THE DEVELOPMENT OF A TECHNIQUE FOR VASCULARISED TRANSPLANTATION OF THE FALLOPIAN TUBE IN THE PIG WITH REFERENCE TO ITS APPLICATION IN THE HUMAN FEMALE

Thesis
for the degree

DOCTOR OF MEDICINE

submitted to the University of Cape Town

by

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November 1974

TO ROSE, JOEL AND ARI

May their many sacrifices one day be reflected in the rejoicing of others who presently yearn for the precious gift of a child.

ACKNOWLEDGEMENTS

The author wishes to express his utmost gratitude to the following people and institutions all of whom have made major contributions to this study:

My wife Rose whose total support has enabled me the privilege of pursuing a dream in an effort to seek the truth.

Professor D.A. Davey, Director and Head of the Department of Obstetrics and Gynaecology, University of Cape Town, for his constant support, encouragement and for the provision of the facilities which have enabled me to conduct this study within his Department.

Professor J.H. Louw, Head of the Division of Surgery, University of Cape Town, who permitted an invasion of the Surgical Laboratories by a team of gynaecologists, and for his inspiration, interest and encouragement.

Professor John Terblanche, Department of Surgery, University of Cape Town, for his unwavering support, understanding, constructive criticism and advice.

Professor C.J. Uys, Head of the Department of Pathology, University of Cape Town, for having personally undertaken the assessment of all histological sections submitted and for his positive support and encouragement at all times.

Drs M.C. Botha and E. Du Toit whose support, criticism and provision of immunological facilities have always been appreciated.

Professor C.N. Barnard for allowing his technical laboratory staff to assist with this study.

The Medical Research Council of South Africa whose major financial contributions enabled the establishment of this research programme.

Dr Rosemary Hickman for her constant support, positive criticism, advice and personal example, all of which have helped me to endure the difficulties involved in biological research.

Professor C.H. van Niekerk and Dr J. Morgenthal of the Department of Agriculture, University of Stellenbosch, Cape, for their co-operation, advice and provision of facilities which enabled us to undertake studies in sheep during the latter stages of this project.

The Heads of Firm of the Department of Obstetrics and Gynaecology, University of Cape Town, for their continuous advice, encouragement and support.

Drs Peter Baillie, Dennis Israelstam, Maurice Katz and Harold Jordaan for their constant encouragement and assistance at all times.

Messrs. Eli Lilly, Davis and Geck, Ledlab and Ethnor Laboratories for their financial support together with donations of pharmaceuticals and surgical sutures.

Messrs. Noristan, Upjohn and Boots for their donations of pharmaceuticals.

The University of Cape Town Staff Research Fund for financial assistance.

Miss Beatrice Becket for her expertly done drawings and illustrations.

Miss Christine Vader for having undertaken the statistical analysis of data.

Miss Jeannie Waskansky for having undertaken the typing of this thesis.

Mrs Anne Schofield for assisting in the classification of publications and experimental results.

Messrs. Robin Henry, S.N. Barnham and M. Bennett for their initial donation of research animals which enabled the commencement of this study.

Mr and Mrs S.N. Barham for the provision of accommodation for all the long-term postoperative animals.

Mr W. Stander for ensuring that laboratory requirements and preparations were always available.

Mr D. Scammell for his continuous assistance with provision and maintenance of the laboratory animals.

Dr Trevor Waner for his enthusiasm, support and prompt advice regarding pre- and postoperative animal problems.

Messrs. G. Jacobson and H. de Zitter for their expert photographic assistance.

Dr P.J. van Biljon, Editor, for permission to reproduce photographs and diagrams previously published in the South African Medical Journal, vol. 48, February 1974, pp. 162 - 164, and October 1974, pp. 2097 - 2104.

A most important group of men whose constant support and encouragement together with persistent hard work have made this study possible, namely Dr David Poole and the staff of the J.S. Marais Surgical Laboratory - Messrs. F. Lotter, F. Barends, H. de Mink, E. Henry, A. Lesch, P. Madlingozi, H. Naki, N. Plato, J. Roussouw, B. Sassman, F. Snyders and D. Tities.

These men have been the life and blood of the research team. Their perseverence, often under most difficult circumstances, will always command not only my utmost appreciation but with it, my respect.

All of my colleagues and friends who have tolerated my trials and tribulations of the past 3 years.

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CHAPTER ONE

INTRODUCTION

1. THE PROBLEM

Infertility poses a serious problem to the gynaecologist. It occurs in 6 - 17 per cent of married females (Browne and McClure Browne, 1964; Jeffcoate, 1969). Pathology of the Fallopian tube is found in 40 - 50 per cent of women investigated for this complaint (Özaras, 1968; Siegler, 1973) and is still the most common cause of absolute sterility (Israel, 1967; Woodruff, 1969).

The results of surgical procedures performed on occluded oviducts are unpredictable (Ten Berge and The Tik Lok, 1954) and are usually extremely disappointing with respect to the number of live births that result (Gellhorn, 1911; Solomons, 1935; Greenhill, 1937; Gepfert, 1939; Castallo, Stock and Wainer, 1950; Siegler and Hellman, 1956; Te Linde, 1962; Crane and Woodruff, 1968; Grant, 1971; Wood, 1971; Siegler, 1973).

The incidence of term pregnancies following all types of tuboplasty considered as a whole may vary from less than 5 per cent (Greenhill, 1937) to more than 35 per cent (Moore-White, 1960; Horne, et al., 1973), but most investigators agree that where the Fallopian tube has been severely damaged, this anatomical and physiological impairment is permanent and irreparable. Operations performed on these oviducts are rarely, if ever, followed by a normal pregnancy.

The inverse relationship between the extent of tubal damage and the subsequent incidence of term gestations has been stressed by numerous authors (Gellhorn, 1911; Schmitz, 1932; Gepfert, 1943; Rutherford, Lamborn and Banks, 1949; Meigs, 1950; Green-Armytage, 1952 and 1957; Pratt, Banner and Huang, 1956; Shirodkar, 1961 and 1966; Peel, 1964; Boyd and Holt, 1973).

Several workers (Green-Armytage, 1937; Ten Berge and The Tik Lok, 1954; Moore-White, 1960; Grant, 1971; Siegler, 1973) have emphasised the principle of careful selection of patients and of operating only on those women in whom the tuboplastic procedure is most likely to be followed by a term pregnancy. When this principle is practised, the operations performed by those who are specifically trained and experienced in the finer techniques of this type of surgery, do appear to yield a significantly more positive outcome. However, even if one accepts the better results reporting live birth rates of approximately 35 per cent which follow tuboplastic procedures (Moore-White, 1960; Palmer, 1964; Grant, 1971; Horne et al., 1973), it is still cogent to question the reproductive outcome of those women whose extensive pathology excluded them from such a surgical programme ab initio. Their numbers are rarely specified in the voluminous literature on tuboplasty, but at certain centres, such as Groote Schuur Hospital, in Cape Town, these women constitute the majority of patients presenting with involuntary sterility.

In 1972, 74 per cent of the 195 patients attending the Family and Fertility Councilling Clinic (F.F.C.C.) at this centre were found to have tubal occlusion. The diagnosis was made on the evidence of two abnormal hysterosalpingograms and in many cases was confirmed at laparoscopy or formal laparotomy.

In 20 per cent of these patients, the tubal pathology was considered to be a localised defect in an essentially healthy organ and therefore surgery was recommended. In the other 80 per cent, the Fallopian tubes had suffered major damage. Most commonly, they appeared as two thinned-out diffuse hydrosalpinges with no recognisable components of their normal anatomical structure. Under these circumstances, it was felt that surgery was inadvisable and these patients were returned to their doctors who had referred them.

Our experience is in keeping with the observations of Gellhorn (1911); Peel (1964); and Shirodkar (1966) who found that where current methods of tubal surgery were applied to this type of clinical material, pregnancies were rarely recorded. At Groote Schuur Hospital, many tuboplasties have been performed on such patients when they insistently requested that surgical correction be attempted. While this practice may be condemned on purely scientific grounds, these operations have been of psycho-therapeutic value to many of them.

Two hundred patients who underwent surgery despite extensive tubal damage during the years 1968 - 1972 at Groote Schuur Hospital have been reviewed. While the outcome of ten of these cases could not be ascertained, reference to the most recent attendance of the remaining 190, showed no evidence of any pregnancy in the succeeding 9 months to 5 years after their operations. The mean number of months over which the patients were observed was 42 (S.D. = 8.1 months).

As patients with extensive tubal pathology constitute the major part of our Infertility Practice at this Hospital, and in view of their present hopeless prognosis, an experimental study of another surgical procedure was commenced.

2. APPROACHES OF OTHER WORKERS

The previous work of many researchers bears testimony to the significance of this problem in the field of human infertility. Attempts to remedy this situation have included the following:

1. Autotransplantation of :
   (a) the vermiform appendix (O'Neill, 1966);
   (b) an isolated segment of vascularised ileum

(Kucharczuk and Green, 1956; Carey et al., 1958; Wingate, Wingate and Lachlan, 1970);

(c) a length of artery or vein (Davids and Bellwin, 1954; Schein and Ferreira, 1956).

2. Reconstruction of a peritoneal tunnel from the ovary to the uterus at the site of the Fallopian tube (Cross and Erskine, 1956; Grant, 1971).

3. Insertion of a silastic tube between the ovary and the uterus including with it a mechanism for transporting the ovum to the endometrial cavity (Wood, Leeton and Taylor, 1971).

4. Bypassing the Fallopian tube by implanting the ovary or a part of it in direct continuity with the uterine cavity (Estes, 1909; Estes, 1924; Estes and Heitmeyer, 1934).

5. Using various culture media and attempting to mimic the physiology of the Fallopian tube. Some workers (Edwards, Bavister and Steptoe, 1969) have combined spermatozoa with ova and have succeeded in extracorporeal fertilisation and cleavage of the zygote with a view to

re-insertion of the developing blastocyst into the uterine cavity.

Until the present time, isolated results of term pregnancies have been obtained by using methods 4 and 5. In general, however, all of these procedures have been extremely disappointing, probably because of the failure to reproduce the normal physiological functions of the Fallopian tube reliably.

3. PHYSIOLOGICAL CONSIDERATIONS

The oviduct has acquired the name of Giuseppe Fallopius who first described this organ in Observationes Anatomicae in 1561. While the tube was originally considered to be a simple conduit for ova from the ovary to the uterus, this concept has changed markedly particularly as a result of the intensive physiological research that has been conducted during the past fifty years.

There are many detailed reviews of this subject which indicate the highly complex and subtle functions of each and every anatomical unit which, considered as a whole, constitutes the Fallopian tube (Hafez and Blandau, 1969; Woodruff and Pauerstein, 1969; Mastroianni, 1970; Thibault, 1972). This organ performs many intricate activities which are vital to normal conception and nidation, which in the human female, takes 3 - 7 days (Rhodes, 1969).

A few of the multiple functions of the Fallopian tube include :

1. The selection and dilution of healthy spermatozoa and their transport, survival, maturation, and metabolism. These activities ensure normal fertilisation which usually takes place within the ampulla.

2. Effective transport of the ovum into the ampullary region of this organ via the fimbriae.

3. Provision of the correct biochemical, hormonal and nutritional environment for fertilisation and subsequent cleavage of the zygote.

4. Adequate preservation and timely transport of the blastocyst into the uterus, directing it to a site of the endometrial layer most adequately prepared to receive it.

4. HYPOTHESIS OF HOMOGRAFT TRANSPLANTATION OF THE FALLOPIAN TUBE

In view of its highly subtle, complex and intricate functions, it is tempting to suggest that only another healthy, viable Fallopian tube would be capable of reliably replacing its severely damaged counterpart.

In practical terms this hypothesis implies replacement of the extensively damaged oviduct by another healthy one obtained from a suitable donor.

Transplantation operations have been developed primarily for patients with lethal disease, but there is no reason why this type of operation, if proved simple and safe, should not be applied to the field of tubal infertility.

5. PREVIOUS GENITAL TRANSPLANTATION

The concept of transplantation of the reproductive organs of the female is not new. Ovarian transplantation performed in human females (Blanco, et al., 1972), tubo-ovarian transplantation (Zhordania and Gotsiridze, 1964; Winston and McClure Browne, 1974), replacement of the uterus together with both Fallopian tubes and their ovaries (Zhordania and Gotsiridze, 1964; Eraslan et al., 1966; Truta et al., 1969; Wingate et al., 1970; Chiapponi et al., 1971; Scott, Pitkin and Yannone, 1971) and vaginal transplantation performed in human females (Papanicolaou, 1971) have all been previously performed.

Pregnancies have been observed where oviducts have been autotransplanted together with their corresponding ovaries (Zhordania and Gotsiridze, 1964;

Eraslan et al., 1966; Truta et al., 1969; Chiapponi et al., 1971; Winston and McClure Browne, 1974) and also after homograft transplantation of the ovary alone (Blanco et al., 1972).

The possibility of vascularised transplantation of the Fallopian tube alone, and thereby excluding significant genetic and ethical sequelae, appears to have been omitted from all these previous studies.

Many of the problems of obtaining healthy viable organs would be minimised by the possibility of access to healthy, live consenting donors. Many patients undergoing total abdominal hysterectomy have normal Fallopian tubes which are often excised and discarded. Thus, if oviduct transplantation were proved to be a reliable method of solving infertility problems, these excised organs could become an abundant source of healthy donor material.

6. SCOPE OF THE THESIS

In accordance with the abovementioned hypothesis, the purpose of this study was to assess the technical feasibility of vascularised transplantation of the Fallopian tube. This would be a pre-requisite to any subsequent research into immunological, hormonal, ethical or other problems.

As there was no recorded technique for performing such an operation, it had to be developed by means of animal experimentation. The initial research was intended to provide some answers to the following questions:

1. Is vascularised transplantation of the Fallopian tube a technically feasible procedure.

2. What are the problems that one may encounter during, and as a result of such an operation.

3. On the basis of the answers to questions 1 and 2, would it be possible to propose a method of performing this procedure in the human female in a relatively simple and safe manner.

CHAPTER TWO

CHOICE OF ANIMAL

1. EXCLUSION OF OTHER SPECIES

2. AN OUTLINE OF THE ANATOMY AND PHYSIOLOGY OF THE REPRODUCTIVE SYSTEM IN THE PIG

3. KNOWN ADVANTAGES AND DISADVANTAGES OF THE PIG AT COMMENCEMENT OF STUDY

CHAPTER TWO

CHOICE OF ANIMAL

1. EXCLUSION OF RABBIT, GUINEA PIG, RAT, BABOON AND DOG

Preliminary dissections performed on these species showed that :

1. The uterine arteries of the rabbit were found to be approximately 0.4 mm in diameter. Vascularised transplantation of the oviduct was not considered to be comparable to the human situation or technically feasible without the use of an operating microscope.

2. These vessels were observed to be even smaller in the guinea pig and the rat.

3. The adult female baboon was noted to have a uterus measuring 2 cm from the top of the fundus to the uterine cervix. The oviducts were approximately a millimetre in external diameter and the uterine arteries approximately 0.3 mm in diameter at the level of the uterine isthmus. The known difficulties encountered in attempting to breed these animals in captivity also

precluded their use in this study.

4. The diameter of the uterine arteries of the average-sized parous adult bitch was 1 - 1.5 mm. In the dog, oviduct transplantation would necessitate opening the peri-ovarian and fimbrial capsule. This dissection would almost certainly damage its normal ovulatory mechanism and thus the bitch was excluded.

While other favourable or unfavourable factors could be considered, the availability of the pig, together with the possibility of obtaining facilities for its pre- and postoperative care, rendered it the animal of choice.

2. AN OUTLINE OF THE ANATOMY AND PHYSIOLOGY OF THE REPRODUCTIVE SYSTEM IN THE PIG

The pig has a bicornuate uterus and each cornu measures from $\pm$ 30 to 60 cm in length and from $\pm$ 1 to 3 cm in diameter depending on the absence or presence of oestrus in the mature animal. The Fallopian tubes are convoluted and 10 - 20 cm in length at maturity. Their abdominal ends are large and possess fimbriae which envelop the ovaries which are suspended by the broad ligament cranial to the lateral boundary of the pelvic inlet.

The relatively short distance between the uterine body and the tubal extremities necessitates that the uterine cornu and Fallopian tubes assume a very tortuous course.

The distal cornu and Fallopian tube receive their main blood supply from the middle uterine artery which originates from the internal iliac artery together with the superior vesical (obliterated umbilical) branch. The ovarian artery on each side is long and tortuous.

These vessels together with their accompanying veins anastomose alongside the genital organs and are also anastomosed to major branches of the internal pudendal vessels which supply the vulva, vagina, cervix and lower parts of the uterus. The uterine and ovarian vessels have an efficient cross anastomosis in the region of the upper cornu and mesovarium.

The gilt usually reaches sexual maturity at 7 months of age. The only certain sign of oestrus in the pig is sexual receptivity to the boar. Hyperaemia and oedema of the vulva are noted 2 to 3 days before the gilt is receptive to the boar, and these signs regress in the middle of oestrus. They indicate the rise and fall of urinary oestrogen concentrations. The average length of the oestrus cycle is 21 ± 2.5 days and this cycle is repeated throughout the year.

Oestrus averages two to three days in duration. The remainder of the cycle is classified as follows:

Met-oestrus, from oestrus to day 4 of the cycle;
Di-oestrus, days 4 to 15;
Pro-oestrus, from day 16 until the onset of oestrus.

Ovulation is spontaneous and occurs approximately 36 hours after the onset of oestrus. Rupture of the follicle extends over a 6- to 7-hour period and the number of ova shed ranges from 10 to 25.

Fertilisation takes place in the oviduct. Transport through this structure is fairly rapid and the majority of ova reach the uterus between 66 and 90 hours after the onset of oestrus.

Spermatozoa reach the oviduct by their own initiative within 6 to 8 hours after copulation. During this act, up to 500 ml of semen may be ejaculated into the long tortuous uterine horns of the sow and spermatozoa may be propelled to the oviduct within minutes of emission assisted by uterine contractions.

The earliest sperm penetration of the ovum is observed approximately 6 hours after mating. If pregnancy occurs, the average length of gestation is 113 $\pm$ 3 days.

3. KNOWN ADVANTAGES AND DISADVANTAGES OF THE PIG AT COMMENCEMENT OF STUDY

Advantages

1. Pigs of the Landrace, Large White and Landrace

X Large White breeds were easily obtainable in the Cape.

2. The University of Cape Town Surgical Research and Liver Research units have established an international reputation for work performed on these animals. All technicians and laboratory assistants were well trained in handling this species.

3. The mature pig has a relatively short and regular oestrus cycle of 21 - 23 days. It was hoped that the regularity of these cycles as well as their occurrence at short intervals would facilitate early conception following surgery.

4. Whilst being of different texture and thickness, the size of the vessels of the pelvis compared favourably to that of the human female. The uterine artery was consistently $\pm$ 1 - 2 mm in external diameter. The uterine and ovarian veins were approximately 2 - 4 mm in diameter. Re-anastomosis of these vessels appeared to be a difficult but feasible proposition.

5. In view of its reputedly benign immunological response to vascularised homografts, the pig would probably be a good experimental animal

because this study was primarily designed to assess the technical problems rather than the immunological hazards of the intended transplant operation.

Disadvantages

1. In the pig, regular oestrus occurs from the age of 180 to 200 days. At this age, the average weight of the animal is 75 - 90 kg. It is cumbersome, aggressive and extremely difficult to handle.

2. Operative procedures with fine instruments are usually performed close to the hands of the operator. This type of surgery conducted deep within the pelvis of the pig would require adaptation for application at this site. Greater difficulties regarding technical problems could therefore be anticipated, but it was felt that these would not be insurmountable.

3. The animals would have to be housed in an overcrowded "temporary sty". This factor, added to their tendency to roll over in the dirt and faeces, rendered sepsis a major hazard.

Because of the availability of the pig and despite these disadvantages, facilities were obtained for the supply and maintenance of a limited number of these animals and the study was commenced.

CHAPTER THREE

DEVELOPMENT OF TECHNIQUE

1. INTRODUCTION

2. DEFINITION OF THE "TUBOCORNUAL UNIT"

3. CONCEPT OF UTERINE ARTERIAL PERFUSION OF OVIDUCT WITH DRAINAGE VIA THE OVARIAN VEIN

4. ANAESTHESIA

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7. SUTURE MATERIALS

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1. General
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CHAPTER THREE

DEVELOPMENT OF TECHNIQUE

1. INTRODUCTION

The attempt to formulate a protocol for vascularised transplantation of the oviduct in the pig was initially complicated by the following:

1. It was necessary for the investigator to devise his own surgical procedure because there was no previous record of vascularised transplantation of the oviduct available for reference.

2. Repeated operative dissections were necessary to clarify the surgical anatomy of the pelvis of the pig. The literature did not provide a sufficiently detailed account of the pelvic vasculature of this animal to enable one to plan the strategy of the operation.

3. Problems regarding the nature and size of the pelvic vasculature of the pig relative to its age or the phase of its oestrus cycle could not be anticipated.

4. While developing the technique, the investigator was undergoing personal training and gaining first-hand experience in the techniques of vascular and microsurgery.

5. Although many surgical instruments and various types of suture materials were available, it was necessary to assess their place in this particular operation.

With the above-mentioned facts in mind, it is clear that the initial experiments could have no formal protocol. This was only established once one had obtained some insight into the problems to be solved, progress that had been made and the directions of further experimentation. The concept of attempting to derive a relatively simple technique that could be modified for use in the human female was always kept in mind.

The details of the original experiments are described in their sequential order in Appendix 1.

The following is a resumé of the knowledge gained from operative experiments performed on 19 pigs before the formulation of a technique. This technique (CHAPTER FOUR) was subsequently utilised for performing three groups of transplantation procedures as described in CHAPTER FIVE.

2. DEFINITION OF THE "TUBOCORNUAL UNIT"

The term "tubocornual unit" has been coined to define the oviduct in continuity with a section of the lateral part of the uterine cornu, the ipsilateral ovarian hilar stump, the uterine artery and the ovarian vein.

This unit was considered to be the minimal amount of tissue required to effect a vascularised transplantation of the oviduct (Fig. 1).

3. CONCEPT OF UTERINE ARTERIAL PERFUSION OF OVIDUCT WITH DRAINAGE VIA THE OVARIAN VEIN

The Fallopian tube has a blood supply derived from two sources, namely the uterine and ovarian arteries. In the pig, its venous drainage is predominantly via the ovarian vein.

Perfusion of the oviduct via the single uterine artery and venous drainage by way of the utero-ovarian vascular communications into the single ovarian vein was considered a significant method of simplifying the operation.

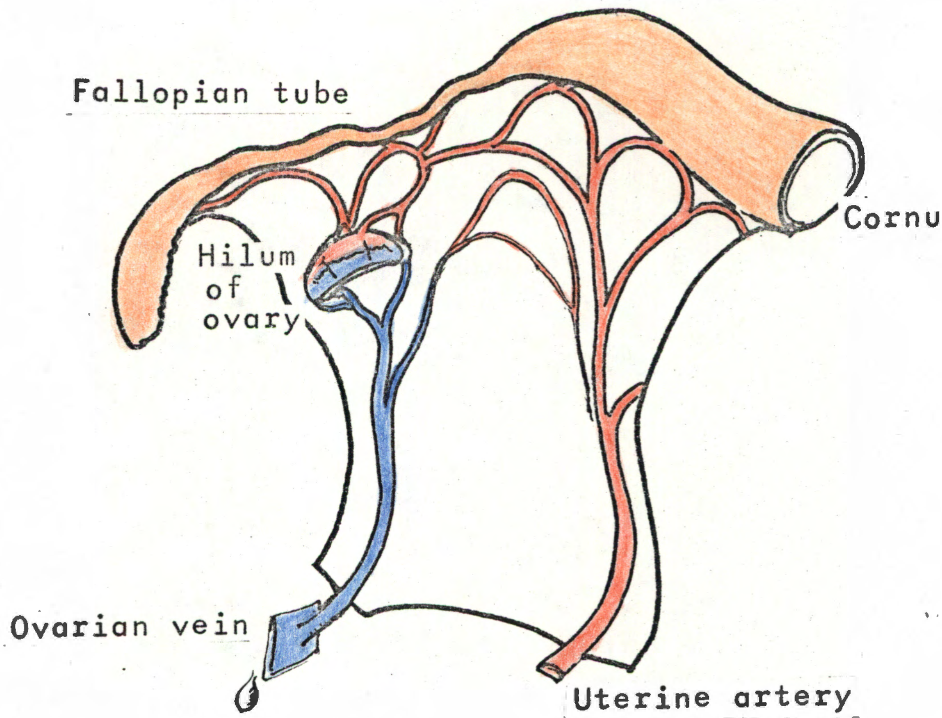

Fig. 1. The "Tubocornual Unit"

4. ANAESTHESIA

Halothane was given with nitrous oxide and oxygen by inhalation through a padded jam tin placed over the snout of the pig. This is usually a reliable and convenient method of induction and maintenance of anaesthesia in this experimental animal. Three pigs (Case Nos. 4, 7 and 13) died of malignant hyperpyrexia resulting from halothane administration. It was therefore necessary to adopt an anaesthetic technique which excluded this agent. Although the large animals were extremely difficult to restrain, anaesthesia was subsequently induced by giving suitable doses of thiopentone sodium (2.5%) via a fine needle inserted into an ear vein. Anaesthesia was maintained via an endotracheal tube (inserted under direct vision) using a Bird positive pressure ventilator with a closed Magill-type circuit.

Diallyl-nortoxiferine (Alloferin) provided adequate muscular relaxation throughout the operative procedures and was reversed by the administration of suitable doses of atropine and neostigmine at the end of each operation.

5. MEDICATIONS

1. Antibiotics

The use of chloromycetin administered intravenously and directly into the abdominal cavity was considered a reliable means of reducing the extent and complications of infection. This antibiotic was also administered intramuscularly during the postoperative phase.

2. <u>The Use of Heparin</u>

Heparin was used as an anticoagulant to facilitate the vascular surgery performed, and in an effort to prevent postoperative venous and arterial thrombosis. It was found expedient to heparinise an animal at the start of a procedure so that adequate haemostasis could be assessed when therapeutic levels of anticoagulant had already been obtained.

Heparin was also combined in a mixture with saline for the purpose of : (i) irrigation of vascular anastomosis in an effort to prevent subsequent thrombosis; (ii) moistening intra-abdominal packing swabs; and (iii) for the instillation of approximately 500 ml into the peritoneal cavity before the abdomen was closed in an effort to reduce the formation of subsequent adhesions.

3. <u>Dosages of Chloromycetin and Heparin Administered</u>

(i) <u>As operation commenced</u>

Heparin 10,000 units intravenously

Chloromycetin 1 g intravenously

(ii) Prior to vascular clamping

Heparin 10,000 units intravenously

(iii) During abdominal closure

500 ml of a normal saline solution containing 2 g of chloromycetin and 5,000 units of heparin/litre intra-abdominally

(iv) On completion of operation

Chloromycetin 1 g intramuscularly

(v) Postoperative therapy - 10 days

Chloromycetin 1 g b.d. intramuscularly

Heparin 10,000 units b.d. intramuscularly

4. Procaine Hydrochloride

Procaine hydrochloride (2 per cent) was found to be a reliable means of producing relaxation of the arteries which were to be transected and re-anastomosed. This agent was repeatedly sprayed onto the ends of the vessels while they were being sutured.

6. INSTRUMENTS

The following instruments were found to be satisfactory and, grouped together, were considered to be the minimum necessary to perform the intended operation:

1. Routine dissection

Scalpel

Cutting diathermy knife

2 pairs of Russian tissue forceps

6 Crafford's haemostatic forceps

6 Crile's haemostatic forceps

1 standard curved scissors

1 large self-retaining retractor

2 large deep Deaver retractors

2 large straight needle holders

1 small straight needle holder

2. Peritoneal and vascular dissection

1 Kilner's plastic scissors

2 atraugrip vascular forceps

Diathermy for cutting and coagulation

1 dozen Lahey's swabs

3. Vascular transection and suturing

1 Oculus loupe with 2-fold magnification

2 straight fine-pointed scissors

4 five-cm rubber-shod bulldog vascular clamps

2 medium-sized Satinsky vascular clamps with atraugrip jaws

1 pair of scissors for excision of vena-caval patch (A. Schweickhardt, Tuttlingen, Germany)

1 fine Stummer delicate-ear forceps with straight smooth jaws

6 rubber-shod straight mosquito artery forceps

1 Castroviejo needle holder

2 micro-suture jeweller's forceps

2 straight Iris forceps

2 curved Iris forceps

7. SUTURE MATERIALS

Vascular pedicles - 00 linen ligatures

Venous anastomoses - double-armed 6 - 0 silk on fine atraumatic taper needles

Arterial anastomoses - 7 - 0 silk on fine atraumatic taper needles

Repair of cornu and broad ligament - 6 - 0 and 3 - 0 polyglycolic acid sutures on ½-circle 20 mm atraumatic taper needles

Abdominal closure - No. 1 and No. 2 chromic catgut on atraumatic taper and reverse cutting needles and No. 1 monofilament nylon.

8. PRACTICAL SURGICAL POINTS

1. General

The midline incision was found to be most suitable. It did not present the problems of the greater vascularity of a paramedian incision (Case No. 1) nor of excessive stripping of tissue planes and consequent infection as observed with a lower abdominal transverse incision (Case No. 8).

The application of sterile skin towels around the wound edges, the instillation of a solution of heparinised saline containing 2 g of chloromycetin/litre into the abdominal cavity prior to closure, and completing an operation with a subcuticular suture all appeared to coincide with a reduction in the incidence of postoperative intra-abdominal and wound sepsis.

Abdominal packs held in place with deep Deaver's retractors provided adequate exposure of the pelvis and lower abdomen. This reduced the need for a larger incision and displacement of bowel out of the abdomen which contributed to the death of the first case.

If the bladder was distended, it was emptied either by gentle bimanual compression, or was displaced out of the abdomen onto a moist sterile swab placed over the pubis and lower angle of the abdominal incision. Catheterisation of the bladder via the urethral meatus was not possible even when efforts included performing a wide episiotomy. Suprapubic cannulation and drainage was not used for fear of urinary peritonitis.

The uterine cornu was found to be extremely large ($\pm$ 50 cm x 3.5 cm) and vascular during oestrus (e.g. Case No. 2), and it was considered inadvisable even to attempt any further operative procedure during this stage of the oestrus cycle.

The uterine arteries were noted to have an external diameter of approximately 0.5 mm in the young gilt (e.g. Case No. 3, aged 3 months). This finding confirmed the need to operate on older animals, preferably at least 6 months of age, where the overall diameter of these vessels was usually of the order of 1.5 - 2 mm.

The ureter was closely related to the medial surfaces of the proximal parts of the uterine artery and its accompanying veins.

2. Specific to the operation of vascularised oviduct transplantation

The peritoneum of the lower abdomen and pelvis contained many fine vessels. It was necessary to cauterise this layer of tissue along the intended paths of dissection prior to its incision in order to maintain adequate haemostasis.

The pelvic vessels were best approached via a midline incision through the posterior abdominal peritoneum. After definition and mobilisation of the internal iliac artery, any vessels required were dissected from this point on the corresponding side.

The uterine arteries were found to have thick walls. These consisted of a fine intimal layer which was surrounded by a wide muscular layer and this in turn was covered by a resilient layer of adventitia. The thick, tough walls of these vessels did not allow insertion of the standard 9 - 0 or 10 - 0 monofilament nylon microvascular sutures. There were no 8 - 0 taper-pointed atraumatic sutures available and thus the finest suture that could be employed was a 7 - 0 silk suture on a taper-pointed needle. Insertion of these sutures was facilitated by lubricating them with sterile liquid paraffin and by using binocular spectacles which provided two-fold magnification of the operative site.

All vascular stay sutures were held in rubber-shod mosquito forceps to prevent damage to the suture material.

The anastomosis of the ovarian vein presented a major problem in the pig. This vessel was extremely thin-walled and fragile. The handling and suturing of the structure required particular care and extreme gentleness.

It was difficult to define the end of this vein once it was emptied of blood (e.g. Case Nos. 5 and 6). This was facilitated by squirting saline at the transected end of the vessel, or watching it closely while an assistant perfused the excised vascularised specimen via the uterine artery.

Completing an adequate end-to-end anastomosis of the ovarian vein was difficult. This type of anastomosis was abandoned in favour of excision of a patch of vena cava surrounding the termination of the ovarian vein into this major vessel. This procedure was simplified by using a pair of angled scissors specifically designed for this purpose (Fig. 2).

Fig. 2. Scissors for excision of vena-caval patch. (Designed by A. Schweickhardt, Tuttlingen, Germany.)

Re-anastomosis of the venous patch was performed with fine 6 - 0 silk double-armed sutures with atraumatic taper-pointed needles. These were repeatedly lubricated with sterile liquid paraffin which facilitated the passage of the sutures and assisted in the prevention of trauma to the edge of the vessel. When using the vena-caval patch technique, a major branch of the uterine vein was often observed to join the ovarian vein just before it entered the vena cava. It was important to preserve this branch to avoid infarcting a section of the uterine cornu.

In dissecting out the "tubocornual unit" it was essential to define and ligate every branch of the uterine artery or the ovarian vein individually. This intricate process ensured adequate haemostasis and reliable perfusion of the specimen.

The lengthy vascular pedicles of the tubocornual unit posed their own specific problems. It was sometimes necessary to insert strategically-sited sutures at various points along the length of the vessel (e.g. Case No. 14) in order to prevent it from kinking. It was also essential to ensure that these did not become twisted (e.g. Case No. 18).

CHAPTER FOUR

TECHNIQUE OF TRANSPLANTATION OF FALLOPIAN TUBE

1. THE DONOR
2. THE RECIPIENT
3. VENOUS ANASTOMOSIS
4. ARTERIAL ANASTOMOSIS
5. CORNUAL ANASTOMOSIS
6. COMPLETION OF OPERATION

CHAPTER FOUR

TECHNIQUE

1. THE DONOR

The abdomen was opened with a sub-umbilical midline incision, by using a cutting diathermy knife. The bicornuate uterus was elevated, while the bowel was displaced with two large swabs which had been moistened with a solution of 5 000 units of heparin in 1 litre normal saline.

The right cornu was elevated (Fig. 3) and an incision in the posterior abdominal peritoneum was made to expose the lower part of the inferior vena cava and the commencement of the right common iliac artery at the bifurcation of the aorta.

Once the right hypogastric artery had been defined, this vessel, together with the proximal portions of the internal pudendal, uterine and superior vesical arteries, were mobilised by dissecting them free of their accompanying veins and surrounding fascia (Fig 4).

At this stage the animal was heparinised by intravenous administration of 20 000 units heparin.

The vascular arcades were then carefully inspected to ensure that the blood supply to the distal uterine cornu and Fallopian tube (oviduct) would not be interrupted.

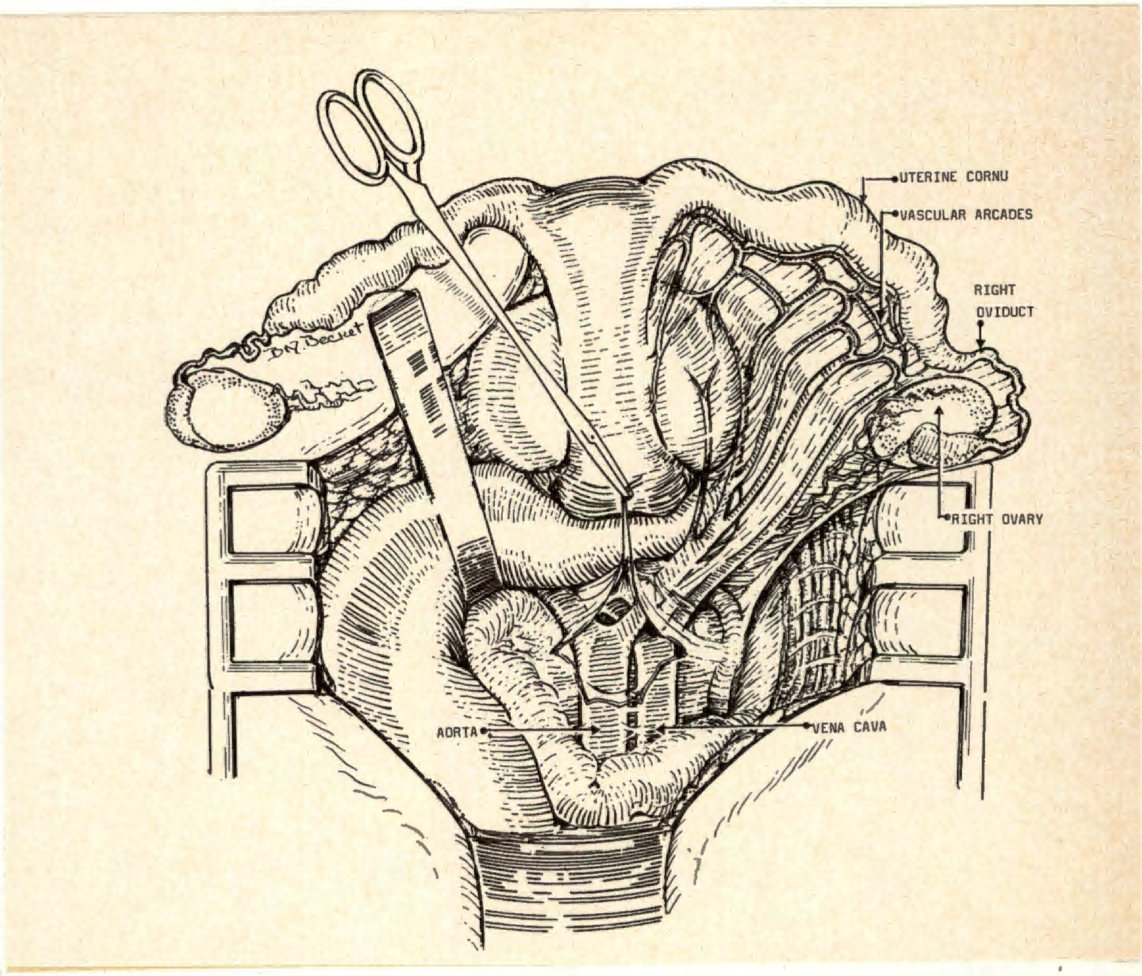

Fig. 3. Appearance of pig genitalia showing initial peritoneal incision to expose commencement of pelvic vessels.

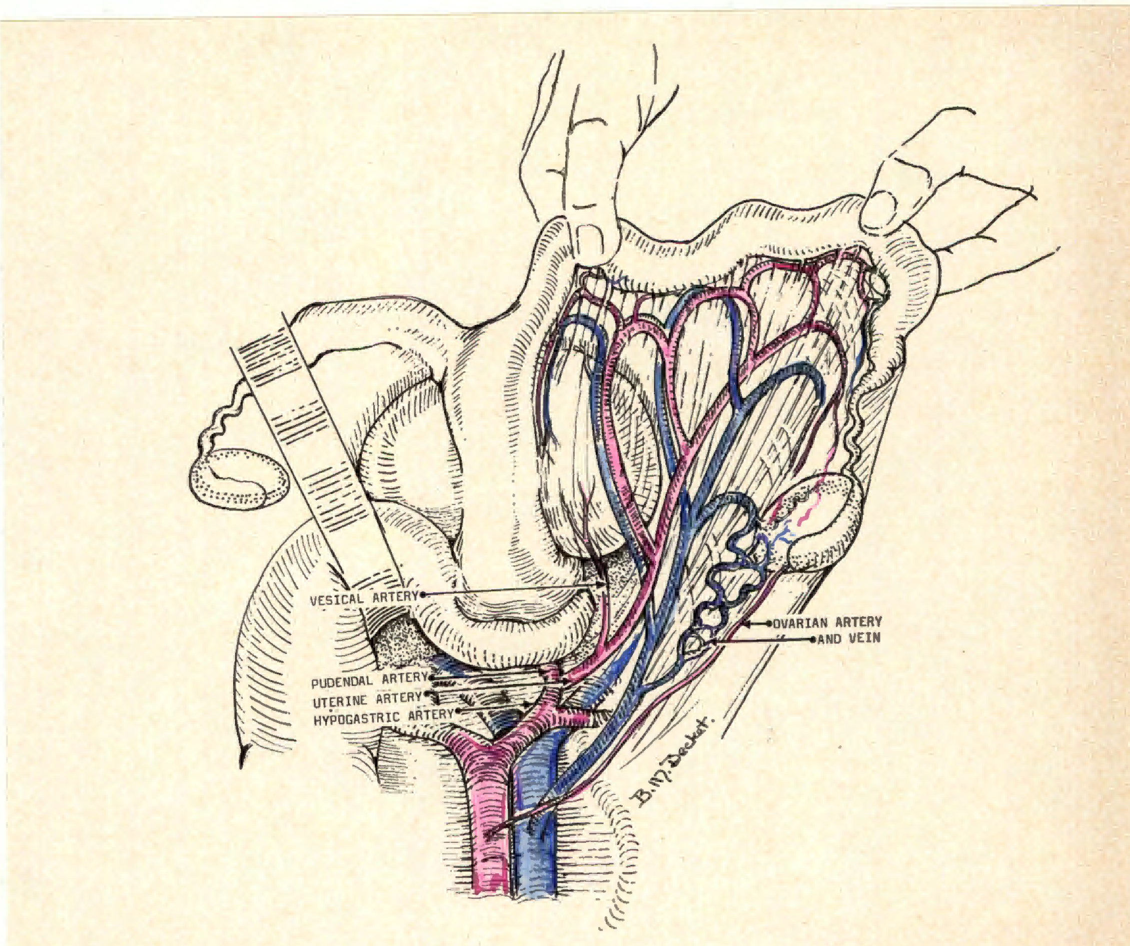

Fig. 4. Blood supply of the proposed site of dissection

The intervascular segments of the broad ligament were cauterised with the diathermy knife (Fig. 5). At this stage, all branches other than those communicating with the intended transplant specimen were doubly ligated and transected. Particular care was taken to ensure that major veins communicating with the ovarian vein were not interrupted by this process.

The vascular arcades were rechecked from both the medial and lateral aspects of the broad ligament. When all other branches had been carefully ligated and divided, the remaining portions of the broad ligament were divided with the diathermy knife.

The operative procedure was now focused on the dissection of the right ovarian vein. All vascular branches other than those arising from the distal uterine cornu and the oviduct were defined, ligated and transected. These included the right ovarian artery, and major venous branches from the right ureter. The ovarian vein was defined right to its termination into the vena cava. Major para-aortic lymph glands in the operative field required careful excision to facilitate clear exposure of the vena cava at this site. This major vessel was then cleared of any fascia, together with the outer adventitia, in the vicinity of the termination of the ovarian vein.

At this stage, the transplant specimen was in continuity with the donor at only three points, viz. the uterine cornu, the uterine artery and the ovarian vein.

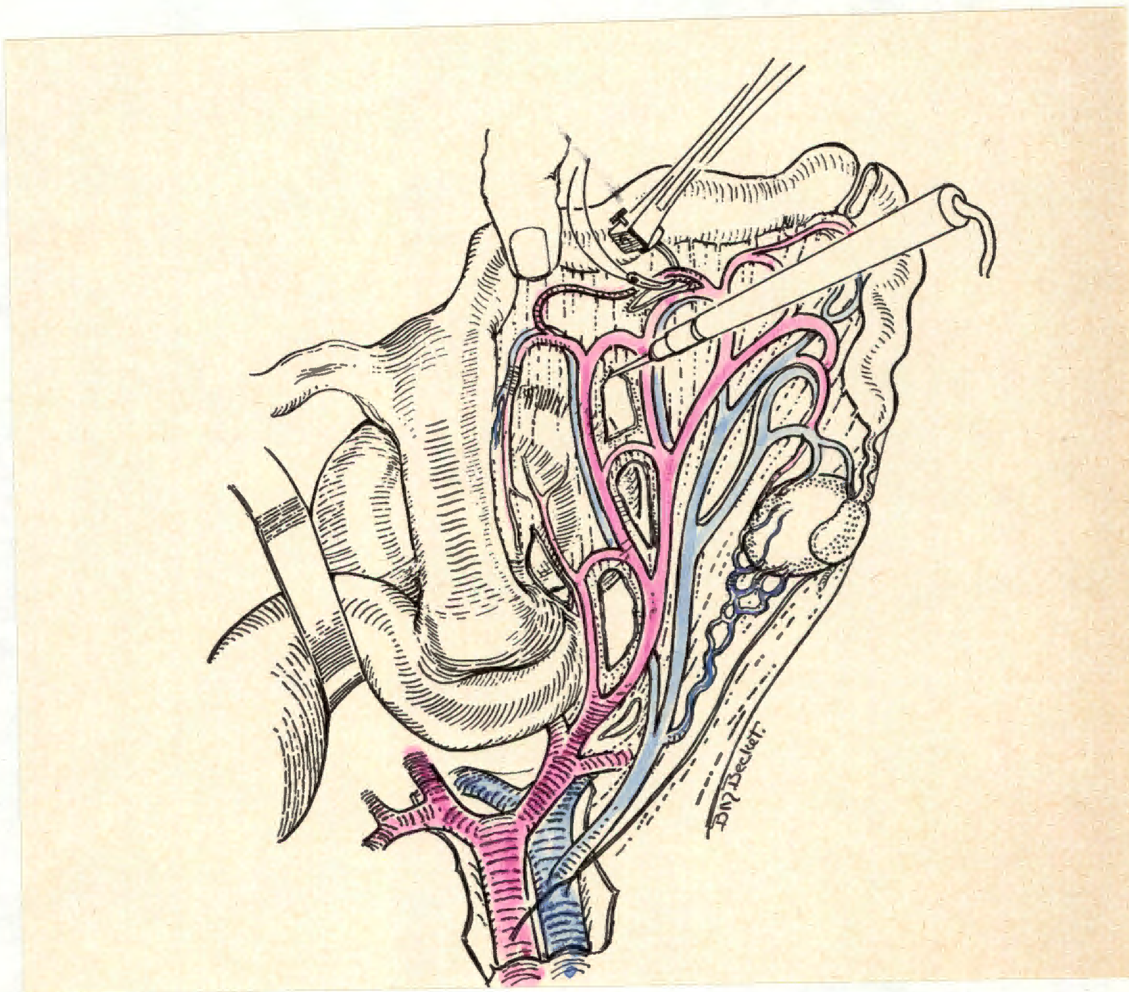

Fig. 5. Assessment and coagulation of vascular arcades. Note the continuous blood supply to oviduct and proposed site of incision.

The superior vesical artery was then ligated and transected, as was the uterine artery. A vena-caval clamp was applied (Fig. 6) and a suitable patch of vena cava was excised around the ovarian vein by means of scissors specifically designed to facilitate this aspect of the procedure.

A fine arterial catheter was then inserted into the uterine artery and the intact donor specimen (Fig. 7) was gently perfused with a solution of Plasmalyte B combined with 10,000 units of heparin and glucose 50 g/litre, cooled to 10° C. The oviduct was kept in a cooled dish containing triamcinolone diacetate (Ledercort) and gentle perfusion was maintained while the operation continued.

The donor vena cava was repaired with a continuous 6 - 0 silk suture. The uterine artery and cornual pedicles were ligated, abdominal packs were removed and the abdomen was closed.

2. THE RECIPIENT

The abdomen was opened with a right paramedian incision approximately 5 cm above the umbilicus and continued subumbilically as a midline incision. Bowel packs were inserted as described previously, but these were placed higher up in the abdomen to facilitate exposure of the lower third of the inferior vena cava.

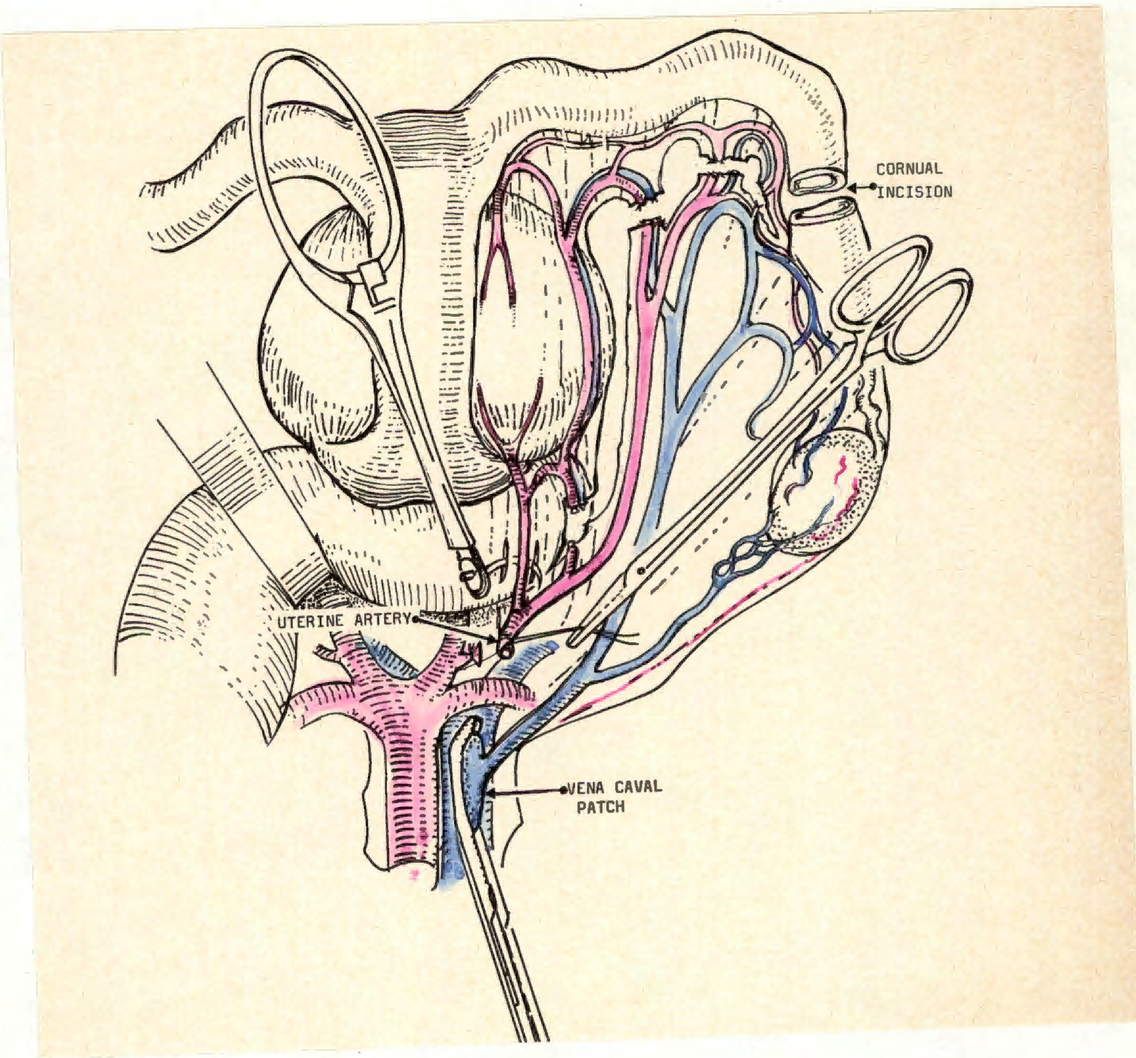

Fig. 6. Application of vena-caval clamp prior to excision of vena-caval patch.

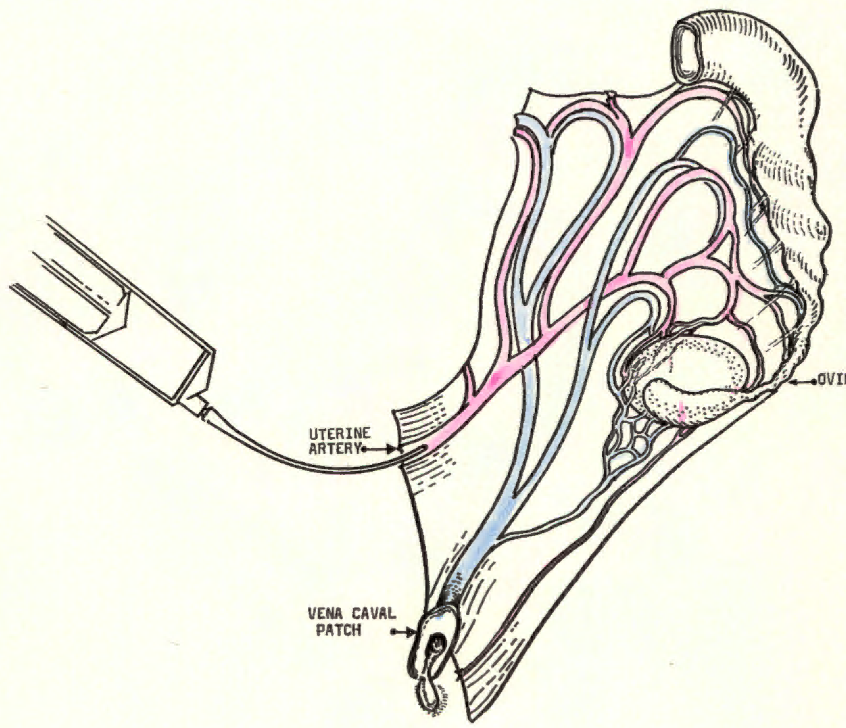

Fig. 7. Diagram showing perfusion of vascularised transplant specimen.

The internal pudendal artery was exposed as described previously, and freely mobilised for its proximal 4 - 5 cm. It was cleared of surrounding fascia.

The inferior vena cava was exposed by diversion of the posterior peritoneum at a point approximately 4 cm above the site of entry of the ovarian vein. This vessel was dissected free of the aorta and its anterior surface was cleared of any surrounding fascia. The right distal cornu and oviduct were then excised.

The recipient sites of cornu, internal pudendal artery and vena cava were now ready to receive the donor specimen (Fig. 8).

3. VENOUS ANASTOMOSIS

Using 6 - 0 silk sutures lubricated with sterile liquid paraffin, the ovarian venous patch was anastomosed in the following manner : after the application of a large vena-caval clamp to the recipient vena cava, a longitudinal incision was made on the anterior aspect of this vessel with a fine scalpel (Fig. 9a) This incision was transformed into a diamond-shaped opening by the insertion of two lateral stay sutures, which were held in small rubber-shod artery forceps (Fig. 9b). These lateral stay sutures, along with two others placed at the upper and lower ends of the vena-caval incision, were then placed through the donor venous patch. This was held in position by ligation of the stay sutures (Fig. 9c). The edges of the anastomosis were approximated

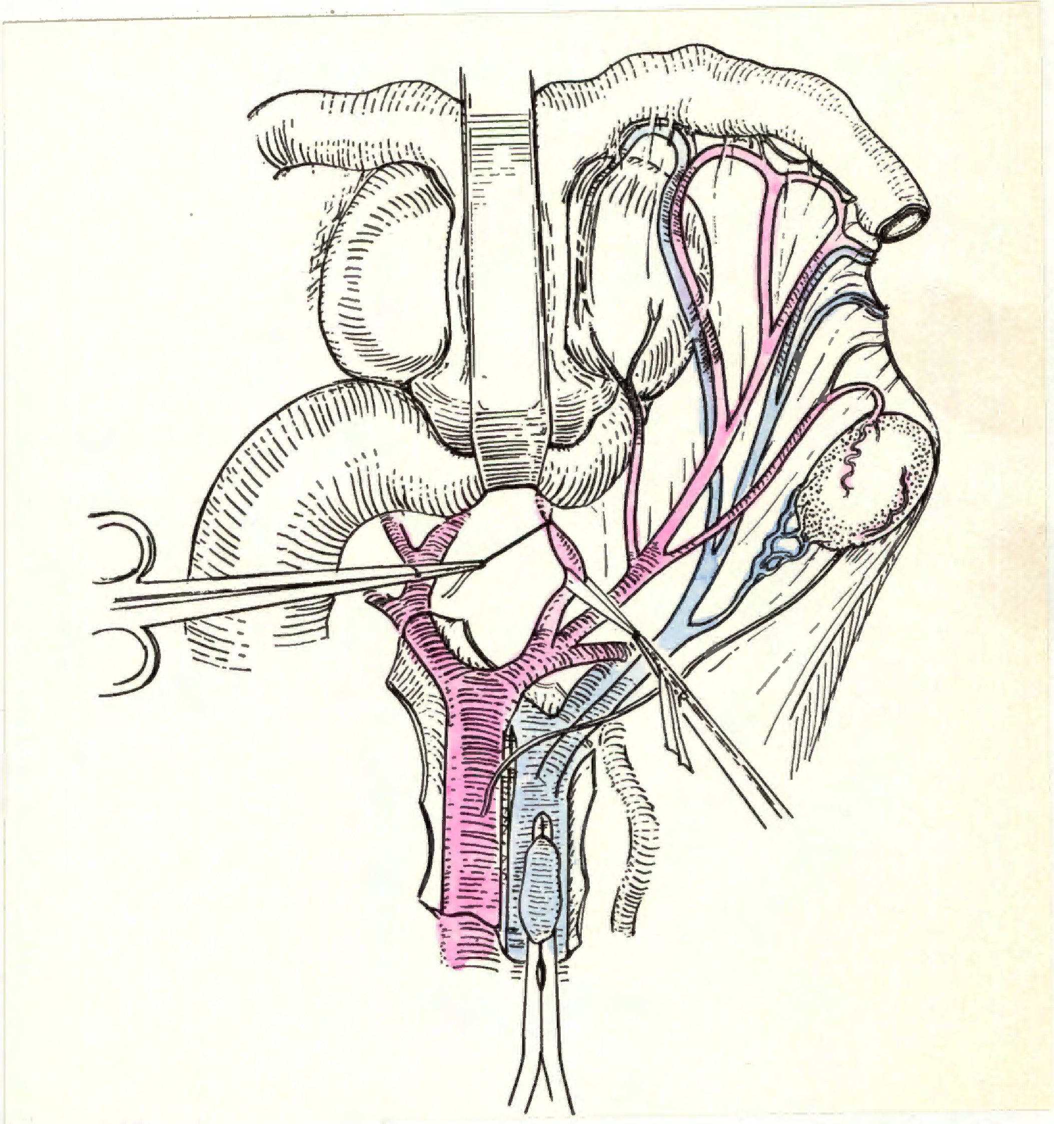

Fig. 8. Oviduct excised and dissection of recipient completed. Note the mobilised internal pudendal artery and application of vena-caval clamp.

by the insertion of a continuous suture line between the stay sutures (Fig. 9d). This suture line was secured at the four suture points by tying it off with one of the ends of the stay sutures. The edges of the anastomosis were repeatedly irrigated with a solution of 10 000 units heparin/litre saline during the insertion of the suture line.

The vena-caval clamp was removed after completion of the anastomosis, which was gently compressed with small, dry gauze dressings for approximately one minute before checking the haemostasis of the suture line. Any bleeding points were closed by the insertion of interrupted 7 - 0 silk sutures.

4. ARTERIAL ANASTOMOSIS

Irrigation of the vessel ends with heparinised saline was performed as described above. In addition, the site of the anastomosis of the opposing arteries was repeatedly sprayed with a 2% solution of procaine hydrochloride. Silk sutures (7 - 0) lubricated with sterile liquid paraffin were used to complete the arterial anastomosis in the following manner: two stay sutures were inserted through the vessel ends at an angle of approximately 120° and ligated (Fig. 10a). Their short ends were held in the rubber-shod ends of small forceps.

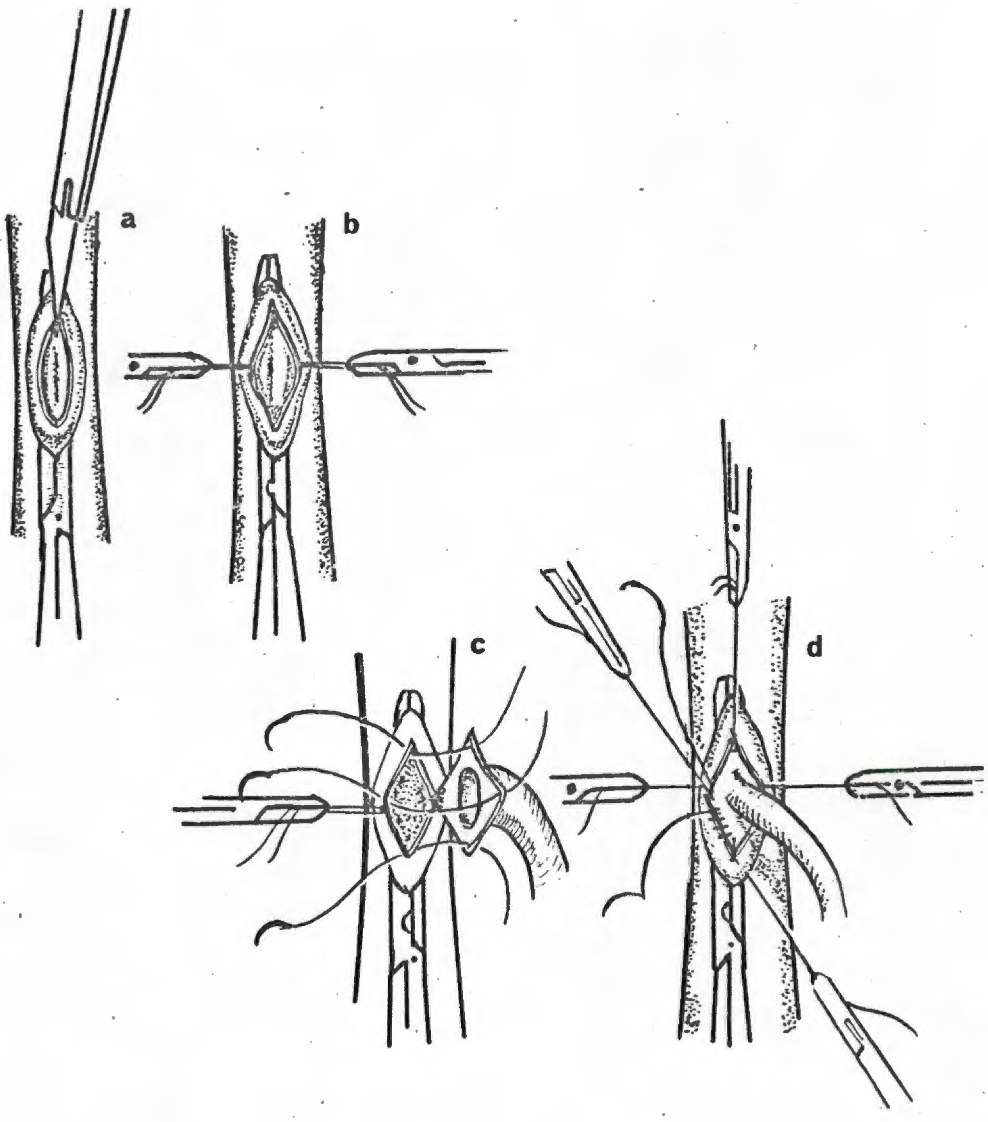

Fig. 9. Patch anastomosis of ovarian vein to recipient vena cava.

The anterior wall of the vessel was then reconstituted by the insertion of a continuous suture line (Fig. 10b). After ligation of this suture line at the distal stay suture, the vascular clamps were released temporarily to expel any clots present in the ends of the vessels. The vessel was now rotated, to make the posterior wall of the vessel anterior (Fig. 10c). This wall of the vessel was closed by the insertion of a continuous suture line through all its layers, as had been performed on its anterior aspect. The vascular clamps were then removed.

5. CORNUAL ANASTOMOSIS

The opposing ends of the cornua were approximated in two layers. A continuous suture of 6 - 0 polyglycolic acid was inserted through the muscular coat, and the endometrial layer was excluded from this suture line. The outer suture line was constituted by interrupted 3 - 0 polyglycolic acid sutures, which were inserted through the serosa and outer muscular layer in such a manner as to cause slight inversion of the cornual anastomosis.

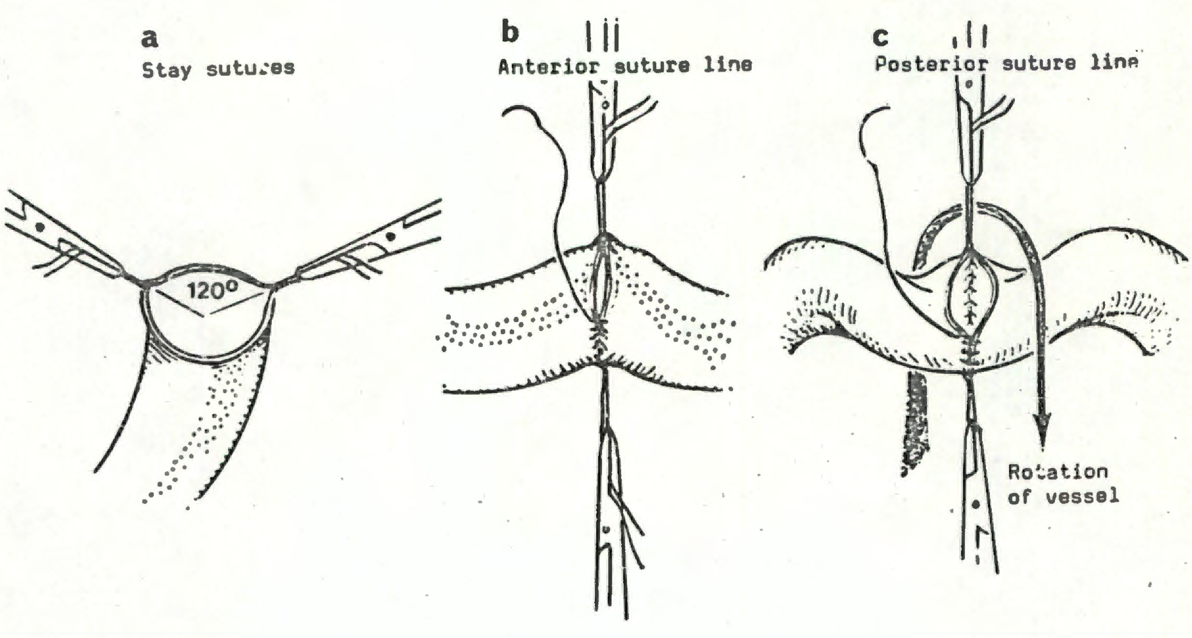

Fig. 10. Technique of completing arterial anastomosis.

6. COMPLETION OF OPERATION

The opposing edges of the donor and recipient broad ligament were approximated with interrupted 3 - 0 polyglycolic acid sutures.

The donor ovary was excised after ligation of its vessels close to the hilum of the structure, which was then sutured to the ovarian ligament of the recipient. The fimbrial end of the transplant specimen was now situated close to the recipient ovary. The appearance of the completed anastomoses of the ovarian venous patch, the uterine artery and the two ends of the cornu is shown in Fig. 11.

The bowel packs were removed, the abdomen was irrigated with a solution containing 5 000 units heparin and 2 g chloramphenicol/litre normal saline. Five hundred millilitres of this fluid were left in the abdomen, which was then closed in layers. A subcuticular nylon skin suture completed the operation.

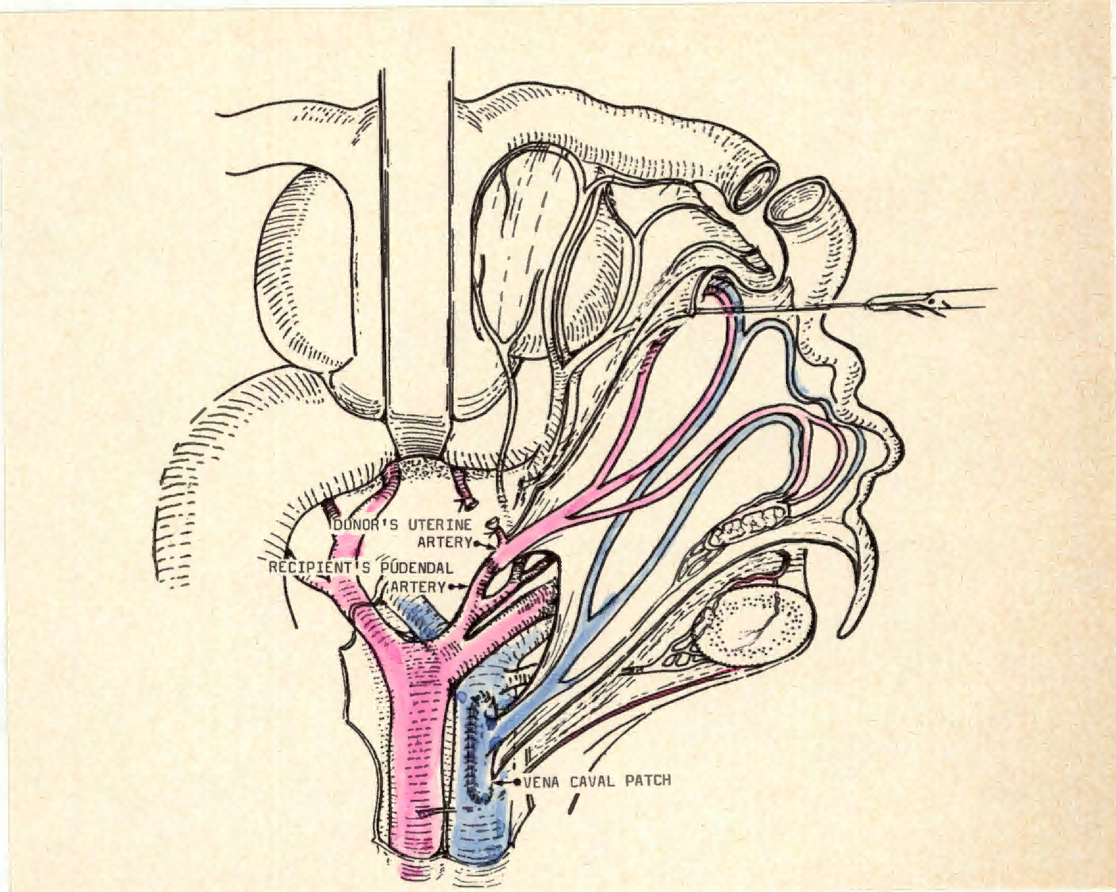

Fig. 11. Transplanted oviduct in situ. (Cornual anastomosis not yet completed.)

CHAPTER FIVE

TRANSPLANT EXPERIMENTS PERFORMED IN THE PIG

1. CLASSIFICATION OF EXPERIMENTS

2. GROUP 1. VASCULARISED HOMOGRAFT TRANSPLANTATION OF THE OVIDUCT

   (a) Type "A" Transplant Procedure

   (b) Type "B" Transplant Procedure

3. GROUP 2. VASCULARISED ORTHOTOPIC AUTOTRANSPLANTATION OF THE OVIDUCT WITH OVARIAN EXCLUSION

4. GROUP 3. VASCULARISED ORTHOTOPIC AUTOTRANSPLANTATION OF THE OVIDUCT TOGETHER WITH ITS IPSILATERAL OVARY

CHAPTER FIVE

TRANSPLANT EXPERIMENTS PERFORMED IN THE PIG

1. CLASSIFICATION OF EXPERIMENTS

The technique described in the previous chapter was used in three groups of transplants classified in TABLE 1.

TABLE 1. CLASSIFICATION OF EXPERIMENTS PERFORMED

		No. of Cases
Group 1	Vascularised homograft transplantation of oviduct	
	(a) Type 'A'	7
	(b) Type 'B'	7
Group 2	Vascularised autotransplantation of oviduct with ovarian exclusion	5
Group 3	Vascularised autotransplantation of oviduct combined with ipsilateral ovary	5

The operative procedures and follow-up were described in these Groups according to the relevant sections of the original protocol as illustrated in Table II.

TABLE II: PROTOCOL FOR TRANSPLANTATION EXPERIMENTS AS PER CASE RECORDS IN ORIGINAL CASE BOOK

DATE

CASE No. AGE

PROCEDURE TIME OF CYCLE — Oestrus / Non-oestrus (quiescent)

DURATION OF OPERATION

A) OPERATIVE DETAILS

PARTICULAR POINTS OF NOTE
VENOUS ANASTOMOSIS
ARTERIAL ANASTOMOSIS
CORNUAL ANASTOMOSIS
GENERAL

B) MEDICATIONS ADMINISTERED

Pre-operative. During operation. Postoperative.

C) LAPAROTOMY FINDINGS

GENERAL APPEARANCE OF ABDOMEN AND PELVIS
PELVIC ADHESIONS

ARTERIAL ANASTOMOSIS — Patent / Thrombosed

VENOUS ANASTOMOSIS — Patent / Thrombosed

CORNUAL ANASTOMOSIS — Patency / Occlusion

ASSESSMENT OF TRANSPLANTED FALLOPIAN TUBE:-
MACROSCOPIC
MICROSCOPIC

D) OVERALL COMMENT

- Viability
- Sepsis
- Rejection
- Technical failure

2. GROUP 1. VASCULARISED HOMOGRAFT TRANSPLANTATION OF THE OVIDUCT

(a) Type "A" Transplant Procedure

The Type "A" transplantation was designed to enable each of two animals to act as both donor and recipient in a single operative procedure. This technique was developed for economic reasons.

When a single animal was both donor and recipient, because it was necessary to remove the ipsilateral ovary with the donor right oviduct, this oviduct, once transplanted, was drawn across the pelvis to the residual left ovary in the recipient. This procedure would have allowed a functional assessment of the transplanted structure to be made provided that the residual "recipient" left oviduct was excised (Fig. 12).

Conception recorded after such an operation could only have taken place by fertilisation of ova from the recipient left ovary via the transplanted right oviduct. Seven Type "A" oviduct homograft transplantations were performed. Their case details are recorded in APPENDIX 2.

(b) Type "B" Transplant Procedure

Once economic circumstances permitted,

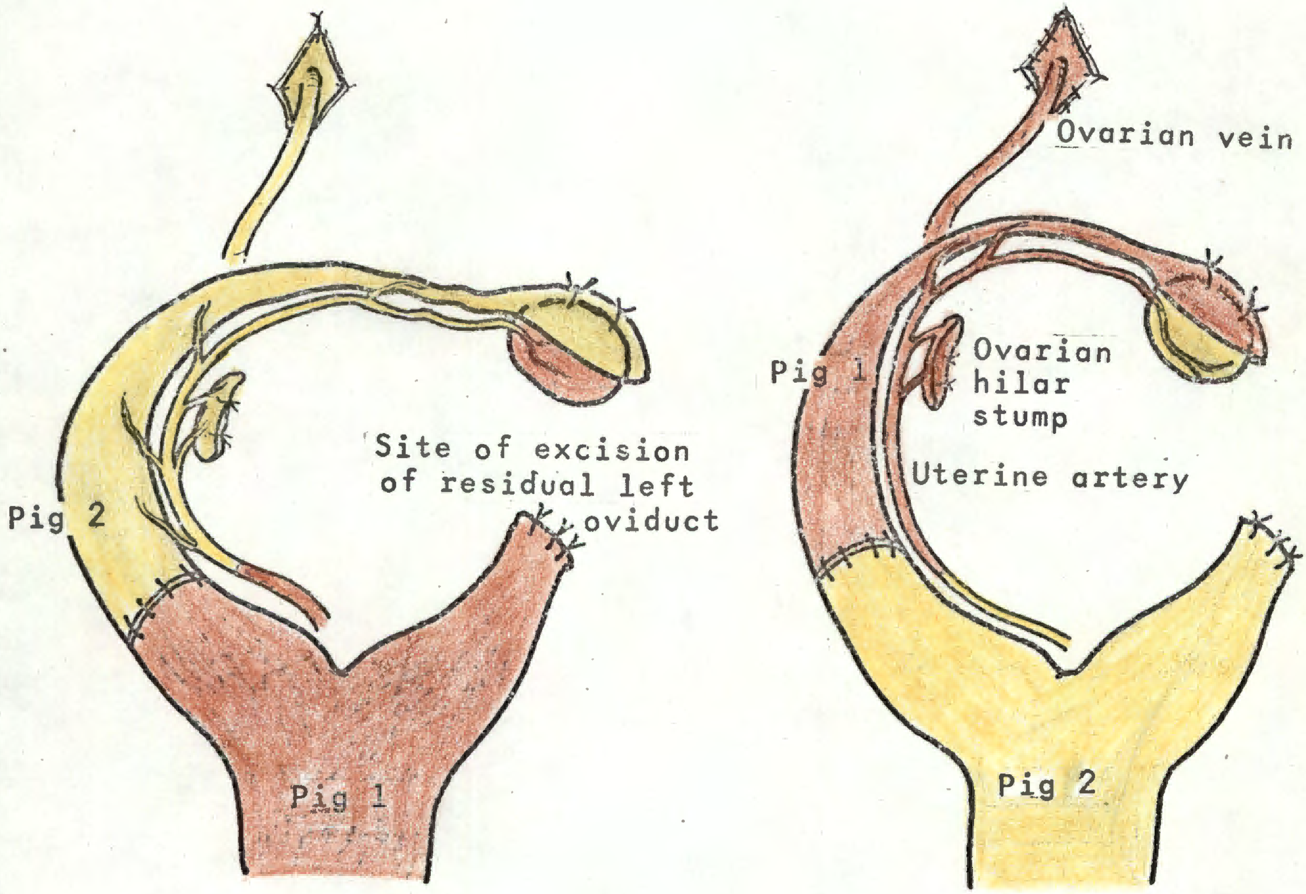

Fig. 12. The Type "A" homograft transplant procedure.

the Type 'A' transplantation operation was abandoned in favour of the simpler Type 'B' procedure. The slight modifications of this operation as compared to the Type 'A' procedure are illustrated in Fig. 13. A separate donor and recipient were used and individual procedures performed in the two animals.

A detailed dissection and removal of the right tubocornual unit was performed on the donor. In the case of the recipient, it was only necessary to define the intended sites of the uterine arterial and vena-caval anastomoses.

Once these vascular anastomoses had been completed, the recipient right oviduct was excised and the cornual anastomosis was performed. The donor right ovary was then excised from the tubocornual unit and its hilar stump ligated. The procedure was completed by performing a left salpingo-oophorectomy in the recipient (Fig. 13). The fimbrial end of the right donor oviduct was placed over the intact right ovary of the recipient. If conception followed such an operation, it could only have occurred by fertilisation of ova from the recipient right ovary via the transplanted right oviduct.

Seven Type 'B' oviduct homograft transplantations were performed. Their case details are recorded in APPENDIX 3.

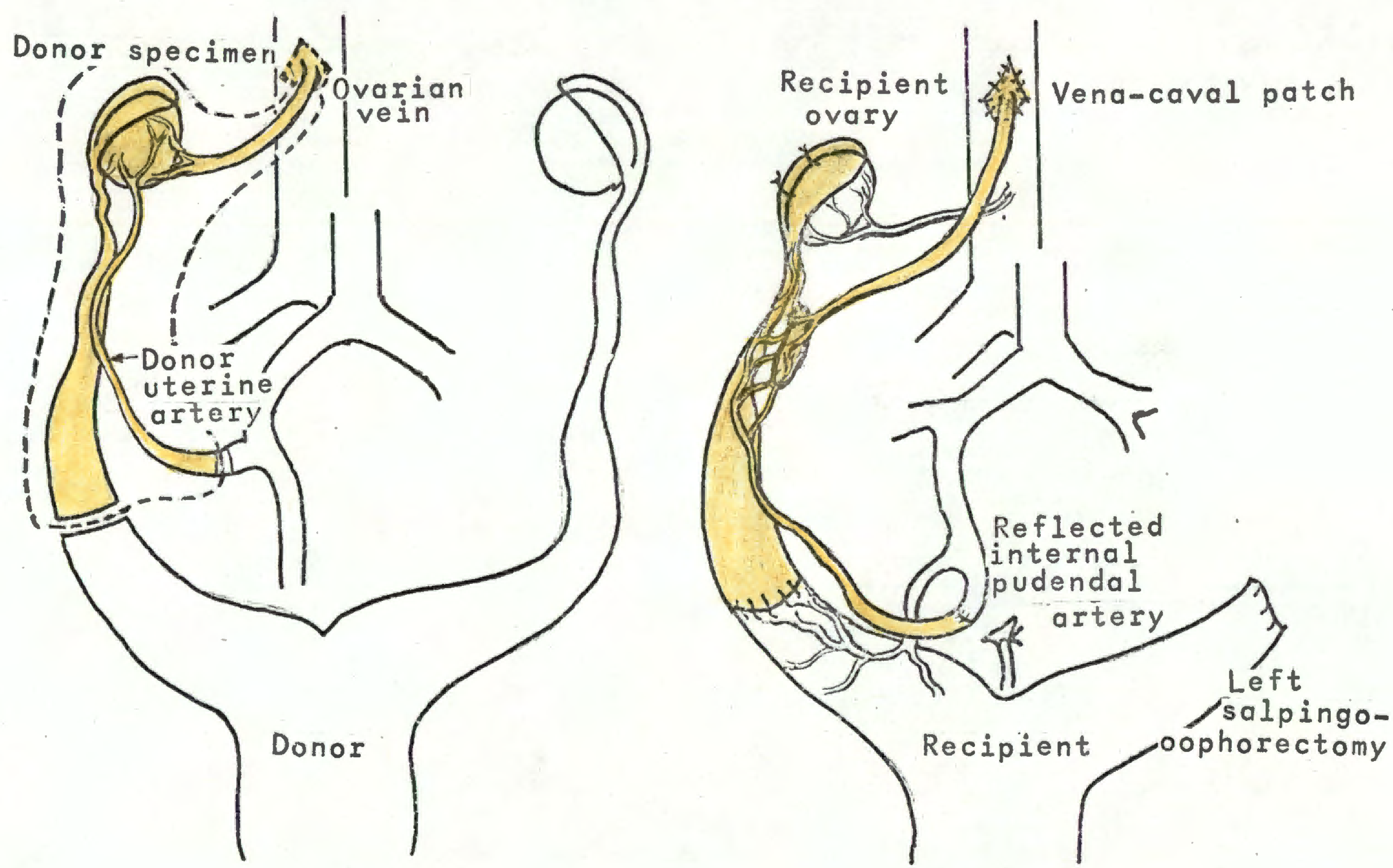

Fig. 13. The Type "B" homograft transplant procedure

3. GROUP 2. VASCULARISED ORTHOTOPIC AUTOTRANSPLANTATION OF THE OVIDUCT WITH OVARIAN EXCLUSION

The operation of vascularised orthotopic autotransplantation of the oviduct was performed using the routine methods of anaesthesia, surgical techniques and medications with the following modifications:

The right "tubocornual unit" was dissected as depicted in Fig. 14. While perfusion was performed, the site of excision of the vena-caval patch was closed with a continuous suture of 6 - 0 silk. The mobilised internal pudendal artery remained clamped with a rubber-shod bulldog clamp.

The excised specimen was then returned to the right side of the same animal and vena-caval anastomosis was performed above the original site of the vena-caval excision using the technique described previously.

The graft uterine artery was then anastomosed to the reflected right internal pudendal artery (Fig. 14). The right ovary was clamped at its hilum, and excised after ligation of its pedicle. The ends of the right cornu were trimmed and re-anastomosed. The operation was completed by performing a left salpingo-oophorectomy as in the Type 'B' homograft transplant. There was no possibility of conception following such an operation.

This experiment was done using comparable vascular techniques to assess the pathological outcome

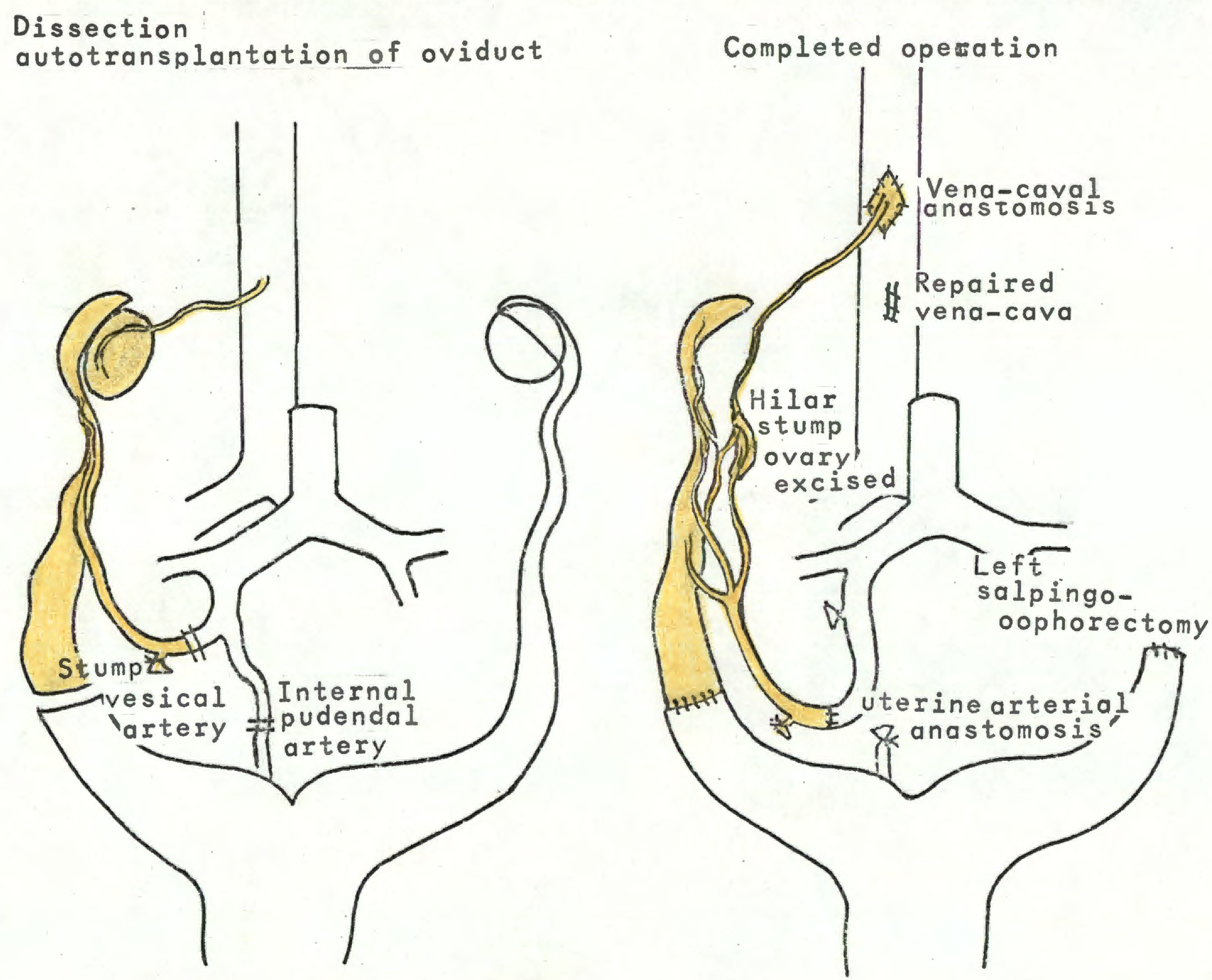

Fig. 14. Vascularised autotransplant of oviduct alone. (Note hilar stump of right ovary, left salpingo-oophorectomy.)

of these procedures without the hazard of rejection in comparison with the homograft transplants. These animals were sacrificed at a much earlier stage than those that had undergone homograft procedures.

Five vascularised autotransplants of the oviduct were performed. Their relevant case details are recorded in APPENDIX 4.

4. GROUP 3. VASCULARISED ORTHOTOPIC AUTOTRANSPLANTATION OF THE OVIDUCT TOGETHER WITH ITS IPSILATERAL OVARY

The operation of vascularised orthotopic autotransplantation of the oviduct combined with its ipsilateral ovary was performed in a manner similar to orthotopic autotransplantation of the oviduct alone.

All methods of anaesthesia, surgical techniques and medications were employed as in the previous experimental procedures (Group 2) with the following modification:

When the venous, arterial and cornual anastomoses had been completed, the ipsilateral right ovary was left in situ (Fig. 15) and not excised and ligated as in all the previously described operations. However, the left tube and ovary were removed and their pedicles were ligated as described in Groups 1 and 2.

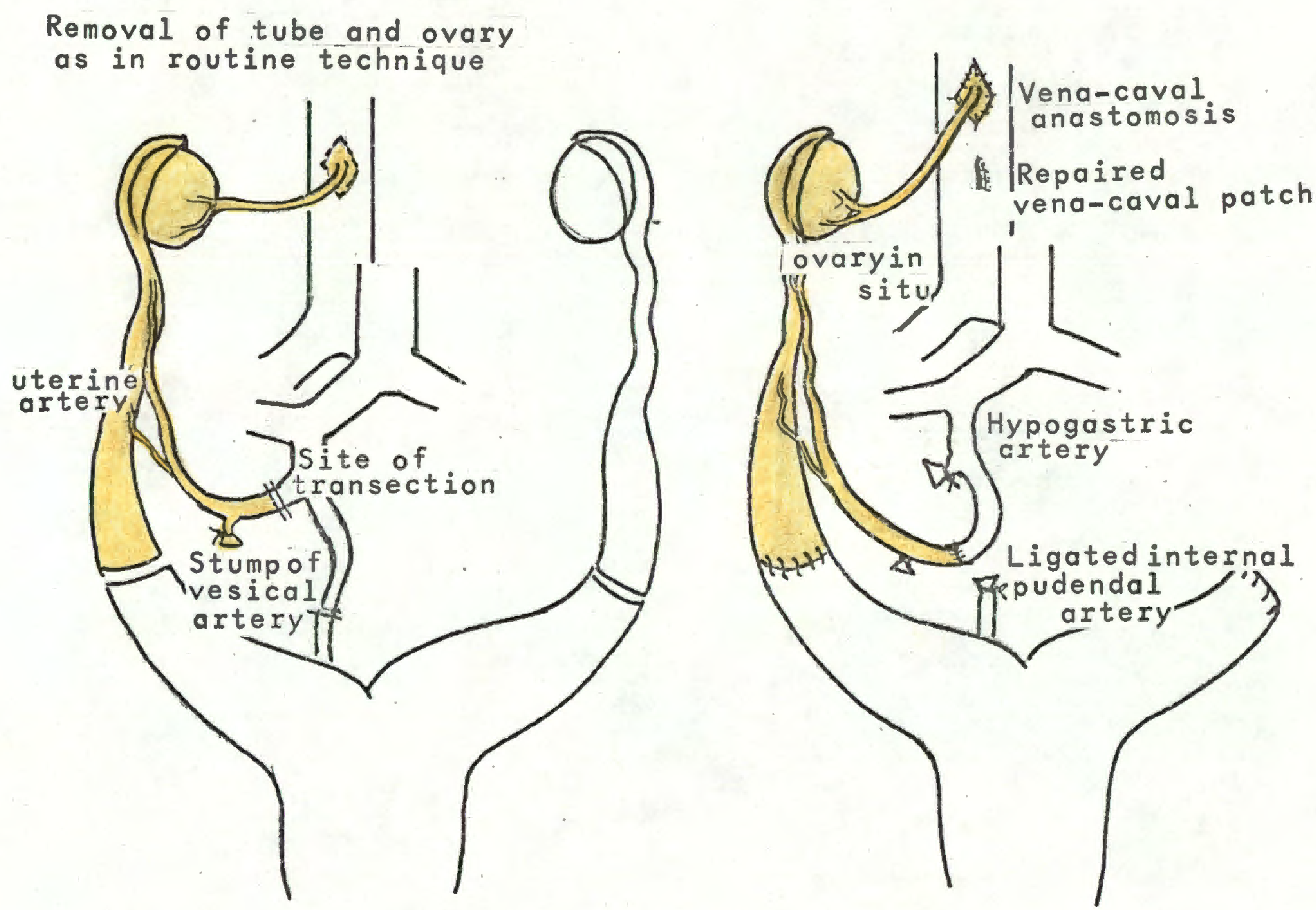

Fig. 15. Vascularised autotransplant of oviduct with ipsilateral ovary. (Note conservation of transplanted right ovary, left salpingo-oophorectomy.)

Other than conservation of the right ovary, the technique used was identical to that employed in the Group 2 series. This operation would allow an assessment of the adequacy of blood supply afforded by the single artery and vein to the tube and its ovary when these were transplanted together. Five such tubo-ovarian autotransplants were performed. Their case details are recorded in APPENDIX 5.

CHAPTER SIX

RESULTS

1. INTRODUCTION

2. COMMENTS

1. Group 1. Vascularised oviduct homograft transplants

2. Group 2. Vascularised oviduct autograft transplants

3. Group 3. Vascularised tubo-ovarian auto transplants

4. Consideration of entire series

CHAPTER SIX

RESULTS

1. INTRODUCTION

Tables 111, 1V and V illustrate the results of the 3 groups of operative procedures performed.

The Type 'A' and Type 'B' series are classified together in group 1 (TABLE 111) as they were both homograft transplants.

Table 1V records the results of the auto-transplants of the oviduct alone. This series (group 2) enables assessment of the technique without the additional hazard of rejection of the transplanted oviduct.

The group 3 series (TABLE V) enables one to assess the adequacy of vascular perfusion by the single uterine artery and ovarian vein to the transplanted oviduct together with its ovary. Excluding the fate of the transplanted ovary, this group may be compared to either of the above 2 groups where the identical blood supply was only intended to nourish the transplanted oviduct alone.

Table V1 illustrates the classification of adhesions used in this study.

TABLE 1 1 1. RESULTS - OVIDUCT HOMOGRAFT TRANSPLANTATION

CASE NO.	STAGE OF CYCLE	DURATION OF SURVIVAL (DAYS)	ADHESIONS ABDOM.	ADHESIONS PELVIC	SEPSIS RELATED TO OPERATIVE PROCEDURE: CONFINED TO TRANSPLANT (SALPINGITIS)	SEPSIS: PERITONITIS	SEPSIS: GENERALISED	OVARY: FUNCTIONAL TISSUE	OVARY: NECROSIS	CORNUAL PATENCY	OVIDUCT PATH. FINDINGS: VIABLE TISSUE ALL LAYERS	OVIDUCT PATH. FINDINGS: VIABLE TISSUE EXTERNAL LAYERS ONLY	NECROSIS	REJECTION	EXTRA SUTURES TO ARTERIAL ANASTOMOSIS	ARTERY	VEIN
GROUP 1a (Type "A")																	
1	non-oestrus	168	+	+++	-	-	-	+	-	p	Disseminated fibrosis - cellular infiltrate of rejection			R	0	T	T
2	oestrus	170	+	+++	-	-	-	+	-	p		+		-	0	T	p
3	non-oestrus	134	+	+	-	-	-	+	-	p	+			-	0	p	p
4	non-oestrus	183	+	+++	-	-	-	+	-	p	+ but no fimbriae			-	4	p	p
5	non-oestrus	168	+	+	+	-	-	+	-	p		+		-	0	T recanalised	p
6	early oestrus	175	+	+++	+	-	-	+	-	p		+		-	0	T recanalised	T
7	early oestrus	*64	+++	+++	+	+	-	+	-	p		+		-	0	T	p
GROUP 1b (Type "B")																	
1	non-oestrus	37	+	+	-	-	-	+	-	p		+		-	0	T	T
2	non-oestrus	107	+	+++	+	-	-	+	-	p		+		-	0	T	p
3	early oestrus	*18	+++	+++	+	+	+	+	-	p		+		-	2	T	p
4	non-oestrus	91	+	+	-	-	-	+	-	p	+			-	2	p	p
5	non-oestrus	91	+++	+++	-	-	-	+	-	p	+ minimal loss of endosalpinx			-	0	T	p
6	non-oestrus	84	+	+	-	-	-	+	-	p	+			-	0	T recanalised	T
7	oestrus	91	+++	+++	+	+	-	+	-	p	+ scattered areas of mucosal fibrosis & atrophy of glands			-	0	T	p

p = Patent T = Thrombosed + = mild ++ = moderate +++ = severe

* = Death due to salpingitis, peritonitis and pneumonia (Type "B") ; * = Death due to volvulus of bowel around adhesion within hernial sac (Type "A")

GROUP 2 TABLE IV. OVIDUCT AUTOTRANSPLANTATION WITH OVARIAN EXCLUSION

CASE NO.	STAGE OF CYCLE	DURATION OF SURVIVAL (DAYS)	ADHESIONS		SEPSIS RELATED TO OPERATIVE PROCEDURE			CORNUAL PATENCY	OVIDUCT PATH. FINDINGS			EXTRA SUTURES TO ARTERIAL ANASTOMOSIS	ARTERY	VEIN
			ABDOM.	PELVIC	CONFINED TO TRANSPLANT (SALPINGITIS)	PERITONITIS	GENERALISED		VIABLE TISSUE ALL LAYERS	VIABLE TISSUE EXTERNAL LAYERS ONLY	NECROSIS			
1	early oestrus	72	+	+	-	-	-	p	+			2	p	p
2	non-oestrus	51	+	+++	-	-	-	p	+			2	p	p
3	non-oestrus	100	+	+	-	-	-	p		+		0	T	p
4	non-oestrus	*41	+	+	-	-	-	p		+		0	T	T
5	oestrus	45	+	+++	-	-	-	p		+ some necrosed tissue in lumen		3	T recanalised	p

* Death due to pneumonia

GROUP 3. TABLE V. AUTOTRANSPLANTATION WITH IPSILATERAL OVARY

CASE NO.	STAGE OF CYCLE	DURATION OF SURVIVAL (DAYS)	ADHESIONS		SEPSIS RELATED TO OPERATIVE PROCEDURE			OVARY			TUBO-OVARIAN GRAFT PATH. FINDINGS			EXTRA SUTURES TO ARTERIAL ANASTOMOSIS	ARTERY	VEIN
			ABDOM.	PELVIC	CONFINED TO TRANSPLANT (SALPINGITIS)	PERITONITIS	GENERALISED	FUNCTIONAL TISSUE	NECROSIS	CORNUAL PATENCY	VIABLE TISSUE ALL LAYERS	VIABLE TISSUE EXTERNAL LAYERS ONLY	NECROSIS			
1	non-oestrus	*10	+++	+++	++	++	++ septicaemia		+	p			+	0	T	T
2	early oestrus	70	+++	+++	++	++	++ pneumonia		+	p			+	0	T	T
3	oestrus	63	+	+++	++	++	-		+	p			+	0	T	T
4	non-oestrus	61	+	+++	++	++	-		+	p		some viable serosal & muscle cells	+	0	T	p
5	early oestrus	56	+++	+++	+	-	-	+	-	p	+ scattered fibrosis of inner layers			2	p	p

* Death due to disseminated sepsis

TABLE VI. CLASSIFICATION OF ABDOMINAL AND PELVIC ADHESIONS

A - Abdominal Adhesions

Mild - +

Isolated, few, fine, flimsy adhesions linking segments of small bowel and/or between sections of small bowel and the anterior and/or posterior abdominal walls.

Moderate - ++

Scattered, thicker, non-vascularised adhesions between segments of small bowel and/or sections of small bowel and the anterior and/or posterior abdominal walls.

Severe - +++

Diffuse, thick, often vascularised adhesions causing extensive matting of multiple loops of small bowel and/or extensive adherence of multiple loops of small bowel to the anterior and/or posterior abdominal walls.

B - Pelvic Adhesions

Mild - +

Isolated, few, fine, flimsy adhesions linking loops of cornu and/or oviduct or cornu and/or oviduct to the ovary with mobility of uterus and adnexal structures.

Moderate - ++

Scattered, thicker, non-vascularised adhesions linking loops of cornu and/or oviduct or cornu and/or oviduct to the ovary with isolated similar adhesions linking the uterus and/or adnexa to neighbouring anatomical structures.

Severe - +++

Diffuse, thick, often vascularised adhesions causing extensive matting of all structures within the pelvis and attaching the uterus and adnexa to neighbouring anatomical structures.

2. COMMENTS

1. Group 1. Vascularised Oviduct - Homograft Transplants (TABLE 111)

The most striking feature of this series was the absence of rejection which was observed in only 1 of 14 cases.

All cornual anastomoses were observed to be patent.

Each recipient ovary contained functional structures (developing follicles or corpora lutea) that were histologically normal.

Peritonitis was present in 3 of the 14 homografts performed (group 1.a, No. 7; group 1.b, Nos. 3 and 7). In these 3 cases, it was associated with salpingitis and in one of them (group 1.b, No. 3) with septicaemia, pneumonia and death of the animal on the 18th postoperative day.

Severe pelvic adhesions were found in 9 of the 14 cases, 4 of whom were also observed to have concomitant severe abdominal adhesions (group 1.a, No. 7; group 1.b, Nos. 3, 5 and 7). Minimal abdominal adhesions were a more common finding as seen in 10 of the 14 cases.

Excluding the loss of fimbrial components in group 1.a, No. 4, viability of all layers of the transplanted oviduct was almost complete in 4 of the 14 homografts (group 1.a, Nos. 3 and 4; group 1.b, Nos. 4 and 6). Three of these 4 cases had patent arteries and veins. A further 2 cases (group 1.b, Nos. 5 and 7) showed viability in all 3 layers of the transplanted oviduct although there were scattered areas of mucosal atrophy and associated fibrosis of the endosalpinx. Of the abovementioned 6 cases where the transplanted oviducts revealed most anatomical normality, 3 of these had thrombosed uterine arteries (group 1.b, Nos. 5, 6 and 7) although recanalisation had taken place in one of them. This case (group 1.b, No. 6) was the only one of these 6 which was found to have a thrombosed ovarian vein.

There were two deaths in the group 1 series. One was precipitated by a volvulus of small bowel around a large abdominal adhesion with its subsequent complications (group 1.a, No. 7). The second death had occurred due to overwhelming infection which was evident in the transplanted oviduct, the abdominal cavity and the lungs at the postmortem examination (group 1.b, No. 3).

Despite the fact that the animals with most viable transplanted tissues had been mated on two successive oestrus cycles prior to their sacrifice, no pregnancies were observed.

2. Group 2. Vascularised Oviduct - Autograft Transplants (TABLE 1V)

The results of these operative procedures were virtually identical to those of the group 1 series. Comments regarding rejection or pregnancy are not possible as these animals were not exposed to these potential sequelae.

Arterial thromboses were found in 3 of the 5 cases, 4 of which had patent ovarian veins. All of the transplanted cornua were patent.

None of the group 2 series had sepsis of the transplanted oviduct or evidence of abdominal peritonitis.

The one death in this batch of animals (Case No. 4) occurred on the 41st postoperative day. It was precipitated by a pneumonia and this complication did not appear to be directly related to the operative procedure.

Scanty abdominal adhesions were found in all 5 cases and severe pelvic adhesions were observed in 2 of them.

Total viability of all layers of the transplanted oviduct was seen in 2 of the 5 cases (Case Nos. 1 and 2) both of which had healthy patent uterine arteries.

3. Group 3. Vascularised Tubo-ovarian Autotransplants (TABLE V)

The most striking findings in this series was the high incidence of extensive necrosis of the transplanted tissues. This was associated with a high incidence of secondary infection in the form of salpingitis, peritonitis and extensive pelvic adhesions.

Although the uterine artery and the ovarian vein were both patent in only one case which revealed most viable tissue, scattered areas of fibrosis were found throughout the tunica propria (Case No. 5). Four of the 5 uterine arteries were thrombosed and a similar outcome had occurred in 3 of the 5 ovarian veins.

The one death in this series was caused by septicaemia and pyaemia which appeared to have its origin as a secondary infection in the necrosed transplanted tissues.

4. Consideration of Entire Series

The only dissimilarity of results in the first 2 series was a higher incidence of sepsis and adhesions in the group 1 as opposed to the group 2 procedures. Paucity of numbers did not allow adequate confirmation of these trends of variation at a level of statistical significance.

The following differences were found between the two types of autografts performed (i.e. group 2 versus group 3):

The transplanted oviduct was extensively necrosed in 4 of the 5 cases submitted to autotransplantation together with their ipsilateral ovaries (group 3), whereas this complication did not occur when the oviduct was autotransplanted on its own (group 2).

	Extensive necrosis of oviduct	No extensive necrosis of oviduct	
Group 2 oviduct alone	0	5	5
Group 3 oviduct & ovary	4	1	5
	4	6	10

P = 0.05

Application of the 4-fold table test (Diem, 1962) revealed that this was statistically significant. The incidence of infection of the oviduct and associated peritonitis was far more common in the group 3 compared to the group 2 series. Use of the 4-fold table test confirmed that this variation was also statistically significant (vide infra).

	Infection of oviduct	No infection of oviduct	
Group 2 Oviduct alone	0	5	5
Group 3 Oviduct & ovary	5	0	5
	5	5	10

P = 0.01

	Peritonitis	No Peritonitis	
Group 2 Oviduct alone	0	5	5
Group 3 Oviduct & ovary	4	1	5
	4	6	10

P = 0.05

There was an apparently higher incidence of arterial and venous thrombosis in the tubo-ovarian transplant series (group 3), but paucity of numbers did not enable establishment of this trend at a statistically significant level.

The most striking feature observed in all series was the very high incidence of thrombosis of the uterine artery. This was seen in 18 of the 24 cases. Ischaemia was responsible for most of the pathological changes observed in the tissues that had been transplanted. In view of the gravity of this problem, an effort was made to assess the various factors that could possibly be implicated in its causation.

Oestrus was not significantly associated with a high incidence of thrombosis.

Severe pelvic adhesions were found in 13 of the 18 cases with arterial thrombosis, whereas they were present in only 3 of 6 cases where the uterine arteries were patent. It was felt that these may have contributed to the occurrence of vascular thrombosis by indicating associated sepsis, traction or compression of the site of the anastomosis. The small numbers did not enable evaluation of this factor at a statistically significant level.

The one feature which was highly significant was the fact that when extra sutures were applied to the uterine arteries to effect adequate haemostasis, 5 of the 7 vessels were patent at the second laparotomy.

When the arterial anastomosis had not required the insertion of extra haemostatic sutures, 16 of the 17 vessels had subsequently become occluded by a thrombus.

Application of the 4-fold table test to this data revealed that the need to insert additional sutures to the uterine arterial anastomosis to effect adequate haemostasis was significantly related to the later incidence of patency of the vessels (vide infra). This was most likely due to the fact that where good haemostasis had been observed, the suture line was too tight and had resulted in stricture and subsequent thrombosis of the artery. Where extra sutures were required, the suture line was looser and had probably not affected the diameter of the vessel anastomosed.

	Thrombosed uterine artery	Patent uterine artery	
Insertion of extra sutures to anastomosis	2	5	7
No extra sutures required	16	1	17
	18	6	24

P = 0.01

A further factor worthy of comment was the amount of viable tissue found in the outer layers of the transplanted oviducts of groups 1 and 2 despite the frequency of arterial thrombosis. Survival of these tissues was surprising and appeared to correlate with the relative absence of sepsis and patency of the ovarian vein.

In the group 3 series, there was virtually total necrosis of the transplanted structure in 4 of the 5 cases. This finding coincided with a higher incidence of venous thrombosis and severe infection which was also most marked in this group.

CHAPTER SEVEN

SUPPLEMENTARY EXPERIMENTS PERFORMED

1. A RE-ASSESSMENT OF THE UTERINE ARTERIAL ANASTOMOSIS

1. Introduction
2. Material and Methods
3. Operative technique
   - (i) modified end-to-end anastomosis
   - (ii) terminal side-to-side anastomosis
4. Completion of operation
5. Subsequent laparotomy
6. Results
7. Comment

2. APPLICATION OF MODIFIED TECHNIQUES OF ARTERIAL AND VENOUS ANASTOMOSES IN A SERIES OF OVIDUCT AUTO-TRANSPLANTS PERFORMED IN THE EWE

1. Introduction
2. Material and Methods
3. Follow-up
4. Results
5. Comment

3. A PRELIMINARY ASSESSMENT OF THE METHOD OF PERFUSION OF THE FALLOPIAN TUBE IN A HUMAN HYSTERECTOMY SPECIMEN

CHAPTER SEVEN

SUPPLEMENTARY EXPERIMENTS PERFORMED

1. A RE-ASSESSMENT OF THE TECHNIQUE OF UTERINE ARTERIAL ANASTOMOSIS IN THE PIG

1. Introduction

On reviewing the results of the three groups of transplants, the most significant cause of failure was the high incidence of thrombosis found at the site of the uterine arterial anastomosis. Only 6 of the 24 anastomoses performed were healthy and patent when assessed at the second laparotomy.

The only clue to the cause of this complication was the significantly higher incidence of vascular patency observed when the suture line had bled vigorously on release of the vascular clamps. Such bleeding had necessitated the insertion of additional haemostatic sutures.

It was felt that this finding indicated that where the original layer of continuous sutures had obtained perfect haemostasis, this was probably because the suture line was too tight and was likely to be associated with a localised stricture of the vessel.

As the thrombotic lesions were probably a reflection of the technique employed to suture the vessels, it was decided to assess the efficacy of two different techniques of uterine arterial suture in an additional study.

2. Material and Methods

Sixteen pigs similar to those operated on previously and all of a comparable age were used for this study. These animals were submitted to laparotomy under the conditions of the previous procedures in regard to pre-, intra- and postoperative therapy.

3. Operative Technique

After dividing the layer of peritoneum of the broad ligament, immediately overlying the uterine arteries, these vessels were dissected free of their accompanying venous branches. The uterine arteries were transected and then repaired using two methods:

(i) Modified end-to-end anastomosis

This was completed as described previously, but in this study, 9 - 0 monofilament nylon sutures were used. These were inserted through the intima of the vessel which had been dissected free of its outer muscularis and adventitia. In addition, a few interrupted 7 - 0 silk sutures were placed through these outer layers in order to ensure their approximation and support for the inner suture line of the anastomosis (Fig. 16).

The following measures were also employed in an attempt to prevent thrombosis. The arteries were transected obliquely. The ends of these vessels were dilated gently to a diameter of approximately 2 mm prior to the insertion of the suture line. The site of the anastomosis was liberally irrigated with a 2% solution of procaine hydrochloride in addition to the heparinised saline to prevent any spasm of the vessel while the anastomosis was being completed.

Particular care was exercised to ensure that the continuous suture lines were kept as relaxed as effective haemostasis would permit.

(ii) Terminal side-to-side anastomosis

In this technique, the ends of the artery were gently dilated and liberally irrigated with a 2% solution of procaine hydrochloride as described above.

After insertion of a fine iris forceps into one end of a vessel, a longitudinal incision through all layers was made on one side. This incision was approximately 5 mm in length and commenced approximately 2 mm from the transected end of the vessel. The distal end of the vessel was then tied off with a 4 - 0 silk suture (Fig. 17).

A longitudinal incision combined with terminal ligation was then performed on the other segment of the transected artery. These two longitudinal incisions were then approximated as a side-to-side anastomosis using 7 - 0 silk sutures lubricated with sterile liquid paraffin employing the technique illustrated in Fig. 18.

4. Completion of Operation

In both groups, the original peritoneal incision was re-approximated with a 4 - 0 atraumatic

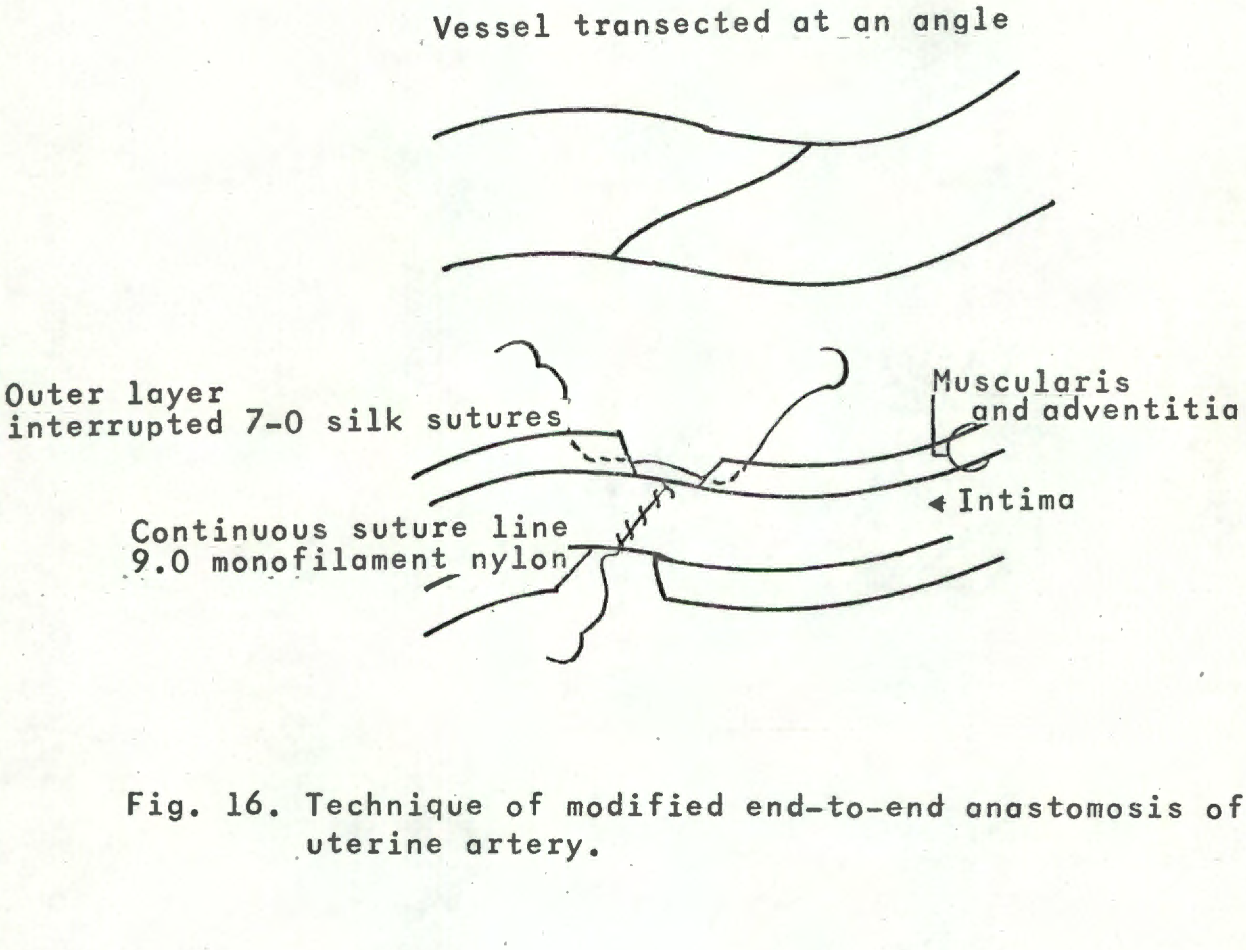

Fig. 16. Technique of modified end-to-end anastomosis of uterine artery.

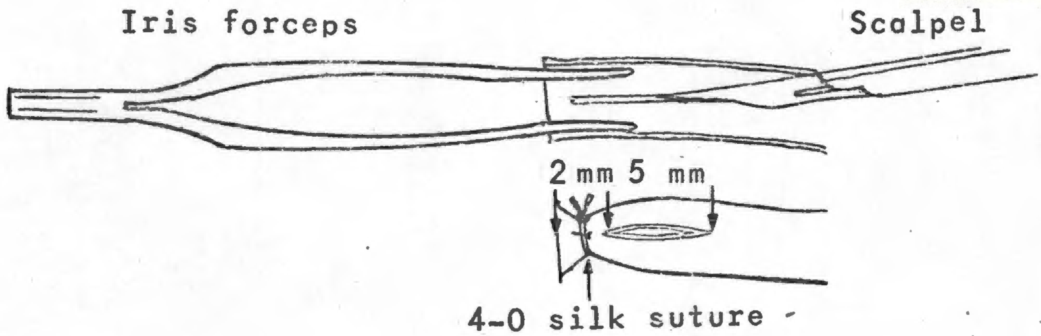

Fig. 17. Preparation of transected end of uterine artery for terminal side-to-side anastomosis.

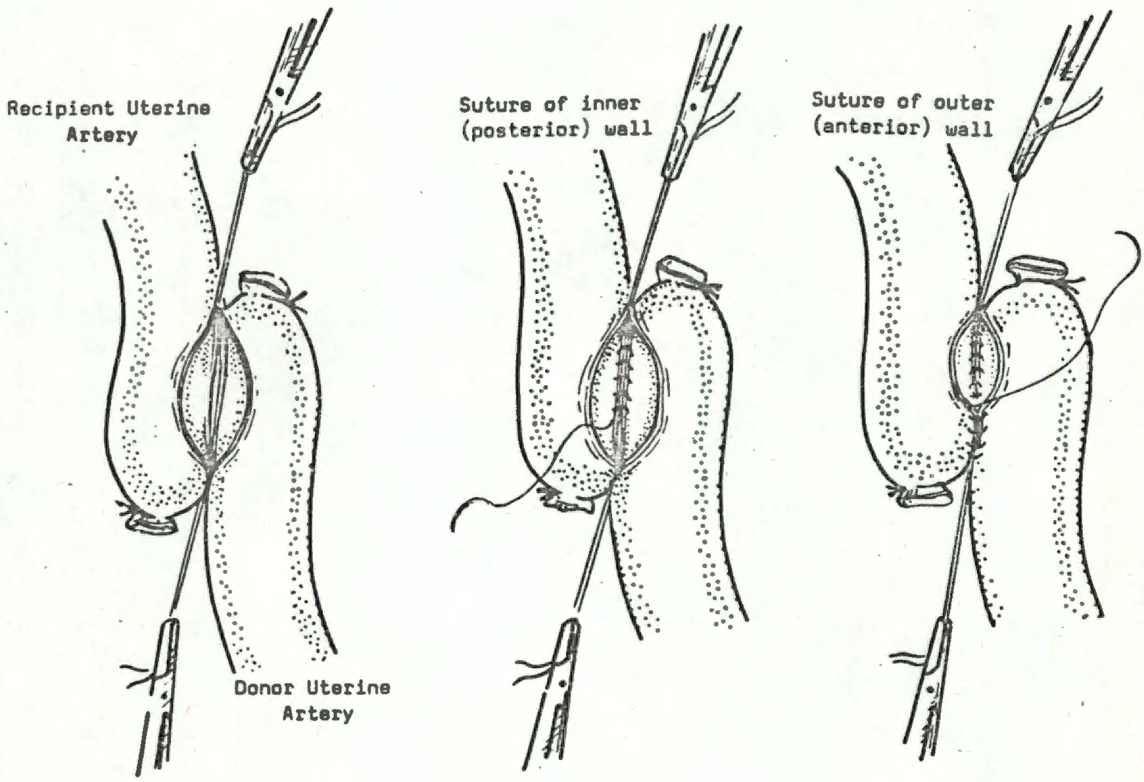

Fig. 18. Technique of terminal side-to-side arterial anastomosis.

polyglycolic acid suture prior to routine closure of the abdomen. The following controls were also performed :

All experiments were carried out during the quiescent phase of the oestrus cycle.

The right and left uterine arteries of an individual animal were always repaired using the different techniques alternately.

The surgeon moved to the corresponding side of the animal to complete the anastomosis.

The technique used for one side in an operation was performed on the opposite side in the next operation (TABLE V11).

5. Subsequent Laparotomy

All animals were submitted to laparotomy 10 - 15 days after the operative procedure. The uterine arteries were dissected out, and after applying a bulldog clamp a few centimetres distal to the site of the anastomosis, the vessel was transected approximately 1 cm beyond the anastomosis. Such transection was either followed by profuse haemorrhage due to patency of the vessel, minimal flow of blood, or no flow at all. Each vessel was then opened through a longitudinal incision commencing proximal and extending at least a centimetre distal to the anastomosis.

Reduced bleeding from a vessel was always associated with an obvious thrombus at the site of the anastomosis. When intense haemorrhage occurred, the intima of the vessel was always noted to be healthy and to have a smooth shiny appearance. As no thrombus was apparent on macroscopic examination and the lumen of the vessel appeared patent, these vessels were not submitted to histological examinations.

6. Results

The observations recorded in the 16 animals included in this experiement are summarised in TABLE V11. Only 2 of 16 uterine arteries re-anastomosed in an end-to-end manner were observed to be patent at the second laparotomy.

The side-to-side technique was clearly a more reliable method of avoiding vascular thrombosis. Eight of the 16 anastomoses completed in that manner were found to be patent.

TABLE V11. RESULTS OF SERIES OF UTERINE ARTERIAL ANASTOMOSES COMPARING END-TO-END WITH TERMINAL SIDE-TO-SIDE ANASTOMOSIS

	End-to-End		Terminal Side-to-Side	
Pig No.	Side Anastomosed	Outcome	Side Anastomosed	Outcome
1	R	T	L	P
2	L	T	R	T
3	R	T	L	P
4	L	T	R	P
5	R	T	L	T
6	L	T	R	T
7	R	T	L	T
8	L	T	R	P
9	R	T	L	T
10	L	P	R	P
11	R	T	L	P
12	L	T	R	P
13	R	P	L	T
14	L	T	R	T
15	R	T	L	P
16	L	T	R	T

R - Right
L - Left

P - Patent
T - Thrombosed

Number patent - 2

Number patent - 8

Analysis of these figures by their application in the 4-fold table test revealed that this difference was statistically significant.

Anastomosis	Vessel Thrombosed	Vessel Patent	Total
End-to-End	14	2	16
Side-to-Side	8	8	16
	22	10	32

$\chi^2 = 5.24$ $\qquad\qquad$ $P < 0.05$

7. Comment

The technique of terminal side-to-side anastomosis was more reliable in securing vascular patency in porcine uterine arterial anastomoses. The larger diameter of the anastomosis combined with spasm of the circular muscle fibres of the vessels which would tend to dilate the anastomotic site were thought to be factors contributing to this finding.

2. APPLICATION OF MODIFIED TECHNIQUES OF ARTERIAL AND VENOUS ANASTOMOSES IN A SERIES OF OVIDUCT AUTO-TRANSPLANTS PERFORMED IN THE EWE

1. Introduction

On the evidence of the previous study, it was decided that further transplant procedures should be modified by performing the uterine arterial anastomosis using the side-to-side technique. The initial results using this method were significantly better than those recorded with the end-to-end technique.

Regarding the ovarian vein, it was decided to assess the efficacy of an end-to-side anastomosis performed onto the recipient's ovarian vein within the brim of the pelvis. This technique, if proven a reliable means of performing an oviduct transplant operation, would render the procedure much safer for application in humans.

2. Material and Methods

Ewes were chosen for this study as they had recently become available. Close examination of their pelvic anatomy showed that this was far more comparable to that of the human female. These findings were particularly applicable with regard to the texture, diameter and situation of the uterine and ovarian vessels (Fig. 19).

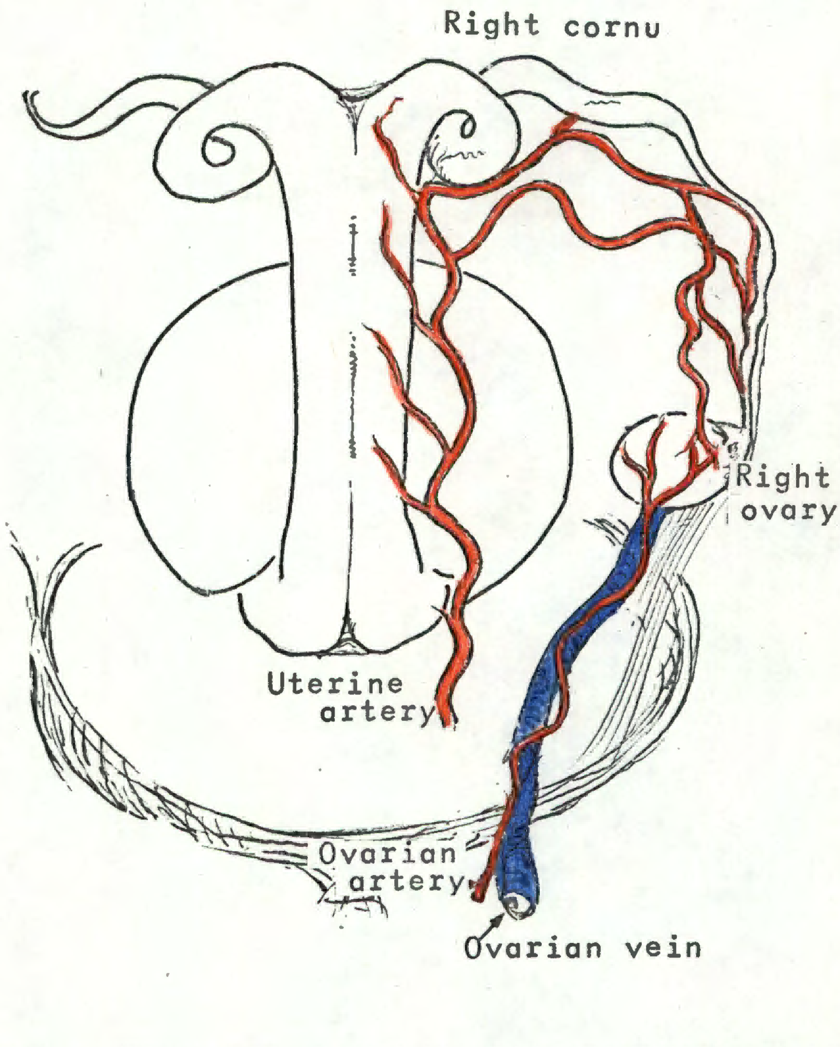

Fig. 19. Vascular anatomy of the right oviduct in the ewe (posterior aspect).

Twelve autograft transplants of the Fallopian tube were performed using the technique previously applied in the pig but with the following modifications :

The left tubocornual unit was dissected out. Its ovarian vein was transected at an angle within the pelvis at a site proximal to its fixation on the posterior aspect of the pelvis.

The left uterine artery was transected at a point parallel to the uterine isthmus. The left tubocornual unit was now totally freed from the host and perfused in the routine manner. The pedicles of the left ovarian vein and the left uterine artery were ligated with 00 linen.

The right ovarian vein was cleared of its overlying peritoneum for a distance of 2 cm at a site within the brim of the pelvis. The right uterine artery was exposed at a site parallel to the isthmus of the uterus.

The left ovarian venous pedicle of the graft was anastomosed to the right ovarian vein in an end-to-side fashion with a continuous 6 - 0 silk suture. (Fig. 20).

The exposed right uterine artery was transected and its distal end was ligated. The proximal end was clamped with a rubber-shod bulldog clamp. The graft

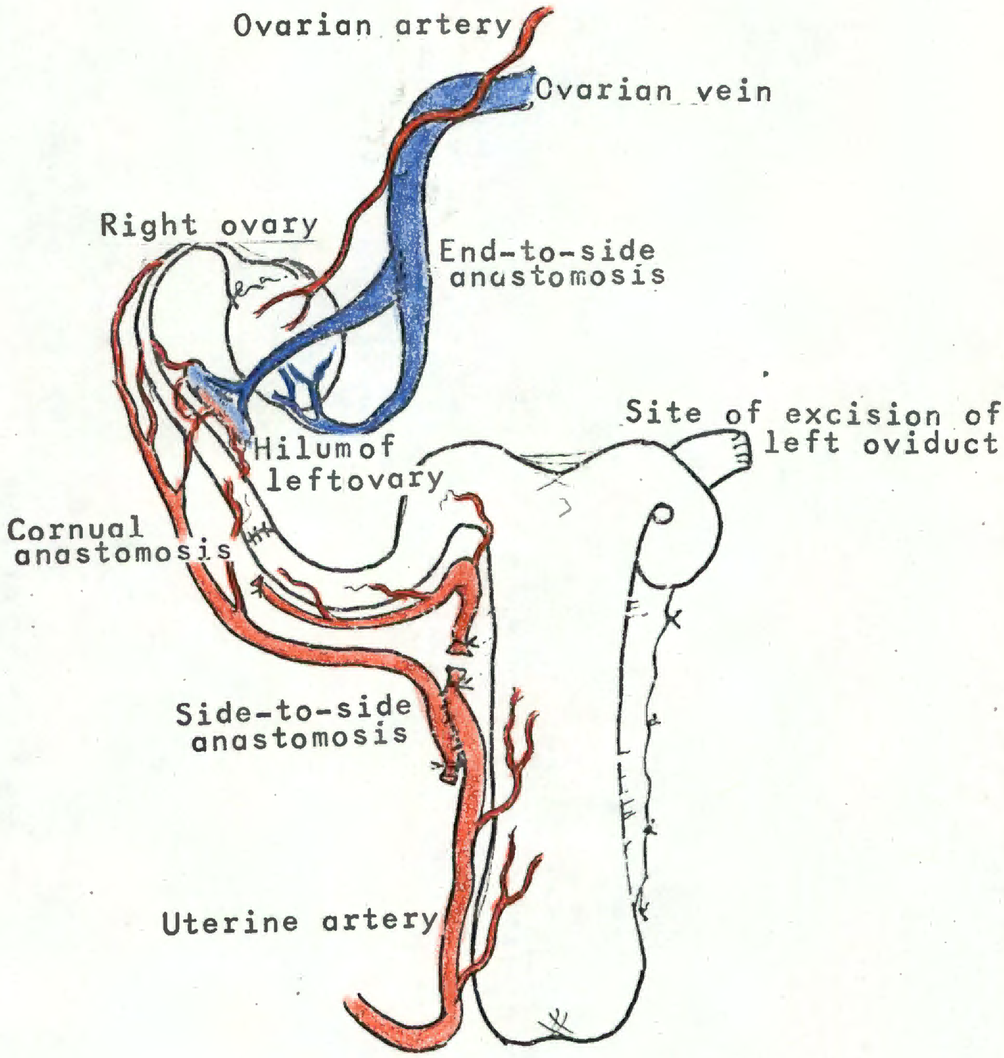

Fig. 20. Technique of heterotopic (right-to-left) autotransplantation of the oviduct in the ewe. (Note side-to-side anastomosis of uterine artery, end-to-side anastomosis of ovarian vein.)

uterine artery was anastomosed to this vessel with a 6 - 0 silk suture using the side-to-side technique described in the previous experiment.

Once the anastomoses were completed, the vascular clamps were released. The right Fallopian tube was excised together with a piece of its cornu and the cornual anastomosis with the graft cornu was performed at this site.

The ovary of the graft specimen was excised and its ligated pedicle was sutured close to the hilum of the right ovary which had remained in situ.

The broad ligament of the graft specimen was sutured to the right broad ligament and a few 6 - 0 polyglycolic acid sutures were inserted to secure the fimbrial end of the transplanted left Fallopian tube over the right ovary.

The abdomen was irrigated with heparinised saline combined with chloromycetin prior to its closure. Routine intra- and postoperative medications were administered.

3. Follow-up

Two of the 12 sheep developed severe postoperative pneumonia and these animals were sacrificed on the 3rd and 4th postoperative days respectively.

The remaining 10 ewes were submitted to exploratory laparotomy approximately 3 months after undergoing the transplant operation.

The animals were not exposed to the possibility of insemination as the operations had been performed during the winter months when local ewes are non-oestrus. The laparotomies were performed to assess the anatomical outcome of the operation. This examination would enable an early assessment of the efficacy or pit-falls of the new technique and whether or not efforts should be made to attempt to cause pregnancy in these animals when oestrus returned.

4. Results (TABLE V111)

In all cases, the graft appeared healthy. This was associated with obvious patency of the uterine artery and the ovarian vein as assessed by digital compression of these vessels in vivo. In the 2 animals sacrificed, absence of any vascular occlusion was confirmed by longitudinal section through the anastomosis of the uterine and ovarian vessels.

5. Comment

The original technique, modified by using a uterine arterial side-to-side anastomosis together with an ovarian vein end-to-side anastomosis, resulted in a successful anatomical outcome in all cases.

TABLE V111. RESULTS OF FALLOPIAN TUBE AUTOGRAFT TRANSPLANTATIONS IN SHEEP

Case No.	Day	Sacrifice/ laparotomy	Uterine artery	Ovarian vein	Appearance of graft
1	3	S	P	P	Healthy
2	4	S	P	P	Healthy
3	92	L	P	P	H
4	90	L	P	P	H
5	96	L	P	P	H
6	94	L	P	P	H
7	93	L	P	P	H
8	95	L	P	P	H
9	92	L	P	P	H
10	90	L	P	P	H
11	91	L	P	P	H
12	94	L	P	P	H
Total 12	-	-	12	12	12

S - Sacrifice

L - Laparotomy

P - Patent

H - Healthy

3. A PRELIMINARY ASSESSMENT OF THE METHOD OF PERFUSION OF THE FALLOPIAN TUBE IN A HUMAN HYSTERECTOMY SPECIMEN

1. Introduction

Since the overall simplicity of the operation was dependent on the concept of using the uterine artery for arterial perfusion, and the ovarian vein (via utero-ovarian anastomoses) for venous drainage, it was essential to conduct a preliminary study to assess whether this method could be used in the human female.

If the method of perfusion could be applied to the human Fallopian tube including its ipsilateral cornu, the only surgical additions to the current methods of tubal implantation would be: a slightly more elaborate technique of cornual implantation; the definitive dissection of the uterine artery and an ipsilateral ovarian vein; and the re-anastomosis of these two vessels in the recipient.

2. Material and Methods

Using a fresh human hysterectomy specimen, the left uterine artery was cannulated with a fine No. 19 gauge polythene catheter which was attached to a 10-ml syringe containing a radio-opaque medium (Urografin).

An X-ray was taken before the Fallopian tube and a section of the ipsilateral cornu were dissected free of the uterus. The hilum of the corresponding ovary was clamped with two artery forceps and the perfusion was continued while successive X-rays were taken.

A similar series of X-rays were taken after dissection of the left cornu and oviduct together with its ipsilateral ovary in the pig.

3. Results

Figs 21a, b and c illustrate the vascular anatomy of the Fallopian tube and its ipsilateral cornu in the human hysterectomy specimen. These may be compared with Figs 22a and b which show the analogous situation in the pig.

4. Comment

Whilst confined to a single case, the vascular anatomy of the human female appeared to be similar to that of the pig, thus allowing vascularised tranplantation of the oviduct with the method employed in the animal transplants.

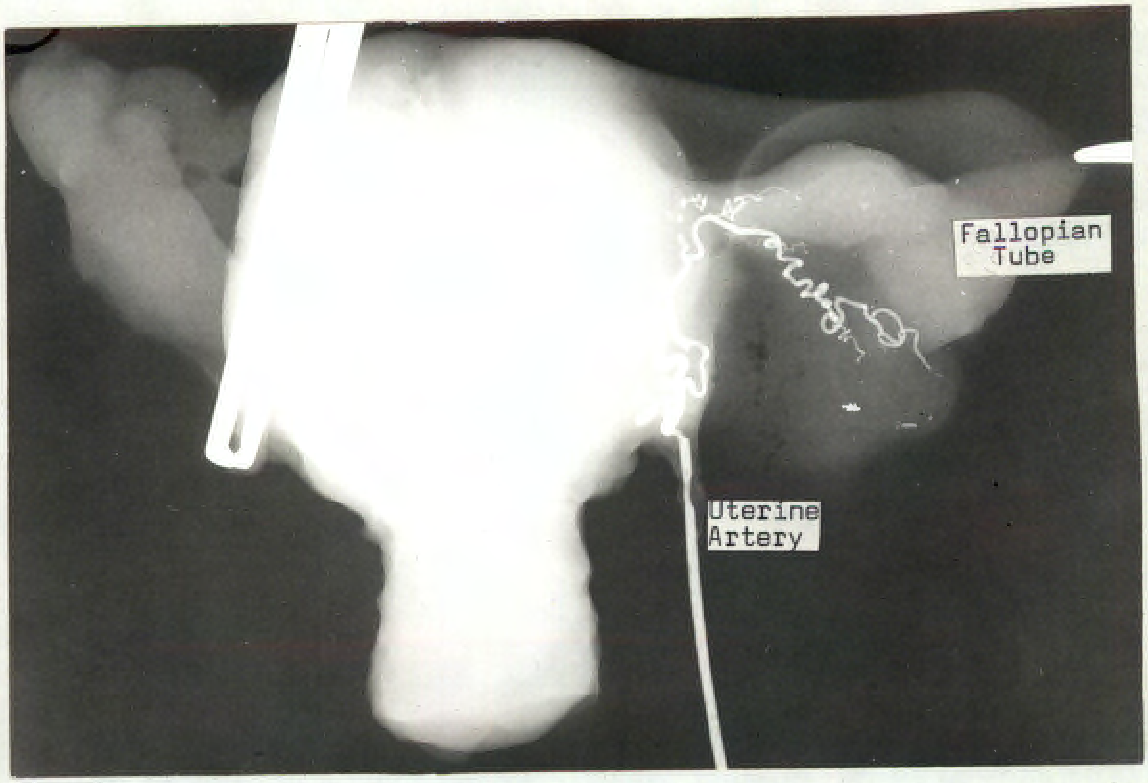

Fig. 21a. Human hysterectomy specimen. Cannula in left uterine artery. Early arteriographic appearance of left Fallopian tube.

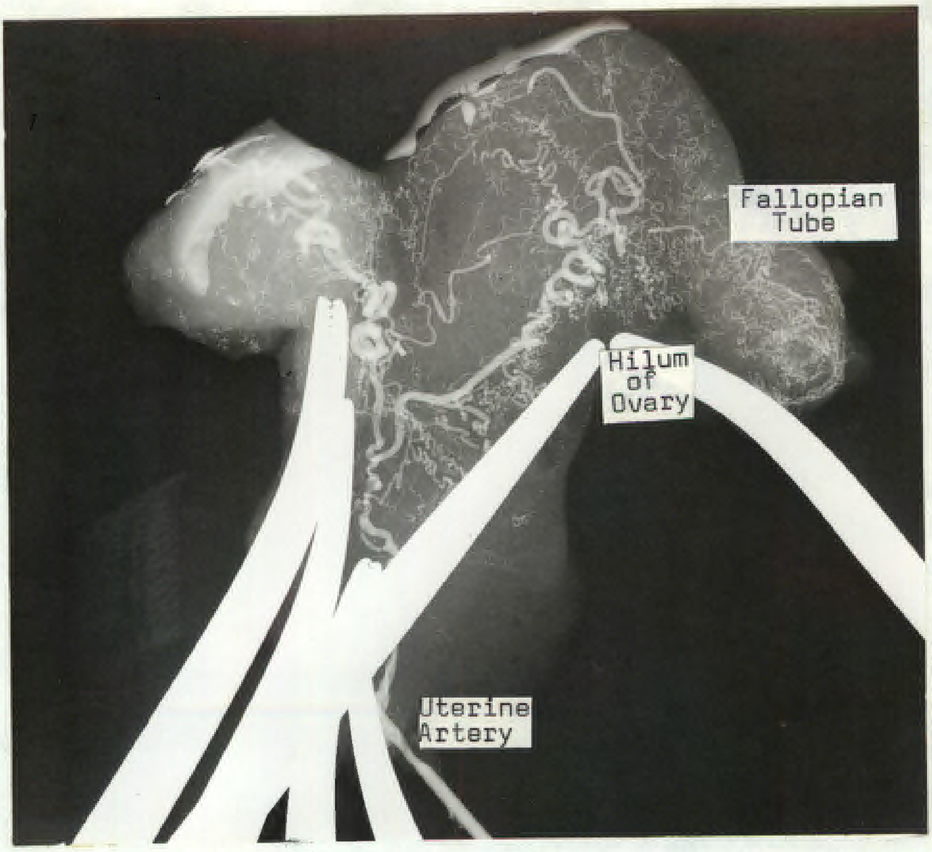

Fig. 21b. Mid-phase arteriogram of human left "tubo-cornual unit"prior to venous filling.

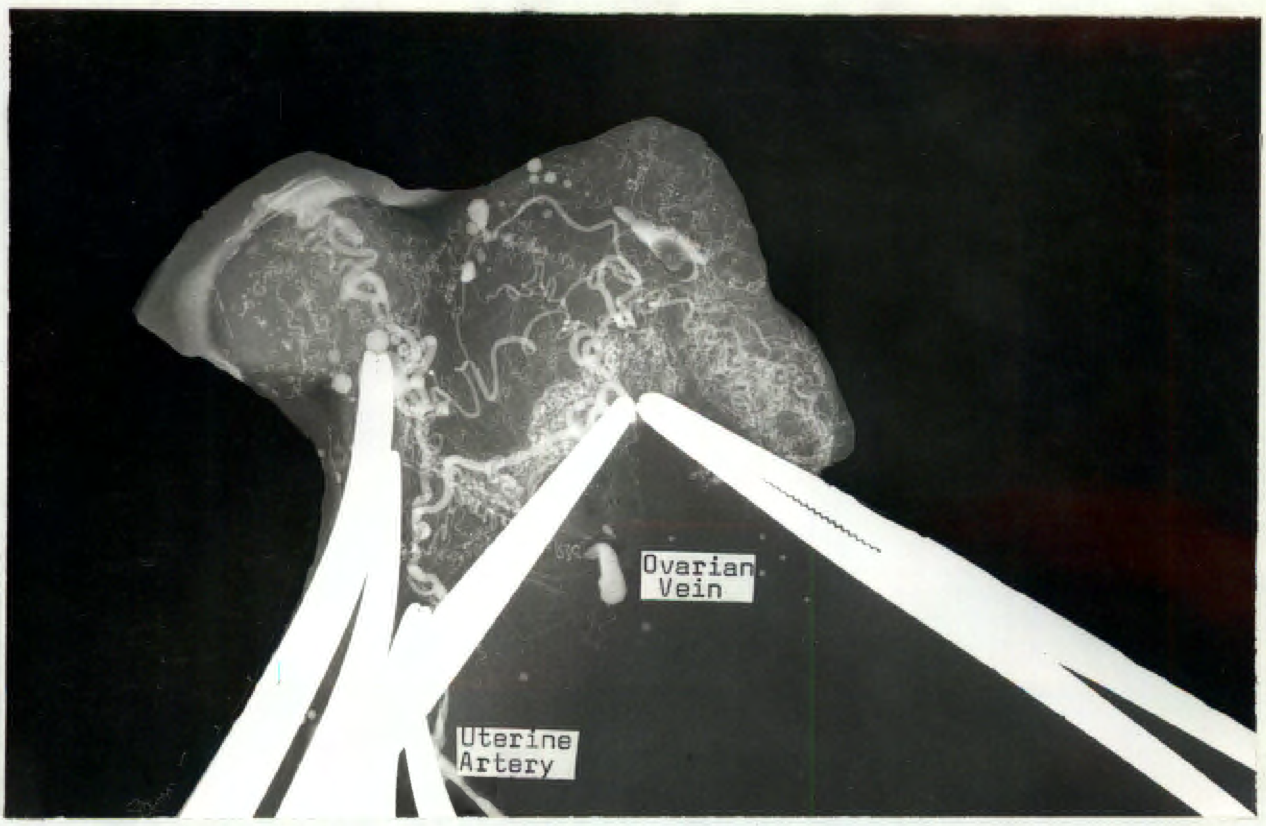

Fig. 21c. Late phase arteriogram of human left "tubocornual unit". (Note ovary clamped at hilum. Venous drainage of Fallopian tube via ovarian vein.)

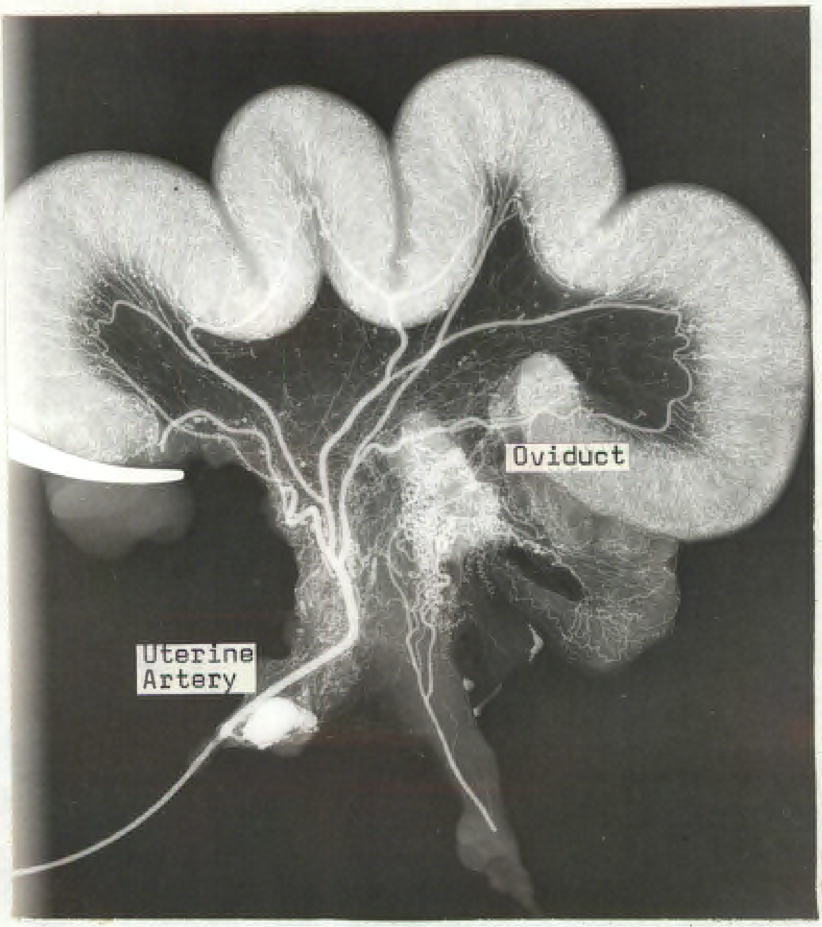

Fig. 22a. Early phase arteriogram of left "tubocornual unit" of pig.

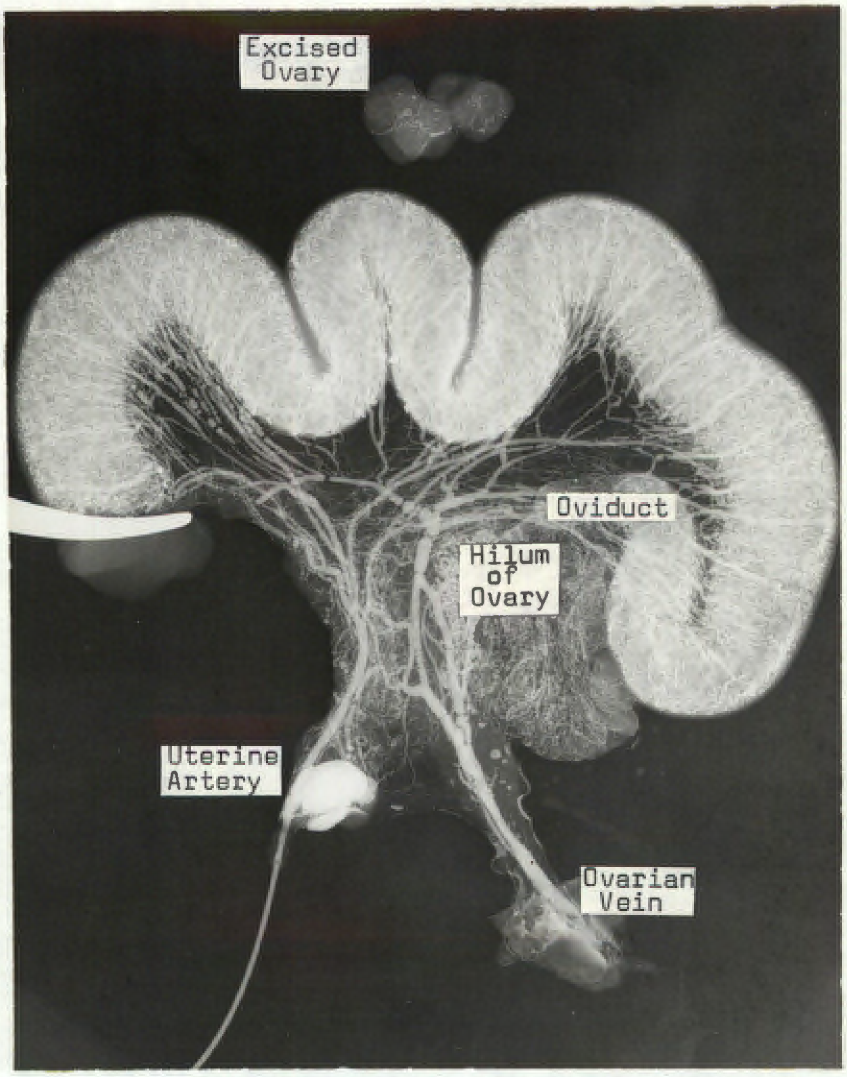

Fig. 22b. Late phase arteriogram of left "tubocornual unit of pig.
(Note ovarian hilum ligated, venous drainage via ovarian vein.)

CHAPTER EIGHT

DISCUSSION

1. INTRODUCTION

1. The Significance of Tubal Occlusion as a Cause of Infertility
2. Possible Methods of Improving the Results
3. The Inverse Relationship Between the Extent of Tubal Damage and the Subsequent Likelihood of Pregnancy after Tuboplasty
4. Methods of Previous Authors
5. The Importance of Tubal Physiology
6. Methods of Replacing Fallopian Tube Function
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CHAPTER EIGHT

DISCUSSION

1. INTRODUCTION

1. The Significance of Tubal Occlusion as a Cause of Infertility

Whilst major efforts are being made to curb the ever-increasing human population of the world, 6 - 17% of marriages are childless (Browne and McClure Browne, 1964; Jeffcoate, 1969). In most cases, such infertility is involuntary. These individuals constitute a significant proportion of the patients presenting to the contemporary gynaecologist. The misery and marital disharmony associated with this problem have been commented on by Solomons (1935), Green-Armytage (1937) and Greenhill (1956).

When the fertility of the male partner has been assessed as normal, the predominant fault found in the female is tubal occlusion (Rutherford, Lamborn and Banks, 1949; Siegler, 1960). This important cause of sterility occurs in 40 - 50 per cent of all patients presenting with the problem of female infertility (Özaras, 1968; Siegler, 1973) and is the most common barrier to child-bearing (Israel, 1967).

The results of surgery performed on the Fallopian tubes remain disappointing (Siegler, 1973). Such operations are subsequently followed by a low conception rate (Wood, Leeton and Taylor, 1971), but "there will be no improvement in the results of these operations unless some surgeons keep trying to improve the technique and the principles involved" (Grant, 1971).

Results of all types of procedures reviewed together with respect to the incidence of subsequent live births recorded are listed in TABLE 1X.

TABLE 1X. LIVE BIRTH RATES FOLLOWING ALL TYPES OF TUBAL SURGERY

Author	% of cases submitted to surgery
Schmitz (1932)	10.03
Solomons (1935)	7.6
Greenhill (1937)	4.4
Gepfert (1943)	3
* Rutherford, Lamborn & Banks (1949)	41.8
Siegler & Hellman (1956)	16.6
Greenhill (1956)	12.3
Martius (1959)	25
Palmer (1960)	22
* Moore-White (1960)	37.5
Mulligan (1966)	21
Swolin (1967)	28
Crane & Woodruff (1968)	10
Özaras (1968)	5.6
Grant (1971)	28
Boyd & Holt (1973)	10.6
* Horne et al. (1973)	38

* Term pregnancy rates > 35%

2. Possible Methods of Improving the Results

The three series (Horne et al., 1973; Moore-White, 1960; and Rutherford, Lamborn and Banks, 1949) reporting live birth rates over 35 per cent cover a span of 25 years. Although the general trend has been towards an improvement of results, these have been extremely variable.

More than half (23) of Rutherford, Lamborn and Bank's 43 cases (1949) had fimbrial occlusion or peritubal adhesions. The minimum of surgery was required and the best results were observed in those cases "where the least had to be done". They submitted their patients to intermittent hydrotubations from 2 to 3 days after surgery until pregnancy was achieved.

Moore-White (1960) operated on 69 carefully selected cases. The best results were obtained for the operation of salpingolysis which was followed by a 50 to 80 per cent success rate with respect to the subsequent incidence of live births. Her 31 per cent term delivery rate for the operation of tubal implantation is comparable to the figures of Johnson (1955), 30 per cent; Green-Armytage (1957), 36.1 per cent and Palmer (1960), 33 per cent. Moore-White (1960) advised plication of the round ligaments and occasionally shortening of the ovarian ligaments. She covered raw areas with an omental patch and poured at least half a pint of warm normal saline into the peritoneal cavity just before closure in the hope of minimising the risk of further adhesions.

Horne et al. (1973) used dexamethasone and promethazine in an effort to reduce the incidence of postoperative adhesions. Whilst these agents appear to have achieved the desired effect, most cases involved salpingolysis, fimbrioplasty or simple dilatation of the fimbriae of an otherwise normal tube (130 out of 240 cases). Shirodkar (1966) commented on the fact that where the fimbriae are present and are of normal length and character, 50 per cent of operations performed on such tubes should be followed by pregnancies.

Moore-White (1960) and Peel (1964) did not think that the use of polyethylene splints and hoods advocated by Castallo (1950), Hellman (1951) and Mulligan, Rock and Easterday (1953), or the use of chorio-amniotic membrane (Ten Berge and The Tik Lok, 1954) or bovine allantoic membrane (Gepfert, 1943) had altered the outcome of these procedures.

Hydrotubations were used by Rutherford, Lamborn and Banks (1949), Shirodkar (1961) and Grant and Robertson (1969).

Castallo and Wainer (1953) have commented on the use of prophylactic antibiotics.

All of these methods together with the use of cortico-steroids and antihistaminics (Horne et al. 1973) do not appear to have altered the outcome of a particular series of tuboplastic procedures significantly.

Many authors (Hellman, 1951; Greenhill, 1956; Moore-White, 1960; Shirodkar, 1961; Grant, 1971; and Siegler, 1973) feel that better figures are achieved by those experienced in tubal surgery, using finer instruments and meticulous methods, operating on highly selected cases.

3. The Inverse Relationship Between the Extent of Tubal Damage and the Subsequent Likelihood of Pregnancy after Tuboplasty

The most significant factor affecting the outcome of a particular operation appears to be the overall state of normality of the Fallopian tube. Better results are obtained when operations are performed on oviducts where the occlusion is a localised defect in an otherwise healthy organ.

The importance of the fimbriae of the Fallopian tube, together with its absolute length, and the state of health of its muscularis and mucosa, has been emphasised by many authors (Schmitz, 1932; Gepfert, 1939; Meigs, 1950; Green-Armytage, 1952; Greenhill, 1956; Moore-White, 1960; Peel, 1964; Shirodkar, 1966; Crane and Woodruff, 1968; Özaras, 1968; and Boyd and Holt, 1973).

Review of the literature regarding the prognosis for tuboplastic procedures performed on selected cases revealed that term delivery rates ranged from a very unfavourable 3 per cent to an apparently favourable 41.8 per cent (TABLE 1X). This relatively successful outcome is not observed very often and there is uniformity of opinion regarding the poor prognosis for the patient with marked hydrosalpinges (Gepfert, 1943; Pratt, Banner and Huang, 1956; and Green-Armytage, 1957). According to Gellhorn (1911) and Ten Berge and The Tik Lok (1954) the presence of extensive hydrosalpinges is a specific contra-indication to the performance of a tuboplastic procedure. Green-Armytage (1957) has commented on the very disappointing outcome when operations are performed on patients who have easily palpable tubo-uterine pathology.

At Groote Schuur Hospital, Cape Town, the majority of patients attending the Infertility Clinic have marked hydrosalpinges or easily palpable tubo-ovarian pathology. The local prevalence of these cases was previously observed by Resnick (1962). The failure to find an authentic report of a single pregnancy when reviewing the folders of 200 such patients submitted to tubal surgery during the years 1968 to 1972, is not surprising. These operations have been performed at the patients' request and in most cases appear to have resulted only in pacifying marital disharmony.

The virtually hopeless prognosis of the patient with gross destruction of her Fallopian tubes has been recognised for many decades. These women form a significant group of any infertility practice. Whilst their numbers are not specified in the literature, it is reasonable to assume that they constitute many of the patients excluded the opportunity of undergoing reparative tuboplastic procedures when other non-tubal factors are found to be favourable.

Their non-selection for current methods of tubal surgery is commendable, but the attempts to resolve their somewhat insurmountable problem must continue.

4. Methods of Previous Authors

The operation described by Estes in which the cut surface of the ovary is implanted in direct continuity with the uterine cavity excluded the Fallopian tube completely. Estes and Heitmeyer (1934) reported a term pregnancy rate of 4 per cent with this procedure, but Rutherford, Lamborn and Banks (1949); Meigs (1950); and Palmer (1960) did not observe a single conception following this operation.

Cross and Erskine (1956) and Grant (1971) attempted to replace the Fallopian tube by constructing a peritoneal tunnel between the ovary and the endometrial cavity. No pregnancies resulted. Substitution of the oviduct by the insertion of a segment of ileum (Kucharezuk and Greene, 1956; Carey et al., 1958), vein and artery transplants (Davids and Bellwin, 1954; Schein and Ferreira, 1956) or the vermiform appendix (O'Neill, 1966) were similarly unproductive.

In 1971, Wood, Leeton and Taylor described a sophisticated silastic tube and reported its use in a patient for 5 months with no conception resulting.

5. The Importance of Tubal Physiology

The procedures described have either excluded the oviduct (Estes' operation) or they have regarded it as a relatively simple conduit.

The Fallopian tube is a very specialised organ, and each anatomical part of this structure has an intricate and highly specific function. Reference to the findings of many workers, as reviewed by Hafez and Blandau (1969), Woodruff and Pauerstein (1969), Mastroianni (1970) and Thibault (1972), dispels any doubt as to the complex physiology of the oviduct. This is summarised in CHAPTER ONE 3.

Its functions are a necessity for the process of conception and subsequent development of the morula and blastocyst. Any attempt to replace the oviduct must recognise these facts.

6. Methods of Replacing Fallopian Tube Function

There are two potential methods of replacing the damaged Fallopian tube. The first approach is to utilise the complex knowledge of tubal physiology and to attempt to reproduce it in the laboratory. In vitro fertilisation and maturation of human oocytes was reported by Edwards, Bavister and Steptoe in 1969. This technique necessitates obtaining ova from the patient and fertilising them in the laboratory with her husband's spermatozoa. Once cleavage has been completed, the blastocyst may be implanted into her uterus. The pregnancy rate achieved after multiple attempts by many workers is virtually zero. (Bevis (1974) has reported 3 live births resulting from this technique in the lay press.) In addition, the quality of life produced under totally artificial conditions at such a sensitive stage of development remains questionable.

Another avenue requiring further exploration is the possibility of homograft transplantation of a healthy Fallopian tube to replace its severely damaged counterpart. This idea is not new. Ritala (1946) performed 5 non-vascularised homograft transplants of the oviduct in human females. Although patency was subsequently demonstrated in all of his cases by means of hysterosalpingograms, no pregnancies resulted and their postoperative course was uneventful. It is unlikely that the transplanted oviducts could have survived the ischaemic insult imposed on them by this procedure which did not include an attempt to restore their blood supply.

In recent years, Peel (1964) and Grant (1971) have commented on the concept of homograft tubal transplantation. To translate this idea into practical feasibility, certain foreseeable problems had to be resolved. These included the development of a relatively simple and safe technique and those related to donor selection, graft rejection and the complications of immunosuppressive therapy, which according to Alexander and Good (1970), have constituted the "backbone of the causes for failure" of transplantation procedures.

As the uterus is not an immunologically privileged site (Truta et al., 1969; Wingate et al., 1970; Scott, Pitkin and Yannone, 1971; Beer and Billingham, 1974), the problem of rejection would be encountered. In addition, ethical, legal and endocrine difficulties would have to be solved.

The purpose of this study was to attempt to solve the initial problems of technical feasibility, a prerequisite before embarking on subsequent research.

7. Previous Gynaecological Transplants

In 1964, Zhordania and Gotsiridze recorded a term pregnancy in one of five ewes where autotransplantation of a portion of their Fallopian tubes had been performed. Omentum had been used to revascularise the segment of tube thus transplanted. According to Eraslan et al. (1966)

restoration of vascular continuity is essential if a consistently viable and fully functional organ is to be obtained following transplantation. His group, together with that of Chiapponi et al. (1971), both recorded pregnancies following total autotransplantation of the uterus together with both its Fallopian tubes and ovaries in the dog. Vascular anastomoses were performed at the level of the internal and common iliac arteries and veins.

Truta et al. (1969) reported that conception had followed autotransplantation of the uterus with both adnexa. His series of homograft transplantation of these organs together with that reported by Wingate et al. (1970) were complicated by rejection in all cases surviving the initial postoperative phase. In these latter two series, dogs were the experimental animals employed, and both groups chose to perform their arterial and venous anastomoses at the aorta and vena cava respectively.

In 1971, Scott, Pitkin and Yannone reported their experience in rhesus monkeys with transplantation of the uterine fundus together with the Fallopian tubes. A subtotal hysterectomy and bilateral salpingectomy were performed. This donor specimen was wrapped in the omentum of the recipient in an effort to revascularise the graft. No pregnancies were observed over a course of 10 months "probably because of tubal occlusion". An adequate blood supply appeared to have been developed but the homografted uteri were rejected within 3 weeks.

In 1974, Winston and McClure Browne reported pregnancies following vascularised tubo-ovarian autotransplantations completed in rabbits with the aid of an operating microscope. Except for the safety of this method described by these workers who re-anastomosed the uterine artery and its corresponding vein in their tubo-ovarian transplants, none of the abovementioned techniques are simple nor relatively safe for human application.

The potential hazards of the other techniques where vascular surgery was performed on the aorta, vena cava or iliac vessels could not be justified for an operation designed to restore a patient's fertility.

The method of Winston and McClure Browne (1974) would appear to be limited by access to an operating microscope. Furthermore, serious ethical objections may be raised against homograft transplantation of germinal epithelium in the human.

It is important to realise that in all of these studies where pregnancies have been recorded, the ovary has never been separated from its ipsilateral Fallopian tube.

Regarding the concept of uterine transplantation, the potential danger of total rejection of this organ, especially during a subsequent pregnancy, must surely be greater than that of rejection of the transplanted Fallopian tube on its own.

None of the abovementioned procedures aimed at providing an answer to the most common human gynaecological transplantation problem. This would appear to be the development of a relatively simple and safe technique enabling vascularised homograft transplantation of the Fallopian tube alone. The research carried out was specifically designed to investigate this possibility.

2. MATERIAL AND METHODS

1. Selection of an Experimental Animal

The ideal experimental subject for this research project would have been an animal whose pelvic anatomy and reproductive physiology closely resembled that of the human female. In considering primates, the local baboon (papio ursinus) was excluded after preliminary dissection had revealed that it was not anatomically suitable because the calibre of its uterine and ovarian vessels would necessitate use of an operating microscope. This type of apparatus was not available. These animals are, in addition, difficult to obtain and to breed in captivity.

A personal appraisal of the pelvic anatomy of the rat, guinea pig, rabbit and dog had also shown that they were similarly unsuitable. It was clear that a larger type of animal, e.g. the ewe or the pig would have to be used. During 1972, when this project was commenced, it was not possible to consider sheep, as there were no facilities for their accommodation or maintenance. The availability of the pig, together with an offer of accommodation for their pre- and post-operative care, made the choice of this animal obligatory. Preliminary dissections of the internal genitalia of this species revealed that the diameter of their pelvic vessels were comparable to those in the human female.

The relatively benign rejection response of the pig to vascularised allografts (Perper, Bowersox and Van Gorder, 1971; Terblanche et al. 1973) might also be advantageous for a project aimed primarily at assessing the technical feasibility of a transplant operation.

2. Problems with the Pig

When this study was commenced, only limited accommodation was available for the pigs. These animals were kept in temporary sties whilst the building of a new Animal House was in progress. Only 2 sties were available and this meant that no animal could be kept at the Medical School for longer than 14 days. The long-term survivors were then transported to a farm 25 miles from the Animal House where sties were available for their further care.

Under these circumstances, it was difficult to keep a close watch over the animals as they were not accessible to daily scrutiny.

The animals were purchased every 2 weeks in batches of 6 and the limited accommodation did not allow a detailed study of their oestrus cycle.

They were observed to be "in oestrus" or "quiescent" when a particular operation was performed. This difficult situation did not allow procedures to be performed relative to the stage of their oestrus cycles. It would have been desirable to operate a few days prior to oestrus with a view to having the animal mated before the expected onset of rejection. In view of the situation described, such precision regarding the timing of operative procedures was unattainable.

Rowson (1962) has described the method and difficulties encountered in performing artificial insemination in the pig. This act requires an expert with access to adequate technical and laboratory assistance. There was no such individual available in the neighbourhood of Cape Town where there has never been a demand for this type of facility for this particular animal.

Whilst working with the pig, facts emerged which were relevant to the handling of this species in general and to the Fallopian tube transplant operation in particular.

Methods used on 20 - 40 kg gilts did not apply when the experimental animals were twice that size. Mature pigs were cumbersome, aggressive and extremely difficult to handle. Three able-bodied men were necessary to coerce them into a transport pen which did not allow the animals much freedom of movement. The beasts could then be anaesthetised with relative ease and minimal risk to the laboratory staff.

Holding the ear of a pig steady in order that an induction dose of thiopentone sodium could be administered intravenously was never an easy procedure. Use of a 35-cm horse laryngoscope was mandatory for visualising the vocal cords and epiglottis. The standard endotracheal tubes were lengthened an extra 10 - 12 cm for these large animals and intubation was always a difficult task. Rapid deaths due to the malignant hyperpyrexia syndrome as described by Harrison et al. (1969) were encountered during the course of this research project. The triggering agent was halothane. This agent, together with suxamethonium and chloroform, may all precipitate the condition (Harrison et al., 1969). Thus muscular relaxation was produced with diallyl-nortoxiferine (Alloferin) which was found to be an excellent means of paralysing pigs. Whilst some of the animals appeared to require exceptionally large doses (50 mg over 4 hours), these were always reversible with atropine and neostigmine.

3. Operative Procedure

A prerequisite to the performance of the detailed vascular dissection and subsequent suture of small vessels was the provision of adequate lighting facilities. This was achieved by using 6 coolspot lamps focused over the operating area, in addition to the mobile adjustable theatre lamp. Use of coolspot lamps did not cause desiccation of the tissues exposed during these prolonged procedures. The oculus loupe provided a 2-fold magnification of the operative site and was found to be an adequate aid facilitating vascular dissection and re-anastomosis. Jacobson (1967) described the difficulty in the adjustment of vision when going back and forth from the loupe to the normal eye-glass area. This observation was confirmed but use of an operating microscope as recommended by Jacobson (1967) was not possible. Such an apparatus is relatively costly and is not likely to be readily available in many hospitals throughout the world in the foreseeable future.

The need to perform vascular anastomoses deep within the pelvis of large pigs rendered these procedures particularly difficult and probably more tedious than the expected situation in the human.

The dissection of the donor "tubocornual unit" was always a lengthy and intricate procedure. This aspect of the transplantation operation demanded a great deal of patience and care. Whilst one was often tempted to traverse the smaller vessel of the broad ligament with a cutting diathermy knife (in order to shorten the length of the procedure), this was not done because it was essential that a water-tight specimen be obtained. The dissection, ligation and transection of every vessel in the broad ligament attached to the graft, provided adequate perfusion without leakage and subsequent haemostasis after the vascular connections of the transplanted specimen had been reconnected.

The excised tubocornual unit was infused with a solution of Plasmalyte B containing 50 g of glucose and 10 000 units of heparin per litre at 10° C. Perfusion with this fluid was used to cool the organ and slow down its metabolism, to wash out blood and to allow an assessment of perfusion of the whole structure. Whilst the solution used was probably adequate for such short-term organ preservation, it lacked the hyperbaric oxygenation and careful control of pH as described by Starzl and Marchioro (1968). Although balanced electrolyte solutions have been used in the past (Marshall, 1971), their lack of colloid osmotic agents was usually followed by oedema and a rising vascular resistance (Pegg and Farrant, 1967, 1968). While these complications were not observed, adequately buffered and oxygenated cryoprecipitated filtered plasma would probably have been a superior solution to have used (Marshall, 1971). Jacobson described his experience with the Castroviejo needle holders in 1967. This instrument was found to be a reliable and effective aid in the completion of small vessel anastomoses. While special blunt dissecting forceps were used by Sun Lee (Arnot et al., 1973),and Jacobson (1967) has commented on the superiority of jewellers' forceps, fine blunt iris forceps were considered adequate aids for completing the uterine arterial and ovarian venous anastomoses.

The attempts to resuture the ovarian vein in an end-to-end fashion were a total failure despite the fact that the vessel was transected at an angle as suggested by Jacobson (1967). This author used an interrupted suture technique assisted by an operating microscope.

The necessity to employ a vena-caval patch technique as adopted in the pig must be conceded to be a failure. Whilst proving to be a reliable means of affecting venous drainage, its inherent danger would render it unsuitable for use in the human female. Subsequent experience with the 'end-to-side' venous anastomosis, as performed on the ovarian veins within the pelvis of ewes provided an alternative,safer and reliable method of completing this part of the operation. This technique would be more suitable for application in a human Fallopian tube transplant operation.

The use of 4 stay sutures before inserting the continuous suture line facilitated distension of the anastomotic area and helped to prevent a purse-string effect at this site. This technique of avoiding stenosis of the anastomotic site was recommended by Foster and Dean (1973), and these authors used it for end-to-side arterial anastomoses. It is possible that slight stenosis of the vena-caval patch around the ovarian vein would not have affected its outflow, but nevertheless, use of this technique avoided the likelihood of this complication.

Sterile liquid paraffin was employed to lubricate the suture material. This facilitated passage of the arterialised silk through the vessel edges. Its anticoagulant properties (Choate, Just-Viera and Yeager, 1964) made it a suitable choice for this purpose.

The uterine arterial anastomosis was commenced by inserting 2 stay sutures 120° apart as described by De Klerk and Ploncard (1972).

While use of finer sutures of 9 - 0 and 10 - 0 monofilament nylon is recommended by various authors (Jacobson, 1967; De Klerk and Ploncard, 1972; and Arnot et al., 1973), it was not possible to insert their fine, soft needles through the thick, tough walls of the uterine arteries of the pig. Atraumatic silk (7 - 0) was used as originally described by Jacobson and Suarez in 1960. Other authors (Engler et al., 1959) have previously performed similar anastomoses on the femoral arteries of the dog which averages an external diameter of 3 mm, with 6 - 0 arterial silk.

Jacobson (1967), De Klerk and Ploncard

(1972) and Arnot et al., (1973) all state that either interrupted or continuous sutures may be employed in the anastomosis of small arteries. The tension of a continuous suture line "should only be enough to approximate the vessel ends" (De Klerk and Ploncard, 1972).

A continuous suture technique was adopted for application in this research programme. Whilst this method was associated with a high incidence of arterial thrombosis in an end-to-end anastomosis, it was far more reliable when used in a side-to-side anastomosis of porcine uterine arteries. It was totally efficacious when used in the uterine arterial anastomosis performed in a side-to-side manner in the Fallopian tube transplants completed in the sheep.

The long vascular pedicles required precise orientation before performance of the vascular anastomoses. This intricate process demanded patience and excessive care as it was otherwise extremely easy to miss a twist in the vessels when they were perfused with clear fluid.

The dosage of intravenous heparin administered (20 000 units) was empirical. Whilst dosages of 5 000 - 10 000 units would be considered adequate for human arterial surgery (De Weese, 1973; and Olcott and Blaisdell, 1973), Engler et al. (1959), working with dogs, employed larger doses equivalent to 20 000 units intravenously combined with 100, 000 units intramuscularly in a 75-kg animal. Although this type of dose prevented thrombosis, it was also associated with an incidence of massive and fatal haemorrhage. This complication was not encountered with the smaller dosages used in the pig transplant operations. The heparin in the recipient animal was not neutralised at the end of the procedure. Terblanche et al. (1968) reported that such neutralisation was unnecessary following hepatic transplantation in the pig. No untoward effects resulted. Heparin (10 000 units) was administered intramuscularly twice daily during the first 10 postoperative days. Whilst a similar regime has been shown to reduce the incidence of postoperative venous thrombosis (Joffe, Immelman and Louw, 1973), it is unlikely that this low dosage would have been adequate to affect the course of any subsequent arterial thrombosis.

The importance of preventing desiccation of transected vessels is well established (Engler et al., 1959; De Klerk and Ploncard, 1972). Heparinised saline was used for this purpose. Donaghy (1967) and Yasargil (1967) have commented on the use of procaine in micro-vascular surgery. This agent is a chemical vasodilator (Rich, 1973) and was applied to the arterial ends in an effort to reduce the vasoconstriction that invariably took place when vessels were handled or transected.

Low molecular weight Dextran (Choate, Just-Viera and Yeager, 1964; Kapur and Gulati, 1967; and Polishuk and Bercovici, 1971) saline (Moore-White, 1960;

Seitz et al., 1973) corticosteroids combined with anti-histamines (Horne et al., 1973; and Seitz et al., 1973) fibrinolysin and heparin (Knightly, Agostino and Clifton, 1962) have all been used to prevent intra-abdominal adhesions.

No particular agent appeared to have absolute advantages over the others. A mixture of heparinised saline combined with 2 g of chloromycetin was therefore used with the double purpose of reducing adhesions and preventing intra-abdominal infection.

Whilst the use of prophylactic antibiotics is contra-indicated in the immunosuppressed human transplantation subject (Evans, 1971), chloromycetin was administered to the pigs pre- and postoperatively. There was no direct evidence in this series, but the administration of this antibiotic appeared to reduce the incidence and magnitude of postoperative septic complications. As no blood counts were obtained, the possibility of this agent having caused bone marrow depression could not be ascertained

Triamcinolone acetonide has been shown to prolong the graft survival of rabbit skin allografts (Klaue, Jolley and Hinshaw, 1971). The incubation of the graft for 60 minutes within a solution of triamcinolone acetonide provided local immunosuppression of the graft without the risks of using systemic immunosuppression. The mean survival time of the grafts treated by Klaue, Jolley and Hinshaw (1971) in this manner was 22.5 days as opposed to

6.1 days in untreated controls.

The use of triamcinolone diacetate in the pig study was totally inadequate. The possibility of it having had any effect as an immunosuppressant is extremely unlikely because (a) the dosage used was only 1 mg/ml whereas the abovementioned workers used 40 mg/ml; and (b) this steroid was not perfused through the transplant specimen and was therefore not applied to all of the graft tissues.

3. EXPERIMENTS PERFORMED IN THE PIG

The type "A" homograft transplantations (group 1.a - TABLE 111) were performed because of the economic need to use a single animal as both a donor and recipient.

Once dissections were confined to the right side and the right ovary was removed together with the right oviduct, there was no ovary available to receive the fimbrial end of the donor oviduct on this side of the pelvis. It was therefore reasoned that the simplest way to use the same animal as a recipient was (a) to transplant the donor's oviduct, ovarian vein and artery back to the right side; and (b) to mobilise the fimbrial end of this organ to the intact contralateral left ovary.

Such a procedure was most unsuitable but was the only way of subsequently attempting a functional assessment of the transplanted oviduct.

The type "B" homografts (group 1.b - TABLE 111) were commenced as soon as provision of accommodation and financial support allowed use of one animal as a donor and another as a recipient for a single transplantation procedure.

This operation enabled one to place the donor right Fallopian tube in its orthotopic position alongside the recipient right ovary. The dissection of the recipient was thereby minimised so that fewer tissue planes were transected. Sterilisation of the contralateral side was completed by performing a left salpingo-oophorectomy. It was hoped that this manoeuvre would (a) ensure that the animal could only conceive via the transplanted oviduct; and (b) facilitate oestrus and ovulation from the remaining ovary on the transplanted side by it being the solitary end organ for gonadotrophic stimulation.

The autotransplants of the oviduct (group 2 - TABLE 1V) were performed as a necessary control. They allowed assessment of the merits of the technique developed, excluding the possible sequelae that might have arisen as part of a rejection response.

The tubo-ovarian autotransplants were performed in order to assess the adequacy of the blood supply provided to both of these structures by the single artery and vein.

4. REVIEW OF RESULTS AND SUBSEQUENT STUDIES

The most striking feature of this study was the high incidence of arterial thrombosis that followed the 3 groups of transplants performed in the pigs. Only 25 per cent of the uterine arterial anastomoses were patent at the subsequent laparotomy. While vascular thrombosis was a significant cause of mortality following the operation of uterine transplantation (Wingate et al., 1970; and Chiapponi et al., 1971), no deaths were directly attributable to this complication in this series. Wingate et al., (1970) reconstituted the arterial supply of their "utero-tubo-ovarian" homografts at the aorta. In the execution of their total uterine transplants, Chiapponi et al., (1971) performed their arterial anastomoses at the proximal part of the internal iliac vessels. The level of the uterine arterial anastomosis chosen in this study, together with that employed by Winston and McClure Browne (1974) would appear to be less hazardous with respect to the occurrence of this complication.

Postoperative haemorrhage has also been recorded as a significant cause of mortality following the operation of total uterine transplantation (Eraslan et al. 1966; Wingate et al. 1970). This complication did not occur in the 3 groups of Fallopian tubal transplants described in this thesis.

There was no comparable study of the incidence of uterine arterial thrombosis in large experimental animals. Occlusion of 75 per cent of the anastomoses performed was evidence of technical failure to complete this aspect of the procedure. The subsequent study comparing the technique of end-to-end with a side-to-side uterine arterial anastomosis, showed that the latter method was significantly superior. When assessed in a preliminary series of sheep autografts, it was totally efficacious. The higher patency rate observed when this technique was employed was probably due to (a) the decreased likelihood of constricting the much larger anastomosis with consequent increase in the flow of blood through the anastomosis; and (b) if vascular spasm was significant, the circular muscles of the vessel walls would cause relative dilatation of an anastomosis performed in the side-to-side manner.

No pregnancies were recorded in the pig study. This finding is not surprising because only 2 animals with viable transplanted oviducts and minimal abdominal and pelvic adhesions (group 1.a - No. 3; and group 1.b - No. 4) were inseminated over only 2 oestrus cycles. Once the pathological sequelae of transplanting the oviducts were appreciated, efforts to obtain pregnancies were abandoned. It was considered far more important to obtain an early assessment of the anatomical fate of the transplanted graft in order that the problems coincident with the operation could be fully appreciated. Conclusions regarding the overall technique and the choice of experimental animal could then be made at a relatively earlier stage of the research programme. Thus the group 2 and group 3 series (TABLES 1V and V) were sacrificed at a much earlier stage.

Fifty-seven per cent of the tubal transplantation operations (groups 1 and 2) were complicated by severe intrapelvic adhesions but only 21 per cent of these animals had marked abdominal adhesions. This discrepancy may well have been due to the instilled intra-abdominal solution accumulating on the inner aspect of the anterior abdominal wall for the animals were standing within 12 hours of the operation in most cases. There was no way in which their postoperative posture could have been controlled in order to concentrate the intra-abdominal fluid around their pelvic organs. Any significant beneficial effect of the intra-abdominal solution could not be substantiated as there were no control animals in whom this technique was not used. Furthermore, the most likely explanation would be that more extensive adhesions would be an expected finding within the pelvis which was the main operative site. The adhesions found were far in excess of those usually encountered in the human pelvis following gynaecological surgery.

Major adhesions associated with a large ventral hernia were responsible for the death of an animal due to a volvulus of bowel on the 64th postoperative day (group 1.a - Case No. 7). This was one of four deaths that followed the 3 groups of operations performed.

Disseminated sepsis originating in the transplanted structure was responsible for the deaths of 2 others (group 1.b - No. 7; and group 3 - No. 1). The fourth death due to pneumonia, in a case where there was no intra-abdominal or pelvic sepsis, on the 41st post-operative day, could not be directly attributed to this particular operative procedure.

Microscopic salpingitis was observed in 43 per cent of the homograft transplants (group 1), none of the tubal autografts (group 2) and all of the tubo-ovarian autotransplants (group 3). The higher incidence of this complication observed in the homografts (group 1) was most likely due to the more prolonged perfusion and extracorporeal handling which invariably took place with these operations. Furthermore, although clean , sterile towels and packs were applied, the same instruments were used for both animals and this practice must be severely criticised.

Operations in groups 2 and 3 were performed under identical conditions. Whilst the group 2 series appeared to have benefited from the more favourable anti-septic circumstances, the group 3 series was complicated by the most sepsis of all 3 groups. These tubo-ovarian autografts (group 3) were complicated by the most extensive necrosis and superimposed secondary infections. These complications were significantly more common in this series and probably reflect the gross inadequacy of blood supply when a single artery and vein were relied upon to perfuse the transplanted oviduct together with its accompanying ovary. This does not appear to be a complication in the rabbit (Winston and McClure Browne, 1974), possibly because the thinner, less muscular arterial wall may predispose to less active spasm on transection than that seen in the pig.

All animals appeared to continue their oestrus function after homograft transplantation of the oviduct. Histological examination of the ovaries showed functional tissue in all 14 homografts. Whilst it is conceded that this is an extremely primitive method of assessing normal ovarian function, it is unlikely that the recipient's ovaries were affected by the vascular manoeuvres inherent in the technique. The recipient's ovarian artery and vein were not disturbed in the homograft transplants performed (group 1) and therefore continued function of the residual gonads would be expected.

Patency of the cornual anastomosis was demonstrated in all cases. Whilst the cornu of the pig is not at all comparable to that of the human female, the fact that an anastomosis of the Fallopian tube itself is entirely avoided by siting the suture line at the cornu, would make it the logical site to choose for the re-anastomosis of the transplanted oviduct. Rejoining the transplant graft at this site would also facilitate total transplantation of every component of the Fallopian tube.

An interesting and surprising finding was the amount of viable tissue observed despite thrombosis of the uterine artery in most of the tubal transplantations performed. The viable tissue was invariably confined to the outer muscular and serosal surfaces of the transplanted oviducts. It is possible that these tissues were nourished by peritoneal fluid.

Other than the fact that only one of the 14 homograft transplantation operations showed definite histological evidence of rejection, no reliable comment can be made regarding the incidence of this complication in this series of homograft oviduct transplantations. Wingate et al. (1970) described the rejection response observed in their series of vascularised "uterotubo-ovarian homotransplantations" performed in dogs as follows: "There was a rapid and substantial increase in the size and weight of the organ system due to marked interstitial oedema of the tissues, accompanied in many cases by rupture of small vessels and extravasation of red blood cells. The inflammatory cell exudate consisted of a mixed population of neutrophil polymorphonuclear leukocytes, occasional plasma cells and monocytoid cells. These findings were uniform throughout the various parts of the transplanted organs". Although these authors also encountered a high incidence of intravascular thrombosis involving large and medium-sized vessels, they could not be certain whether this finding was due to the surgical procedure itself or a primary manifestation of rejection.

Scott, Pitkin and Yannone (1971) performed homograft transplants of the uterus together with the Fallopian tubes in monkeys and obtained revascularisation of the grafts by wrapping them in omentum. These workers described a similar rejection response and commented on the histological appearance of a progressive inflammatory mononuclear cell infiltration and marked oedema of all layers of the uterus. "Although rejection of the endometrium was more rapid than with the myometrium, gradually all layers of the uterine wall and Fallopian tube assumed a non-viable appearance and were replaced by a hyaline amorphous material".

The rejection response is generally much less severe in the pig (Herbertson, Millard and Ansell, 1971). Some authors have commented on its unique ability to handle vascularised allografts (Perper, Bowersox and Van Gorder, 1971; Terblanche et al., 1973). According to Herbertson (1973), the macroscopic and microscopic features of allografts may have an extremely variable range of appearance. Rejection may be a distinct intermittent process with phases of allergic injury alternating with periods of partial recovery. Furthermore, he states that this is most often seen when the antigenic disparity between donor and recipient is relatively slight and that the transplant may then survive for long periods despite occasional episodes of rejection. Herbertson (1973) also describes the unique situation of temporary allograft reaction which may follow liver transplantation in the pig. The short-lived allograft reaction may occur during the first month or so after transplantation but the recipient later becomes unresponsive to the graft and the reaction subsides completely. Terblanche et al. (1973) have stressed how this mild rejection response can be missed if biopsies are not taken during the second week following hepatic transplantation in the pig. These authors have also suggested that rejection may be less severe in the smaller percentage of renal allografts that survive transplantation in this animal.

The findings noted in this series of vascularised transplantations of the Fallopian tube are extremely difficult to interpret for many reasons.

The macroscopic features of the shrunken and fibrosed oviducts, whilst possibly a manifestation of a rejection response, were more likely to be a manifestation of progressive ischaemia coincident with the high percentage of uterine arterial thrombosis.

The changes observed were most probably due to technical failure because (a) there was no histological evidence of the rejection response within the vessels themselves; (b) the surviving viable tissues showed no disseminated mononuclear infiltration; and (c) a similar high incidence of primary thrombosis was recorded in the subsequent study comparing the 2 techniques of uterine arterial anastomosis.

Although primary thrombosis would render the grafts avascular and thus there would be no cellular infiltration, the absence of a disseminated cellular mononuclear infiltrate at the adjacent cornu which was invariably viable was not in keeping with a rejection response.

While a short-lived rejection response may have been missed because of the grafts not being biopsied during the second week post transplantation, such biopsy was not practical. Furthermore, the high incidence of salpingitis as evidenced by the appearance of organisms and more commonly many polymorphs within the lumen of the graft complicated the histological assessment further.

It is true that where the uterine arteries were patent in 3 vascularised homografts (group 1.a - Case Nos. 3 and 4; group 1.b - Case No. 4) there was no evidence of rejection. Only one case had definite macroscopic and microscopic evidence of this complication.(group 1.a - Case No. 1). These findings indicated that the rejection response was not a major handicap encountered when performing vascularised transplantations of the Fallopian tube in the pig.

Excluding the incidence of sepsis, the

pathology of the group 2 series of autotransplants was very similar to that seen in the homograft series. This observation is not surprising and correlates with the benign rejection response noted in the homograft operations. The most striking complication of all 3 series was the high incidence of arterial thrombosis.

The results of the subsequent study comparing an end-to-end with a terminal side-to-side arterial anastomosis (CHAPTER SEVEN 1) showed that the later technique was far more effective. A significantly lower incidence of arterial thrombosis occurred when the side-to-side method was employed. Use of interrupted sutures to complete an end-to-end anastomosis was not assessed. This method is preferred by Yasargil (1974) and its efficacy at the site of the uterine artery in the pig remains unknown. Utilisation of the uterine arterial side-to-side anastomosis, together with an ovarian vein end-to-side anastomosis was shown to be an extremely reliable means of transplanting a Fallopian tube in the ewe (CHAPTER SEVEN 2). The radiographic appearance of the dissected human hysterectomy specimen (CHAPTER SEVEN 3) confirmed that utilisation of the uterine arterial and ovarian venous vascular connections near the hilum of the ovary to obtain perfusion of the Fallopian tube, was comparable to the concept applied in the pig studies. Whilst the evidence is presented from only one case, it is not unreasonable to surmise that the application of this principle may also be feasible in the human female.

Although the application of this technique would necessitate sacrificing the ipsilateral ovary of the donor, it would give the operation the 2 attributes of simplicity and relative safety in the recipient.

5. PROPOSED TECHNIQUE FOR TRANSPLANTATION OF THE FALLOPIAN TUBE IN THE HUMAN FEMALE

In practical terms, the human recipient surgical procedure would merely entail dissection and exposure of the uterine artery at the level of the isthmus of the uterus. The ipsilateral ovarian vein would require division of a short section of its overlying peritoneal covering at a suitably chosen site near the brim of the pelvis. A section of the corresponding uterine cornu would be cored out with a reamer as currently performed in the operation of tubal implantation. Following the anastomosis of the donor ovarian vein to the recipient ovarian vein in an end-to-side manner, the donor uterine artery would be joined to the proximal end of the previously mobilised recipient uterine artery in a side-to-side fashion. The distal end of the recipient uterine artery would be ligated just beyond the anastomotic site. The donor cornu would then be re-implanted into its prepared site of the recipient cornu (Fig. 23). Whilst this suggested technique is purely speculative at present, its

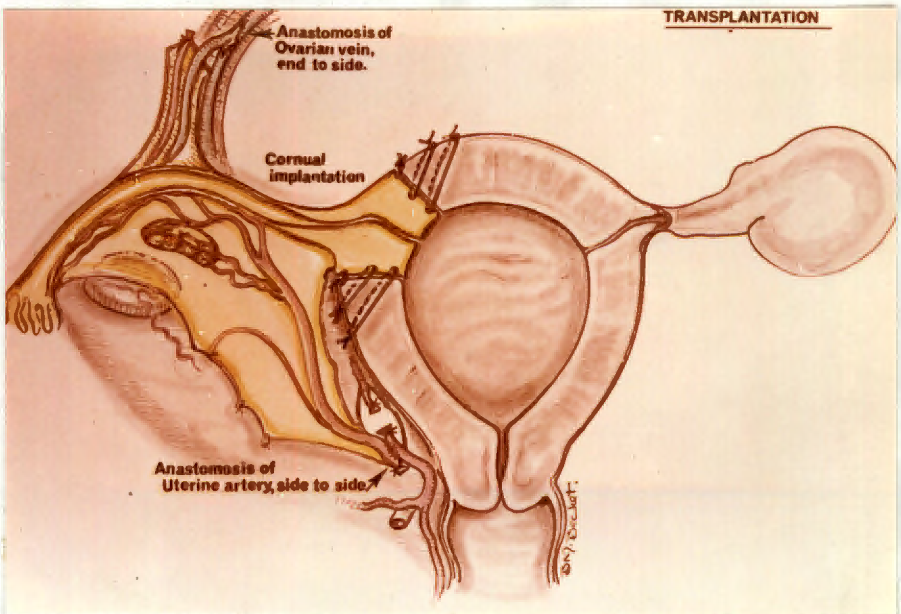

Fig. 23. Proposed technique for vascularised transplantation of the Fallopian tube in the human female.

efficacy was demonstrated in the sheep autografts. It would certainly give the operation of Fallopian tube transplantation simplicity and relative safety. Should complications ensue, although lesser measures could be employed, the most drastic surgical consequences envisaged would be a hysterectomy easily afforded by having sited the vascular anastomoses well within the range of the standard abdominal hysterectomy procedure.

CHAPTER NINE

SUMMARY AND CONCLUSIONS

1. SUMMARY

2. CONCLUSIONS

CHAPTER NINE

SUMMARY AND CONCLUSIONS

1. SUMMARY

Infertility resulting from occluded Fallopian tubes remains a significant gynaecological problem.

In view of the disappointing results that follow reparative surgery performed on extensively damaged oviducts, a study was undertaken to explore the technical feasibility of replacing these organs by performing vascularised Fallopian tube transplants.

Pigs were chosen for this study primarily because of their availability and because the size of their uterine and ovarian vessels appeared to be comparable to the same vessels in human females.

A preliminary series of experiments using 19 pigs resulted in the development of a technique for vascularised transplantation of the Fallopian tube.

This technique which used the uterine artery and the ovarian vein to vascularise the oviduct was considered to be a relatively simple method of effecting transplantation of this organ.

The technique was evaluated in pigs by performing 14 homografts and 5 autografts of the Fallopian tube, followed by 5 tubo-ovarian autografts.

After subsequent macroscopic and microscopic assessment, 3 of the 14 homografts were viable with proven vascular patency, all of their cornua were patent and only one case had definite evidence of rejection.

Only 2 of the 5 oviduct autografts were completely viable with patent vascular anastomoses, all of their cornua were patent and no sepsis of these transplanted grafts was observed.

Tubo-ovarian autotransplantation using a single artery and vein to vascularise the graft (as in the previous two series) was complicated by extensive necrosis and secondary infection following on thrombosis of the artery of the graft which occurred in 4 of the 5 cases. The residual tubo-ovarian transplant was almost completely viable. All of the transplanted cornua in this series were also patent.

Although no intra-operative deaths occurred whilst performing the 3 series of pig Fallopian tube transplants, 3 of the 4 post-operative deaths were caused by infection which originated in the graft in 2 cases. This complication must be recognised as a relatively small but distinct hazard of a Fallopian tube transplant operation. The 5th death was caused by a volvulus of bowel around a major adhesion within a large hernia and associated extensive peritonitis.

The major problems encountered in the pig were arterial thrombosis, extensive pelvic and abdominal adhesions, salpingitis and peritonitis.

Although this study was primarily aimed at assessing the anatomical and pathological fate of the transplanted Fallopian tubes, 11 of the 14 pigs submitted to homograft transplantation of the oviduct were subsequently mated with a boar during 2 oestrus cycles, but no pregnancies resulted.

As most pathological sequelae of the transplants were due to failure to maintain arterial patency of the grafts, a subsequent study was undertaken to compare two techniques of uterine arterial anastomosis. Thirty-two anastomoses were performed using a continuous suture technique.

The results of this study showed that terminal side-to-side uterine arterial anastomoses (50% vascular patency) were significantly more efficacious than end-to-end anastomoses of these vessels (20% vascular patency).

The original technique of transplantation was changed so that a uterine arterial side-to-side anastomosis was used in combination with an ovarian vein end-to-side anastomosis. (The previous method had employed a uterine arterial end-to-end anastomosis together with an ovarian vein vena-caval patch anastomosis to vascularise the graft.)

This modified technique was evaluated in a series of autotransplants of the Fallopian tube which were completed in ewes. Each of the 12 sheep operated on were subsequently found to have viable oviducts with patent arteries and veins.

A subsequent arteriographic study of a human Fallopian tube and cornu dissected from a single hysterectomy specimen, showed that its vascular anatomy and perfusion of the graft tissue using the uterine artery and the ovarian vein, were comparable to that seen when an arteriogram was performed on a similar specimen dissected from a pig.

A hypothetical technique of performing a vascularised transplantation of the Fallopian tube in the human female was described.

2. CONCLUSIONS

Transplantation of the Fallopian tube using the uterine artery and the ovarian vein to vascularise the graft is a technically feasible operation. This was demonstrated anatomically in only 3 of 14 homografts of the Fallopian tube performed in pigs, and subsequently in each of 12 heterotopic autografts of the oviduct carried out in ewes.

No pregnancies were recorded and the functional result of this operation remains inconclusive. Nevertheless, the anatomically viable successes are encouraging and indicate that the concept of homograft transplantation of the Fallopian tube aimed at seeking a cure for human females who have extensive disease of their occluded oviducts, should be submitted to further research.

The pig is not a suitable animal model for further experimentation in the field of vascularised Fallopian tube transplants. Besides being cumbersome, extremely difficult to handle and presenting additional technical problems, its vascular complications together with those of sepsis and extensive adhesion formation appear to be in excess of those observed in other available species.

In the pig, the low incidence of rejection of the homograft Fallopian tube transplants presented in this thesis was in keeping with previously observed benign rejection responses of this species to vascularised homografts at other sites. This observation in pigs must therefore be extrapolated with extreme caution regarding the expected more virulent rejection responses, that may subsequently be encountered when homograft Fallopian tube transplants are performed in other species.

Regarding suitable animal models, preliminary work using the ewe suggests that this animal will be a far more suitable experimental model for further research in this field.

The fact that all of the cornual anastomoses of the pig oviduct transplants were subsequently found to be patent, suggests that if human Fallopian tube transplants were to be performed by joining the contiguous cornu of the donor oviduct to the excised cornual site of the recipient uterus (as suggested in this thesis), a high incidence of cornual and tubal patency may result.

Whilst the pig uterine cornu is different to that of the human, sutures passing through the cornu of the donor specimen in the human would avoid direct trauma to the lumen of the Fallopian tube completely. Furthermore, this site of anastomosis of the transplanted Fallopian tube would facilitate transplantation of every anatomical component of this organ.

If the proposed technique of performing transplants of the Fallopian tube in human females was ever proved to be a reliable operation for the cure of certain cases of infertility, it would have the highly desirable characteristic of being relatively simple, requiring freely available and inexpensive surgical equipment, and it could therefore be performed in many centres.

CHAPTER TEN

PROPOSED FURTHER

STUDIES

CHAPTER TEN

PROPOSED FURTHER STUDIES

The ewes submitted to the operation of heterotopic (left-to-right) autotransplantation of their Fallopian tubes (CHAPTER SEVEN 3) must be mated when their oestrus cycles return. If pregnancies are observed, this experiment would prove that, excluding rejection, transplantation of the Fallopian tube alone to a heterotopic site and a foreign ovary (using the method described in this thesis) may be followed by normal conception and nidation. Whilst pregnancies have been noted when the Fallopian tube is transplanted together with its ipsilateral ovary, there appears to be no documentation in the literature of a pregnancy following transplantation of the Fallopian tubes alone to a heterotopic site and a foreign ovary.

Until pregnancies are observed in these specific circumstances, the concept of transplanting the Fallopian tube alone, as a potential method of curing infertility caused by extensively damaged oviducts, must remain suspect.

If pregnancies are observed, a series of non-immunosuppressed Fallopian tube homografts should be performed in ewes. These grafts should be removed at 2- to 3-day intervals and submitted to macroscopic and microscopic examination in order that the rejection response at this site may be more thoroughly understood.

If rejection is observed (a likely finding), then bearing in mind the possibility of performing this operation in humans where the simplest and safest techniques of immunosuppression will have to be employed, the following further experiments are proposed:

A series of sheep Fallopian tube homograft transplants should be carried out, and the operations timed in such a manner that attempts at conception could be undertaken prior to the occurrence of extensive rejection. It is just possible that nidation may be successfully completed prior to rejection resulting in functional destruction of the graft. This type of protocol would be acceptable for a human Fallopian tube transplant operation as it would avoid the use of immunosuppressive therapy.

If the abovementioned method is not feasible, a series of sheep Fallopian tube homograft transplants should be conducted using local techniques of immunosuppression, e.g. triamcinolone acetonide perfused through the graft. The effect of this local form of immunosuppressive therapy on grafted oviducts should then be evaluated by examining the grafts macroscopically and microscopically after removal at 2- to 3-day intervals. If local immunosuppressive techniques are shown to delay rejection for a suitable length of time, a further series of sheep Fallopian tube homograft transplants should be performed using local immunosuppressive therapy, and an effort should be made to obtain pregnancies in these animals.

If it is not possible to circumvent rejection with a local technique of immunosuppressive therapy applied to the graft, then a series of sheep Fallopian tube homograft transplants should be done using adequate doses of systemic immunosuppressive agents.

If normal term pregnancies are only achieved using systemic immunosuppression, then the overall concept of homograft transplantation of the Fallopian tubes in human females would become an extremely controversial matter in view of the multiple well-documented hazards of systemic immunosuppression previously observed in man. In particular, if a human recipient were to die because of sepsis during systemic immunosuppression administered for a non-life-saving operation with a definite risk of infection, this would be morally and ethically indefensible.

If suitable results are obtained during the abovementioned research programme and a relatively safe and reliable method of obtaining pregnancies from homograft Fallopian tube transplants is found, then studies of homograft transplants of the Fallopian tube in human females using methods researched in the animal laboratory would be justified. The Fallopian tube transplant operation would be clinically and ethically acceptable in most quarters if it were proved to be reliable safe and, in particular, possible without the use of systemic immunosuppression.

It is hoped that these further studies may yet result in the advent of a method of curing a significant number of infertile patients whose current prognosis remains somewhat hopeless.

APPENDIX 1

A sequential description of the experiments performed in the development of a technique for vascularised transplantation of the Fallopian tube in the pig.

CASE No. 1

Age of pig - 5 months   Operating time - $7\frac{1}{2}$ hours

PROCEDURE: Dissection and Assessment of Anatomy

Anaesthesia was induced with halothane, endotracheal intubation was performed and anaesthesia was maintained with a mixture of nitrous oxide, oxygen and halothane using a Bird positive pressure respirator.

The anterior abdominal wall was shaved, painted with tincture of iodine and sterile drapes were applied. The abdomen was opened through a right paramedian incision and the bowel withdrawn onto the draping towels to improve exposure.

In dissection, particular attention was paid to the relations and blood supply of the pelvic organs. This procedure occupied $7\frac{1}{2}$ hours. The bowel became progressively dilated, the animal progressively hypothermic and it died a few hours after the operation. Three litres of 10% Invert Sugar in Ringer's lactate and 400 ml of 4.2% sodium bicarbonate had been infused intravenously.

POINTS OF NOTE:

The paramedian incision was extremely vascular due to the multiple branches of vessels running anteriorly through the rectus abdominis. Prolonged exposure of the bowel with associated ileus appeared to cause refractory shock in the animal. A technique of packing off the bowel within the abdomen would have to be adopted.

The uterine arteries of the pig were extremely long and narrow. Their walls contained a thick layer of muscularis and adventitia. The lumen on transection was 0.5 - 1 mm in diameter. A fine instrument would have to be found to dilate the lumen.

The uterine vein was closely related to the ureter, and one of its major branches joined the ovarian vein before its entry into the vena cava. The predominant venous drainage of the uterus and its appendages was via the ovarian veins. These were extremely thin-walled. It was difficult to define their edges due to their relative transparency once they had been emptied of blood.

All pelvic veins of the pig were found to tear easily with minimal trauma, demanding extreme care in dissection.

CASE No. 2

Age of pig - 6 months   Operating time - $1\frac{1}{2}$ hours

PROCEDURE: Further Assessment of Pelvic Anatomy - The Problem of Oestrus

Anaesthesia was performed as in Case No. 1. Using a cutting diathermy knife, the abdomen was opened through a subumbilical midline incision. The bowel was packed off with two abdominal packing swabs.

FINDINGS:

This animal was found to be in maximal oestrus. The uterine cornua were 50 cm in length, 3 - 4 cm in diameter (cf 15 cm x 1.5 cm in Case No. 1), and very convoluted. Major dilatation and vascularity of the pelvic vessels precluded further surgery and the abdomen was closed.

POINTS OF NOTE:

The subumbilical midline incision was less vascular. The bowel could be adequately retracted with packing swabs and Bonney's and Deaver's retractors.

It would be advisable to avoid operating if the animal was assessed as being in mid-oestrus.

ASSESSMENT OF OESTRUS:

This was done very simply by noting whether the gilt had marked swelling of the vulva, and whether the animal stood still if the weight of one's two hands were applied to its hindquarters.

CASE No. 3

Age of pig - 3 months   Operating time - $1\frac{1}{2}$ hours

PROCEDURE: Assessment of Pelvic Anatomy - The Small Pelvic Vessels of the Young Pig

Anaesthesia was induced and maintained as described in the aforementioned two Cases.

Laparotomy was performed using a sub-umbilical midline incision.

FINDINGS:

The cornua measured $\pm$ 10 cm x 1 cm. The uterine arteries were $\pm$ 0.5 mm in external diameter.

POINTS OF NOTE:

While the younger animal was much easier to handle, it was clear that vascularised oviduct transplantation would be technically impossible without the use of an operating microscope.

Although oestrus would be a problem, larger animals would have to be used when available. This would add to the expense of the project (cost - ± R35 per large animal), but it was hoped that the chances of conception would also be higher in an animal whose oestrus cycle was well established.

CASE No. 4

Age of animal - $5\frac{1}{2}$ months   Operating time - nil

PROCEDURE: Induction of anaesthesia was performed as in the previous cases with halothane, nitrous oxide and oxygen.

FINDINGS:

Within minutes of inducing anaesthesia, the animal's limbs were observed to be rigid and in intense muscle spasm.

The pig's temperature rose rapidly and the animal died within 5 minutes of the induction. This was the first encounter with the malignant hyperpyrexia syndrome. This anaesthetically-triggered syndrome has a strong genetic factor and has been observed in 25 per cent of Landrace pigs used in the University of Cape Town Laboratories. Once this condition is established, the prognosis is very poor, death occurring within minutes in most cases. It is a response to various agents including halothane, scoline and chloroform (Harrison et al., 1969).

POINTS OF NOTE:

In considering other methods of anaesthesia, thiopentone sodium could be administered into an ear vein via a fine scalp-vein set but large animals were difficult to restrain for this. In view of the fact that the animals used were mainly of the cross Landrace/Large White variety, it was hoped that hyperpyrexia would not often occur.

CASE No. 5

Age of animal - $5\frac{1}{2}$ months   Operating time - $4\frac{1}{2}$ hours

PROCEDURE: Assessment of Pelvic Anatomy

Laparotomy was performed using a sub-umbilical midline incision. The bladder was distended to $\pm$ 20 x 12 cm and obstructed access to the uterus and oviducts. Multiple efforts to catheterise the bladder via the vulva and cloaca were unsuccessful. It was then emptied by bi-manual compression.

The uterine artery and vein were dissected out from the lateral aspect of the broad ligament. The ureter was closely related to the uterine artery on its medial aspect. Thus the uterine artery required mobilisation at its origin from the internal iliac artery in the median plane. The origin of the internal iliac artery was approached via the posterior peritoneum in the midline.

The peritoneal surfaces of the posterior pelvic wall and broad ligaments were extremely vascular. It was necessary to carefully coagulate each section of the peritoneum before incising it with the pair of scissors. This afforded adequate haemostasis. An atraugrip dissecting forceps and a pair of Kilner's plastic scissors were considered to be satisfactory for this type of delicate dissection. The uterine artery was incised with a pair of De Lee arteriotomy scissors and dilatation of its lumen to ± 1.2 mm was satisfactorily achieved with a Stummer fine grasping forceps. (Fig. 24).

Attempts to re-anastomose the uterine artery with 9 - 0 sutures proved that the fine needle would not penetrate the resilient muscularis and adventitia, and continued to bend at each attempt.

The uterine vein was held on two aspects with haemostatic forceps and transected. It was not possible to identify the edges of the ends of the vein and the procedure was then abandoned. The abdomen was closed.

<u>POINTS OF NOTE</u>:

Adequate haemostasis of the vascular peritoneum was achieved by coagulation prior to its incision. The pelvic vessels were best approached by an initial midline incision of the posterior peritoneum over their origin from the common iliac artery.

The Kilner's plastic scissors and atrau-grip vascular dissecting forceps were satisfactory instruments for the dissection of the vascular anatomy. The Stummer fine grasping forceps proved an excellent means of dilating the uterine artery when in spasm.

7 - 0 silk on a tapered needle was more suitable for penetrating the thickened muscularis and adventitia of the pelvic vessels in the pig and micro-vascular 9 - 0 and 10 - 0 sutures were discarded.

A means of defining the edges of the veins would have to be found. This was one of the most difficult technical problems encountered.

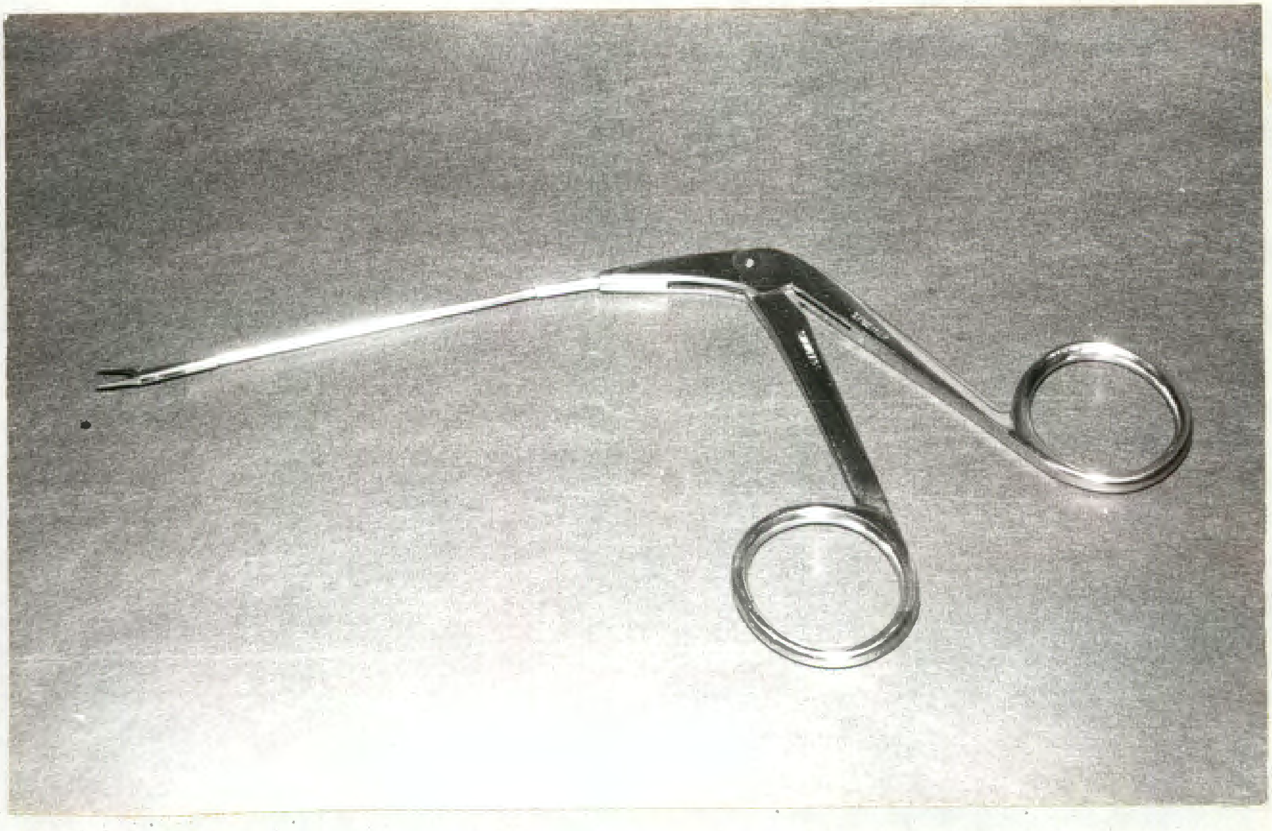

Fig. 24. The Stummer fine grasping forceps.

CASE No. 6

Age of animal - 5 months   Operating time - $4\frac{1}{2}$ hours

Stage of cycle - non-oestrus

PROPOSED EXPERIMENT : Attempt at Autotransplantation of Left Tubocornual Unit to Corresponding Site on Right Side of Uterus

In view of the knowledge and experience gained by the previous procedures, it was intended to attempt to dissect out the left distal cornu and Fallopian tube as an intact vascularised unit. This specimen would be perfused with a cooled electrolyte solution.

The right uterine artery and a suitable vein would then be dissected and prepared to receive the left Fallopian tube and its distal cornu. The right Fallopian tube and cornu would be excised.

Re-anastomosis of the artery, vein and cornu of the specimen would then complete the procedure.

Thus in principle, this would be a left-to-right vascularised autotransplantation of the oviduct.

PROCEDURE:

Laparotomy was performed using a subumbilical midline incision. The animal was given 10 000 units of intravenous heparin. The left distal cornu and ovary were elevated enabling careful inspection of their vascular arcades. The left uterine artery and the corresponding ovarian vein were identified and freed from the surrounding peritoneum. Ensuring that an intact arterial and venous circulation was preserved to provide an adequate blood supply for the distal part of the left cornu and its oviduct, all other branches were dissected out, ligated and transected. The left ovary was ligated at its hilum and excised. A vascularised tubocornual specimen was removed. Using a fine polythene catheter, this was perfused with a solution of Plasmalyte B containing 10 000 units of heparin and glucose 50 g/litre cooled to 10° C.

The whole specimen was almost cleared of its blood within seconds suggesting that the vascular dissection and estimation of sufficient arterial and venous arcades to the distal cornu and oviduct had been satisfactory. Whilst perfusion was maintained by an assistant, further dissection continued in the following manner:

The right uterine artery was exposed by

dividing the peritoneum covering it on the medial aspect of the broad ligament. The right distal cornu and oviduct were excised by successive clamping, transection and ligation of their corresponding pedicles of broad ligament and accompanying blood vessels.

A right lumbar vein was exposed by division of the posterior peritoneum. The right uterine artery was exposed and cleaned of adventitia and fascia at the site selected for anastomosis. This vessel was then clamped with a rubber-shod bulldog clamp and its distal end ligated.

The left tubocornual specimen was placed in the right iliac fossa and its arterial pedicle was held close to the right uterine arterial pedicle to enable the arterial anastomosis to be completed (Fig. 25).

An attempt was then made to perform a venous anastomosis. The prepared lumbar vein was clamped with a rubber-shod bulldog clamp, its distal end was ligated, and the vessel was transected. The vein of the transplant specimen was virtually transparent and its end could not be adequately defined. Despite multiple efforts, it was not possible to secure the ends of the two veins. The procedure was abandoned, hysterectomy was performed and the abdomen was closed.

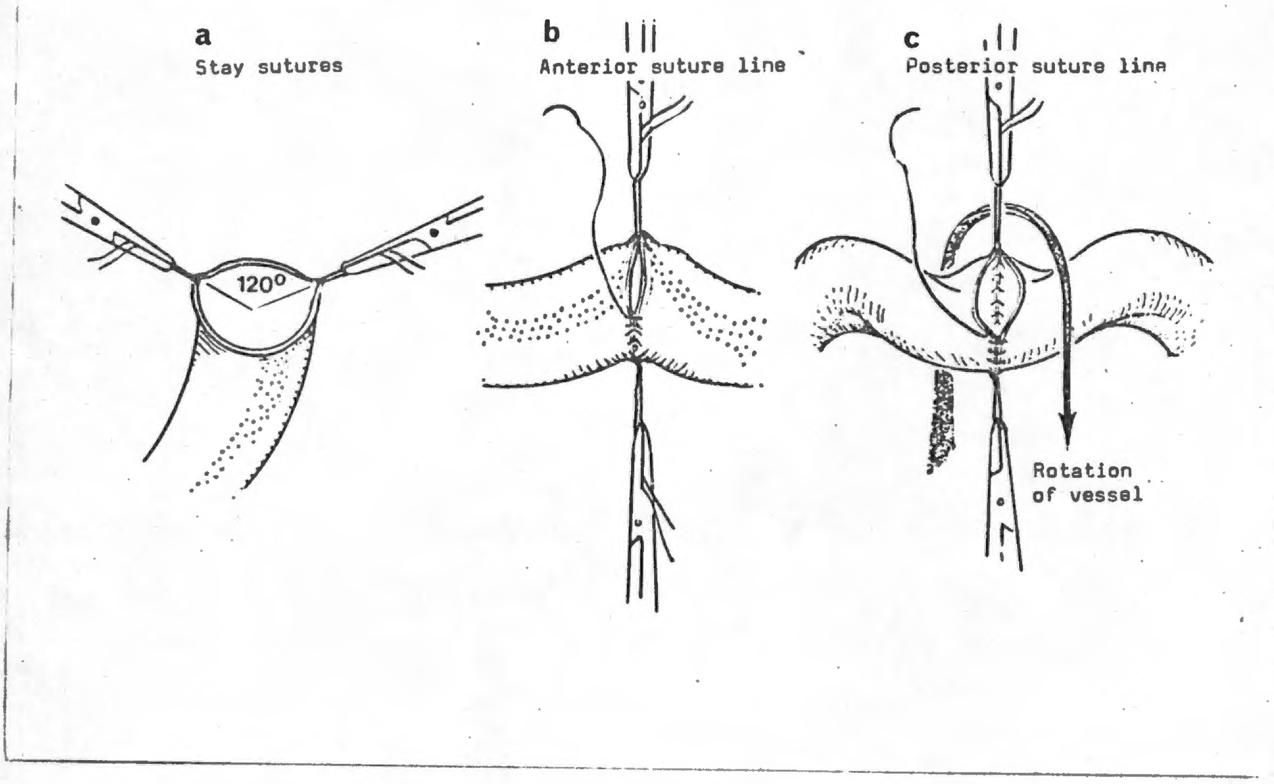

Fig. 25. Technique of completing arterial anastomosis.

POINTS OF NOTE:

Whilst tedious and time-consuming, the distal oviduct could be successfully dissected out with an accompanying artery and vein. Perfusion of the specimen appeared to be adequate as assessed clinically. Anastomosis of the uterine artery appeared to be satisfactory using the 7 - 0 greased suture material.

Venous isolation, definition and a method for its re-anastomosis was a major problem. Dissection of both sides of the broad ligament, together with the posterior peritoneum was extensive and caused concern because of the duration of the dissection and the hazards of sepsis and adhesion formation. However, the need to confine preliminary experimentation to one animal at a time would necessitate an extensive procedure if one was going to attempt autotransplantation of the distal cornu and oviduct from one side to another.

CASE No. 7

Age of animal - 6 months   Operative time - nil

Stage of cycle - quiescent

PROCEDURE: Death due to Malignant Hyperpyrexia Triggered by Halothane (cf Case No. 4).

Anaesthesia was induced with halothane, nitrous oxide and oxygen in the routine manner. The animal developed malignant hyperpyrexia and died within minutes of the induction.

CASE No. 8

Age of animal - $5\frac{1}{2}$ months   Operating time - $4\frac{1}{2}$ hours

Stage of cycle - quiescent

PROPOSED OPERATION:

Left-to-right vascularised autotransplantation of the distal cornu and oviduct through a modified Pfannenstiel incision.

PROCEDURE:

Anaesthesia was induced and maintained with a gaseous mixture of halothane, nitrous oxide and oxygen. The animal was given an intravenous injection of 10 000 units of heparin. The abdomen was opened with a modified Pfannenstiel incision. The bowel was packed off with bowel packs which provided excellent exposure of the pelvic organs. The left oviduct together with the distal cornu was elevated and an assessment was made of the vascular arcades. Dissection and removal of the left tubocornual unit were performed as described in Case No. 6. Particular care was taken with haemostasis.

The uterine artery was cannulated with a fine No. 17 gauge polythene arterial catheter, and the structure was perfused with a solution identical to that used in Case No. 6.

The right uterine artery was exposed and dissected free of surrounding tissues ± 2 cm above the right ureter. The adventitia and surrounding fascia were gently removed from the vessel at the site chosen for transection and anastomosis.

The right Fallopian tube and distal cornu were then excised. The superior haemorrhoidal vein was dissected free of surrounding structures and prepared for anastomosis to the ovarian vein of the transplant specimen.

The perfused specimen was then placed in the right iliac fossa. The two opposite sides of the haemorrhoidal vein were held on stay sutures of 7 - 0 silk and the vessel was then transected after clamping its distal end. The proximal end was held in a gentle rubber-shod bulldog clamp.

The two corresponding sides of the ovarian vein were found by squirting saline at the lumen of the vessel with a No. 21 gauge needle. The previous sutures were now passed through the ends of the donor vein and then ligated (Fig. 26). These provided two angle sutures, and their free ends were held with rubber-shod small mosquito forceps. The vessel wall was closed using the

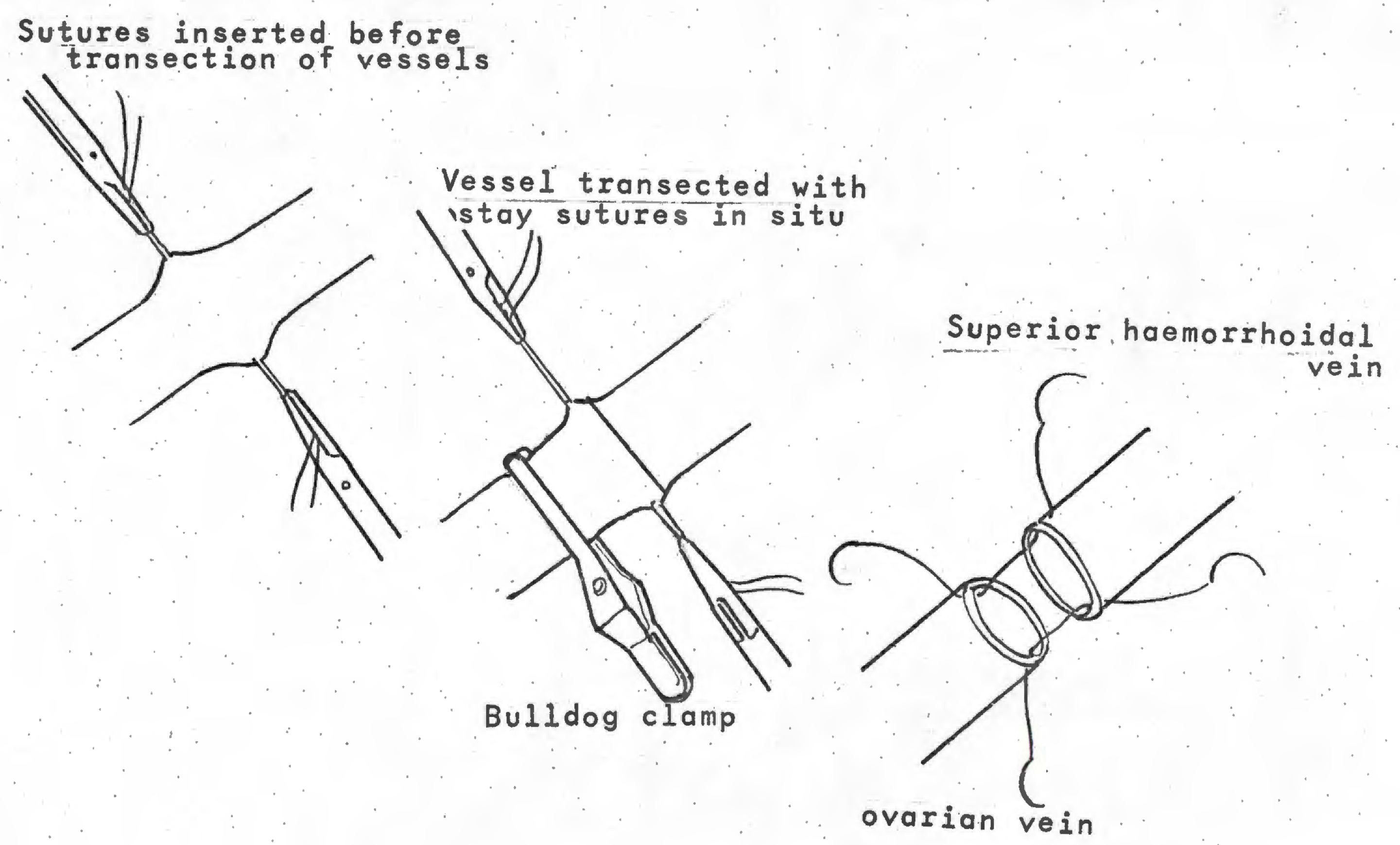

Fig. 26. Technique of inserting stay sutures prior to vascular transection (used in an attempt to facilitate completion of venous end-to-end anastomosis).

method described for the uterine artery in Case No. 6.

The right uterine artery was clamped with a soft rubber-shod bulldog clamp. Its distal side was ligated and the vessel was transected. The end of the left uterine artery was approximated with the end of the proximal part of the right uterine artery.

The anastomosis between the two ends of these vessels was performed as in Case No. 6 using 7 - 0 silk. The vascular clamps were then removed. The proximal ends of the vessels were gently squeezed a few times and vascular perfusion of the transplanted structure was observed.

The ends of the right cornu and the transplantation specimen were trimmed and sutured together in two layers with 6 - 0 polyglycolic acid sutures. The fimbrial end of the transplanted Fallopian tube was placed over the right ovary and sutured in place with two fine 7 - 0 silk sutures.

The stump of the left cornu was inverted and sutured in two layers with 4 - 0 silk sutures. The left ovary was excised and discarded.

The transplanted specimen appeared to be congested and there was doubt as to the adequacy of the blood flow through the venous anastomosis which appeared to be narrowed. Despite this observation, the transverse incision of the abdomen was closed in three layers: A continuous chromic 1 suture in the longitudinal plane through the peritoneum and extraperitoneal fat; interrupted chromic 1 sutures through the sheath in the transverse plane; and interrupted No. 1 silk mattress sutures through skin and subcutaneous fat in the transverse plane.

POSTOPERATIVE MANAGEMENT:

Five thousand units of heparin were administered intravenously to the animal after abdominal closure. One gram of chloromycetin was given intramuscularly.

FOLLOW-UP:

The animal appeared to be very sleepy for about 36 hours postoperatively. Later it developed extensive wound sepsis. The was followed by severe abdominal distension on the 13th postoperative day and the animal died on the 14th postoperative day.

POSTMORTEM FINDINGS:

Gross wound sepsis was noted and there

was extensive pelvic and generalised abdominal peritonitis. The transplanted structure together with the right ovary appeared to be infarcted and gangrenous. Both the artery and vein were thrombosed.

POINTS OF NOTE:

The transverse incision appeared to contribute to the severe wound sepsis. On closure of the abdomen there had been apparent venous congestion of the unit. Inadequate venous drainage could have caused infarction and subsequent necrosis of the transplanted structure. In subsequent operations a particular effort would be made to avoid narrowing of the anastomotic suture line of the vein.

CASE No. 9

Age of animal - 6 months   Operating time - $3\frac{1}{2}$ hours

Stage of cycle - quiescent

PROPOSED OPERATION:

Attempted left-to-right vascularised tubocornual autotransplantation.

Anaesthesia was induced and maintained as described in Case No. 8. The abdomen was opened with a subumbilical midline incision. The left oviduct and distal cornu together with accompanying ovary were dissected out and perfused as described in Case No.8. The left ovary was excised after ligation of its pedicle just proximal to the hilum. The right uterine artery was prepared as described in Case Nos. 6 and 8.

A major lumbar vein was dissected out on the right side of the lower lumbar vertebra and prepared for anastomosis to the left ovarian vein. Anastomoses of the vein, artery and cornu of the donor specimen from the left side of the uterus to the prepared sites on the right side of the pelvis were completed using the same techniques applied to Case No. 8. The only anatomical difference was the use of a large right lumbar vein for end-to-end anastomosis to the left ovarian vein. Particular care was taken to avoid tight suturing of this anastomosis. In addition, two fine 7 - 0 silk sutures were used to attach the fimbrial end of the grafted left oviduct to the right ovary.

On removal of the vascular clamps, the transplanted structure appeared to be well perfused. At this point, it was felt that the procedure had been technically satisfactory. The abdominal packs were removed, and the abdomen was closed. At the end of the procedure, it was noted that an extra litre of fluid had been rapidly infused accidentally, and the animal was in pulmonary oedema. This was confirmed clinically by auscultation of the chest, and by noting the frothy fluid pouring out of the endotracheal tube. Treatment was unsuccessful.

POINTS OF NOTE:

It was felt that the overall strategy of the transplantation procedure was proceeding favourably. One could now attempt to apply the technical knowledge gained to the concept of a homograft transplant procedure.

The anaesthetic assistant was instructed in the principles of intravenous fluid therapy and the importance of vigilant observation of drip rates. It was hoped that such a simple yet fatal accident would be avoided in any future experiment.

CASE NOS. 10 & 11

Age of animals - both 6 months   Operating time - $7\frac{1}{2}$ hrs

Stage of cycle - both quiescent

PROCEDURE: Attempted Homograft transplantation of a Vascularised Oviduct Together with the Distal Uterine Cornu.

The donor animal was anaesthetised in the routine manner. The right uterine cornu and oviduct were identified and elevated.

The right hypogastric artery was selected as suitable for perfusion and the redundant branches not directly responsible for perfusion of the transplant specimen were ligated and transected. This included ligation of the superior vesical and internal pudendal vessels which were doubly tied with 00 linen sutures (Fig. 27).

The right ovarian vein was similarly dissected free of surrounding structures and all branches including a major division from the right ureter were ligated and transected. The residual peritoneal folds supporting the right oviduct, cornu and ovary were incised with the diathermy knife.

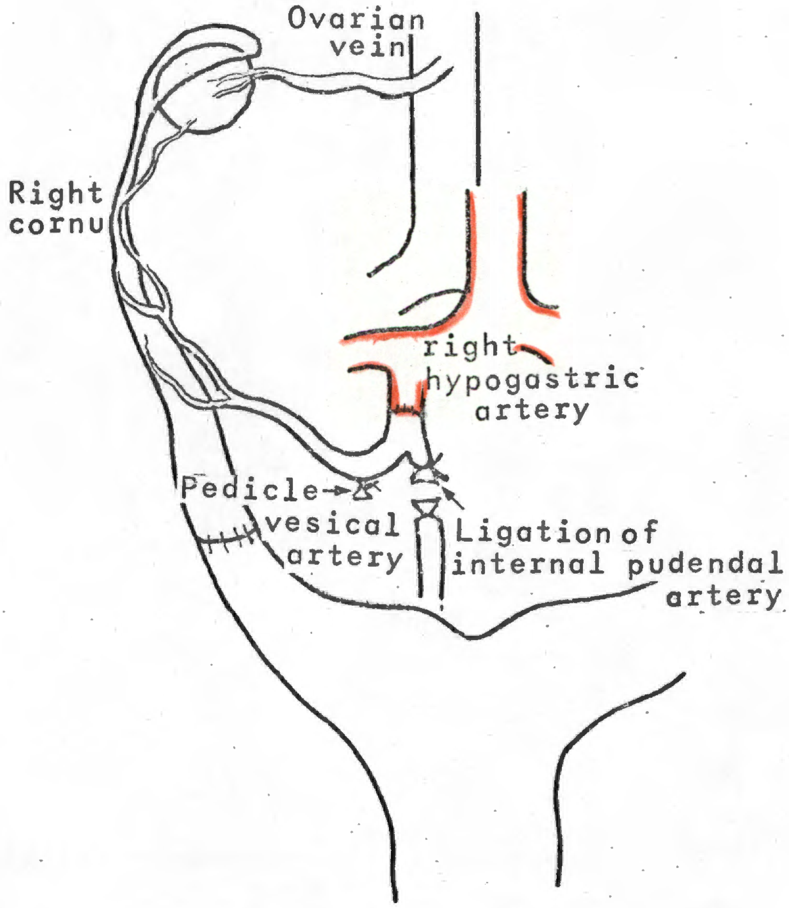

Fig. 27. Selection of right hypogastric artery as arterial pedicle of graft.

When the intact specimen had been successfully dissected out, perfusion was begun via a fine polythene catheter as described in previous chapters. By this time, the operation had been in progress for $3\frac{1}{2}$ hours.

The recipient was anaesthetised and the abdomen opened through a subumbilical midline incision. The right distal cornu and oviduct were dissected out as described above. However, in this Case, the uterine artery and a lumbar vein were prepared to receive the respective donor arterial and venous pedicles (Fig. 28).

Arterial anastomosis between the uterine artery of the recipient and the donor hypogastric artery was completed using the technique described previously (Cases 6,8,& 9). Extreme difficulty was encountered in defining the ends of the venous pedicles. Once defined, attempts were made to insert satisfactory angle sutures and to perform a venous anastomosis. The tissue was extremely fine, fragile and relatively transparent. Despite multiple attempts, completion of a venous anastomosis could not be achieved, and the procedure was thus abandoned. The transplanted tissue was removed, vascular pedicles were ligated and the abdomen was closed.

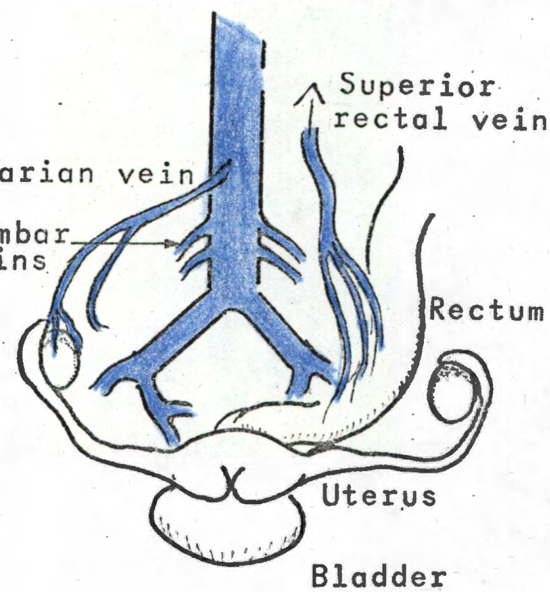

Fig. 28. Potential sites for venous anastomosis in the recipient.

POINTS OF NOTE:

Adequate dissection and removal of an intact specimen while prolonged and tedious, appeared to be satisfactory.

The fragility and relative transparency of the thin-walled pelvic veins of the pig constituted a major technical problem. In this regard, it was felt that stay sutures should be inserted into the vessel wall before transection.

The fact that the donor arteries were of a smaller diameter than expected had necessitated use of the hypogastric artery in this experiment. The diameter of this vessel was suitable for anastomosis to the transected uterine artery of the recipient. To allow for such anatomical aberrations, the precise technique for each case would have to be decided after inspection of the vessels.

CASE NOS. 12 & 13

Age of animal - 5½ and 6 months, Operating time - 4 hours respectively

Stage of cycle - both quiescent

PROPOSED OPERATION:

Attempted homograft transplantation of vascularised oviduct together with its distal uterine cornu.

Donor : The animal was given 10 000 units of heparin intravenously. After routine anaesthesia and dissection, the right tubocornual unit was removed and perfused as described in Case No. 10, except that on this occasion the uterine artery was transected at a point approximately one centimetre proximal to its division with the superior vesical artery.

Recipient : Anaesthesia was induced in the routine manner but the animal developed malignant hyperpyrexia and died. At this stage, it was decided to return the transplant specimen to the donor. Such an autotransplant procedure would provide an important technical exercise especially in regard to the venous anastomosis.

Stay sutures were inserted at 2 points on the two ends of the transected vein using 7 - 0 silk sutures. The short ends were held in rubber-shod mosquito forceps and the long ends were used to complete the anastomosis.

Taking particular care to avoid excessive tension in the suture lines, the anastomosis was completed. Arterial anastomosis was performed as described previously (Case No. 6).

On release of the vascular clamps, the tubocornual unit appeared to be well perfused, and the ends of the cornu were approximated with 6 - 0 polyglycolic acid sutures. At this stage, it was noted that the transplanted oviduct had become severely cyanosed. Inspection of the venous anastomosis revealed a slight narrowing of the lumen of the vessel at the suture line which caused inadequate venous drainage with resultant infarction of the transplanted oviduct.

The specimen was excised after application of suitable clamps. The 3 pedicles were ligated and the abdomen was closed. The animals died on the 7th day from peritonitis.

POINTS OF NOTE:

Halothane anaesthesia would be abandoned. A satisfactory method of anastomosing the ovarian vein would have to be found. The severe wound sepsis and peritonitis appeared to be related to unsatisfactory postoperative housing as other workers were experiencing similar problems with their research animals.

However, an attempt to prevent or minimise this complication would be made by:

(a) Use of prophylactic antibiotics administered to the animals intravenously during the operation, into the abdominal cavity prior to closure of the abdomen, and intramuscularly during the first 10 postoperative days.

(b) Sterile towels would be placed on the wound edges when inserting the skin retractors in an effort to reduce the transfer of pathogens from the skin edges.

(c) A subcuticular suture would be used to close the skin. This might reduce the introduction of organisms into the wound as compared to the routine type of mattress skin sutures.

CASE NOS. 14 & 15

Age of animals - both 6 months   Operating time - $6\frac{1}{2}$ hours

Stage of cycle - both quiescent

PROPOSED OPERATION:

Homograft transplantation of vascularised oviducts.

PROCEDURE:

The donor animal was kept in the transport cage to assist in restraining it and anaesthesia was induced with thiopentone sodium (2.5%) administered intravenously via an ear-vein. Muscular relaxation was achieved with diallyl-nortoxiferine 10 mg given intravenously. Intubation was effected and the anaesthetic was maintained with nitrous oxide and oxygen. Further doses of diallyl-nortoxiferine (2 - 5 mg) were administered when required during the procedure. Both animals were anticoagulated by administration of 10 000 units of heparin intravenously shortly after commencing the operation.

Case No. 14 (Donor)

The right oviduct together with a section of distal uterine cornu was dissected out as described in Case No. 10. The transplant specimen was obtained intact with the uterine artery and ovarian vein as described previously. The specimen was perfused in the routine manner.

Case No. 15 (Recipient)

The animal was anaesthetised and anaesthesia was maintained as described in Case No. 14. Dissection and removal of an intact vascularised right tubocornual unit was performed as described in Case No.14 and the specimen was perfused in a similar manner.

VENOUS TECHNIQUE:

In both cases, 7 - 0 sutures were inserted at 4 points on the ovarian vein before it was transected. Such transection was effected so that the stay sutures were abutting on the edges of the vessel when it had been cut.

Having made the initial transection as close to the distal (donor side) sutures as possible (Fig. 29a), the excess venous tissue was grasped with the vascular dissection forceps and a second transection line was effected as close to the proximal layer of stay sutures as possible (Fig. 29b).

Having removed both venous pedicles in the above manner, anastomosis of the veins was achieved by holding the 2 ends together and by inserting the stay sutures through the opposite venous edge (Fig. 29c).

Once 3 suitable stay sutures had been inserted and ligated, the remainder were gently withdrawn. Anastomosis was now completed by placing a row of continuous sutures around the vessel. Care was taken to ensure that the suture line was not constricted, and it was tied off when meeting with each stay suture.

The venous anastomosis was completed between the donor venous pedicle from Case No. 14 into Case No. 15 as described above. The arterial anastomosis was then performed between the end of the transected uterine arterial pedicle (from Case No. 14) and the reflected internal pudendal artery of Case No. 15. Silk sutures (7 - 0) were used, and the technical details were as described in Case No. 6.

The transplanted cornual end was then anastomosed to the recipient (Case No. 15) cornual stump

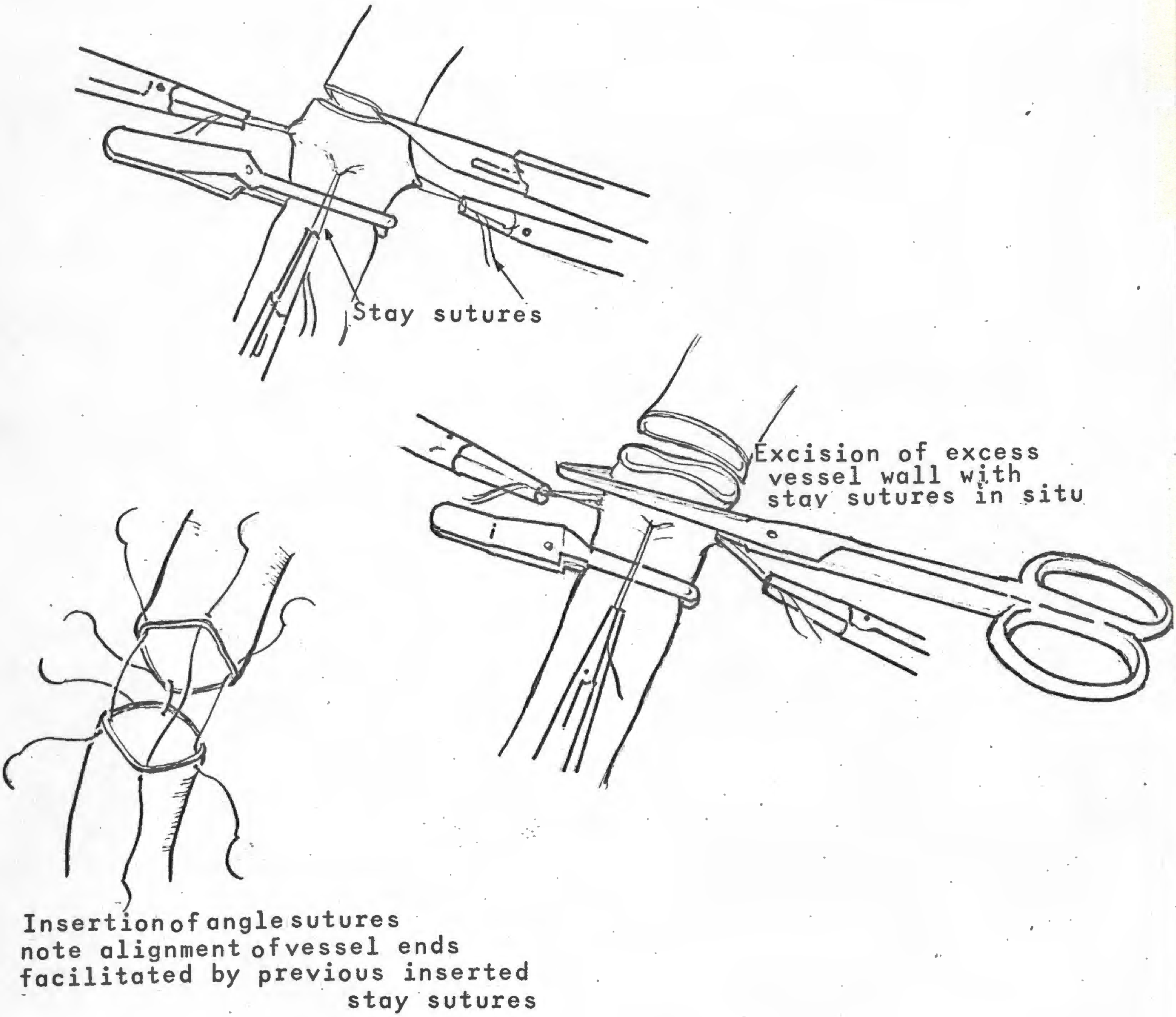

Fig. 29. Insertion of multiple stay sutures prior to transection of ovarian vein. (One of the methods used in the attempts to complete an ovarian vein end-to-end anastomosis.)

after fresh excision of the ends of these structures. This anastomosis was completed in 2 layers in the following manner :-

(a) An inner layer of continuous sutures was inserted using 6 - 0 polyglycolic acid, and an effort was made to exclude the endometrium from this suture line.

(b) Interrupted 3 - 0 polyglycolic acid sutures were then placed around the anastomosis. These were inserted through the outer serosal surface of the uterine cornu on each side and tended to cause slight inversion of the suture line (Fig. 30).

The free peritoneal edges beneath the cornua were approximated with a few interrupted 3 - 0 polyglycolic acid sutures. On release of the vascular clamps, sound pulsation of the artery was noted and at this stage, the transplanted structure appeared to be well perfused. Re-inspection of the vascular pedicles revealed that their length might still present problems which had not been anticipated. Such unsupported length tended to cause kinking of the vessels, particularly to the ovarian vein, which tended to kink at the suture line (Fig. 31).

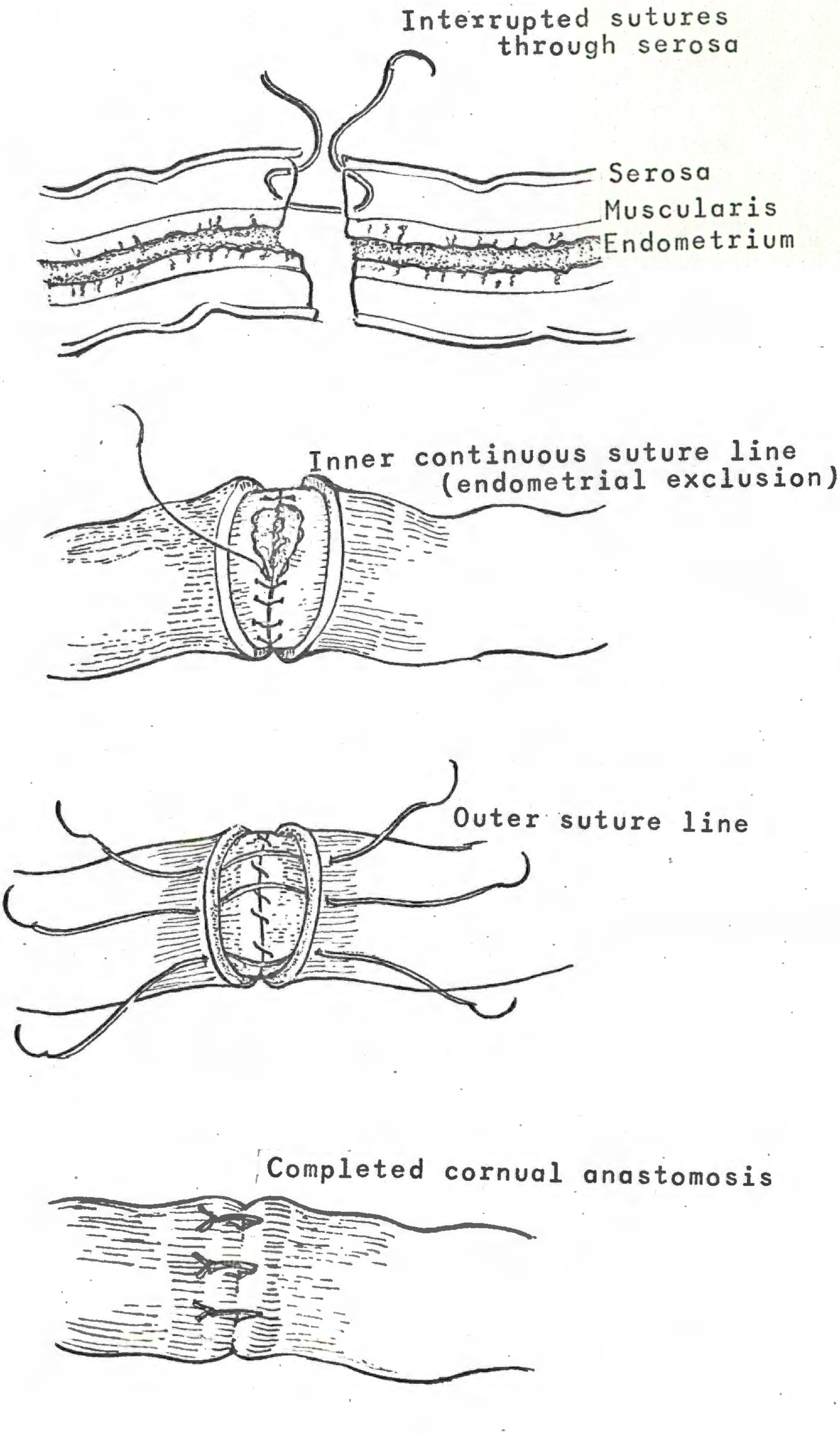

Fig. 30. Method of completing cornual anastomosis.

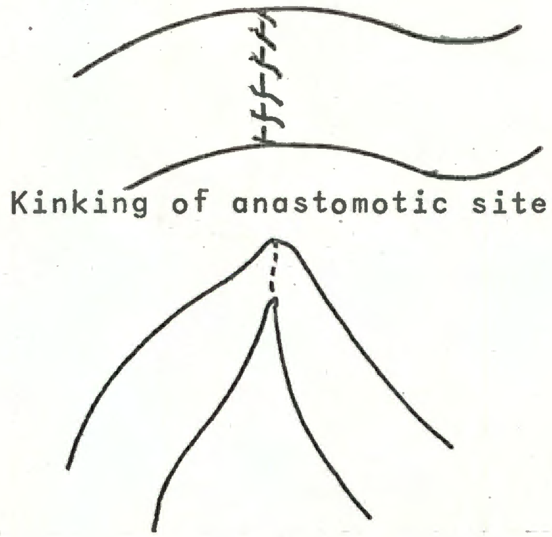

Fig. 31. Effect of long unsupported venous pedicle on vascular anastomosis.

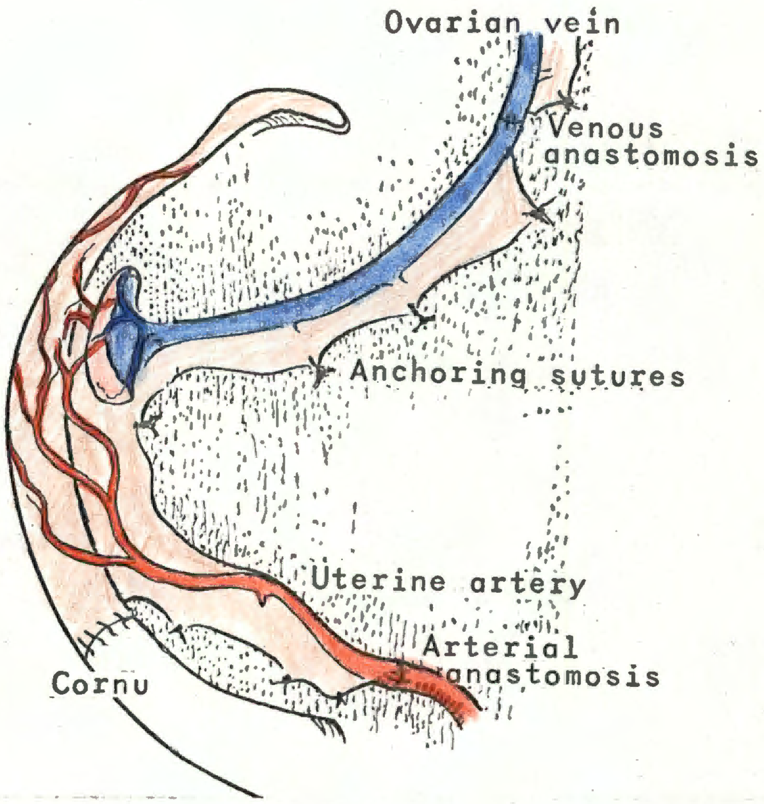

Fig. 32. Kinking of vascular anastomoses and pedicles prevented by insertion of anchoring sutures.

An effort to prevent this was made by inserting a few 5 - 0 chromic sutures between the adventitia and fascia surrounding the vessels and the posterior peritoneal wall as shown in Fig. 32. After insertion of these sutures, perfusion appeared to be adequate.

A solution of 5 000 units of heparin combined with 2 g of chloromycetin in a litre of normal saline was used to wash out the pelvis and lower abdomen. Approximately 400 ml were left in situ and the abdomen was closed.

Case No. 14

The perfused donor specimen of vascularised distal cornu and oviduct was transplanted into Case No. 14 in a manner similar to that described above. On completion of the vascular anastomosis, perfusion appeared adequate. A few supporting sutures for the vessels were also inserted as demonstrated in Fig. 32.

The abdomen was washed out with a solution of chloromycetin in heparinised saline. Approximately 400 ml of the solution was left in situ and the abdomen was closed. A further 5 000 units of heparin was administered to both animals intravenously after completing the operation. The muscular relaxation induced with diallyl-nortoxiferine was reversed by intravenous administration of 1.2 mg of atropine followed by 1.5 mg of neostigmine methyl sulphate. Spontaneous respiration was observed in both animals and they were transported to postoperative boxes with their endotracheal tubes in situ. These were removed a few hours later when the animals were fully conscious.

CASE No. 16

Age of animal - $5\frac{1}{2}$ months

Stage of cycle - quiescent

CASE No. 17

Age of animal - 6 months

Stage of cycle - early oestrus

Operating time - $6\frac{1}{2}$ hours

PROPOSED OPERATION:

Vascularised homograft transplantation of the right oviduct from Case No. 16 to Case No. 17 and vice versa.

PROCEDURE:

The anaesthetic technique, the dissection and perfusion of the right tubocornual unit were performed in a manner similar to that described in the previous experiment (Case Nos. 14 and 15).

Case No. 17

The donor specimen from Case No. 16 was successfully transplanted into Case No. 17. Venous, arterial and cornual anastomoses were performed in a manner similar to that described for Case No. 15. On release of the vascular clamps, the transplanted structure appeared to be well perfused but the arterial anastomosis was bleeding excessively at 2 sites which were sutured with interrupted 7 - 0 silk sutures. The pelvic peritoneal cavity was irrigated with the routine abdominal irrigation fluid as described previously and approximately 400 ml were left in situ. The abdomen was closed.

Case No. 16

The distal cornu and oviduct together with its vascular pedicles, which had been successfully dissected out from Case No. 17, was now transplanted into Case No. 16. The specimen had been adequately perfused in the routine manner.

Difficulty was encountered in completing the venous anastomosis. Despite excision and repetition of this suture line in a manner similar to that described in Case No. 15, the venous outflow was inadequate. The graft became progressively cyanosed and congested and it was therefore removed. The 3 major pedicles were ligated and the abdomen was closed.

FOLLOW-UP - CASE NOS. 14, 15 & 17:

These 3 cases were submitted to repeat laparotomy 2 days after the initial procedure to assess the fate of the transplanted structures.

FINDINGS:

In each case, the transplanted tubocornual unit was infarcted with obvious venous thrombosis beginning in the vicinity of the ovarian venous suture line. In Case No. 17, a distinct thrombus was also noted at the arterial anastomosis in addition to that observed in the ovarian vein. Such thrombosis at the arterial suture line was not seen in the other 2 cases. In view of the obvious macroscopic pathology, histological analysis was not required.

POINTS OF NOTE:

The new anaesthetic technique appeared to be satisfactory and avoided use of agents that could precipitate malignant hyperpyrexia. Such anaesthesia required the administration of repeated doses of diallyl-nortoxiferine, but this had been effectively reversed with suitable doses of atropine and neostigmine.

Using this technique, the animals regained consciousness very shortly after the completion of a procedure.

As no evidence of obvious wound sepsis or early peritonitis was seen in these 3 cases, the various manoeuvres used to prevent infection (cf Case No. 12) seemed successful.

The technique used for the venous anastomosis was not allowing adequate venous drainage. This had contributed to the 3 cases of venous thrombosis and infarction observed at laparotomy. If end-to-end anastomosis was anticipated in these extremely thin and unsupported structures, kinking or slight narrowing of the lumen at the suture line remained a major problem. This had occurred despite considerable care to prevent excessive tension in the venous suture line.

It was decided to attempt to dissect out the right ovarian vein up to its termination in the inferior vena cava. At this site, a patch of vena cava would be excised around the vein. This could be used for reanastomosis to the vena cava in the recipient and would avoid the likelikhood of anastomotic narrowing.

CASE No. 18

Age of animal - 6 months
Stage of cycle - quiescent

CASE No. 19

Age of animal - 6 months
Stage of cycle - quiescent

Operating time - 7 hours

PROPOSED OPERATION:

Homograft transplantation of vascularised right tubocornual unit using vena-caval patch technique.

PROCEDURE:

Anaesthesia was induced with intravenous thiopentone sodium and maintained with nitrous oxide, oxygen and diallyl-nortoxiferine.

The dissection of the right tubocornual unit was performed in a manner similar to that described in the previous 4 experiments with the following modifications applied to the venous technique:-

The ovarian vein was dissected up to its termination in the vena cava. There were many small branches but 3 main vessels, which appeared to drain the ureter, iliolumbar region and para-aortic lymph nodes, required identification and careful ligation (Fig. 33). It was also necessary to ligate and transect the ovarian artery and to remove the para-aortic lymph nodes in the region of the commencement of the vena cava for adequate exposure. Once all branches of the ovarian vein had been divided, and the vena cava had been cleared of surrounding fascia in the region of the ovarian vein, a vena-caval clamp was applied (Fig. 34) and a patch of vena cava was excised together with the termination of the right ovarian vein. This site of excision was then closed with a 6 - 0 silk suture. The transplant specimen was perfused in the routine manner.

For re-anastomosis of the vena-caval patch into the recipient, the vena cava was exposed approximately 4 cm above the previous site of entry of the ovarian vein. It was mobilised free from the aorta and its anterior surface was cleared of surrounding fascia. A vena-caval clamp was applied and a longitudinal incision made in the anterior surface of the vein (Fig. 35a). This was held open by 2 lateral 6 - 0 silk sutures which converted the longitudinal slit into a diamond-shaped opening (Fig. 35b).

The donor ovarian vein was then placed alongside the recipient vena-caval slit, and 4 double-armed 6 - 0 silk stay sutures were inserted and ligated (Fig. 35c).

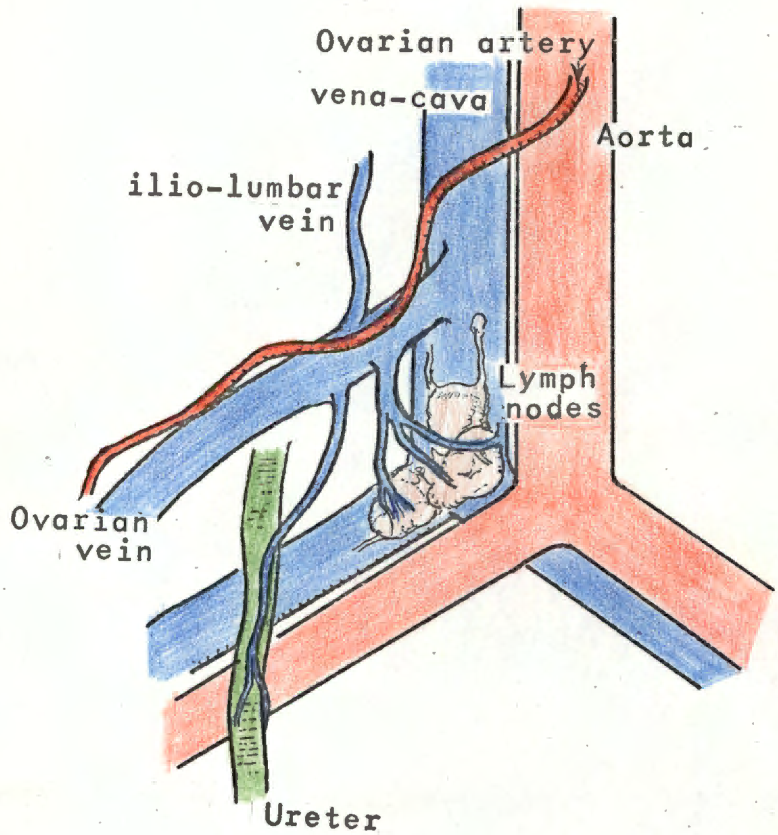

Fig. 33. Surgical anatomy relevant to dissection of ovarian vein to vena cava in the pig.

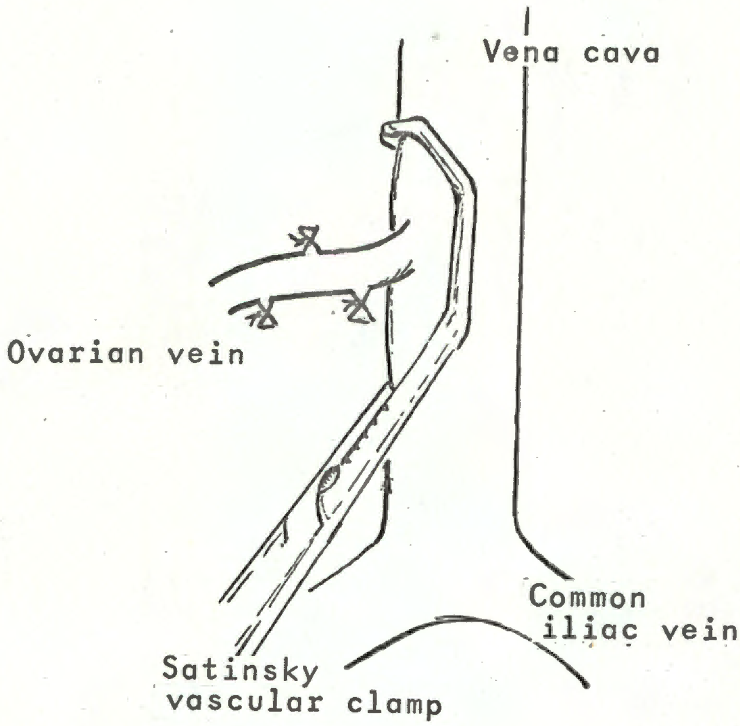

Fig. 34. Method of applying Satinsky vascular clamp prior to excision of vena-caval patch contiguous with end of ovarian vein.

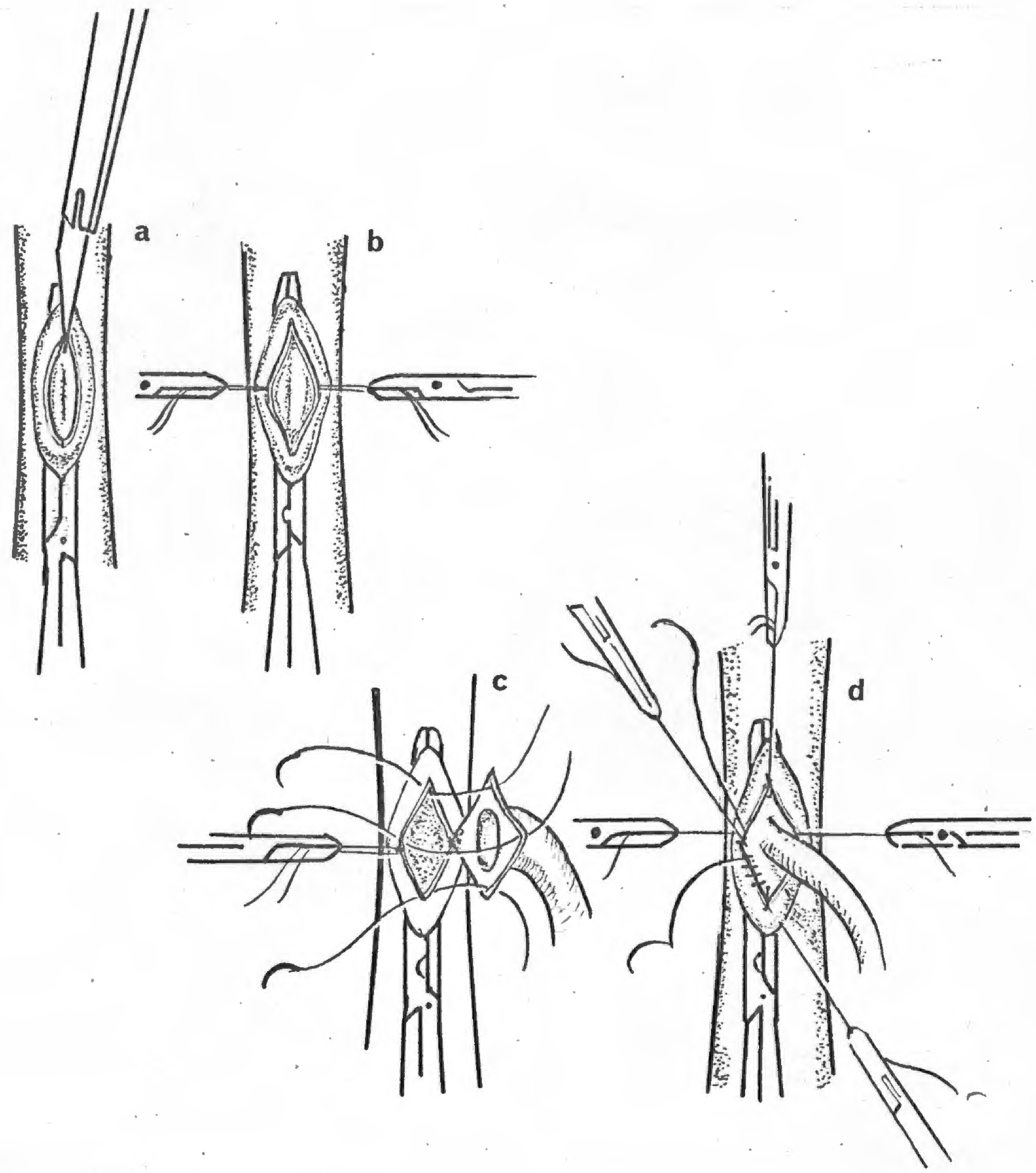

Fig. 35. Patch anastomosis of ovarian vein to vena cava.

The appearance of the aligned edges of the ovarian venous patch and the incised vena cava was now a diamond-shaped ostium, and the edges were approximated by a continuous 6 - 0 silk suture between the 4 stay sutures (Fig. 35d).

Once the vena-caval patch had been sutured in place, the lateral stay sutures were cut ± 2 mm above their knots and the vena-caval clamp was released. The anastomosis site was gently compressed with dry gauze swabs, and these were then removed to check that haemostasis was adequate. Additional 7 - 0 silk sutures were used to close any bleeding points. The upper and lower stay sutures were then cut, and gauze swabs were placed around the suture line for approximately 2 minutes before a final check to ensure that there was no defect in the suture line. In Case No. 19, 2 extra haemostatic sutures were required to achieve adequate haemostasis of the vena-caval patch. The arterial and cornual anastomoses were then completed as described previously.

Following release of the arterial clamp, the transplanted tissue was noted to become increasingly congested. The venous outflow was inadequate. On careful inspection, this appeared to be due to one of the haemostatic sutures which had caused occlusion of the ovarian venous outflow. Although an attempt was made to re-establish adequate flow, this was unsuccessful.

The transplanted tubocornual unit was removed and its pedicles were ligated. An attempt was made to complete the transplantation procedure by inserting the previously dissected tubocornual unit from Case No. 19 into Case No. 18.

The venous patch was secured as described in Case No. 19. In this case, the suture line had no leaks and the insertion of haemostatic sutures was not necessary. The arterial anastomosis was completed in the routine manner using 7 - 0 silk sutures.

The cornu was adequately perfused on release of the vascular clamps. The long arterial pedicle was at this stage noted to be twisted, and there was no means of securing it in a straight manner. Thus the graft was excised and the abdomens of both animals were closed in the routine manner.

POINTS OF NOTE:

The anaesthetic technique was once again confirmed to be satisfactory.

Whilst tedious and time-consuming, the venous patch technique appeared to be an answer to the previous problems encountered when performing a venous anastomosis. Although the patch had been spoilt by the extra haemostatic sutures in Case No. 19, the patch inserted in Case No. 18 had provided excellent venous drainage for the transplant specimen. The lesson learned from Case No. 19 was to ensure that adequate care be taken in the insertion of any haemostatic sutures on the venous patch suture line in the future.

The positions of long arterial and venous pedicles would require double checking before commencing their anastomoses. This would avoid the accidental twisting of a pedicle that had occurred in Case No. 18. Furthermore, it would be necessary to insert a few anchor sutures to avoid kinking of the pedicles. The siting of these sutures would have to be carefully chosen to ensure that they did not in themselves cause kinking.

The overall impression at the conclusion of this experiment was that by correcting all the mistakes that had occurred to date, it would soon be possible to perform a technically adequate homograft transplantation of the oviduct in the pig.

The overall strategy of the procedure depended on a concept of obtaining an adequate arterial blood supply from the uterine artery and satisfactory venous drainage via the ovarian vein

APPENDIX 2

Case reports of type "A" homograft transplantation procedures

CASE No. 1

Age of animal - $4\frac{1}{2}$ months

Operating time - $5\frac{1}{2}$ hours

Stage of cycle - non-oestrus

Date of operation - 20.9.72.

POINTS OF NOTE:

Venous Anastomosis: A routine vena-caval patch anastomosis was performed using 6 - 0 silk sutures. The initial, longitudinal incision performed on the recipient vena cava was too extensive and required closure of its superior aspect. This repair was made with a continuous 6 - 0 silk suture (Fig. 36).

Arterial Anastomosis: In view of the small calibre of the pelvic arteries found in the recipient, it was necessary to anastomose its reflected internal iliac artery to the uterine artery of the donor.

Mobilisation of the recipient internal iliac artery required extensive adventitial dissection to avoid kinking. The anastomosis was completed in the routine manner using 7 - 0 silk sutures.

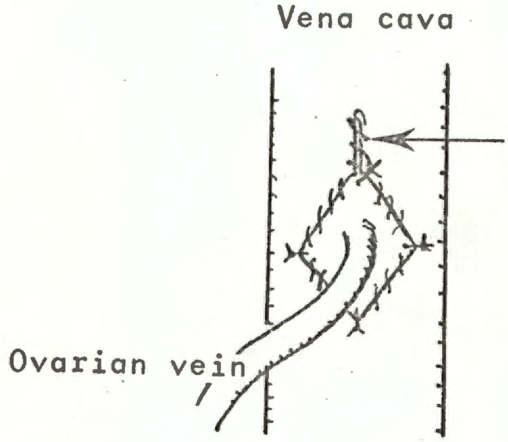

Fig. 36. Repair of excess vena-caval incision above site of patch anastomosis.

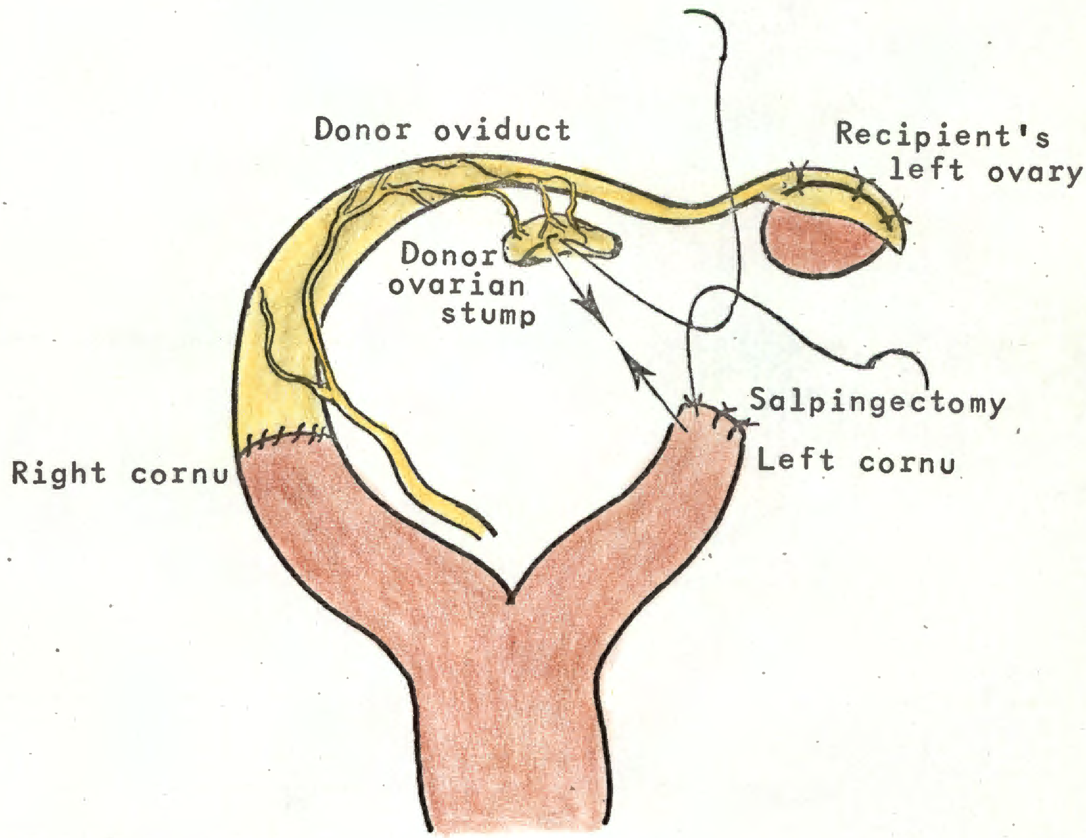

Fig. 37. Fixation of donor right ovarian pedicle to distal end of recipient's left cornu. (Note excision of recipient's left oviduct. Fine sutures inserted to attach donor's fimbriae to recipient's left ovary.)

Cornual Anastomosis: This was done in the routine manner using a continuous suture line of 6 - 0 polyglycolic acid sutures, oversewn with a few interrupted 3 - 0 polyglycolic acid sutures.

General

A single fixation suture was inserted on the posterior abdominal wall to support the long arterial pedicle and to prevent it from kinking.

The fimbrial end of the transplanted right Fallopian tube was attached over the recipient's left ovary with three 4 - 0 silk sutures.

The donor ovary was excised in the routine manner and its hilar pedicle was tied to the pedicle of the excised recipient left distal cornu (Fig. 37).

MEDICATIONS ADMINISTERED

Routine dosages of chloromycetin and heparin were administered as described in CHAPTER THREE 5. 3.

POSTOPERATIVE COURSE

This was uneventful.

DATE OF SACRIFICE: 7th March 1973

DURATION OF SURVIVAL: 167 days

LAPAROTOMY FINDINGS:

On opening the abdomen, there were a few adhesions found in the anterior general abdominal cavity. The bladder appeared healthy with no evidence of vascular impairment. The pelvic organs were covered in multiple adhesions. These had resulted in gross kinking of the uterine cornua and the coils were matted together by extensive fine adhesions. Identification of the transplanted oviduct with its artery and vein was extremely difficult.

When identified, the transplanted tissue appeared as a cord of pink fibrous tissue. Both the artery and vein had a similar pale-pink sclerosed appearance. Careful examination of the major sites of anastomosis revealed thrombosis of the artery and the vein and the cornual anastomosis was patent but ended in a narrow segment of fibrosed tissue distal to the anastomosis.

There was no obvious evidence of active inflammation or sepsis. The residual ovary appeared normal. Cysts of clear fluid were noted at the site of the transplanted fimbriae.

MACROSCOPIC ASSESSMENT:

1. Probable failure of adequate perfusion of the transplanted tissue resulting in aseptic fibrosis.

2. No overt evidence of active inflammation due to rejection or sepsis.

3. Multiple peritubal adhesions.

4. The residual ovary was viable.

5. The technique of attaching the right tube to the left ovary together with the extensive adhesions had resulted in gross mechanical distortion of the oviduct and should be abandoned.

HISTOLOGICAL ASSESSMENT:

Both the artery and the vein had evidence of thrombosis together with fibrous replacement of their walls. In some parts of the vessels there was endothelial swelling with an inflammatory response compatible with rejection.

Histology of the transplanted cornu showed a florid infiltrate of inflammatory cells compatible with rejection (Fig. 38). The fimbrial end of the tube was completely replaced by fibrosis. The ovary contained follicular cysts and 2 old corpora lutea.

OVERALL COMMENT:

The transplanted structure was virtually entirely fibrosed and this finding together with arterial and venous thrombosis was in all probability due to a combination of rejection and the technical failure of the vascular surgery. The extensive peritubal and intrapelvic adhesions noted may have also played a part.

Fig. 38. Rejection of transplanted oviduct. (Note diffuse infiltrate of mononuclear cells.)

CASE No. 2

Age of animal - 6 months   Operating time - $4\frac{1}{2}$ hours

Stage of cycle - oestrus   Date of operation - 19.10.72

POINTS OF NOTE:

Venous Anastomosis: Satisfactory.

Arterial Anastomosis: This was completed by anastomosing the donor uterine artery to the recipient internal pudendal artery in the routine manner.

Cornual Anastomosis: This was performed in the routine manner.

General

A suture joining the donor and recipient broad ligamentory edges was inserted through the peritoneal aspect of the anterior abdominal wall to support the elongated vascular pedicles.

<u>MEDICATIONS ADMINISTERED</u> : All routine medications were administered.

<u>POSTOPERATIVE COURSE</u>: This was uneventful.

<u>DATE OF SACRIFICE</u>: 27th April 1973.

<u>DURATION OF SURVIVAL</u>: 170 days.

<u>LAPAROTOMY FINDINGS</u>:

Few adhesions were present in the anterior abdominal cavity. The pelvic findings were very similar to those noted in Case No. 1. There were extensive adhesions matting the extremely kinked uterine cornua together. The transplanted structure appeared to be fibrosed but in this Case some viable fimbrial tissue was observed around the residual ovary. This structure was viable and appeared to be filled with small functional cysts.

<u>Arterial Anastomosis:</u> A small thrombus was present at the site of the anastomosis. The vessel appeared to be extensively fibrosed.

<u>Venous Anastomosis</u>: No thrombus was evident at this site but the vessel was narrowed and fibrosed.

Cornual Anastomosis: This was patent but the transplanted structure had narrowed into a shrunken fibrosed oviduct. There was no obvious evidence of active inflammation, rejection or sepsis.

MACROSCOPIC ASSESSMENT:

Probable vascular failure with ischaemic fibrosis or possibly this is the end stage of rejection of this organ.

HISTOLOGICAL ASSESSMENT:

The venous anastomosis was healthy, but the vessel wall was predominantly replaced by fibrous tissue.

The site of anastomosis of the uterine artery showed proliferating fibrous tissue and remnants of smooth muscle. A section through the middle of this vessel showed a similar appearance of smooth muscle combined with partial replacement by fibrous tissue. There was no evidence of any inflammatory or rejection response noted.

The transplanted cornu - while some areas of viable muscle cells were noted, there was extensive fibrosis of this structure. This appearance was compatible with the progressive onset of ischaemia. Very few inflammatory cells were observed. The ovary contained follicular cysts and the remnants of a recent corpus luteum. Some viable fimbriae were present.

Some of the cystic structures submitted were collections within occluded lymphatics.

OVERALL COMMENT:

The findings were compatible with a slow, progressive thrombosis of the artery resulting in ischaemia and subsequent fibrosis of the transplanted structure. Viability of areas of muscle cells were noted in the cornu and there was no evidence of any rejection response in any of the histological sections examined.

These findings were not caused by rejection but were the end result of the vascular surgery.

CASE No. 3

Age of animal - $4\frac{1}{2}$ months

Operating time - 4 hours

Stage of cycle - non-oestrus

Date of operation - 25.10.72

POINTS OF NOTE:

Venous Anastomosis: This was performed in the routine manner without complications.

Arterial Anastomosis: In view of the very small calibre of the vessels noted, the internal iliac artery was chosen as the level for transection of the donor artery and this was anastomosed to the corresponding vessel in the recipient. Both vessels had an external diameter of $\pm$ 2 millimetres.

These vessels lying deep in the pelvis were sutured with difficulty. Arterial thrombosis was anticipated although the transplanted organ appeared well perfused when the abdomen was closed.

Cornual Anastomosis: This was performed in the routine manner.

MEDICATIONS ADMINISTERED:

All routine medications were given.

POSTOPERATIVE COURSE: This was uneventful.

DATE OF SACRIFICE: 8th March 1973.

DURATION OF SURVIVAL: 134 days.

LAPAROTOMY FINDINGS:

Minimal adhesions were observed throughout the abdomen and pelvis. The transplanted oviduct appeared healthy throughout its entire length, and the fimbrial end was wrapped around a healthy ovary filled with multiple haemorrhagic corpora lutea. There was no evidence of infection or rejection. Arterial, venous and cornual anastomoses were all patent and appeared to be healthy.

MACROSCOPIC ASSESSMENT:

There appeared to be total viability of the transplanted structure (Fig. 39).

Fig. 39. Healthy appearance of transplanted oviduct.

HISTOLOGICAL ASSESSMENT:

Other than a slight serosal reaction, all sections of the transplanted cornu, Fallopian tube and fimbriae appeared healthy and viable with no cellular infiltration (Fig. 40a and Fig. 40b).

Both the ovary and vein had a normal appearance although a slight inflammatory exudate was observed at the sites of anastomosis.

OVERALL COMMENT:

From an anatomical point of view, the transplant was entirely satisfactory as assessed by macroscopic and microscopic examination of the transplanted organ. The sacrifice was regretted as it was possible that this particular case might later have proved the intended functional feasibility of the procedure.

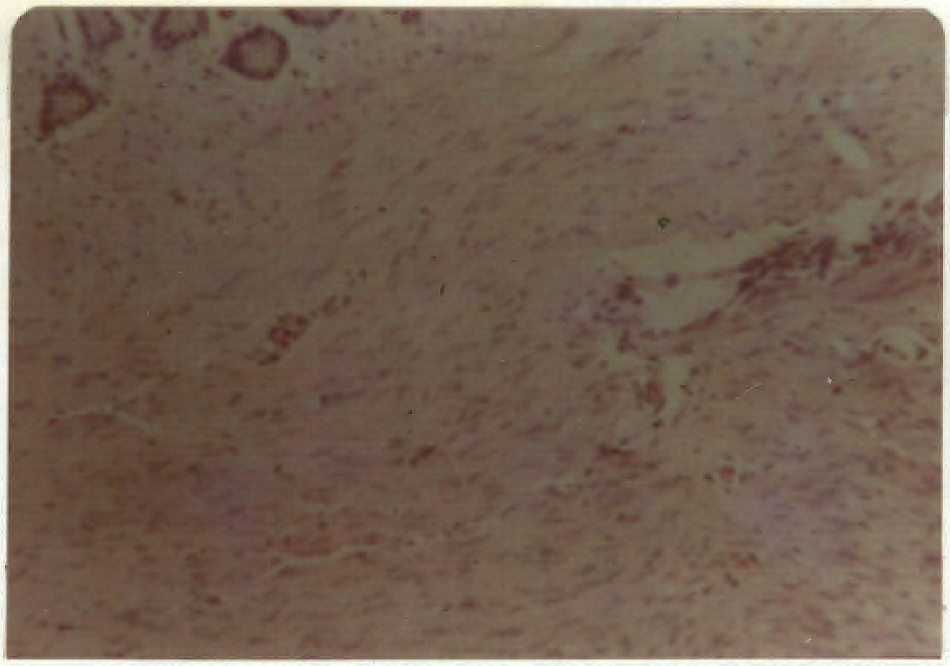

Fig. 40a. Microscopic section of transplanted oviduct. (Note healthy tissues and absence of cellular infiltrate; cf. Fig. 38.)

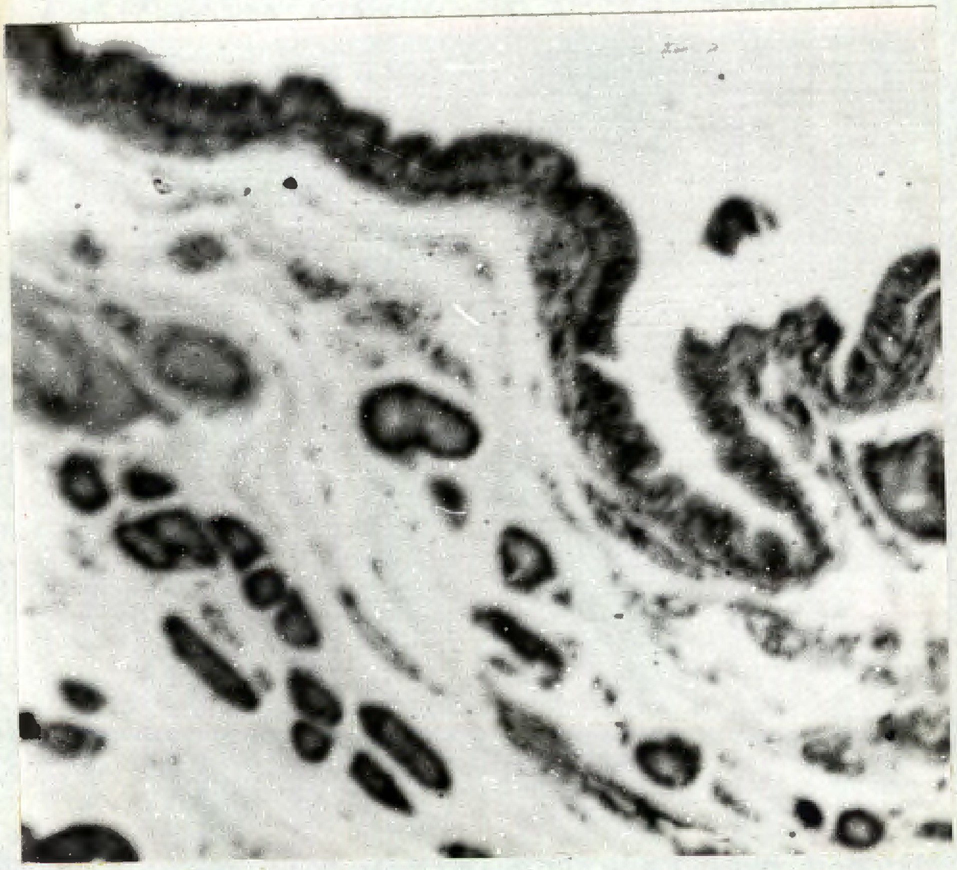

Fig. 40b. Microscopic section showing healthy endosalpinx of transplanted oviduct.

CASE No. 4

Age of animal - 6 months   Operating time - 4½ hours

Stage of cycle - non-oestrus Date of operation - 26.10.72

POINTS OF NOTE:

Venous Anastomosis: This was performed satisfactorily using 6 - 0 silk suture material as described previously.

Arterial Anastomosis: The donor uterine artery was anastomosed to the reflected internal pudendal artery of the recipient. Both vessels were $\pm$ 1.2 mm in diameter and the anastomosis was completed with difficulty. On release of the vascular clamps, there was excessive blood loss from the arterial anastomosis. It was felt that the suture line was too loose and 4 interrupted 7 - 0 silk sutures were inserted before adequate haemostasis was obtained.

Cornual Anastomosis: was completed in the routine manner using 6 - 0 and 3 - 0 polyglycolic acid suture material.

General

The artery was supported by a single

suture inserted on the posterior aspect of the uterus. The transplanted organ appeared well perfused when the operation was completed.

MEDICATIONS ADMINISTERED:

All routine medications were given as described previously.

POSTOPERATIVE COURSE:

This was complicated by the development of an incisional hernia.

DATE OF SACRIFICE: 27th April 1973.

DURATION OF SURVIVAL: 183 days.

LAPAROTOMY FINDINGS:

A very large ventral hernia ± 18 cm x 12 cm was observed on the anterior abdominal wall at the site of the previous operation. On opening the abdomen, there were only a few adhesions present in the general abdominal cavity. The pelvic organs were encompassed by gross adhesions which caused fairly marked kinking and distortion of the cornua and oviduct.

The uterine artery and the ovarian vein were isolated with difficulty but both appeared to be patent. The cornual anastomosis was patent and had a healthy appearance. Although the transplanted oviduct looked viable, it had a somewhat shrunken and relatively fibrosed appearance. This assessment was difficult because of the extensive adhesions covering the genital organs. The recipient cornu was markedly hypertrophied, measuring $\pm$ 40 cm x 2½ cm, and such an appearance was in keeping with oestrus. The ovary was slightly enlarged and appeared to be filled with multiple old corpora lutea and some follicular cysts.

<u>MACROSCOPIC ASSESSMENT</u>:

1. The most dominant feature was the extent of the pelvic adhesions present.

2. The vascular surgery appeared to have been successful.

3. The transplanted oviduct was probably viable but the fimbrial end of this structure could not be recognised separately from the peri-ovarian adhesions.

4. There was no obvious evidence of active infection or rejection.

HISTOLOGICAL ASSESSMENT:

The uterine artery was patent and had a healthy lumen with no inflammatory response. The ovarian vein was patent. There was slight intimal thickening but no inflammatory cells were present.

Sections of the transplanted cornu just distal to the anastomosis showed viable cornu with no inflammatory or rejection response. There was no evidence of any previous salpingitis. Sections of the oviduct showed a healthy viable appearance, and there was no evidence of rejection. The serosa of this structure was surrounded by extensive connective tissue.

The ovary was covered in extensive connective tissue. No recognisable fimbriae were present. The ovarian cysts were confirmed to be old corpora lutea and there were also two fresh haemorrhagic corpora lutea present.

A lymph node present in the specimen submitted showed slight follicular hyperplasia, but it was not particularly reactive.

OVERALL COMMENT:

The most striking features of this case were the extensive peritubal and peri-ovarian adhesions. There was no evidence of sepsis. There were no signs of rejection and although the anastomosed vessels were patent, the transplanted structure was not totally viable in that no recognisable fimbriae had been found.

Ovarian function had been normal as assessed by the cyclical occurrence of oestrus prior to and on the date of the laparotomy.

CASE No. 5

Age of animal - 6 months   Operating time - $4\frac{1}{2}$ hours

Stage of cycle - non-oestrus   Date of operation - 8.11.72.

POINTS OF NOTE:

Venous Anastomosis: In this case, 2 vena-caval clamps were applied prior to the insertion of the donor venous patch as it was felt that this would provide better access for the insertion of the sutures at the site of the anastomosis (Fig. 41a). Whilst this was true, it was also almost the cause of fatal haemorrhage. As the clamps were removed, there was severe haemorrage from 2 perforations of the vena cava at sites compatible with the points where the distal ends of the vena-caval clamps had been applied to the vessel.

While compression of the vena cava was performed above and below this site, repair of these tears was completed with a continuous line of 6 - 0 silk sutures at each site respectively (Fig. 41b). Approximately 300 ml of blood was lost before haemostasis was secured.

Arterial Anastomosis: This was performed between the uterine artery of the donor and the reflected internal pudendal artery of the recipient.

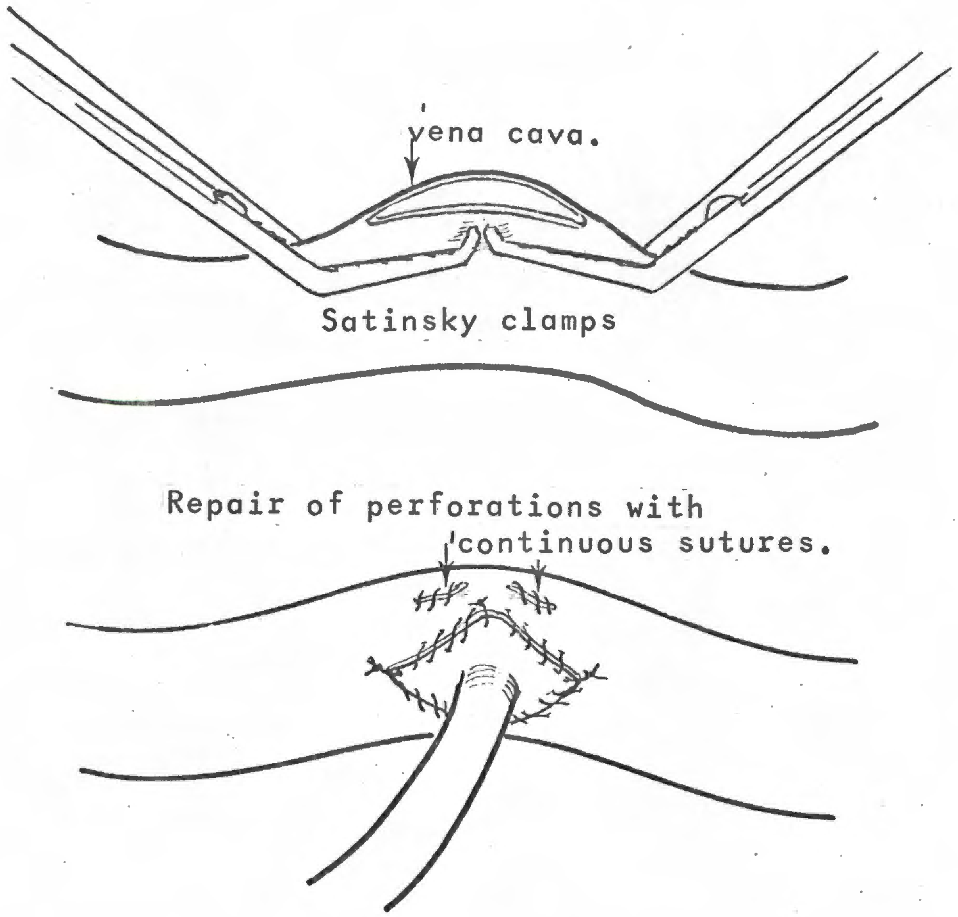

Fig. 41. Application of two Satinsky clamps to vena cava. (Note perforations caused by ends of clamps being sited on vessel wall.)

Cornual Anastomosis: This was effected in the routine manner.

General

The perforations of the vena cava did not appear to affect the final appearance of the transplant specimen or its venous drainage as assessed at the end of the operation. The occurrence of this trauma was a reminder that these clamps were not designed for application onto a vessel wall as described in this case. Whilst access to the site of anastomosis had been improved, this had almost been at the expense of the animal's life.

MEDICATIONS ADMINISTERED:

All routine medications were given.

POSTOPERATIVE COURSE:

This was uneventful.

DATE OF SACRIFICE: 27th April 1973.

DURATION OF SURVIVAL: 168 days.

LAPAROTOMY FINDINGS:

There were virtually no generalised abdominal adhesions observed. Minimal peritubal adhesions were noted. Large peri-ovarian cysts occupying an area of 14 cm x 20 cm were found around the residual ovary. These were filled with clear serous fluid and it appeared that this was an exudate trapped within adhesive fimbriae. Multiple cysts were noted in the ovary and there appeared to be old corpora lutea present. The artery appeared to be fibrosed but bleeding took place when it was transected. The vein appeared to be somewhat shrunken but patent. The cornual anastomosis was patent, but the transplanted oviduct appeared as a somewhat shrunken, relatively fibrosed band leading to the left ovary.

There was no external evidence of active sepsis, inflammation or rejection.

MACROSCOPIC ASSESSMENT:

The peri-ovarian cysts appeared to be fluid trapped within the remnants of the transplanted fimbriae. The large hyperplastic residual cornu $\pm$ 40 cm x 4 cm was compatible with oestrus. The transplanted specimen appeared to be somewhat fibrosed, possibly the end result of rejection, but more likely the result of progressive ischaemia.

HISTOLOGICAL ASSESSMENT:

The artery showed evidence of thrombosis and a finely recanalised lumen. In many parts, the vessel wall was virtually replaced by a cord of fibrosis. Very little inflammatory response was noted. The vein was oedematous but there was no thrombus present within its lumen. Vena comitantes were noted on its external surface, with a slight cellular reaction within their endothelial surfaces.

Haemosiderin deposits were observed close to the endothelial aspect of the main vein but cellular response was virtually absent. The cornu and transplanted oviduct appeared to be viable, but contained a florid infiltrate of pus cells and scattered mononuclear cells.

Viable muscular and connective tissue was noted around the purulent infiltrate which was confined to the inner surface of these structures. The inner folds were filled with connective tissue and only scanty glandular elements were observed.

A lymph node draining the area showed marked follicular hyperplasia and the presence of mononuclear cells. The ovary contained follicular cysts, a corpus albicans and a haemorrhagic corpus luteum.

The peri-ovarian cysts were lined by a fibrous wall containing some smooth muscle. Grossly dilated lymphatic channels were also present. No structure was clearly recognised as viable fimbria.

OVERALL COMMENT:

There was no definite evidence of rejection of the transplanted oviduct. The uterine artery had clearly been thrombosed and was partially recanalised. The ovarian vein was patent. The transplanted oviduct, although shrunken, was predominantly viable, but severe destruction of the endosalpinx had occurred. There was also evidence of a chronic salpingitis present and this was confined to its lumen.

The abovementioned features were in the main compatible with ischaemia following arterial thrombosis and subsequent chronic salpingitis. The peri-ovarian cysts could well have been caused by fluid trapped within the fibrosed remnants of the fimbrial end of the oviduct, but were also the result of extensive dilatation of the blocked lymphatic channels.

CASE No. 6

Age of animal - 6 months   Operating time - 4 hours

Stage of cycle - early oestrus   Date of operation - 8.11.72

POINTS OF NOTE:

Venous Anastomosis: This was performed satisfactorily in the routine manner.

Arterial Anastomosis: Dissection of the internal pudendal artery was complicated by the formation of an acute aneuysmal dilatation in the vessel wall. This occurred because of excessive dissection of the peri-vascular connective tissue in an effort to clear and mobilise the distal part of this vessel. As a result of this complication, the internal pudendal artery was transected just distal to the previously ligated branch of the uterine artery. This did not allow much anterior mobilisation of the vessel and thus its positioning for suture was deep within the pelvis.

Despite the additional technical difficulty, this anastomosis was completed in the routine manner as described previously.

Cornual Anastomosis: This was completed using 6 - 0 and 3 - 0 polyglycolic acid suture material as described previously.

MEDICATIONS ADMINISTERED:

The routine medications were all given.

POSTOPERATIVE COURSE:

This was uneventful.

DATE OF SACRIFICE: 1st May 1973.

DURATION OF SURVIVAL: 175 days.

LAPAROTOMY FINDINGS:

On opening the abdomen, there were no adhesions observed between the bowel and the anterior wall. The bowel was bound to the bladder by multiple adhesions which were also found distorting the pelvic structures.

The residual cornu was extremely convoluted and kinked by multiple adhesions. It measured approximately

4 cm x 40 cm and had an appearance compatible with the oestrus phenomenon.

The uterine artery looked like a fibrosed cord-like structure and its site of anastomosis appeared to be thrombosed. The transplanted ovarian vein was only recognised with difficulty as a similarly fibrosed cord-like structure. Its anastomosis at the vena cava was clearly occluded. The cornual anastomosis was patent and showed no obvious evidence of inflammation, sepsis or rejection. The transplanted cornu and oviduct were shrunken and somewhat fibrosed. No fimbrial structures were recognised and the residual ovary had a healthy polycystic appearance.

MACROSCOPIC ASSESSMENT:

The findings were compatible with arterial thrombosis and consequent ischaemic fibrosis of the transplanted structure. The possibility of rejection would have to be excluded. The residual ovary appeared to contain normal functional cysts.

HISTOLOGICAL ASSESSMENT:

The transplanted cornu near the site of the anastomosis was viable. Its mucosal layer was infiltrated with many plasma cells. A few plasma cells were also noted in the muscle layer.

Sections of the transplanted oviduct showed viable serosa and muscular tissue but there were only scanty areas of viable endosalpinx noted. These were also infiltrated with some plasma cells which were confined to the surface mucosa.

The arterial anastomosis was completely obliterated by an old organised thrombus and there was also evidence of recanalisation of this structure. No inflammatory response was noted.

No healthy venous tissue was found. The remains of the ovarian vein appeared as aggregates of elastic tissue in areas of fibrosis. The ovary appeared healthy and contained multiple follicular cysts, corpora lutea and a corpus albicans.

<u>OVERALL COMMENT</u>:

Arterial thrombosis was confirmed together with occlusion of the ovarian vein in this case. Despite these findings, the outer serosa and muscular parts of the transplanted structure had remained viable as assessed histologically. The fact that cellular infiltration was confined to the lumen of the structure was more in keeping with a diagnosis of a chronic salpingitis, than that of rejection.

The final appearance was in keeping with arterial and venous occlusion and subsequent endosalpingitis, most likely due to technical failure at the original operative procedure. Features of the rejection response were absent.

CASE No. 7

Age of animal - 6 months   Operating time - 5 hours

Stage of cycle - early oestrus   Date of operation - 15.11.72

POINTS OF NOTE:

Venous Anastomosis: This was performed using 6 - 0 silk sutures in the routine manner.

Arterial Anastomosis: The donor uterine artery was anastomosed to the reflected internal pudendal artery of the recipient.

Cornual Anastomosis: was completed in the routine manner.

MEDICATIONS ADMINISTERED:

All routine medications were given.

POSTOPERATIVE COURSE:

This was complicated by the development of a large incisional hernia.

DATE OF DEMISE: 25th January 1973.

DURATION OF SURVIVAL: 64 days.

POSTMORTEM FINDINGS:

The abdomen was grossly distended and resonant. An incisional hernia measuring 25 cm x 20 cm was noted over the site of the operation. Infarcted large and small bowel that had undergone volvulus around an adhesion was found within the lower abdomen and the ventral hernia.

The involved bowel was grossly distended and it appeared to be gangrenous. Approximately 500 ml of sersanguinous fluid was present in the abdominal cavity. Gross pelvic adhesions were noted.

The transplanted oviduct was difficult to define but appeared somewhat necrosed with thrombosis of the small vessels within the broad ligament. The site of anastomosis was patent and the proximal end of the transplanted structure appeared viable.

Remnants of the fimbrial end of the oviduct appeared to be incorporated in an abscess around the ovary which had a polycystic appearance. Whilst difficult to define, both the artery and vein of the specimen appeared to be somewhat shrunken and relatively fibrosed.

The lungs, liver, stomach and kidneys appeared to be healthy.

MACROSCOPIC ASSESSMENT:

Death due to torsion of bowel around a large adhesion with associated infarction and peritonitis. The transplanted tissue appeared to be infected and it was probable that both the artery and the vein were thrombosed.

HISTOLOGICAL ASSESSMENT:

Sections of bowel submitted showed features of infarction and peritonitis over its surface. The arterial anastomosis was filled with an organised thrombus. The venous anastomosis and sections of the vein draining the transplant site appeared healthy and patent. Sections of cornu taken near the site of anastomosis appeared viable in all layers. There was virtually no inflammatory infiltrate present at this site. Sections of the oviduct showed that in most areas it was viable, but there was ulceration of the endosalpinx and an associated marked acute on chronic inflammatory cellular infiltrate.

Sections of the ovary showed developing follicles and a large corpus luteum. The fimbrial end of the oviduct had no mucosal cells present and its wall was replaced by granulation tissue following on an inflammatory reaction. Sections of the kidney, lung, and liver were all healthy.

OVERALL COMMENT:

Death due to torsion of bowel and associated peritonitis. Viability of sections of outer coats of the transplant structure. Scattered areas of viable endosalpinx but associated acute or chronic salpingitis and scanty evidence of rejection. The features were compatible with ischaemia to the transplant structure and this was confirmed by the presence of thrombosis in the transplant uterine artery.

APPENDIX 3

Case reports of type "B" homograft transplantation procedures

CASE No. 1

Age of animal - $6\frac{1}{2}$ months   Operating time - 6 hours

Stage of cycle - non-oestrus   Date of operation - 17.4.73

POINTS OF NOTE:

Venous Anastomosis: The recipient vena-caval incision was too large and required repair to its upper part as described in Case No. 1 of the Type "A" transplantation procedures.

Arterial Anastomosis: The arterial anastomosis between the donor uterine artery and the reflected internal pudendal artery of the recipient was considered satisfactory and no additional haemostatic sutures were required when the vascular clamps were removed.

Cornual Anastomosis: The cornual end-to-end anastomosis was completed in the routine manner.

General

The fimbrial end of the transplanted oviduct was sutured in place over the recipient ovary with 2 fine 6 - 0 polyglycolic acid sutures.

MEDICATIONS ADMINISTERED:

Routine dosages of chloromycetin and heparin were administered as described in CHAPTER THREE 5. 3.

POSTOPERATIVE COURSE:

The animal contracted pneumonia 32 days after the operation. In view of the fact that this illness did not show a rapid response to treatment, the pig was brought in from the farm and sacrificed. This procedure was performed to avoid any delay and subsequent autolysis of the tissues that could occur if the animal had subsequently died on the farm.

DATE OF SACRIFICE: 24th May 1973.

DURATION OF SURVIVAL: 37 days.

LAPAROTOMY FINDINGS:

There were no adhesions observed in the peritoneal cavity but a few were present within the pelvis. The transplanted cornu and oviduct appeared viable but shrunken and fibrosed. The site of cornual anastomosis was patent. The artery and vein were fibrosed cord-like structures.

The residual ovary had a polycystic appearance but did not appear to be enlarged.

MACROSCOPIC ASSESSMENT:

There appeared to have been failure of the blood supply to the transplant specimen and yet it appeared viable despite its shrunken and fibrosed appearance. There was no obvious evidence of inflammation, sepsis or rejection. The ovary appeared healthy and functional. Pneumonia was present in the lungs.

HISTOLOGICAL ASSESSMENT:

The artery was occluded by a thrombus. Whilst a few mononuclear cells were present at the site of the anastomosis, there was no striking evidence of rejection having been responsible for this. The vein was also occluded by a thrombus.

Other than a slight inflammatory response observed at the site of the cornual anastomosis, the cornua on either side appeared to be healthy and viable. Further sections of the transplanted oviduct showed that there were areas of viable tube but the endosalpinx was generally ischaemic and there was atrophy of its mucosal surface, loss of the glands and replacement by fibrosis. The serosal surface and muscle wall were viable in most sections submitted to examination. A slight mononuclear infiltrate was noted in some areas but these were very scanty and not sufficiently impressive to suggest a rejection response.

Sections of the ovary revealed the presence of developing follicles together with follicular cysts. Examination of sections of lung confirmed the presence of many pus cells and bacteria within the alveoli together with a fibrinous exudate on the pleural surface.

OVERALL COMMENT:

The pathology noted appeared to have been caused by progressive ischaemia. Parts of the transplanted oviduct had undergone ischaemic necrosis and fibrous replacement. It was partially atrophic. However, despite the thrombosed artery and vein, it appeared to be viable in many areas examined, notably the muscularis and the serosa.

Despite the presence of some inflammatory cells, this did not suggest any obtrusive rejection response. The findings in the pelvis appeared to be unrelated to the presence of pneumonia which the animal had contracted a month after the operation.

CASE No. 2

Age of animal - $6\frac{1}{2}$ months   Operating time - 4 hrs 10 mins

Stage of cycle - non-oestrus   Date of operation - 24.4.73

POINTS OF NOTE:

Venous Anastomosis: The ovarian vein was torn off at the point of commencement of the venous patch. The vessel was thus cut at an angle above the tear and an end-to-side anastomosis was completed. This anastomosis appeared to provide an adequate venous drainage for the transplant.

Arterial Anastomosis: This was performed between the donor uterine artery and the reflected internal pudendal artery of the recipient in the routine manner. No extra haemostatic sutures were required and perfusion of the transplanted structure was very satisfactory.

Cornual Anastomosis: This was completed as described previously.

General

Two fine 6 - 0 polyglycolic acid sutures were inserted to hold the fimbrial end of the transplanted oviduct over the recipient ovary.

MEDICATIONS ADMINISTERED:

All routine medications were given.

POSTOPERATIVE COURSE:

This was uneventful.

DATE OF SACRIFICE: 9th August 1973.

DURATION OF SURVIVAL: 107 days.

LAPAROTOMY FINDINGS:

Whilst there were minimal adhesions in the general abdominal cavity, extensive adhesions were present in the pelvis between the loops of cornua. The uterine artery appeared as a fibrosed cord and the site of its anastomosis appeared thrombosed. The ovarian vein looked somewhat shrunken, but its site of anastomosis was patent.

The transplanted structure was somewhat thinned and dilated and appeared to contain some necrotic material within its lumen. The cornual anastomosis was patent and had a healthy appearance.

The ovary appeared to be healthy and polycystic.

MACROSCOPIC ASSESSMENT:

The changes were compatible with vascular failure and possible infection or rejection.

HISTOLOGICAL ASSESSMENT:

The artery had disintegrated into a fibrous cord. There was evidence of tissue destruction and replacement by elastic tissue. The slight inflammatory response noted was more likely to be a manifestation of infection than that of rejection. The arterial anastomosis contained an old organised thrombus. Minimal cellular reaction was noted.

The venous anastomosis was patent and healthy. The vein itself was replaced by a cord of fibrosed tissue. No inflammatory cells were noted. The cornual anastomosis appeared to be healthy and totally viable cornu was noted on both sides of the anastomosis.

No evidence could be found of any active rejection response. The external layers of the transplanted oviduct appeared to be viable, but the endosalpinx was necrosed and infiltrated by some plasma cells and macrophages. These cells were confined to this site which was in keeping with a chronic endosalpingitis. The ovary was healthy and contained follicular cysts.

OVERALL COMMENT:

The changes observed were most likely due to ischaemia with the possibility of an associated low-grade chronic endosalpingitis. The mild cellular response observed was more in keeping with this diagnosis rather than that of rejection.

It was interesting to observe that the outer layers of the transplanted structure had remained viable despite the loss of its blood supply.

Failure to obtain arterial patency was the most likely cause of the abovementioned pathological findings.

CASE No. 3

Age of animal - 6 months   Operating time - $4\frac{1}{2}$ hours

Stage of cycle - early oestrus   Date of operation - 3.5.73

POINTS OF NOTE:

The Venous Incision was slightly long for the vena-caval patch and therefore required partial repair as in Case No. 1.

The Arterial Anastomosis was completed between the donor uterine artery and the reflected internal pudendal artery of the recipient. Two extra sutures were required to effect adequate haemostasis after removal of the vascular clamps.

The Cornual Anastomosis was completed in the routine manner.

General

A single 3 - 0 polyglycolic acid suture was utilised to attach the fimbrial end of the transplanted oviduct to the recipient ovary.

MEDICATIONS ADMINISTERED:

All routine medications were given.

POSTOPERATIVE COURSE:

The animal developed a pneumonia on the 15th postoperative day and it died 3 days later.

DATE OF DEMISE: 21st May 1973.

DURATION OF SURVIVAL: 18 days.

POSTMORTEM FINDINGS:

Examination of the thoracic cavity confirmed a diagnosis of pneumonia and empyema. On opening the abdomen, there was evidence of diffuse peritonitis and approximately 500 ml of purulent fluid was seen between the loops of bowel and in the pelvis.

Multiple adhesions were observed around the residual cornu and the transplanted oviduct both of which were filled with purulent material.

The ovary contained multiple follicular cysts and was covered by a fairly solid envelope of purulent material. The cornual anastomosis was patent. The arterial anastomosis was filled with a thrombus but the venous anastomosis was patent.

MACROSCOPIC ASSESSMENT:

Diffuse peritonitis and associated pneumonia. Partial necrosis and salpingitis of the transplanted oviduct most probably due to ischaemia. Technical failure followed by arterial thrombosis.

HISTOLOGICAL ASSESSMENT:

A thrombus was noted in the lumen of the uterine artery at the site of the anastomosis. Necrosis of the media of the vessel wall was seen with early calcification at this site. The occlusive thrombus showed no features of a rejection response.

The venous anastomosis was healthy. No thrombus was present in its lumen but a slight mononuclear cell infiltrate was noted in its wall. The transplanted oviduct and associated cornu were extensively necrosed but a subserosal muscle layer was noted to be viable. Mucosal necrosis was evident and this was infiltrated by polymorphs and some monocytes.

The fimbrial end of the transplanted oviduct was completely necrosed and a marked infiltrate of inflammatory cells was present. The recipient cornu was viable but contained an inflammatory exudate within its lumen compatible with the appearance of an acute salpingitis.

The ovary was viable but had an acute inflammatory exudate on its surface.

The sections of lung confirmed the presence of pneumonia and a purulent exudate was present on the pleural surface. A thick purulent exudate covered the surface of the spleen which appeared to be hyper-reactive.

OVERALL COMMENT:

Technical failure with arterial thrombosis, ischaemic necrosis of the transplanted oviduct and subsequent salpingitis. Death due to diffuse peritonitis, pneumonia and probably associated septicaemia.

CASE No. 4

Age of animal - $6\frac{1}{2}$ months   Operating time - 4 hours

Stage of cycle - non-oestrus   Date of operation - 8.5.73

POINTS OF NOTE:

The Venous Anastomosis was performed in the routine manner and this part of the operation was uneventful.

The Uterine Artery of the donor was transected just proximal to the point at which its lumen was joined by that of the vesical artery.

The vessel was anastomosed to the reflected internal pudendal artery of the recipient in the routine manner. Two extra sutures were required to effect adequate haemostasis once the vascular clamps were released.

The Cornual Anastomosis was completed using the routine technique.

MEDICATIONS ADMINISTERED:

All routine medications were administered.

POSTOPERATIVE COURSE:

Other than the development of some stitch abscesses and a small incisional hernia ± 5 cm x 3 cm, this was uneventful.

DATE OF SACRIFICE: 7th August 1973

DURATION OF SURVIVAL: 91 days.

LAPAROTOMY FINDINGS:

A few fine adhesions were noted in the general abdominal cavity. No adhesions were observed in the pelvis. A small area of fibrosis was noted on the lower part of the right side of the bladder.

The uterine artery appeared to be healthy and patent. The venous anastomosis appeared to be patent and the vein had a healthy appearance. The cornual anastomosis was patent. Other than a slight stricture, it appeared to be normal and there was no evidence of any sepsis or rejection.

The transplanted oviduct looked completely normal and its fimbrial end was readily identified. The ovary contained many small functional cysts ± 3 mm in diameter.

MACROSCOPIC ASSESSMENT:

A technically successful procedure with total viability and no evidence of rejection or infection.

HISTOLOGICAL ASSESSMENT:

Other than a slight round cell infiltrate, the uterine artery and its site of anastomosis appeared healthy and patent. The vein was normal and its site of anastomosis was healthy and patent.

The cornual anastomosis showed total viability although a slight round cell infiltrate was present. All sections of oviduct examined showed complete viability in all layers. There was very little inflammatory cell infiltrate present and all layers were completely healthy.

The ovary was normal, follicular cysts were noted and the overlying fimbriae were viable. A pelvic lymph node submitted showed slight follicular and sinus hyperplasia but this did not appear to be related to the transplant.

OVERALL COMMENT:

A remarkably normal-looking transplanted oviduct with both vessels patent. No evidence of sepsis or rejection. The operation had been entirely successful with regard to the anatomical appearance of the transplanted structure 91 days after the procedure.

CASE No. 5

Age of animal - 6½ months   Operating time - 4 hrs 15 min

Stage of cycle - non-oestrus   Date of operation - 10.5.73

POINTS OF NOTE:

Venous Anastomosis: This was effected in the routine manner.

The Arterial Anastomosis between the donor uterine and recipient reflected internal pudendal artery was uneventful.

Routine Cornual Anastomosis was performed.

MEDICATIONS ADMINISTERED:

All routine medications were administered.

POSTOPERATIVE COURSE:

This was uneventful.

<u>DATE OF SACRIFICE</u>: 9th August 1973.

<u>DURATION OF SURVIVAL</u>: 91 days.

<u>LAPAROTOMY FINDINGS</u>:

Extensive adhesions were found between the bowel, the anterior abdominal wall and covering the pelvis. There was no overt evidence of sepsis or inflammation and the pelvic organs appeared to be healthy.

The uterine artery appeared to be thickened and thrombosed. The ovarian vein appeared to be fibrosed but its site of anastomosis appeared healthy and patent. Other than a slightly shrunken appearance, the transplanted oviduct with its adjacent cornu looked viable and healthy. The cornual anastomosis was patent.

<u>MACROSCOPIC ASSESSMENT</u>:

Despite the thrombosis of the uterine artery and the fibrosed ovarian vein, the transplanted structure appeared to be viable with no overt evidence of sepsis or rejection. Extensive pelvic adhesions were present.

HISTOLOGICAL ASSESSMENT:

The uterine artery was completely occluded by an organised thrombus and there was very little cellular reaction present. In some areas the collapsed artery was surrounded by some plasma cells and lymphocytes. No rejection reaction was noted at the site of the anastomosis but an inflammatory response was noted around the suture material and this had the appearance of minute stitch abscesses.

The venous anastomosis appeared healthy and there was very little in the way of an inflammatory reaction present. Viable oviduct and cornu were observed and there was minimal loss of the endosalpinx noted. A minimal cellular response of mononuclear cells, plasma cells and occasional eosinophils was noted at the site of the cornual anastomosis. If this was an immune response, it was absolutely minimal and of a very low order. Sections of donor broad ligament contained viable vessels with no inflammatory cellular infiltrate.

The ovary appeared healthy and no inflammatory cells were present. Developing follicles, follicular cysts and atretric follicles were observed. No recent corpus luteum was noted.

OVERALL COMMENT:

Despite the arterial occlusion, the transplanted structure was viable and all coats of the oviduct appeared relatively healthy. Minimal reaction was present and there was no overt evidence of active inflammation or rejection. It was possible that the smaller healthy vessels in the broad ligament represented vascular adhesions which had helped to nourish the graft.

CASE No. 6

Age of animal - 6 months   Operating time - 4 hours

Stage of Cycle - non-oestrus   Date of operation - 15.5.73

POINTS OF NOTE:

The Venous Anastomosis was performed in the routine manner.

Arterial Anastomosis: This was performed between the donor uterine artery and the reflected internal pudendal artery of the recipient. The anastomosis was considered technically sound and no extra sutures were required to effect haemostasis when the vascular clamps were released.

The Cornual Anastomosis was completed in the routine manner. The fimbrial end of the transplanted oviduct was attached to the ovary with two 6 - 0 polyglycolic acid sutures.

MEDICATIONS ADMINISTERED:

All routine medications were given as described previously.

POSTOPERATIVE COURSE:

Other than the development of stitch abscesses on the skin sutures, this was uneventful.

DATE OF SACRIFICE: 7th August 1973.

DURATION OF SURVIVAL: 84 days.

LAPAROTOMY FINDINGS:

Two small stitch abscesses were present on the skin surface. The abdomen was almost entirely free of adhesions. The adhesions were present over the pelvic structures which appeared healthy with no obvious foci of infection, inflammation or rejection.

The uterine artery was thrombosed and thickened. The ovarian vein appeared to be occluded at the site of anastomosis, but healthy endothelium was noted.

The cornual anastomosis appeared healthy. It was patent and the transplanted oviduct appeared viable and healthy but was kinked by fine adhesions. The ovary was healthy and there appeared to be evidence of recent corpora lutea present. It was surrounded by small cysts which appeared to be fimbrial in origin.

MACROSCOPIC ASSESSMENT:

Arterial and venous thrombosis. A viable tube was present and there was no evidence of sepsis or rejection.

HISTOLOGICAL ASSESSMENT:

The uterine artery was completely occluded by organised and partially recanalised thrombus. In some areas, the artery was thickened by intimal proliferation and a narrowed lumen was noted. There was little in the way of an inflammatory reaction.

The venous patch was occluded but the surrounding tissue showed minimal inflammatory response. The vein contained an old occluded thrombus with prominence of the vascular epithelium and a mild inflammatory response.

Both sides of the cornual anastomosis were viable in all layers and a mild mononuclear cell infiltrate was observed. The oviduct appeared completely viable in all layers and there was virtually no inflammatory cell infiltrate noted.

The ovary was viable and primordial follicles, follicular cysts and an old corpus luteum were all observed. No recognisable fimbrial tissue was present.

OVERALL COMMENT:

The transplanted structure was grossly and histologically viable despite the evidence of arterial and venous thrombosis. Whilst pelvic adhesions were present, there was no evidence of active sepsis. The cellular reaction was extremely mild, unobtrusive and most likely the result of ischaemia. If part of a rejection response, it was of a very low order.

CASE No. 7

Age of animal - 6½ months   Operating time - 5 hours

Stage of cycle - oestrus   Date of operation - 22.5.73

POINTS OF NOTE:

A particularly small length of cornu measuring approximately 3 cm was transplanted with the oviduct.

The Venous Anastomosis was completed without complication in the routine manner.

The donor uterine artery was anastomosed to the reflected internal pudendal artery in the usual way, and no extra haemostatic sutures were required.

Routine Cornual Anastomosis was completed using 6 - 0 and 3 - 0 polyglycolic acid sutures.

MEDICATIONS ADMINISTERED:

All routine medications were administered.

POSTOPERATIVE COURSE:

This was uneventful.

DATE OF SACRIFICE: 21st August 1973.

DURATION OF SURVIVAL: 91 days.

LAPAROTOMY FINDINGS:

Extensive adhesions were noted throughout the lower abdominal cavity. Loops of bowel were bound over the pelvis by multiple adhesions and these required extensive and careful dissection to eventually free the pelvic organs. There were many small abscesses present within the pelvis. These were found between the loops of hypertrophied cornu which had an oestrus appearance.

The transplanted oviduct and cornu appeared viable but appeared to contain a purulent inflammatory exudate. The cornual anastomosis was patent. The uterine artery appeared to be thickened and thrombosed. The ovarian vein had a shrunken appearance but its anastomosis appeared patent and healthy.

MACROSCOPIC ASSESSMENT:

Extensive intra-abdominal and pelvic adhesions. Extensive salpingitis and associated intra-pelvic abscesses. The transplanted tube appeared viable despite the uterine artery thrombosis.

HISTOLOGICAL ASSESSMENT:

The uterine artery was occluded by an old thrombus. The venous anastomosis was patent and healthy. Minimal inflammatory reaction was noted in the adjacent tissues. Viable tissues were noted on both sides of the cornual anastomosis. The inner layer of the cornu contained a definite infiltrate of mononuclear and plasma cells together with layers of polymorphs within the lumen.

There was atrophy of glands with connective tissue replacement. These findings were compatible with salpingitis rather than a rejection phenomenon, as the infiltrate was not observed in the muscle layers of the transplanted tissue.

The oviduct appeared viable but its inner mucosa also showed a moderate infiltrate of mononuclear cells, plasma cells and polymorphs. The mucosal glands were cystic and dilated and some subserosal fibrosis was observed. Abscesses were seen on the outside of the tube.

The ovary was healthy. Developing follicles were seen together with a recent corpus luteum.

OVERALL COMMENT:

The transplanted structure was viable but involved in active salpingitis together with intra-pelvic abscesses. Arterial thrombosis was confirmed. There was no definite evidence of rejection. The ovary was anatomically normal.

APPENDIX 4

Case reports of group 2 - vascularised autograft oviduct transplantation procedures (ovary excluded).

CASE No. 1

Age of animal - 6½ months   Operating time - 6 hours

Stage of cycle - early oestrus   Date of operation - 25.9.73

POINTS OF NOTE:

The initial arterial anastomosis was not considered satisfactory. It was therefore excised and this part of the procedure was repeated. The anastomosis required two extra interrupted sutures to effect adequate haemostasis.

DATE OF LAPAROTOMY: 5th December 1973.

DURATION OF SURVIVAL: 72 days.

MACROSCOPIC ASSESSMENT:

There were minimal adhesions between the bowel and the anterior abdominal wall. Scanty adhesions were noted within the pelvis. The transplanted oviduct appeared healthy but was bound to the posterior abdominal wall. The cornual anastomosis was patent.

The uterine artery and the ovarian vein both appeared to be patent and healthy.

HISTOLOGICAL ASSESSMENT:

Sections of the cornual anastomosis, transplanted cornu and oviduct all appeared totally viable and healthy. The uterine artery and the ovarian vein were both patent and healthy.

OVERALL COMMENT:

The transplanted specimen was totally viable with arterial and venous patency. There was no evidence of sepsis or inflammation.

CASE No. 2

Age of animal - 6 months   Operating time - $3\frac{1}{2}$ hours

Stage of cycle - non-oestrus   Date of operation - 15.10.73

POINTS OF NOTE:

When the vascular clamps were released, blood loss from the arterial anastomosis was considered to be excessive. Adequate haemostasis was achieved by the insertion of two additional sutures to the completed suture line.

DATE OF LAPAROTOMY: 5 December 1973.

DURATION OF SURVIVAL: 51 days.

MACROSCOPIC ASSESSMENT:

Minimal adhesions were noted in the general abdominal cavity but extensive adhesions were present within the pelvis. The cornual anastomosis was patent. The transplanted structure appeared viable and healthy throughout its length and the fimbrial end was clearly recognisable. The cornu and oviduct were extensively kinked by the multiple adhesions present. Both the uterine artery and the ovarian vein appeared to be healthy and patent.

HISTOLOGICAL ASSESSMENT:

This confirmed totally viable and healthy cornu and oviduct. There was minimal inflammatory reaction. The artery and vein were both patent and healthy.

OVERALL COMMENT:

This was a technically successful procedure. There were extensive adhesions present in the pelvis but there was no active sepsis or inflammation. The transplanted structure was viable and its artery and vein were patent.

CASE No. 3

Age of animal - $6\frac{1}{2}$ months Operating time - $3\frac{1}{2}$ hours

Stage of cycle - non-oestrus Date of operation - 23.10.73

POINTS OF NOTE:

The anastomosis between the uterine artery and the reflected internal pudendal artery was performed with excellent haemostasis and no extra sutures were required.

DATE OF LAPAROTOMY: 31st January 1974.

DURATION OF SURVIVAL: 100 days.

MACROSCOPIC ASSESSMENT:

Virtually no adhesions were observed in the lower abdomen or in the pelvis. The transplanted oviduct and cornu appeared viable but somewhat shrunken, atrophied and fibrosed.

The cornual anastomosis was patent with no evidence of active inflammation or infection. The artery resembled a fibrosed cord and its anastomosis was thrombosed.

The venous anastomosis was patent but the vein appeared to be somewhat shrunken and fibrosed.

HISTOLOGICAL ASSESSMENT:

The transplanted oviduct was viable throughout its muscular layer and outer serosal surface. There was no endosalpinx present. Examination of the transplanted cornu adjacent to its anastomosis revealed viability in all layers. A cellular reaction of histiocytes was also observed at this site.

The uterine artery was thrombosed and sections of the vessel wall were replaced by connective tissue. The venous anastomosis was healthy. The residual venous structure appeared as a combination of elastic tissue and associated fibrosis.

OVERALL COMMENT:

The findings were compatible with vascular occlusion and progressive ischaemic changes to the transplanted oviduct.

CASE No. 4

Age of animal - 6 months   Operating time - $3\frac{1}{2}$ hours

Stage of cycle - non-oestrus   Date of operation - 21.1.74

POINTS OF NOTE:

The vena-caval incision was too large and required repair at its upper end. The operation was otherwise uneventful.

DATE OF LAPAROTOMY: 3rd March 1974.

DURATION OF SURVIVAL: 41 days. This animal died of pneumonia on the 41st postoperative day.

MACROSCOPIC ASSESSMENT:

Minimal adhesions were observed throughout the abdomen and pelvis. The transplanted oviduct appeared to be shrunken, atrophic and fibrosed. There was no evidence of obvious sepsis or necrosis. Both the uterine artery and the ovarian vein including its site of vena-caval anastomosis appeared to be thrombosed.

HISTOLOGICAL ASSESSMENT:

The smooth muscle and serosal surface of the transplanted oviduct appeared viable. The inner surface of the endosalpinx was replaced by fibrous tissue and isolated areas of necrosis.

Whilst there was a moderate infiltrate of histiocytes, there was no evidence of sepsis noted. Both the arterial and venous anastomoses were filled with organised thrombus.

OVERALL COMMENT:

The transplanted oviduct was viable in its outer coats but mainly revealed the pathology of aseptic ischaemic necrosis with fibrous replacement of the inner layers of the transplanted tissues.

CASE No. 5

Age of animal - 7 months   Operating time - 4 hrs 15 mins

Stage of cycle - oestrus   Date of operation - 22.1.74

POINTS OF NOTE:

After completion of the vena-caval anastomosis it was noted that there were two obvious leaks in the suture line. Adequate haemostasis was achieved by the insertion of single sutures at these two points. A routine arterial anastomosis was performed between the uterine and reflected internal pudendal arteries. Three additional sutures were required to achieve adequate haemostasis. The cornu was re-anastomosed in the routine manner.

DATE OF LAPAROTOMY: 7th March 1974.

DURATION OF SURVIVAL: 45 days.

MACROSCOPIC ASSESSMENT:

Whilst there were minimal adhesions noted in the general abdominal cavity, there were extensive adhesions present in the pelvis and around the genital organs.

The transplanted oviduct appeared partially viable, but it was somewhat shrunken and fibrosed. Its lumen appeared to be filled with pus. A small section of its fimbrial end was viable. The cornual anastomosis was patent. The ovarian vein appeared to be healthy and patent.

The uterine artery resembled a fibrosed cord and was obviously thrombosed. The residual cornua were grossly hypertrophied in a classical oestrus-like manner.

HISTOLOGICAL ASSESSMENT:

The transplanted oviduct and cornu were extensively fibrosed. Whilst some outer serosal and muscle tissues appeared viable, the inner layers revealed necrosis, loss of the endosalpinx and replacement with fibrous tissue. Necrosed tissue filled the lumen of the structure as an amorphous eosinophic mass and there was no cellular infiltration of this material. The uterine artery was thrombosed but recanalisation of its lumen had occurred. The ovarian vein appeared healthy, and there was no thrombus present in its lumen. The site of anastomosis was patent with minimal adjacent cellular reaction.

OVERALL COMMENT:

The changes were compatible with progressive ischaemic necrosis followed by a fibrous tissue response. There was no evidence of active sepsis.

APPENDIX 5

Case reports of group 3 - vascularised autotransplants of oviduct with ipsilateral ovary

CASE No. 1

Age of animal - $6\frac{1}{2}$ months   Operating time - 5 hours

Stage of cycle - non-oestrus   Date of operation - 7.6.73

POINTS OF NOTE:

Venous, arterial and cornual anastomoses were performed without event. The ovary was conserved.

POSTOPERATIVE COURSE:

The animal became ill on the 8th postoperative day and died 2 days later.

DATE OF POSTMORTEM: 17th June 1973.

DURATION OF SURVIVAL: 10 days.

MACROSCOPIC ASSESSMENT:

The lungs had the appearance of bronchopneumonia, the spleen appeared reactive and the kidneys appeared somewhat oedematous on cut section.

The abdomen contained approximately 500 ml of purulent fluid and there was clearly evidence of peritonitis. Purulent and fibrous material was seen between adjacent segments of the small bowel and between the convoluted cornua and oviducts within the pelvis.

The transplant appeared as an enlarged, totally necrosed and septic specimen. The dilated necrotic oviduct appeared to contain a cast of necrotic and purulent material. Both the artery and the vein were thrombosed.

HISTOLOGICAL ASSESSMENT:

The transplanted oviduct showed extensive necrosis particularly of the endosalpinx and inner aspect of the muscular layer. There was also evidence of extensive suppurative inflammation compatible with a florid, severe salpingitis. These changes were also observed at the site of the cornual anastomosis.

The transplanted ovary was completely necrotic. Many inflammatory cells were noted amongst areas of necrosis and scattered areas of calcification. The smaller venules observed were occluded by thrombus.

The uterine artery was occluded by a thrombus which was undergoing organisation. Areas of calcification were noted in its walls. The ovarian vein was completely occluded by thrombus and areas of dystrophic calcification were noted in its walls.

Sections of lung examined revealed pyaemic abscesses. Sections of kidney showed evidence of focal embolic nephritis compatible with septicaemia and pyaemia. The spleen showed evidence of a septic reaction. The heart was normal. Other than vascular congestion, the sections of liver examined were normal.

OVERALL COMMENT:

Death had occurred due to severe septicaemic and pyaemia. This was linked to severe suppurative inflammation of the transplanted oviduct and ovary and an associated peritonitis.

The transplanted specimen had undergone extensive necrosis and this was associated with a severe suppurative inflammatory process. It was felt that the most likely course of events had been ischaemia, necrosis and subsequent secondary infection.

CASE No. 2

Age of animal - 6 months   Operating time - 5 hours

Stage of cycle - early oestrus   Date of operation - 12.6.73

POINTS OF NOTE:

Venous, arterial and cornual anastomoses were performed without event and the ovary was conserved.

POSTOPERATIVE COURSE:

The animal did not thrive and required intermittent courses of antibiotics to maintain it in a relatively healthy state during its postoperative course.

DATE OF SACRIFICE: 21st August 1973.

DURATION OF SURVIVAL: 70 days.

MACROSCOPIC ASSESSMENT:

In view of the fact that the animal had never been completely healthy as assessed clinically following the operation, a full postmortem was performed.

Abdominal findings: Extensive adhesions were noted in the lower abdomen and pelvis. Approximately 200 ml of serous fluid was found in the abdominal cavity.

The transplanted oviduct and ovary both appeared to be necrosed and the inner aspect of the dilated oviduct was filled with necrotic caseous-looking material.

The uterine artery and the ovarian vein both had the appearance of a fibrosed cord-like structure and both appeared to be thrombosed.

The lungs were relatively solid in consistency and had the superficial appearance of a bronchopneumonic pneumonic process. The heart, kidneys, spleen and liver appeared to be normal on macroscopic examination.

HISTOLOGICAL ASSESSMENT:

The transplanted oviduct and cornu were almost totally necrotic and infiltrated with inflammatory cells. In some areas, a thin rim of surviving outer muscle cells was noted beneath the serosal surface of the structure. Obvious bacterial colonies were noted within the necrotic and purulent material. The cornual anastomosis showed normal cornu with some inflammatory cells on one side and necrotic and infected cornu on the other.

The transplanted ovary was entirely necrotic and infiltrated with inflammatory cells. An inflammatory exudate was present on the surface of the broad ligament. Its vessels were necrotic and some contained thrombi. The uterine artery and the ovarian vein were both filled with thrombus and the vessel walls were partially necrosed and partially replaced by a fibrous tissue response.

Sections of lung examined revealed pyaemic abscesses and a suppurative pneumonia. The splenic pulp contained numerous inflammatory cells and findings were consistent with the appearance of a septic spleen. Sections of the heart, liver and kidneys were normal.

OVERALL COMMENT:

The transplanted tissues had undergone extensive necrosis and there was evidence of secondary infection and gross suppuration.

The animal had probably suffered bouts of septicaemia and pyaemia and this had resulted in the suppurative pneumonia and pyaemic abscesses present in the lungs.

These findings explained its failure to thrive during the postoperative phase. Failure to provide an adequate blood supply for the transplanted tissue appeared to be the prime factor resulting in the overall pathology noted.

CASE No. 3

Age of animal - 6 months   Operating time - 3 hrs 45 mins

Stage of cycle - oestrus   Date of operation - 19.6.73

POINTS OF NOTE:

Venous, arterial and cornual anastomoses were performed without event and the ovary was conserved.

POSTOPERATIVE COURSE: This was uneventful.

DATE OF SACRIFICE: 21st August 1973.

DURATION OF SURVIVAL: 63 days.

MACROSCOPIC ASSESSMENT:

There were scanty adhesions present in the lower abdominal cavity. This contrasted with the pelvic findings, where there were fairly extensive adhesions found between the kinked and convoluted sections of the cornua.

The transplanted specimen appeared as a fairly large necrotic tubo-ovarian mass (Fig. 42). A longitudinal incision of this structure resulted in a cast of purulent material falling from within the lumen. Its outer surface resembled the rugae of the oviduct mucosa.

The cornual anastomosis was patent. The ovary appeared to be necrosed and infected. Both the uterine artery and the ovarian vein were occluded by thrombi.

HISTOLOGICAL ASSESSMENT:

The transplanted oviduct and its contiguous cornu were extensively necrosed. In some areas, the wall of the oviduct was thickened and there was evidence of a chronic infective process present. The "cast" of purulent-looking material was indeed a cast of necrotic tubal mucosa and tunica propria with inflammatory cells noted on its outer surface. It had literally sloughed from the inner layer of the oviduct and was lying free within the lumen. Marked necrosis was seen in the sections of ovary examined, but in some areas it was partially viable. These areas appeared as viable connective tissue resembling ovarian stroma, but there were no recognisable follicles, corpora lutea or corpora albincantes seen. A marked chronic inflammatory reaction was present.

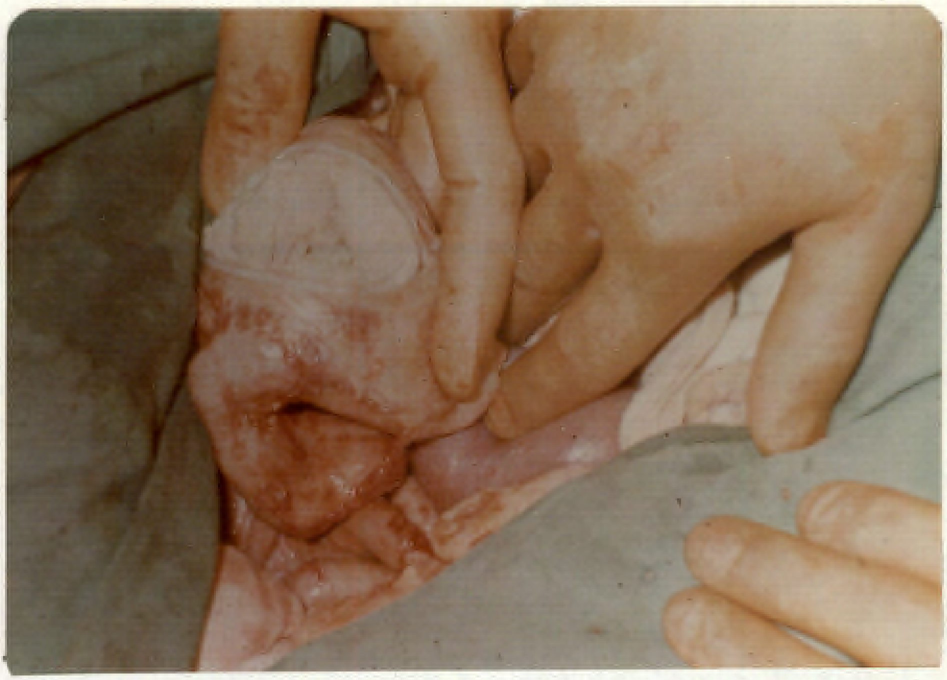

Fig. 42. Appearance of necrotic cast of oviduct and tubo-ovarian abscess in a case of tubo-ovarian auto-transplantation.

The transplanted cornu showed a fair amount of viable tissue present close to the site of the cornual anastomosis. This included viable mucosa in some areas but it was otherwise necrosed. There were many inflammatory cells and histiocytes present at this site.

The uterine artery and the ovarian vein were both occluded by organised thrombus. A pelvic lymph node submitted to histological examination showed reactive inflammatory changes.

OVERALL COMMENT:

Vascular failure resulting in extensive necrosis and associated sepsis. The inner mucosa had leterally sloughed into the lumen of the transplanted structure as a necrotic septic cast.

CASE No. 4

Age of animal - 7 months   Operating time - 4 hours

Stage of cycle - non-oestrus   Date of operation - 21.6.73

POINTS OF NOTE:

Venous, arterial and cornual anastomoses were completed without complication after the excised specimen had been perfused in the routine manner.

POSTOPERATIVE COURSE: This was uneventful.

DATE OF SACRIFICE: 21st August 1973.

DURATION OF SURVIVAL: 61 days.

MACROSCOPIC ASSESSMENT:

Minimal adhesions were found in the general abdominal cavity. Extensive adhesions were found in the pelvis, particularly between the convolutions of the cornua.

The cornual anastomosis was patent but opened into the transplanted specimen which had the appearance of a dilated bag of necrotic tubo-ovarian tissue. On incising the oviduct, a purulent necrotic cast of its inner surface fell away from within the lumen of the structure as seen in the previous case.

The ovary appeared to be necrosed. The uterine artery was thrombosed but the ovarian vein appeared healthy and patent at its site of anastomosis.

HISTOLOGICAL ASSESSMENT:

The external muscular layer and sub-serosal surface of the transplanted oviduct appeared to be viable. The mucosa and lamina propria were completely necrotic and contained an infiltrate of inflammatory cells. Once again this necrotic mass had the appearance of a sloughed cast of the inner layers of the transplanted oviduct.

Where the tube was viable, its inner surface contained a marked inflammatory response where the mucosa and lamina propria had sloughed. This inflammatory response included many histiocytes, foamy giant cells and other chronic inflammatory cells.

Some viable tissue was observed in the outer layers close to the site of the cornual anastomosis, but the mucosal layer was necrotic and contained an inflammatory cellular reaction.

The ovary was only recognisable as some viable connective tissue stroma. Many macrophages, histiocytes and giant cells were observed on its outer aspect together with a chronic inflammatory infiltrate. This reaction appeared to be a response to the necrotic tissue present. No normal ovarian structures could be identified.

A pelvic lymph node examined was reactive with follicular hyperplasia, and inflammatory cells were present in the sinusoids.

The uterine artery was occluded by old organised thrombus. The ovarian vein was identified, its wall was extensively replaced by connective tissue, but no thrombus was seen at the site of anastomosis which was patent. The sections of heart, liver, kidney and lungs examined were all normal. The splenic pulp contained a moderate infiltrate of chronic inflammatory cells.

OVERALL COMMENT:

This case was very similar to Case No. 3 of this series. The findings were compatible with severe ischaemia, extensive necrosis and evidence of chronic sepsis and inflammatory reaction.

The inner layer of the transplanted oviduct had sloughed into the lumen. The ovary was also necrosed and contained no recognisable normal physiological components.

CASE No. 5

Age of animal - Operating time - 4 hours

Stage of cycle - early oestrus Date of operation - 26.6.73

POINTS OF NOTE:

The arterial anastomosis appeared to be leaking excessively at two places when the vascular clamps were released. Adequate haemostasis was achieved by inserting a single suture at each of these sites.

The venous and cornual anastomoses were completed in the routine manner and were uneventful components of the procedure.

POSTOPERATIVE COURSE: This was uneventful.

DATE OF SACRIFICE: 21st August 1973.

DURATION OF SURVIVAL: 56 days.

MACROSCOPIC ASSESSMENT:

Many adhesions were noted in the general abdominal cavity in addition to the extensive adhesions present within the pelvis. These were particularly concentrated between the convolutions of the uterine cornua.

The transplanted oviduct appeared to be viable and healthy in its general appearance but appeared to be septic in some areas. It was hypertrophied as was the residual cornu and this appearance was compatible with a normal oestrus response. The cornual anastomosis was patent but slightly stenosed.

The ovary appeared to be viable and healthy and some functional cysts were noted in the cortex. Both the uterine artery and the ovarian vein appeared to be patent.

HISTOLOGICAL ASSESSMENT:

The transplanted oviduct was clearly viable in its outer and inner mucosal layers, but inflammatory cells were present. These were compatible with an acute superimposed on a chronic salpingitis. A fair amount of fibrosis was seen in the tunica propria. Examination of sections of transplanted cornu close to the site of cornual anastomosis revealed viable muscularis and mucosa but the latter layer was infiltrated with a moderate number of plasma cells and polymorphs.

The ovary was normal and healthy. Follicular cysts and primordial follicles were seen. There were no inflammatory cells observed at this site.

The uterine artery was patent but there was slight thickening of the intimal surface. The ovarian vein appeared to be healthy although its intima was also thickened. The venous anastomosis was healthy.

A regional lymph node taken from the pelvis showed a moderate inflammatory reaction. Sections of the kidneys, liver, heart, lungs and spleen examined were all normal.

<u>OVERALL COMMENT</u>:

There was vascular patency with a viable oviduct and functional ovary but the transplanted tube contained evidence of chronic salpingitis. Extensive pelvic adhesions with gross distension of the cornu and transplanted oviduct compatible with an oestrus response were seen.

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