HUMAN DECIDUAL SPIRAL ARTERIAL STUDIES

PART VI*: POSTMORTEM CIRCULATION STUDIES ON AN *IN SITU* PLACENTA

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Placental insufficiency has many facets. A large part of the problem of placental insufficiency is concerned with an adequate maternal and foetal placental circulation, as well as with the relationship of the two circulations to one another. Further study of this aspect may therefore yield very interesting results.

The material for examining the foetal placental circulation is freely available and, by injecting various dyes, rubber solutions or other materials, the circulation may be observed during the injection, the villi may be dissected, or studies may be done after corrosion. X-rays may be taken after a radio-opaque dye has been injected.

Though a fairly good understanding of the intervillous-space (IVS) circulation may be obtained by injecting individual spiral arterioles, it is nevertheless impossible to gain a comprehensive knowledge of the general distribution of spiral arterial flow, because there are probably always some of the spiral arterioles which are either not detected or are too small to inject.

It is now an acknowledged fact that the foetal placental tissues depend on an adequate maternal arterial inflow for health and survival. The peculiar round or oval subdecidual infarcts, which are found especially in the toxaemic group of patients, have been an enigma until recently. My earlier studies have shown[7,8,11] how coagulative blood from the spiral arterioles flows into the IVS, where it produces subdecidual red infarcts. If a substance such as liquid latex is injected *via* the intact uterine artery and the spiral arterial circulation into the IVS, to solidify there, then such an artificial lesion should conform to the pattern of infarcts mentioned above.

During the previous studies of the spiral arterioles[7-11] the techniques were constantly adapted to the demands of the material available and the aims of the study. Some of the abovementioned features can, however, only be convincingly demonstrated in an *in situ* placenta. Corroborative evidence of other features may also be obtained with the aid of such a specimen. *In situ* specimens are very rare; only one has become available during the past 2 years, which represents 16,000 deliveries. It will now be dealt with in some detail.

Case Report

M.S., a 33-year-old gravida 5, para 3, had only one significant feature in her past history — a ruptured ectopic for which a right salpingectomy was done in 1959.

During the pregnancy under review she booked at 28 weeks with a blood pressure of 120/75 mm.Hg, no albumin or sugar in the urine, no oedema, and 174 lb. in weight. She attended 5 times until the 36th week (5 September 1961), when the following data were recorded: blood pressure 130/90 mm.Hg, urine normal, slight oedema of the legs, and the weight 177 lb. From the 36th week she failed to attend at the antenatal clinic, because, according to her husband, she did not feel well and she complained of severe headaches and swelling of the feet. On the afternoon of 4 October she developed epigastric pain in addition to the headaches. At 4 a.m. the next morning generalized convulsions commenced, yet the relatives failed to notify the Obstetric Flying Squad, a mere 2 miles distant, until an hour had elapsed. By then she was having a sixth fit. On arrival the patient was found to be deeply comatose with a blood pressure of 220/120 mm.Hg, solid albuminuria, gross oedema, and in labour. In spite of the administration of 5 ml. of rectal 'avertin' on arrival of the Flying Squad, ¼ gr. of morphine at 6.30 a.m. and another 5½-ml. dose of avertin at 9 a.m., the blood pressure failed to respond despite the adequate sedative effect of the drugs. At 10 a.m. she became cyanosed and the rate of respiration, which was Cheyne-Stokes in nature, was decreased to 10 per minute. The blood pressure fell to 130/70 and then suddenly rose to 210/110 mm.Hg. This was followed by a sudden final collapse and death. The foetal heartbeat had ceased and cardiac massage was of no avail.

On postmortem examination a massive left subarachnoid haemorrhage, typical eclamptic liver, and pale haemorrhagic kidneys were found. The uterus with foetus and placenta *in situ* was removed *in toto*. This specimen was used for the investigation.

METHOD OF INVESTIGATION

The pathologist had delivered the 7 lb. 3 oz.-baby through a longitudinal anterior uterine incision, and had severed the cord 4 inches from the chorionic surface of the placenta. The placenta was 7½ inches in diameter, ¾-inch thick near the cord, roughly round, and situated posterolaterally in the right cornu. The chorionic surface presented no abnormal features. A number 15 Luer-lock needle, with a polythene tube attached to it, was inserted into the right uterine artery; this artery was selected because most of the placenta overlay it.

The artery and its ramifications were flushed through with a 1% sodium citrate solution. During these injections there was a gradual distension of the intervillous space, at first focal, then generalized. Compression of the placenta after injecting 100 ml. of sodium citrate solution was followed by drainage, mostly through the right uterine veins, but also through the incision into the anterior uterine wall. This flushing of the uterine artery and IVS followed by compression and drainage was continued until the returning fluid became clear.

The incision of the uterine wall was thereafter extended towards the left side of the fundus, at the one end, and the lower segment at the other. By doing this the entire placental surface could now be laid flat, yet nearly all the branches of the right uterine artery, which was thought to represent the main arterial supply of this placenta, could be preserved. The incised edges were carefully sutured with a continuous dermalon thread to prevent the escape of the radio-opaque dye during injection of the uterine artery.

The specimen was now positioned on an X-ray machine capable of 6 exposures per second, with the area of the uterine muscle on which the placenta was implanted flat on the plate. The machine was set at 4 frames per second for 2 seconds, then 2 frames per second for 1 second and thereafter one exposure per second for 2 seconds. In

* Parts I - V were published elsewhere.[7-12]

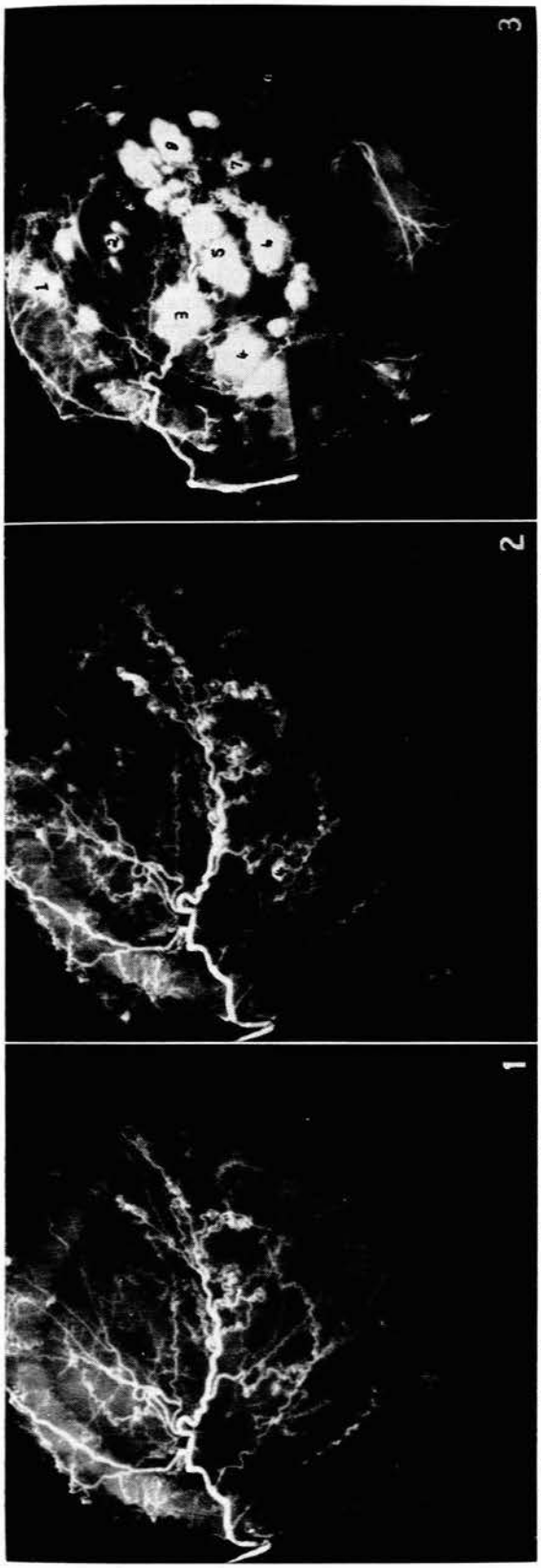

Fig. 1. X-ray taken 2 seconds after the injection was begun and after approximately 20 ml. of radio-opaque dye had been injected into the right uterine artery. *Fig. 2.* X-ray taken after 4 seconds and after approximately 32 ml. of dye had been injected. *Fig. 3.* X-ray after 80 ml. of radio-opaque dye had been injected.

order to reduce the hazard of occluding the smaller ramifications with an oily solution, thereby prejudicing the planned further procedures, the water-soluble radio-opaque preparation 'diagonal' was used for the injection. The forceful injection of 40 ml. of diagonal into the uterine artery was commenced simultaneously with the X-ray exposures. By the end of 5 seconds all 40 ml. had been injected. After injection of a further 40 ml. another exposure was made, followed by yet another 40 ml. and an X-ray.

At this stage 80 ml. of liquid latex, coloured with red vegetable carmine dye, was injected into the right uterine artery. By this means a lateral view of the distribution of the liquid dye, which reached the IVS *via* the spiral arterioles, would be obtained, and, in addition, the radio-opaque diagonal would be washed from the vessel so that an unobstructed radiological view of the foetal circulation might be obtained after injecting it. Before proceeding, a check X-ray was performed to make certain that all the diagonal had been flushed out of the uterine artery.

A polythene tube was then tied into each of the 3 umbilical vessels. These were in turn flushed with sodium citrate solution until the returning fluid was clear. Whilst injecting the arteries, the fluid returned through the vein and vice versa. The umbilical arteries were then injected with 10 ml. of diagonal each so that the larger branches could be filled. It was thought that by using a relatively small volume of dye, the confusion which would be caused by dye starting to flow from arterial into venous foetal placental circulations, could be averted. An X-ray photograph was taken after each umbilical arterial injection. The umbilical vein was then injected with 20 ml. of diagonal and a final exposure made.

The entire specimen was thereafter placed in 10% formol saline for 3 weeks, after which it was longitudinally cut into $\frac{1}{2}$-inch-thick strips. These were then numbered in serial order and each examined in turn.

RESULTS

Figures 1 - 5 had all been positioned at approximately the same angle. For clarity's sake some of the corresponding individual collections of dye, and later dye plus liquid latex in the IVS, had been numbered (Figs. 1 - 5). *Individual numbers refer to the same collections throughout.*

Fig. 1 was the eighth X-ray taken, 2 seconds after the injection was begun and after approximately 20 ml. of dye had been injected. Nearly the entire right uterine artery as well as its branches are filled with dye, yet only at No. 1 has it commenced to pass into the IVS.

Fig. 2 is the eleventh X-ray plate taken, 4 seconds after the injection was begun and after approximately 32 ml. of dye had been injected. Dye starts to appear at Nos. 4 and 8 and around No. 5. Fig. 3 is the thirteenth X-ray taken after 80 ml. of intra-arterial dye had been injected. The radio-opaque material has entered the IVS through a number of spiral arterioles and these collections gradually increased in size as the dye accumulated.

Fig. 4 was taken after a further 40 ml. of radio-opaque dye had been injected through the uterine artery (a few ml. of which drained away), followed by 80 ml. of red liquid latex. In addition, each of the umbilical arteries

were injected with 10 ml. of diagonal. It clearly shows that, excepting for two small branches, all the foetal placental arteries directly enter the collections of dye and latex which had entered the IVS through the decidual spiral arterioles.

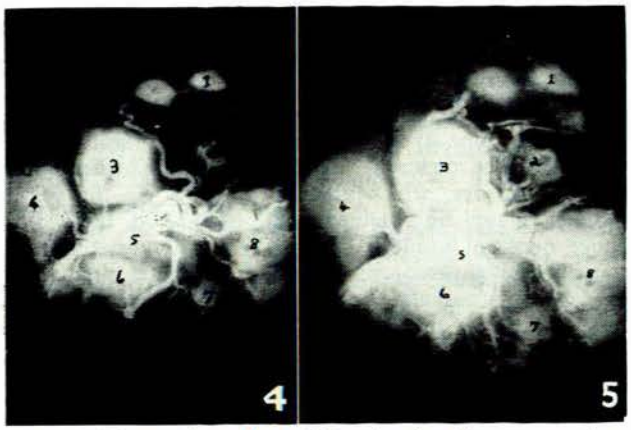

Fig. 4. X-ray after about 120 ml. of radio-opaque dye and 80 ml. of liquid latex had reached the IVS *via* the right uterine artery and spiral arterioles. In addition the umbilical arteries and their ramifications were also partially injected.
Fig. 5. IVS dye and latex as well as the umbilical arteries and vein distribution were shown.

In Fig. 5 the umbilical vein had been injected in addition to the above features being present. Also, the venous distribution conforms mainly to the spiral arterial inflow collections of dye and latex.

Fig. 6* is a cross-section of the placenta and uterus after fixation in 10% formalin saline. The serous surface of the uterus is folded upon itself so that the placenta is situated anteriorly, to the right, and posteriorly to the uterine wall.** Three subdecidual collections of liquid latex are present. The smallest of the three (C) traverses only about half the depth of the IVS, whereas the others (D and E) reach the chorionic plate. The first two are homogeneous. The largest one is starting to separate into an outer homogeneous layer of latex and villi (E) as opposed to the centre (F) which is nearly solid latex.

Figs. 7, 8 and 9* were not obtained from this specimen since the technique employed precluded such an opportunity. However, they are included to demonstrate some severe types of abnormalities encountered in the toxaemia-eclamptic group of cases. Fig. 7 shows a necrotic spiral arteriole which has ruptured intradecidually and from there through the decidual plate into the placenta. From the damaged spiral arteriole (Fig. 8) coagulative blood entered the IVS, where it clotted subdecidually. The lesion can be seen to separate into two layers — on the outside, clot with a few villi incorporated in between; on the inside, solid clot. Fig. 9 not only demonstrates how a damaged spiral arteriole may become aneurysmal, but also a somewhat older red-infarct pattern-A.[11] The border of necrotic villi which forms the outer layer is much thicker; the central clot is relatively small.

* See colour illustration on opposite page.
** B-B-B is the uterine muscle and A-A-A the decidua.

DISCUSSION

X-radiology is a well-recognized method by which the circulation in many parts of the body is studied. Its usefulness depends largely on the nature of the circulation to be studied. If the vessels are small and form a complex three-dimensional structure, such as the foetal placental circulation, interpretation of the films should be very guarded. This applies especially to the finer villus ramifications. Kiffner[6] showed that anastomoses occurred on some plates which, on stereoscopic X-rays, were not seen. Only when the placentas were also X-rayed with the foetal surface on the cassette could many of the apparent anastomoses be discerned as vessels projected across one another. Bacsich and Smout[3] and Szendi[12] re-emphasized this aspect. Tobin,[13] Adler[1] and Dankmeijer and Landsmeer[4] attempted to circumvent this difficulty by injecting a mixture of radio-opaque material and vinylite, celluloid or methacrylester; these preparations could be corroded after X-rays had been taken. By this method the corrosion preparation then serves as a guide to the interpretation of the X-rays.

Several procedures were specially introduced in the present investigation as a safeguard against the above objections to the use of X-rays. By extending the incision of the anterior uterine wall, the vessels, which would have filled with dye and become superimposed on to those on the posterior wall, were eradicated. In addition the entire basal surface of the placenta was now in one plane, approximately ½ inch from the cassette, so that even the smaller blood vessels would be sharply in focus. The X-rays were taken in rapid succession so that the dye could be followed along its course. By this method it was nearly always possible to determine which vessel was proximal and which distal. From a preliminary study of X-rays of the maternal arterial inflow, and the knowledge of the foetal placental circulation (as determined by the technique previously described[7]) it was quite obvious that it was most unlikely that this technique would give accurate results if employed in the examination of the finer ramifications of the foetal placental circulation.

Before injecting the foetal circulation, the maternal circulation was injected with coloured liquid latex. In the first instance this removed all the radio-opaque dye from the uterine artery and spiral arterioles. Secondly, it resulted in solid collections of radio-opaque dye plus latex in the IVS which, after fixation in 10% formalin, also indicated the distribution of spiral arterial inflow into the IVS. The check X-ray confirmed that no radio-opaque dye was left in the uterine artery and its ramifications, but that collections persisted around the spiral arterial inlets into the IVS.

For several reasons only a relatively small amount of radio-opaque dye was injected into the cord vessels. As mentioned earlier, it is thought that there are other far more accurate ways of studying the finer ramifications of this three-dimensional structure, so that there was no object in trying to outline these vessels with radio-opaque material in this study. The confusion which may result when dye starts to return *via* the veins, or vice versa, during an injection of umbilical arteries or veins, was in this way forestalled. It is clear from Figs. 4 and 5 that the cotyledons had developed around the spiral arterial inlets into the IVS. On the whole the larger foetal placental

vessels enter the larger collections of dye. There may be several possible reasons for an absence of collections of IVS dye at the foetal arterial ramifications anteriorly and posteriorly in Fig. 4. The spiral arterioles which should have supplied these areas may have been cut during the uterine incision; these areas may have been supplied by the uninjected left uterine artery; possibly not enough dye was injected or the head of pressure to fill them was too low; or the vessels may have become thrombosed as a result of the pathological process which had triggered the eclamptic fit. Careful study of all the uterine arterial ramifications in this specimen have, however, failed to reveal clear evidence of any intra-arterial obstructions to arterial flow.

Arts[2] emphasized the fact that a clear understanding of the maternal and foetal placental circulations is of fundamental interest, not only to gain an accurate physiological insight, but also to be able to grasp the essential concepts in the understanding of pathological states such as toxaemia, placental infarction, and accidental haemorrhage. The wisdom of this statement, especially with regard to the pathological conditions, has been amply confirmed before.[7-11] Additional experimental evidence was sought to confirm that the pathogenesis of intra-placental infarcts does conform to the distribution of spiral arterial inflow into the IVS. To mimic the true pathological state a substance had to be selected which would be liquid when injected (conforming to blood which becomes coagulative during its passage through damaged spiral arterioles), yet will solidify soon after reaching the IVS (as does the blood from such spiral arterioles). In addition, it may just be possible that similar to red-infarct pattern-A[11] the villi may become adherent to form an outer layer of villi, the injected material (which conforms to the layer of necrotic villi and blood-clot in between) and a central subdecidual collection of pure injection material conforming to the central clot of this type of lesion. Liquid latex was selected as the test material. The injection was carried out relatively slowly to give the latex which had spread furthest an opportunity to rubberize. In this way spread throughout the IVS was prevented (which would have interfered with the interpretation of the IVS spread from any individual spiral arterial inlet), and in addition the outer rubberized layer prevented further spread while the centre was still filling with latex. The smaller red patch of latex shown in Fig. 6 of this report is somewhat larger than the collection shown in Fig. 3 of the report by Earn and Nicholson.[5] The large amount of latex which they injected had filled nearly the entire IVS, thus the distribution from the various individual spiral arterioles is not demonstrated in their Figs. 1 or 2. The larger collection of latex shown in Fig. 6 of this report is starting to separate into the abovementioned two layers (E and F). It would probably soon have resembled Fig. 12.[11]

Figs. 8 and 9 amply demonstrate the two layers of the pattern-A red infarcts. Fig. 8 shows the smallest and most recent pattern-A red infarct which was encountered during the entire study, yet it already shows the characteristic two layers of these lesions. As the lesion becomes larger, or when of longer duration, the layering becomes much more obvious (Fig. 9).

The clinical implications of the spiral arterial lesions with their resultant intraplacental infarction are several-fold. Intervillous-space circulation, and therefore foetal oxygenation and nutrition, are probably interfered with to a greater extent than suggested by the relatively few villi which are completely disrupted. Some of the coagulative material which reached the IVS may drain back into the decidual venous circulation; this sometimes results in sudden obstruction, rupture and accidental haemorrhage; the obstruction to spiral arterial inflow may result in undue proximal strain on a damaged section of the arteriole, with aneurysm formation (Fig. 9), eventual rupture, and accidental haemorrhage; and in some cases the damaged spiral arterioles rupture without prior red-infarct formation (Fig. 7). Potentially the results are similar to the abovementioned.

An artificial 'lesion' which resembles a true intraplacental pattern-A red infarct has thus been created by the liquid latex on reaching the IVS *via* the decidual spiral arterioles. This clearly shows that the distribution of both pattern-A and B red infarcts conform to that of spiral arterial inflow.

SUMMARY AND CONCLUSIONS

In a combined radiological and liquid-latex-injection study of the maternal and foetal circulations, the following features were demonstrated:

1. Decidual, spiral arterial inflow openings into the intervillous space (IVS) are distributed diffusely, though they are more concentrated in some areas than in others.

2. The calibre as well as the site in the uterine arterial tree from which the spiral arteriole is derived seem, to a large extent, to determine the amount of dye which reaches the IVS through a particular arteriole.

3. Foetal cotyledons develop around the sites of spiral arterial inflow into the IVS.

4. When liquid latex is injected through the uterine artery and reaches the IVS *via* the spiral arterioles, the distribution conforms exactly to that of intraplacental red infarcts. The way in which this technique experimentally illustrates the development of pattern-A[11] red infarcts is discussed, and some of the clinical implications are mentioned.

I wish to thank Prof. James T. Louw for the opportunity to make this experiment. The valuable, unspoilt specimen which was used in this study was saved solely by the vigilance of Dr. Cecil J. T. Craig. Dr. Chris R. Rainer-Pope assisted with some of the X-rays and Mr. D. Middleton with some of the photographs.

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