decidua and syncytium. The weight of the placenta, at this time, must represent the weight of the foetal vessels because the weight of the chorion and umbilical cord can be regarded as negligible. It follows that any increase in placental weight with advancing maturity, will represent quite accurately the growth of the foetal vessels which compose the cotyledons. At 16 weeks the placenta weighs from 20 to 40 grams, and at 40 weeks now weighs from 125-160 grams. This is, on an average, a fourfold increase in weight and demonstrates placental growth quite effectively. It does not however indicate which portion or portions of the placenta participate in the growth. The increase in weight of the placenta from 12 weeks until 28 weeks is in the order of 100 grams. This represents a weight increase of 6 grams per weeks. From 28 weeks until 40 weeks the increase is much less - only 40 grams and this represents a weekly increase of 3.3 grams. These results are shown graphically in Figure 35 and individual values in Figure 34. The greatest rise in weight occurs from the 20th until the 28th weeks. Thereafter the weight increases but not quite at the same rate. It will be apparent therefore that placental weight increase occurs throughout pregnancy. As a matter of interest the foetal gain in weight, in average values, during pregnancy has been superimposed on Table 1. It will be seen that although the foetus gains weight throughout pregnancy the same great increase in weight occurs from the 16th until the 28th week of pregnancy. The foetus weighs some 300 grams at 16 weeks but by the 28th week now weighs 2000 grams. This is an increase of 1700 grams or 140 grams per week. From the 28th week until full term the foetus gains another 1000 grams which represents an increase of 80 grams per week. It is apparent therefore that the foetus and placenta gain weight at much the same rate and in the same time. This correlation serves to confirm the impression that the foetal development depends largely on the condition of the placenta.

The Cotyledon Count.

The distinction between large, medium and small cotyledons is not hard and fast. All gradations in size are seen between large and small cotyledons. The cotyledon count is, in consequence, somewhat arbitrary and depends on the judgement of the investigator. In addition it is sometimes difficult to decide whether a cotyledon is a separate structure or part of the system of branches in a larger cotyledon. Each of the twenty placentae in this series was investigated in a similar fashion and the counts can be regarded as reasonably comparable.

The totals of cotyledons counted, in the twenty placentae examined, showed a striking variation. At 16 weeks maturity placentae could have as few as 109 cotyledons and as many as 197. At 40 weeks maturity, in a similar fashion, placentae could have as few as 130 cotyledons and as many as 265. This total of 265 cotyledons was the highest recorded in the series. Curiously enough, it was approached by a 20 weeks placenta which had 246, and a 24 weeks placenta which had 249 cotyledons.

The variation in the cotyledon count between placentae of different maturities is of some interest. If placental growth was brought about by an increase in the numbers of cotyledons, as pregnancy advances, it would be reasonable to assume that older placentae would possess more cotyledons than the less mature placentae. This finding has not been borne out in the present investigation. On the contrary it has been shown that at 12 or 16 weeks a placenta can possess more cotyledons than a placenta at term. Also a placenta at 20 weeks can possess almost twice the number of cotyledons as a full time placenta. These findings indicate quite strikingly that numerical increase of cotyledons is not a feature of placental growth. On the contrary, the findings can only be explained on the basis that the number of cotyledons possessed by any placenta is peculiar to the individual organ, and indicates further that this number is fixed early in pregnancy and is not altered by the duration of pregnancy.

The Size of the Cotyledon.

It has been shown that the diameter of the placenta increases steadily during pregnancy and is not restricted to any particular period or periods of development. The increase in size of the cotyledons shows a similar steady increase and illustrates and underlines the mode of placental growth. This will be discussed in the following paragraphs.

The Large Cotyledon.

A large cotyledon may measure as little as 1.5 cm. and as much as 3 cm. at 16 weeks maturity.

At full term it may have attained a length of 4 to 6 cm. A maximum increase in length of four times is thus possible. For the other periods of maturity smaller but similar increases in length have been noted. The increase in length of the large cotyledon does not necessarily demonstrate that increase in bulk is also taking place at the same time. The bulk of the cotyledon however does increase in a comparable fashion with its length. This is reflected in the increasing size and visibility of the many branches and especially of the peripheral fringe of small vessels which is such a prominent feature of the mature placenta. The cotyledon is a three dimensional structure and an increase in its breadth does not adequately convey the amount of increase in bulk. For this reason the breadth has not been noted, but as an indication of increase in size, the breadth increases in a similar fashion to the length. The measurements obtained in this series would indicate that placental growth is a maintained process during pregnancy.

The Medium Cotyledon.

The medium cotyledon is not such a large structure and its system of branches never quite so numerous. It is sometimes as long, and occasionally even longer than the large cotyledon. During pregnancy it shows the same growth pattern of increase in length and breadth but it never becomes such a bulky structure. A medium cotyledon may measure as little as 1.5 cm. and as much as 5 cm. at 16 weeks maturity. As maturity advances increase in length takes place but it is not so great as with the large cotyledon. For example the maximum length obtained in a full term placenta was 4 cm. The increase in length is accompanied by an increase in bulk but never to the same degree as its larger companion. The number of branches is always less and the fringe of peripheral vessel less striking. In some placentae the differentiation between medium and large cotyledons is less obvious and the counting of each rather arbitrary. However, although the separate counts may be inaccurate the total count can be regarded as accurate.

The Small Cotyledon.

This cotyledon is very small and rarely attains a length of more than 2 cms. The length does not increase very much with increasing maturity although the bulk increases and branches become

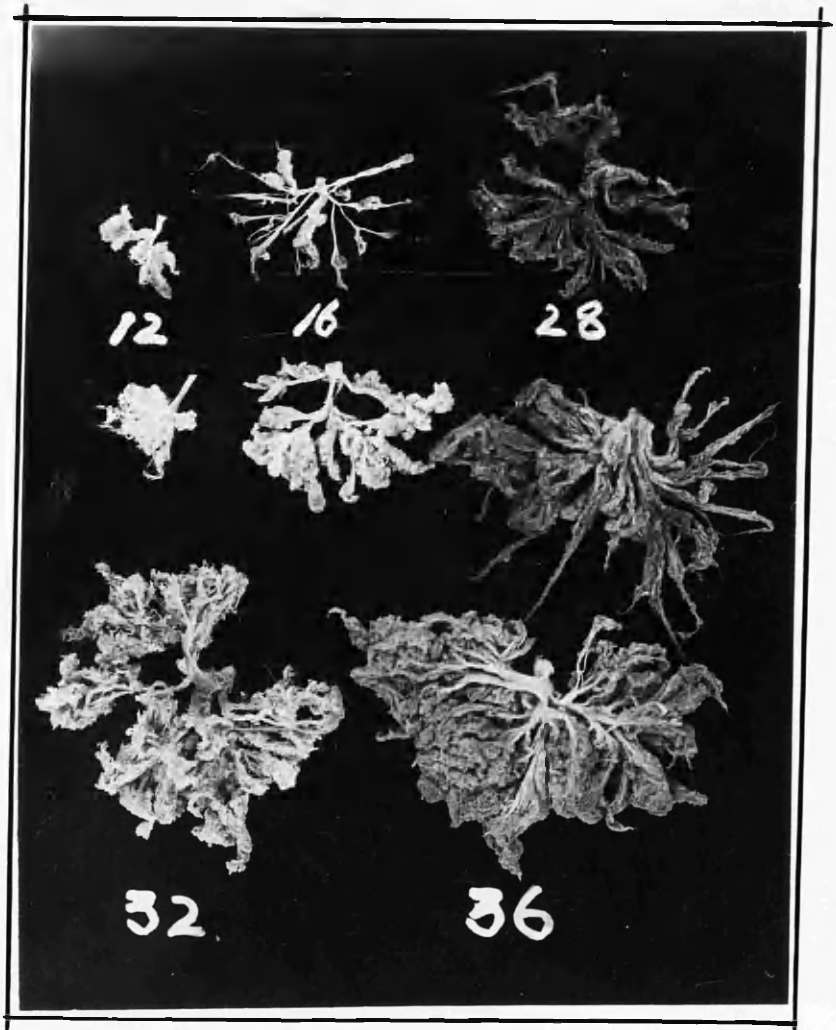

Figure 32.

The increase in size of large cotyledons is illustrated by this photograph. The numbers refer to the maturity of the cotyledon in weeks. The great increase in size is apparent between cotyledons at 12 weeks and the cotyledon at 36 weeks. It will be noted that although the size increases yet the general plan of the cotyledon is maintained. The branches become larger as maturity advances and the peripheral fringe of small vessels more and more abundant.

more obvious. It has usually a simple structure with few main branches, and arterioles and venules with their related capillaries are produced sooner. This cotyledon is most common under the chorion and at the periphery. It appears to fill up the bare areas of chorion which intervene between the origins of the cotyledonary vessels after they have perforated the chorion. They are frequently adherent to the maternal chorion and to related cotyledons. They are small and weigh very little and have been disregarded as an important factor in determining placental growth. It is difficult, at times, to distinguish small cotyledon from their medium sized companions and all gradations in size may exist between them.

The Weight of the Cotyledon.

The placenta has been observed to increase steadily in weight with advancing maturity. It was pointed out previously that the weight of the placenta, after digestion, must represent for all practical purposes the weight of its foetal vessels. Any increase in placental weight would indicate therefore an increase in the weight of the cotyledons. This fact has been borne out by

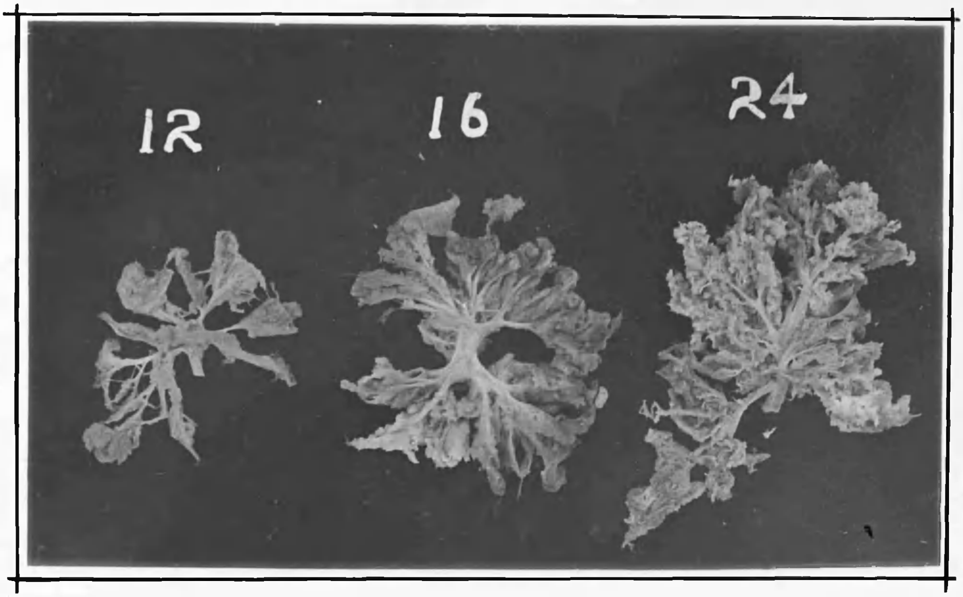

Figure 33.

The growth of the cotyledon is illustrated in another way by this photograph. The numbers indicate maturity in weeks. A large cotyledon is shown at 12 weeks and the increase in size by 16 weeks is apparent. At 24 weeks maturity a sub-cotyledon is shown which is obviously larger than the entire cotyledon at 16 weeks. The great increase in density of the peripheral fringe of capillaries is also very apparent.

this investigation and indicates in a very real way the increasing bulk of cotyledons as maturity advances. This particular part of the investigation is perhaps the most significant and important in indicating the pattern of placental growth. A large cotyledon may weigh as little as 0.44 gram and as much as 2.94 gram at 16 weeks maturity. At full term a large cotyledon may weigh 5.53 gram and even as much as 6.02 gram. This represents an increase from the minimum weight to the maximum weight of almost fourteen times! At the other periods of maturity similar and smaller increases can be noted although the steady pattern of weight increase has been obscured by some of the less mature placentae showing quite large weights. For example large cotyledons weighed 6.98 grams and 7.0 grams at 24 and 30 weeks respectively and demonstrates once again the tremendous weight increase from the 12th to the 28th week of pregnancy.

The medium cotyledon shows a similar increase in weight with maturation. At 12 weeks maturity a medium cotyledon weighs .073 gram. At term a similar cotyledon now weighs 0.5 gram in one instance and 0.8519 gram in another. This represents an increase of four and 12 times respectively. A much greater increase in weight was noted with a placenta of 28 weeks maturity. A medium cotyledon weighed 2 gram and this is 27 times the weight of a medium cotyledon at 12 weeks maturity! In general it has been observed that the medium cotyledon increases in weight with maturation exactly in the same fashion as the large cotyledon. Since the large and medium cotyledons compose the bulk of the placenta it is apparent that these increases in weight must indicate that placental growth takes place both in diameter and in thickness. This growth is a progressive and sustained process during the whole of which pregnancy. The marked exceptions to this rule provided by some of the less mature placentae which appeared to grow excessively, was a puzzling feature and some explanation must be afforded for this phenomenon. Further observation indicated a possible key to this problem and this will be considered in the next paragraph.

The Weight - Count Ratio.

In the course of this investigation it became apparent that there was a distinct relationship between cotyledon count and placental weight. Where the total cotyledon count was low, the cotyledons were larger and weighed more. In contrast where the total cotyledon count was high, the cotyledons were smaller and weighed less. For example at 16 weeks, in one placenta, the cotyledon count was only 109 but the large and medium cotyledons weighed 2.94 and 0.33 gram respectively. In another 16 weeks placenta the count amounted to 165 but the large and medium cotyledons weighed only 0.848 gram and 0.243 gram respectively. At 40 weeks maturity this relationship also held true. In one full term placenta the count was 140 but the cotyledons weighed 6.02 gram. and .8519 gram. In contrast another term placenta had 265 cotyledons but they weighed only 5.53 gram and 0.5 gram respectively. The relationship between placental weight and cotyledon count can be expressed as a weight-count ratio. The placental weight at each of the periods of maturity investigated was divided by the total number of large and medium cotyledons. It will be seen from the table that this ratio gradually rose, from 0.28 at 12 weeks to a maximum of 2.2 at full term. This ratio, if expressed in graphic form against maturity would take the form of a rising curve and this is shown in Figure 35. The ratio expressed clearly the underlying pattern in placental growth. This pattern can be expressed as the progressive increase in weight and size of a fixed number of cotyledons. If the cotyledon count increased, during growth of the placenta, with the weight of the placenta then it would follow necessarily that the weight count ratio would remain at or near the original figure of 0.28 at 12 weeks. Instead, the figure gradually rises to a maximum of 2.2 at full term. This indicates quite certainly that during placental growth there is one fixed value, namely the number of cotyledons.

Only one exception was found in the whole series. This was a placenta at 32 weeks weighing 175 gram and possessing only 42 large and medium cotyledons. This gave a weight-count ratio of 4.0 which was quite the highest obtained. No explanation can be offered for this result. It is possible that by mistake a placenta was obtained from a patient whose pregnancy was grossly abnormal.

1	2	3	4			5			6		7
Maturity Weeks	Diameter after Digestion Cms.	Weight after Digestion Gm.	Cotyledon Count			Cotyledon Size Cms.			Cotyledon Weight Gm.		Wt/Count
			Large	Med	Small	Large	Med	Small	Large	Medium	
12	8	30	14 (104)	90 164	60	3	3	1·5	1·52	0·073	0·28.
16	10	20	6 (56)	50 165	109	3	2·5	2·0	0·848	0·243	0·35.
16	10	30	20 (70)	50 170	100	2	1·5	1·0	0·89.	0·16	0·41.
16	9	40	21 (85)	64 197	112	1·5	1·0	1·0	0·44	0·145	0·50.
16	8	20	6 (36)	30 109	73	3·5.	5·0	2·0	2·94	0·33	0·55
20	12	30	5 (126)	121 246	120	2·5.	2·0.	1·0	—	0·130	0·23.
20	14	35·5	20 (70)	50 160	90	4·0	3·5.	2·0	1·34	0·64	0·50.
24	14	90	13 (59)	46 201	152	2·5.	2·5.	1·5	6·575	0·637	1·5
24	14	200	23 (113)	90 249	136	5·0.	3·5.	1·5	4·5.	0·39	1·6
24	13	125	17 (64)	47 182	128	3·5.	2·75	2·0	6·98.	1·17	1·9
28	15	125	12 (67)	55 224	157	4·0	3·0.	1·0	3·01	0·712	1·82
28	16	135	21 (71)	50 177	106	3·0.	2·5.	1·5	4·0.	2·0	1·9
30	12	65	12 (40)	28 229	189	2·5.	2·0	1·5	7·0	1·5	1·6
32	11	70	21 (47)	26 112	65	4·0	5·0	2·5	4·53	0·361	1·5
32	16	150	15 (57)	42 144	87	3·0	2·5	1·0	7·36	1·58	2·6
32	13	175	13 (42)	29 141	109	5·0.	4·0.	2·0	6·05	0·36	4·1
34	14	90	16 (57)	41 188	131	3·0.	2·0	2·0	4·39	2·15	1·5
36	15	150	17 (69)	52 203	134	4·0.	4·0	2·0	5·06	0·987.	2·1
40	18	160	18 (75)	57 265	190	4·0	3·0	1·75	5·53	0·50	2·1
40	18	125	20 (55)	35 130	75	6·0.	4·0	2·0	6·02.	0·8519	2·2

Figure 34.

Commentary.

If this investigation is correct in indicating that placental growth takes place by the progressive increase in size and weight of a fixed number of cotyledons, certain conclusions can be drawn. If the cotyledons are fixed in number then they must also be fixed in position, apart from an increase in size. This implies that the maternal vessels supplying and draining the placenta are also fixed in number and position. These would also increase in size during pregnancy but, with reference to the placenta their position would be fixed. The anatomical arrangements of the maternal and foetal circulation would not therefore be makeshift arrangements which have developed in a haphazard way during pregnancy. On the contrary, the vascular arrangements would have been present since the placenta was fully formed and developed in size and complexity to meet the ever increasing needs of the foetus. From a theoretical point of view it could be argued that such a permanent vascular arrangement has manifold advantages over a makeshift one. When the placenta has completed its initial growth at the end of the third month

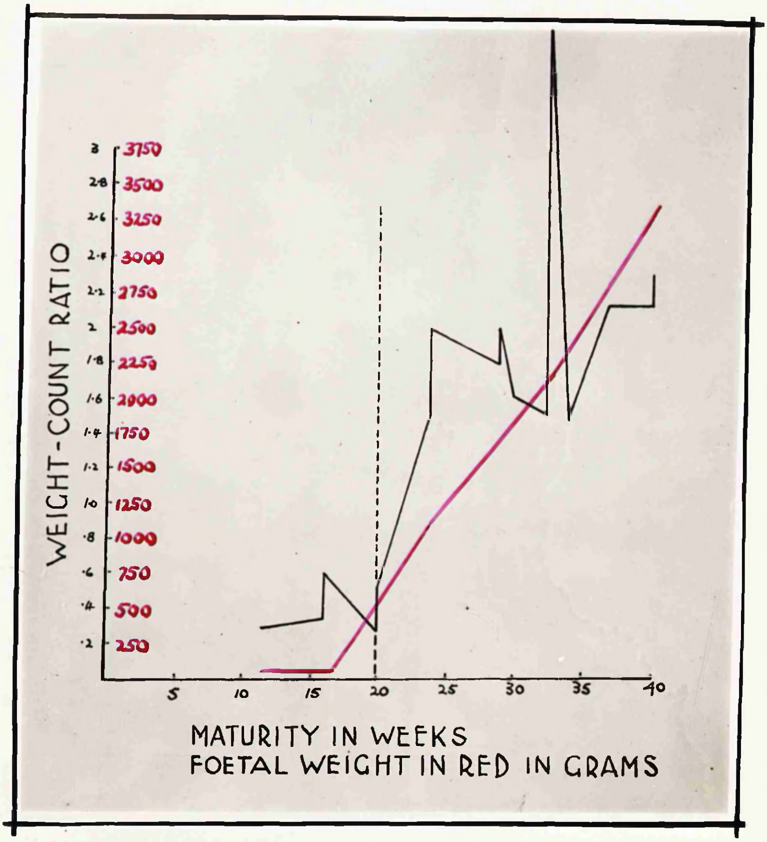

Figure 35.

This graph shows the relationship between advancing maturity and the weight-count ratio. It is evident that with rising maturity the weight-count ratio also rises. Superimposed on this graph is another showing the increase in foetal weight with advancing maturity. This correlation has been referred to in the text.

of pregnancy it would be difficult to conceive new maternal vessels siting themselves at the most advantageous sites for the supply and drainage of maternal blood. The various points in relation to the development of foetus and placenta will be considered at greater length in the final discussion. The growth of the cotyledon is illustrated by Figures 32 and 33.

The results of the investigation are shown in Figure 34. Figure 35 illustrates increased foetal weight with growth superimposed on a graph showing the relationship of the weight/ count ratio and placental maturity.

PART VII.

A Discussion of the Foetal Placental Circulation.

Introduction.

The anatomy of the placenta, as described in this thesis, is rather complicated. It is proposed therefore to discuss the present findings in relation to previous work, section by section. By doing so it is hoped that a clearer understanding of the present findings will be obtained.

Part One.

The Technique of Digestion.

In the practice of histology, as already related, trypsin and other proteolytic ferments have been employed to identify protein in histological sections. The application of this principle to produce a technique which would demonstrate the foetal placental circulation, is quite new and a marked departure from previous techniques. The placental preparation which is obtained after digestion is extremely suitable for demonstrating the anatomy of the placenta. The mode of technique has been described in detail in Part 1.

The placental preparation has several advantages over the cast of the foetal vessels which is obtained by the usual injection-corrosion technique. The principle advantage of this method lies in the fact that the foetal vessels are preserved and can be used to check the results. No such check is possible when the foetal vessels have all been corroded and removed by acid. It follows that artefact can be guarded against and eliminated. There are other advantages. For example the method is much quicker and easier to perform. A placenta can be prepared completely within three days as against the seven or more days required by the injection-corrosion technique. In addition few placentae need be rejected because of vessel rupture and spilling of filler. The method also is quite certain and consistent in its results provided the basic technique is applied correctly.

From the view point of scientific investigation the digested placenta is most suitable. The actual vessels can be seen and dissection carried out with accuracy. Cotyledons can be separated from their neighbours under direct vision and individual cotyledons dissected into their constituent sub-cotyledons. This accurate dissection permits the investigator to obtain a clear picture of the relationship of cotyledons to each other. This is most important in a three-dimensional structure such as the placenta.

In conclusion, it is the belief of the writer that this technique of digestion will enable our knowledge of placental anatomy to be carried beyond the present stage of "first approximation". The systematic application of this technique, in the future, will it is believed place placental anatomy and pathology on a firm scientific basis. In doing so it will help to elucidate so many of the clinical problems confronting the obstetrician at the present time.

Part Two.

The Gross Anatomy of the Placenta.

Previous Work.

The injection of radio-opaque substances into the foetal vessels and the casts obtained after injection-corrosion techniques have, in the past, provided the basic structure of the placenta. It is necessary to remember in any discussion that these techniques are subject to artefact and against this background previous work can be judged. Kellog, Davis and Arnolski (1924); Spanner (1935); Romney and Reid (1951); Wilkin (1954), have provided in their published work a composite picture of placental anatomy. The anatomy of the placenta is, in essence, the anatomy of its blood vessels. It follows, that fillers would adequately demonstrate the gross foetal circulation. However, penetration of vessels is often incomplete or absent and the casts obtained are necessarily fragmentary. The casts obtained have demonstrated that the umbilical arteries anastomose before the insertion of the cord. Thereafter each umbilical artery divides and sub-divides in a dichotomous fashion. At each division a proportion of these vessels perforate the chorion and enter the placenta where they end in cotyledons. This provides for a concentric mode of distribution. Anastomosis between adjacent arteries, on the chorion, has been claimed frequently. Romney and Reid (1951) have claimed to demonstrate anastomosis between adjacent arteries at the periphery of the placenta. Their anastomosis would infer that a dual arterial blood to a cotyledon is possible. The veins lay below the arteries on the chorion and followed a course, more or less the same as the arteries.

Present Work.

The present work has shown that the dichotomous pattern of division on the chorion is not quite correct. The division of each umbilical artery and the subsequent divisions are three-dimensional. At each of the divisions on the chorion and at other times deep arteries are derived from the under surfaces of the chorionic trunks. They pass at once into the placenta and are not seen superficially. These deep vessels can be as large as the primary and subsequent divisions and end in cotyledons.

It has been noted that all the arterial and venous branches on the chorion end in cotyledons. Some of these may be extremely small. This raises the question of the source of placental nutrition since no vessels were seen which appeared to have the specific function of nutrition. The absence of such vessels has been commented on previously by Zeek and Assali (1952). The findings would suggest that the placenta is nourished directly by the maternal blood.

There has been no evidence, in the placentae examined, of any arterial anastomosis between superficial branches of the umbilical arteries or between individual branches in each half of the placenta. Also the arteries supplying the cotyledons are quite separate from each other. The absence of a dual blood supply to cotyledons raises important clinical questions in regard to placental lesions and foetal survival. These questions will be considered later at greater length.

A number of investigations have shown the presence of occlusive structures in the veins of the placenta. These occlusive devices have been considered to possess a sphincteric action with the function of limiting or restricting the venous return from the placenta. Spanner (1935) considered that they were present along the whole venous tree. Danesino (1950) considered they were present also and particularly in the veins within cotyledons and the veins draining cotyledons. In this work there has been no suggestion of sphincters in the veins examined, and so far as the casts of vein are concerned it is reasonable to conclude that some of these occlusive devices were produced by artefact. The possibility of these structures remains and further work will be necessary to confirm or deny their presence.

Arterio-venous anastomosis have been described by Danesion (1950) who found it present particularly in the region of the insertion of the cord or at the base of the large villous trunks. No evidence of such anastomosis has been found so far. The veins and arteries run side by side, especially when supplying cotyledons, and they appear to be quite separate in their courses.

Part Three.

The Anatomy of the Cotyledon.

Previous Work.

In the past, investigators have used the terms "villus", "cotyledon" and "lobe" more or less synonomously. In this present work the term 'cotyledon' is quite distinct from either villus or lobe. In the text care has been taken to make a clear distinction between them.

Bumm (1893) described the cotyledon as a tree-like structure with its most peripheral branches attached to the maternal decidua. Spanner (1935) suggested that the villus (cotyledon) passed downwards from the chorion and entered the decidua where, after a variable distance, it emerged and passed up again into the placenta. This is the well-known "chandelier" arrangement of the villus. It has been confirmed by some workers and just as vigorously denied by others. Stieve

(1948) said that this arrangement was quite untrue, and Romney and Reid (1951) were of a similar opinion. In contrast Wilkin (1954) confirmed Spanner and so did Danesion and Weidermann (1955).

Wilkin (1954) likened a cotyledon to a drum. It was hollow in the centre and possessed walls with a profusion of small branches. He noted also that the cotyledon cast on the maternal aspect possessed a gap. This he termed the crown (couronne) and suggested that it was related to the entry of maternal blood. He was of the opinion, that in view of the structure of the cotyledon, the capillary bed was most concentrated at the periphery and the decidua. Romney and Reid (1951) were also of the opinion that the capillary bed was most dense nearest to the decidua.

A spiralling of the vessels, both arterial and venous, has been noted by many writers including Spanner (1935); Romney and Reid (1951); Wilkin (1954) and Danesion and Weidermann (1955). This spiralling has been noted most commonly in the vessels supplying cotyledons. It has been likened as analagous to the spiralling of endometrial vessels and produced by the same oestrogenic hormone. The spiral has been regarded as a device intended to slow the flow of foetal blood leaving or entering the placenta.

Present Work.

The anatomy of the cotyledon as demonstrated by this investigation, is quite new and has not been described previously. This demonstration has been due entirely to the digestion technique which preserves the actual cotyledon. The vessels of the cotyledon can be dissected free and seen in their entire course. The cotyledon has been described as a cone-shaped structure with its apex to the chorion and its base resting on the decidua. The division of a cotyledon into sub-cotyledons, by a system of branching resembles the structure of a tree. The division of the primary trunk of the cotyledon into a number of secondary branches, which also produce by their branching the sub-cotyledons, has been demonstrated. These divisions tend to keep to their main course whilst giving origin to smaller lateral branches. The bulk of the small vessels are borne at the periphery of the placenta and within the cotyledon comparatively few small branches are derived. It is these smaller branches which ultimately produce arterioles and venules, and those in turn bear the capillaries. This arrangement implies that the capillary bed is peripheral and in greatest concentration nearest to the decidua. The concentration of capillaries would be least within the cotyledon. A feature of the anatomy is the bare areas of chorion between the cotyledonary vessels at their points of perforation of the chorion. These bare areas are normally occupied by small cotyledons but the capillary concentration here would be much less than at the decidua. The views of Romney and Reid and Wilkin are confirmed with regard to the disposition of the capillary bed.

The cotyledon is most firmly attached to the decidua by the branches of one of its sub-cotyledons which is usually present most peripherally. This sub-cotyledon appears to have become modified, either in whole or part, for the purpose of fixation. The trunks of the sub-cotyledon contain few vessels and these show varying degrees of occlusion by endarteritis. The vessels appear small in relation to the bulk of the trunk. In some trunks vessels are quite absent. These fixing trunks end in the decidua. They fill imperfectly with filler and would not be seen by the injection-corrosion technique. At the periphery of the placenta smaller cotyledons show the same modification for fixation. Their characteristics and disposition have been described in detail previously. The remaining areas of the cotyledon fill normally with filler and appear to be the functional elements in the cotyledon. The vessels nearest to the decidua often enter it and after a variable distance emerge and pass upwards into the placenta. The vessel trunks above these most peripheral branches show the same curved course but do not enter the decidua. The "chandelier" arrangement of Spanner is confirmed by this investigation but with the difference that it is only the most peripheral branches which enter decidua. The gap or crown demonstrated by Wilkin may represent the area of fixation since the fixing trunks would not permit filler to enter and would subsequently be corroded away leaving a gap.

The fashion in which the sub-cotyledons are related to each other and to neighbouring cotyledons in a mosaic-like arrangement has been demonstrated for the first time. This arrangement ensures a continuity of placental tissue throughout the entire length and thickness of the placenta. From a functional point of view cotyledons are continuous structures although derived separately from the chorion.

Spiralling has been observed in the vessels supplying cotyledons, especially smaller cotyledons derived from the main cotyledonary trunks. The spirals have been simple and consisting of two to three turns. The spiral is produced by the efforts of the artery or vein to reach its companion vessel and run side by side. Many of these smaller vessels are derived at a different level from their companions and a change of direction is necessary before they can be reached.

It has been demonstrated for the first time that a placenta contains approximately 200 cotyledons. These can be sub-divided into large, medium and small in the proportion of 10, 50 and 150 cotyledons respectively.

Part Four.

The Anatomy of the Villus & Its Capillary Structure.

Previous Work.

The complete capillary vessel has never been demonstrated. The reason resides in the techniques employed. For example, with injection-corrosion methods the fillers such as latex and vinyl acetate rarely reached the capillaries and if they did the penetration was incomplete. The capillary cast was necessarily fragmentary and this no doubt explains the variance of previous opinions. Spanner (1935) described long capillary structures. In contrast, Romney and Reid (1951) considered that capillaries, although extremely numerous, were relative short structures. They based this opinion on the observed gap between the arterial and venous ends of the capillary vessel which they found to be 1 mm. or less. It should be pointed out that they did not obtain complete capillary casts.

The actual appearance of the capillary bed has been visualised by many writers. Stieve (1940, 1948) likened the capillary area to a fringe made up of a three-dimensional lattice work (gitterzotten). This lattice work resembled a sponge which contained maternal blood within its interstices and in consequence no free maternal blood would exist. The interstices of the sponge, he urged, would be lined by syncytium derived from adherent villi and in effect producing a multitude of little channels. He believed that all villi should be regarded as adherent and never free. This would give the capillary bed a 'labyrinthine' structure, such as is found in other animals. Spanner had regarded the villi as hanging free in a lake of maternal blood and producing a capillary bed which was essentially "villous". Hamilton and Boyd (1951) have considered that Stieves views on capillary bed structure to be correct in the main. They doubted however whether all villi could be regarded as fixed to each other by syncytial adhesion. Stieve (1948) has also suggested that villi not only share syncytium but also blood vessels. This has been doubted by Hamilton and Boyd (1951). Hamilton and Boyd have also put forward the theory of "reverse circulations" in the capillary bed. They have pictured that the maternal and foetal bloods flow through the capillary bed in opposite directions. This arrangement would, they urged, ensure time for an efficient transfer of oxygen to the foetus.

Present Work.

The actual appearance of the capillary vessel has been demonstrated for the first time. It has been noted that capillary vessels vary in their complexity. The first capillaries given off by the parent arterioles and venules are usually simple loops, but the later vessels become more complicated structures. These show convolutions in three dimensions and are very long. The final vessels show extreme convolutions and resemble renal glomeruli. The preservation of syncytium has been of great value in the study of the villus. The syncytium reproduces externally the convolutions of the vessel within as a series of lobules over its surface. It is clear therefore that the villus is not a simple structure resembling a gloved finger, but a multi-lobulated structure in three dimensions. Many of the villi are enmeshed with each other and show syncytial adhesion. It has been suggested that some of the syncytial adhesion seen between villi in histological preparations, really represents lobules derived from the same parent villus. In this event it would be possible for "villi" to show a sharing of blood vessels, although the shared vessels would represent the common capillary vessel within the parent villus. The present work would suggest that villi can be both free and adherent by syncytium. The extreme picture of a "labyrinthine" capillary bed, as presented by Stieve, is not supported. However the maternal blood would never really be free as a lake. On the contrary it would, for all purposes be within the meshwork of the capillary bed.

The arterial and venous ends of the capillary vessel are close to each other, as noted by Romney and Reid, but this gives no indication of the great length of the capillary. The convolutions of the capillary vessel could not have been visualised by these workers.

Part Five.

The Maternal Aspect of the Placenta.

The maternal aspect of the placenta has been described and its features interpreted in the light of the anatomy demonstrated by the present investigation. The composition of the placental lobes has been shown for the first time and the significance of the white calcified areas on the placenta made clear.

It has been shown that the deep fissures of the maternal placental surface penetrate between the lobes, for a considerable depth. These fissures are lined by maternal decidua and it is only above the decidua that continuity of cotyledons is again established. The oval openings in the deep fissures have been regarded as the openings of maternal vessels. They have also been shown to be similar to the oval openings around the periphery of the placenta. By dissection it has been demonstrated that these oval openings all drain into the same deeper vessels within the decidua. The convex surface of the lobes also shows small oval openings which are not conspicuous and require careful search. These must also represent the openings of maternal decidual vessels. They can be found at all areas of the placenta. The lobes of the placenta have been shown to be composed of aggregations of cotyledons, the numbers of cotyledons depending on the size of the lobe. The shallow fissures represent and mark the boundaries between adjacent cotyledons and sub-cotyledons. The white areas of calcification, over the lobes and around the margins of the deeper vessels, have been demonstrated to mark the implantation sites of the fixing trunks. It has been suggested that these areas indicate endarteritis in the related foetal vessels and their numbers an indication of the extent of endarteritis present in the placenta. The mature and especially, the post-mature placenta present many calcified areas, and the same frequency is noted in placentae delivered from mothers with hypertension and pre-eclampsia. The "low-reserve" placenta found in such cases may be one in which the endarteritic change within its vessels has been greatly exaggerated. The transfer of oxygen would be diminished because more and more foetal capillaries were being destroyed. The "low reserve" state might only be apparent at labour when foetal distress develops early. This question will be discussed later.

The anatomy of the maternal aspect of the placenta is concerned with and related directly to the maternal blood supply and the maternal placental circulation. This investigation has been concerned with the foetal placental circulation but certain deductions can be made with regard to the maternal circulation. The convex surface of the lobe is formed by the most peripheral areas of the cotyledons which contain the greatest concentration of capillaries. The concentration has been shown to be less under the chorion and least within the centre of the cotyledon where the larger trunks are dividing and sub-dividing. It follows from this that the greatest obstacle to the passage of maternal blood will be offered nearest to the decidua. It seems reasonable therefore to deduce that in this area maternal blood would need to have its greatest pressure. In fact a systolic pressure would be necessary to ensure that the capillary bed would be penetrated. Once the capillary bed is penetrated there would be much less resistance within the cotyledon and maternal blood could flow more freely to the sub-chorionic area. At this level the maternal blood could pass in all directions under it and fairly freely. The drainage of blood could then be effected through the large oval openings in the decidua of the deep fissures and at the periphery. It follows from this that the smaller openings over the lobes may represent maternal arterial openings and the larger openings, maternal venous openings. The maternal placental circulation which has been described differs from the uni-directional blood flow envisaged by Spanner. He described the maternal blood being drained away by the "marginal sinus" at the periphery. Like Hamilton and Boyd (1951) this author has not seen a true marginal sinus. Occasionally large venous channels may be seen at the periphery of the placenta but these are inconstant and never form anything in the nature of a continuous sinus. Hamilton and Boyd (1950) envisaged venous drainage taking place from all parts of the basal plate and maternal arteries opening into the placenta in the same fashion.

Part Six.

The Growth of the Definitive Placenta.

Previous Work.

The technique of digestion presented in this thesis and the details of placental anatomy described subsequently, have permitted for the first time an investigation into the growth of the definitive placenta. The lack of knowledge of placental growth has been due entirely to the absence of a suitable technique. In these circumstances it is not surprising that very few observations have been made on placental growth.

Spanner (1935) believed that the placenta did not grow in circumference during the second half of pregnancy but only in thickness. Stieve (1948) believed that circumferential growth occurred throughout pregnancy but not growth in thickness during the second half of pregnancy. Hamilton and Boyd (1950) agreed with Stieve that circumferential growth did occur throughout pregnancy but this did not exclude the possibility of interstitial growth. These writers considered that growth in thickness did take place throughout the whole of pregnancy but was greatest from the fourth to the seventh month. In regard to the maternal blood supply of the placenta there has been no attempt to investigate how this is continued and developed with placental growth. There is a popular impression that the placenta grows like a fungus across the internal surface of the uterus and progressively acquires connections with maternal vessels in its growth. The foregoing is the sum total of knowledge concerning growth of the definitive placenta. It indicates the urgent need for investigation of this aspect of placental anatomy.

Present Work.

The account of placental growth given in Part Six is original and has not been described previously.

The placenta at the end of its initial development has been shown to possess a fixed number of cotyledons. These do not increase with advancing maturity but instead become longer, broader and heavier. The cotyledons have been described as large, medium and small. The bulk of the placenta has been observed to be composed of the large and medium cotyledons. These number approximately ten large and fifty medium with perhaps one hundred and fifty small cotyledons in addition. The total number of cotyledons varies with each placenta but this would seem to indicate both the natural variations in placental size and errors in enumeration. It is not possible to count all the small cotyledons but since they are small and light, it is unlikely that they exert much influence on placental growth. The number of cotyledons possessed by a placenta would appear to be a fixed genetic endowment.

It has been shown that the large and medium cotyledons increase in length, breadth and weight during pregnancy. The increase is both gradual and sustained and would indicate that placental growth both in diameter and thickness is taking place throughout pregnancy. It has been pointed out previously that if the larger cotyledons are fixed in number they must also be fixed in position to the uterine wall. It follows from this that uterine growth will take place at the same rate as placental growth. It also follows that the maternal vessels which supply the placenta in the earlier months will also be the same at term. They will of course be larger and have shared in the same growth as the placenta. This fixed relationship between placenta and uterus would appear in theory, at least, to be a much more satisfactory way of ensuring an efficient transfer of oxygen to the foetus. The siting of the maternal vascular openings in the deep fissures and the similar vascular openings at the periphery of the placenta suggests an arrangement which has been present throughout pregnancy.

The cotyledon at twelve weeks is a miniature of the cotyledon at forty weeks. The same main divisions are present but they have become progressively larger. The sub-cotyledons share in the increase. A sub-cotyledon at twenty four weeks will be as large or larger than a whole cotyledon at twelve or sixteen weeks. A subcotyledon at term will be as large or larger than a whole cotyledon at twenty four weeks.

It has been shown that although cotyledons are continuous in a functional sense they are separate anatomically and do not possess a dual blood supply. If this is related to function it indicates that disaster can befall one or more cotyledons without involving the rest of the placenta. Foetal survival with perhaps only a half of the placental functioning, is possible. On the other hand since the cotyledons are fixed in number any pathological lesion involving the loss of cotyledonary tissue cannot be made good. If the process is of long duration more and more placental tissue can be destroyed and the environment of the foetus will become more and more unfavourable as pregnancy progresses. The appearance of the areas of calcification in the mature placenta and their relation to endarteritic change in the related foetal vessels is one example of a long-standing change which may become pathological and prejudice foetal survival. This change is obviously of importance in post-maturity where these areas are usually plentiful and indicates that oxygen transfer to the foetus is becoming more and more difficult. The importance of foetal anoxia in relation to foetal survival has been pointed out by many workers including Eastman (1936); Seward (1950); Barcroft (1946); Werthemann, Reiniger and Theolan (1950); Guilhem, Pontomner, Baux and Bennet (1952); Taylor, Tillman and Blanchard (1954), and more recently by Walker (1954). Walker (1954) has shown very convincingly the importance of foetal anoxia in post-maturity. It is assumed that the placenta can cope with foetal oxygen requirements until labour interferes with oxygen exchange. This type of placenta has often been termed the "low reserve" placenta. From the present work it is reasonable to assume that the volume of foetal villi through which oxygen exchange can take place may have been much reduced by the destruction of the placental capillaries following upon the Progressive endarteritis which develops with maturity in the larger foetal vessels.

The close relationship between placental function and foetal development is clearly demonstrated by comparing the weights of both at the various stages of pregnancy. Although the placenta increases in size and weight throughout pregnancy there is a period of especially rapid development from the 16th to the 28th weeks. Comparison of foetal and placental weights shows that the curve of growth in both instances pursues a similar course.

In conclusion it is apparent that the placenta is well adapted to ensure foetal survival. The presence throughout pregnancy of an efficient arrangement of maternal and foetal blood systems ensures a continuity of oxygen exchange. The placenta is well adapted to withstand local lesions since each cotyledon has its own blood supply. The destruction of one cotyledon does not imperil the remainder. On the other hand destruction of a cotyledon, for example by infarction, almost always involves the maternal supply at that point, and the inability to form new cotyledons to tap new sources of maternal supply is a disadvantage. This inability no doubt helps to explain the dangers to the foetus in conditions such as pre-eclampsia where such lesions are common.

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