EXPERIMENTAL VENOUS RECONSTRUCTION

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CONTENTS

SUMMARY OF INVESTIGATION

The Author proposed a method of enhancing the patency of venous grafts using an arteriovenous fistula. A pilot study was initiated to test the feasibility of venous grafting in the iliac veins and to gain expertise with an experimental model. The initial experiment provided equivocal results using isotopic autografts and a further study was initiated using polyamide (Dacron) grafts, in conjunction with an arteriovenous fistula.

In another related study the iliac veins were replaced with autografts and allografts, each bearing a competent valve; in this project a fistula was demonstrated to have no effect on the patency of the grafts.

The effect of an arteriovenous fistula was investigated in some detail with intra-operative blood flow measurements using an electromagnetic blood-flow recorder. An effort was made in each series to correlate the flow-rate through the graft with their subsequent size. The size of the grafts was measured in the experimental animal by serial venography.

RELEVANCE OF EXPERIMENTS TO THE SCIENCE AND PRACTICE OF SURGERY

Blood flow may be sluggish or stagnant in the venous system without coagulation necessarily occurring. In contrast a venous graft readily thromboses unless active steps are taken to prevent this. The reasons for the ready thrombosis of vein grafts are poorly understood and provide a marked contrast with the patency of arterial grafts. This study is an attempt to find ways of enhancing the patency of vein grafts.

Numerous authors have commented on the beneficial effects of increased blood flow through a venous graft in relation to its continuing patency, and several workers have speculated on the reasons for this. Up to the present time no author has attempted to quantify the flow through a venous graft and relate this to its patency. This is surprising, as several authors have increased the graft blood flow by means of an adjacent arteriovenous fistula but have then failed to relate this increase to the subsequent size of the graft or its patency.

The present author set out to measure blood flow in relation to the vein grafts and then study the subsequent size of these grafts by means of venography.

It was hoped that these observations would provide some understanding of the way in which blood flow is related to the size and fate of venous grafts.

The Author's experimental work has relevance to surgical practice, where a successful technique of venous grafting could fill a surgical need. At the present time grafts in the venous system are rarely performed, an expression of failure rather than lack of clinical requirements.

PREFACE

In contrast to the great advances made in arterial surgery over the past 25 years, the results in the field of venous replacements still leave much to be desired. Of the hundred or so papers published since 1950, many have produced encouraging results, but none have given surgeons the confidence to carry out venous grafting as a recognised clinical procedure in the same way as arterial grafting.

This study is an attempt to delineate some of the factors which may be of significance in venous reconstructuve surgery, in an effort to provide a basis for its wider application in two types of clinical situations: they are (1) the replacement of large proximal veins which are occluded either by extrinsic pressure or internal obliteration; (2) the insertion of valves into the popliteal and/or femoral veins when their function has been destroyed by past thrombosis and subsequent organisation.

Venous obstruction and valvular incompetence of major veins constitutes a small but significant problem in clinical practice, which at the present time is not amenable to current surgical techniques. Wider understanding of the problems of venous reconstruction, initially by experimental work, should be the way of altering this situation.

HISTORICAL SURVEY AND REVIEW OF THE LITERATURE

Techniques of venous anastomosis and venous grafting have been studied intermittently since the 19th Century - indeed the first successful venous anastomosis recorded was performed by Eck. (1897), he joined the portal vein to the inferior vena cava, a procedure subsequently used by many experimental physiologists and surgeons.

Payr (1900) attenpted the anastomosis of a human femoral vein by invaginating it over a cylinder of Magnesium, and Clermont (1901) published several successful cases of anastomosis of the inferior vena cava, using a continuous everting mattress suture. Alexis Carrell's published works describe experimental vascular surgery in mammals, including techniques of venous grafting. (Carrell 1902). His comments on the technique of vascular suture are apposite in the field of venous anastomosis and were used by the Author in the experiments described later.

The first attempt at venous grafting (as opposed to venous anastomosis) was reported by Exner (1903). He transplanted autogenous segments of jugular vein 4 cms long into the vein on the opposite side in two dogs, using the prosthesis described by Payr. Thrombosis developed in both animals. Jensen (1903) in a similar series, using a suture technique, had a little more success. Subsequent reports, include an attempt by Borst and Enderlen at replacement of the jugular vein with a carotid allograft in the dog (Kunlin 1953); restoration of the popliteal vein in man with a xenograft sheep vein by Doyen (Kunlin 1953); and an experimental replacement of the inferior vena cava by Jeger and Israel (Kunlin 1953). The results of the experiments were for the most part inconclusive.

Virtually no experiments concerning venous reconstruction work were published between the years 1905 and 1947, and the renewal of

interest in venous surgery coincides with the renaissance in vascular surgery generally at the end of and after World War II. The paper by Johns is the first in modern literature and reveals the early preoccupation with different methods of suture, his work compared suture and non-suture methods of anastomosis in veins (Johns 1947).

It is convenient to discuss the experimental venous work of the last twenty five years in categories related to the site of these grafts, as this has a bearing on their success rate and makes discussion more convenient.

The following review is limited to systemic vein grafts, in the experimental situation.

SUPERIOR VENA CAVA GRAFTS: SVC obstruction is an uncommon clinical problem which presents as venous engorgement of the head, neck and upper limbs associated with plethora and oedema of that region. The commonest cause for this is malignant disease either primary or secondary, although a small proportion of cases are due to benign tumours, cysts and chronic fibrosing mediastinitis.

SVC obstruction is often fatal. Resection of the offending tumour may be possible, but often the SVC is intimately involved with the obstructing growth and a by-pass procedure has to be contemplated. In this situation the SVC cannot be used directly as it is relatively short and cannot be mobilised. Various workers have cast around for a suitable alternative. From the 1950s up to the present time there appears to be no consistently successful practical alternative to the SVC in such a by-pass procedure. Expressed in different ways and occasionally not mentioned directly the various authors discussed below have felt it behoved them to find such a suitable alternative material in the experimental animal which they could apply to the clinical situation and this was the motivation for their publication.

Direct anastomosis of the azygous vein to the right auricle, or its distal cut end to the SVC, in the presence of an experimentally produced SVC obstruction, was first performed by Gerbode with satisfactory results (Gerbode 1949); his aim being the relief of an SVC obstruction by a simple technique; however, in these cases only one suture line was required, a procedure known to be less hazardous than a free graft (Dale 1963). This procedure has limited application due to the anatomy of the azygous vein and the length available for by-pass.

The first successful report of preserved allografts and synthetic tubes was by Deterling and Bhonslay (1955). Their best results were with polyester (Dacron) and polyamide (Nylon) grafts using a continuous suture technique and stay sutures. Polyvinyl alcohol grafts (Ivalon) were also used but these all stenosed. Aortic allografts have been used in other series but stenosis was the usual occurrence (Ashburn et al. 1956; Enerson and Galante 1957). In a further series in Enerson's paper, nylon rings were used to support the anastomotic lines and this was found to be more successful. In contrast to the allografts, Moore and his co-workers found that fresh autogenous aorta remained patent in every SVC graft (Moore and Ribiri 1958; Moore et al. 1962). He used the SVC as a standardised site in order to compare the suitability of different types of graft material in this position. It is perhaps unfortunate that he picked a site which is relatively favourable for most types of graft, (a fact not so obvious in 1962 as it is now) so that differences between graft materials are not so clear cut. The following year they published a further series using preserved aortic xenografts, again with satisfactory patency rates (Moore and Mendelbaum 1963). In 1964 Moore summarised his results in the SVC (Moore and Young 1964). He comments on the unsuitability of the present materials and says that synthetic materials are probably the most

practical, as tissue grafts are unavailable or difficult to use; in descending order of success he found that autogenous tissues, polytetrafluoroethylene (Teflon), allografts and polyester grafts all gave acceptable results in the canine experimental model. Many of these grafts were observed by venography for over a year, and the number of animals used enhanced the validity of the results. It is pertinent to note that the polyester grafts used were all pre-treated with toluene di-isocyanate to make them more rigid.

Botham and his co-workers used a hollow sponge prosthesis made of Teflon in the SVC with reasonable success in twenty animals (Botham et al. 1960). They experimented with synthetic grafts as the latter appear "the most logical, feasible and applicable". This was followed by a report from East and Muller (1960) using a Teflon woven prosthesis after an artificial caval occlusion several months before. Heparin was used peri-operatively in these animals with no apparent benefit. In the introduction to their paper they reviewed the symptoms and signs of SVC obstruction and commented on its causes. Their review of the literature led them to conclude that autogenous vein was the best substitute for vein replacement, but this was impossible, and thus synthetic grafts were the next best alternative.

Howard and his associates reported little success with SVC replacement using a variety of materials; only tracheal allografts and Teflon grafts externally supported were of any use (Todd et al. 1963). They attribute the success of these materials to their relative rigidity and say that this is necessary in a low pressure system like veins. They also commented unfavourably on low molecular weight dextran and warfarin which they used concurrently with the grafting procedures in an effort to prevent graft thrombosis. They state that two essential principles must be borne in mind when choosing a synthetic graft;

semi-rigidity to keep the graft from collapsing, porosity inherent in the knitted character of the graft, to allow tissue growth so that the graft may be permanently incorporated as part of the vascular system. In a further series of Teflon grafts using a carotid jugular fistula there were enhanced patency rates when the fistula was used (Mitsuoka and Howard 1966). Their reason for experimenting with an arterio-venous fistula was the appearance of several papers reporting its successful application in venous grafting. The increase in intramural pressure with a fistula (Bryant et al. 1958) and the consequent graft rigidity appeared to fit in with the concept of enhancing graft patency mentioned previously. They noted that a carotid jugular arteriovenous fistula had no effect on the pressure within the SVC, which remained near the pre-operative level. They comment that other factors must be responsible, but the evidence for any one is so far inconclusive. In this paper Mitsuoka and Howard also noted that the length of the Teflon grafts had a marked effect on patency, as might be expected.

Experience with carotid jugular fistulas was also reported in papers by Schenin and Jude (1964) and Holt and Lewis (1965), in both cases using Teflon grafts, as they comment that this appears to be the best material currently available. Referring to earlier papers Schenin mentions that the low venous velocity has received much of the blame for SVC graft failure, and that concomitant azygous ligation improved the results of grafting, by increasing the rate and volume of the venous flow through the graft. He postulates that an arterio-venous fistula should have a similar effect. In both papers the patency rate of the venous grafts was enhanced in the presence of a fistula, the results being particularly impressive in Holt's paper where thirty-four animals were studied for nearly two years. Schenin and Jude also reported their experience with Dacron and autogenous vein

in conjunction with the fistula, and obtained similar results with a total of twenty-two animals studied over five months (Schenin and Jude 1964).

In this connection it is notable that Dale (1963) obtained better results with the SVC grafts, (Dacron, Teflon and autogenous vein) with azygous vein ligation. He comments that on removing a major collateral i.e. the azygous vein, there is an increased flow in the SVC.

Two authors reported their experience using a mechanical stapling device for anastomosis (Takaro et al. 1962; Sylvestri and Intini 1968). The theoretical benefit of this device is the speed with which the anastomosis is completed, and the standardisation of the diameter between graft and recipient vein. In Sylvestri's paper autogenous veins were used with apparently complete success in one year, although venograms were not performed in the intervening period so thrombosis and recanalisation may have occurred. Takaro and his colleagues used this device with success in direct cavo-caval anastomosis, and they comment on the speed and ease with which suture was performed. Their comments on the porosity and relative rigidity of the synthetic grafts are instructive. They conclude that with two grafts of similar porosity, graft rigidity is the important factor in determining patency and with the treated polyester grafts they used, the more rigid (but less porous) grafts were more successful than the collapsible but more porous ones. They go on to say that rigidity and biological reactivity of the graft material appears to be of more importance than porosity from the standpoint of long term patency.

INFERIOR VENA CAVAL GRAFTS: In the introduction to their paper, Ohara and his colleagues outlined some of the reasons why the great veins of the thorax and abdomen may have to be substituted on occasion (Ohara et al. 1957). They state that the inferior vena cava (IVC) may

have to be excised in the course of radical operations for malignant disease and point out that excision of the IVC above the renal veins is invariably fatal. From these observations they conclude there is a need for a suitable venous replacement and they go on to report their experiences with three types of graft material. They had no success with silicone rubber tubes nor with alcohol preserved allografts in the IVC, and only partial success with polyamine resin tubes (Amylan). Unfortunately, their experience with each group of grafts was small, and they did not follow the fate of their patent grafts for more than three weeks, barely time enough to guarantee that they would remain patent. Bryant and his colleagues reported similar experience with polyester (Orlon), Nylon and Teflon grafts. All these grafts failed although he had considerable success with the fresh autografts (Bryant et al. 1958). He comments that the inadequate experimental results associated with the use of replacements for the vena cava suggest a need for further investigation of the problem.

Bower and his associates in a large series compared several methods of IVC replacement, using cross clamping for ten minutes as a control (Bower et al. 1960). They were concerned with the failure of allograft and plastic materials compared with autograft replacement and were looking for the factors which influenced the discrepancy in their results. They had reasonable success with autografts and partial success with allografts. All the synthetic materials used gave inferior results. They attribute the failure of the synthetic materials to an initial stenosis at the proximal end of the graft and go on to say that this may be due to the decreased intraluminal pressure within that end of the graft. They suggest the use of an arteriovenous fistula as a means of increasing the intraluminal pressure. Demetz and his colleagues say that the replacement of venous

defects remains one of the unsolved problems in vascular surgery (Demetz et al. 1961). They found that human fibrinolysin had no effect on the patency of autografts or a variety of plastic prosthesis (Nylon, Dacron and Teflon). All the prosthetic grafts thrombosed. This study clearly demonstrated the superiority of autogenous material over the currently available synthetic substitutes.

After his successful experience with SVC grafts using external support in the form of a ring around the anastomosis, Todd and his fellow workers had some success using this method with Dacron grafts in the IVC, and again tracheal grafts were relatively successful (Todd et al. 1963). Their overall patency rates were much lower in the IVC than the SVC, a fact which they only mention but do not comment upon, or try to explain. Noszczyk commented on the encouraging results obtained with synthetic grafts using external support, reported in the literature (Noszczyk 1971). In a small series he was able to demonstrate the effect on patency rates of polyester fibre grafts in the IVC with the elegant use of stainless steel wire. Stainless steel wire as an external support has been successfully used earlier for IVC replacement (Shore et al. 1964; Caballero et al. 1969). Both these authors were looking for methods of improving the patency of autografts in the IVC, which fare badly compared with the SVC. In the Italian paper, the authors state that the simple wire rings which supported the anastomosis, tended to angulate and they modified these rings by attaching a bar perpendicular to the ring which ran alongside the graft. This prevented angulation of the support and was more satisfactory.

A different approach to the problem of unsuccessful IVC grafts was adopted by Inokuchi and Ono (1966). They mention the lack of success of synthetic grafts in the IVC and the unavailability of suitable autogenous grafts. They used polyester grafts which had been placed in a

canine aorta several weeks before, and were covered in pseudointima. Although the pseudointima became necrotic and was replaced they were able to demonstrate a distinct advantage over controlled grafts (using fresh polyamide).

On somewhat similar lines, Padula and his colleagues (Padula et al. 1969) reported the use of an autogenous tube produced by a reaction to the implantation of a Silicone rubber (Silastic) cylinder into canine muscle. Four weeks after implantation the tube of autogenous tissue was re-implanted into the IVC. The results obtained were not very dramatic, with half the grafts remaining patent. This does not represent an advance over autogenous vein replacement in this site.

Ashton and his co-workers investigated the use of Silicone rubber as a venous prosthesis using a porous woven graft, as the physical properties of this material appeared suitable, i.e. rigid yet porous (Ashton et al. 1969). Using grafts up to 10 cms long they reported a patency rate better than most authors experienced in this site. They explain the relative success of this material in terms of its somewhat rigid structure which prevents graft compression by fibrous tissue. This material seems to have potential as a venous substitute but there are no further reports of its use in the literature. The results of Ashton and his colleagues compare favourably with the reported use of Silastic reinforced Dacron for IVC replacement by McCaughan who had no success at all with short grafts (McCaughan 1969). He was hoping that the semi-rigid properties of this material combined with its trivial tissue reactivity would minimise fibrosis and subsequent thrombosis. An aspiration that was not borne out in practice.

Sauvage and Gros (1960) compared preserved allografts and autografts and found that all the aortic allografts stenosed. With fresh autografts all were successful. This was a small series and it is

difficult to draw any serious conclusions but in the discussion at the end of the paper they mention thrombosis and contracture (among others) as complications of venous grafting. They go on to say that preserved aortic allografts are particularly prone to these complications and that autogenous vein is the material of choice although it is rarely of suitable calibre. In Sauvage's series compilation* autografts were used, a technique also used by others to increase the size of the donor jugular veins (Earle et al. 1960; John et al. 1961; Shore et al. 1965). In Earle's paper there was some success in the distal IVC grafts but John and his colleagues had none. The experience of Collins and his co-workers with fresh autogenous aorta was similar to that quoted above (Collins et al. 1960). There were no successful grafts in his animals. The impasse of IVC graft failure was circumvented by Scheinin and Jude (1963). They showed that autogenous jugular veins could be grafted into the IVC with a superior patency rate to those in the control group, if a femoral arteriovenous fistula was used. Ths fistula was closed after one month. They briefly discuss the factors involved in successful venous grafting and state the single most important factor appears to be blood flow through the graft. They quote Dale and Scott (1963) and Bryant and his colleagues (1958) as evidence to support this statement, and emphasize that the increase in blood flow need only be temporary for as soon as healing along the suture lines has occurred, the risk of graft thrombosis is minimal. These results were confirmed in the following years by Stansel (1964) and Steinan, Alpert and Haimovici (1966) using plastic grafts (Teflon and Dacron). These authors used

* This is a technique whereby two pieces of narrow vein are split longitudinally, opened out and then sutured together as they lie side by side. The composite vein is then joined into a cylinder nearly twice the diameter of the original vein.

an arteriovenous fistula for the same reasons as Scheinin and Jude, although in addition they mentioned the increase in venous pressure produced by a fistula. Stansel states, however, that the increase in blood flow is more pronounced than the increase in pressure and attributes the beneficial effect of an arteriovenous fistula to the increase in blood flow. Mitsuoka and Howard (1968) used Teflon grafts in the IVC in a series of experiments illustrating the beneficial effect of external support and a distal arteriovenous fistula. They also demonstrated that closing the fistula after three weeks did not effect the subsequent graft patency. This was a follow-up to their earlier work (Mitsuoka et al. 1966) using Teflon grafts in the SVC. The cumulative effects of external support and an arteriovenous fistula are well demonstrated in this paper.

In contrast to the abdominal IVC, grafting procedures in the intra-thoracic IVC are much more successful. There are two reports on the use of knitted Teflon grafts in the thoracic IVC with good results in both cases (Davalos et al. 1960; Hambraeus et al. 1962). Davalos and his colleagues were looking for a suitable material to use in Baffes procedure (Baffes 1957), where a graft is inserted between the left atrium and the great vessels. Both series were moderately large and the grafts were studied for several months. In Hambraeus' series there was a significant difference between the series of thoracic grafts and a further group of abdominal grafts in the IVC, which the authors attribute to the differences in pressure exerted on the grafts in these two sites.

Maclean and his fellow workers comment on the previous reports of graft stenosis in the literature, and use this as the reason for experimenting with a graft of Ivalon supported by rigid plastic rings (Maclean et al. 1959). They had reasonable success with this

prosthesis, and it compared well with the fresh aortic allografts they used for comparison, both series of grafts were observed for many months.

Two authors have discussed the low pressure characteristics of veins in relation to graft failure, and then have suggested testing this hypothesis with porto-caval grafts. The portal venous pressure is higher than that in the IVC and it is argued that a graft communicating between these vessels would be sustained by the pressure difference. Symbas and his colleagues contrasted the success of porto-caval shunts with portal vein grafts (Symbas et al. 1966; Foster et al. 1965). Allografts and Teflon grafts were unsuccessful in the portal vein unless intensive Heparin therapy was instituted for the first week, and even with this treatment half of the grafts thrombosed. Using Teflon grafts and allografts for porto-caval anastomosis there was a very high patency rate without the use of Heparin, and the authors attributed this success to the pressure gradient between the portal vein and the IVC.

GRAFTS IN THE JUGULAR VEIN: Little attention has been given to the external jugular vein as a site for venous grafting, although papers concerned with this area report favourable results with autogenous vein grafts.

Consistently successful replacement of the internal jugular vein would be a useful adjunct to block dissection of the neck, for one jugular vein must be left in situ in a bilateral procedure to safeguard the patient's life.

Egdhal and associates reported on the use of grafts with external support i.e. Silicone lined polyethylene, and had good results especially when the supports were small or contained large perforations (Egdhal et al. 1954). Using the silicone-lined polyethylene material

for the graft was completely unsuccessful. They comment that the supporting structure of the graft must be porous enough to allow the ingrowth of granulation tissue, which infiltrates the graft substance. Schauble and his colleagues reported similar success with unsupported autografts and like Egdhal had no synthetic grafts patent in their series (Schauble et al. 1959). They comment that the jugular grafts are in an isogravitational blood flow, a statement which is difficult to relate to the usual position of a dog's neck.

Haimovici and his co-workers reported favourably on the use of autogenous bypass grafts using end-to-side anastomosis to the jugular vein (Haimovici et al. 1963). They thought that this technique was more applicable to the clinical situation than end to end anastomosis. However, they found that there were more failures when the grafts were used as a collateral circulation, i.e. the blood flow was reduced through the graft.

GRAFTS IN THE FEMORAL VEINS: Many authors have turned their attention in the experimental animal to femoral vein grafts as they present a useful model. The femoral vein in the dog is of a reasonable size and is readily accessible throughout its length, being mainly subcutaneous. In addition, the external jugular vein is of comparable size and so provides a suitable donor site for grafts. So it is not surprising that the majority of experimental venous grafts relate to autografts in the femoral vein. Bryant and his colleagues in an early and often quoted paper, had successful results with femoral vein replacement using autografts (Bryant et al. 1958). They then tried to repeat this success with Nylon grafts using an arteriovenous fistula. Their reasons for using a fistula (the first recorded time in the literature for experimental vein grafts) are not clearly stated, though they do discuss the effect of venous pressure on graft patency

in relation to SVC and IVC grafts, and by inference assume that the increased pressure caused by the adjacent arteriovenous fistula would enhance the patency of their plastic grafts. This hypothesis was first proposed by Kunlin (1953). Two completely different methods of fistula construction were used by Bryant and his colleagues, but there were only four grafts in each group so no valid conclusions can be drawn. It is of significance, however, that he was able to keep Nylon grafts patent in the femoral vein by using a fistula, a fact which did not escape the attention of later workers.

Smith and Schisgall (1963) repeated and extended earlier work with a series of femoral autografts using a more conventional side-to-side femoral arteriovenous fistula. They comment on the low pressure and blood flow characteristics of the venous system, and note that vein grafts are successfully used in arterial surgery. In using an arteriovenous fistula, they were hoping to mimic the conditions found in the arterial system. They had a series of controlled grafts and the dogs were studied for several months. Two-thirds of the grafts were patent overall but there was no significant difference between the two groups of grafts. These findings were confirmed by Johnson and Eiseman (1969) using two different types of arteriovenous fistula to alter the patency of femoral autografts with control grafts on the opposite side. Although the only failures were in the control grafts, the total number of grafts was too small to draw any conclusions. Levin and his co-workers in a further series of femoral autografts were also unable to demonstrate a beneficial effect of an arteriovenous fistula, although their results may have been more conclusive if the grafts had been studied for a longer period (Levin et al. 1971). These three papers all demonstrate high rates of patency in femoral autografts. With such favourable graft material in what is now known to be a

favourable site, it is perhaps the overiding influence of these two latter factors which obscures the effect of an arteriovenous fistula on patency.

Mitsuoka and Howard (1968) using a temporary arteriovenous fistula attempted to graft Teflon into the ilio-femoral segment in dogs. Rings of rigid plastic were used to support the anastomotic line externally, but their grafts all thrombosed. (This was part of a series of grafts discussed earlier). Since Schauble, Anylan and Postlethwait (1959) reported considerable success with autografts in femoral vein replacement, several large series have confirmed these results (Silver et al. 1961); Cerino et al. 1963; Waddell et al. 1964; McLachlin et al. 1965). In the latter papers, continuing valvular function was also seen in many of the grafts. In another large series, De Weese and Niguidula (1960) had little success with the autografts performed early in their experiments but their later results were excellent - presumably due to the improvement in technique. They also report continuing valve function in their successful grafts. Only two papers have reported poor results with femoral autografts, although it is perhaps significant that both these authors were using several different adjuvant techniques to enhance patency, and these may have affected the results (Baird et al. 1964; Eadie and De Takats 1966).

Experience with allografts (both fresh and preserved) has been reported (Schauble et al. 1959; Earle et al. 1960; Waddell et al. 1964). All three papers demonstrate much lower patency rates with this material compared with autografts, although the fresh allografts gave better results than the preserved ones.

The role of anti-coagulant and fibronolytic agents in venous grafting has not been studied in great detail up to the present time

and the results are inconclusive. From theoretical considerations this would seem to be a useful method of enhancing graft patency and a logical way of overcoming the thrombotic tendency of the grafts during the first few weeks. Haimovici and his colleagues reported favourably on the consecutive use of heparin and coumarin (Haimovici et al. 1963). O'Neill and Foster (1966) had similar results using Heparin alone, but they were not enthusiastic about its use. De Weese and Niguidula (1960) reported inconclusive results with Heparin.

Baird and his associates demonstrated that fibrinolytic agents and Heparin prevented thrombosis of the venous grafts in the early post-operative period but the effect was not great (Baird et al. 1964). Demetz and his co-workers found fibrinolytic agents of no value with a variety of IVC grafts (Demetz et al. 1961). Dextran solutions have been used by Just-Viera (1963) and Yaeger (1964) without any success either. The role of anticoagulants in canine grafting is complicated as dogs have resting heparin activity in the blood, making controlled experiments difficult and streptokinase does not activate fibrinolytic activity in canine blood by itself. On theoretical grounds the use of low molecular weight dextran and Heparin would appear to be a useful adjunct to venous grafting, at present time there is little experimental evidence that it contributes in any way to graft patency.

Only Mitsuoka and Howard's paper (1968) so far directly compares effect of differing lengths of prosthetic grafts on the patency rate, and as expected there were more failures in the group with the longer grafts. An examination of the literature on auto-grafts, however, suggests that length is not an important factor in successful grafting as the patency rates of the long grafts are comparable with the others. There is not enough data on other graft materials to draw many conclusions, but it appears that the very short grafts i.e. 2 cms or less,

and the long grafts i.e. over 6 cms fare better than the ones of intermediate length.

Moore (1963) has pointed out that late occlusion of venous grafts rarely occurs and that grafts which retain their patency beyond a critical early period are likely to remain patent. This phenomenon which is discussed by Haimovici and his colleagues in their review, has been utilised by two authors in deciding when to close experimental arteriovenous fistulae (Steinman et al. 1966; Scheinan & Jude 1963).

DISCUSSION:

From inspection of the papers on experimental grafting in the literature, it is clear that SVC grafts are more successful than any other. With the exception of femoral vein grafts, the success rate (which varies from two-thirds to one-third depending on the site) appears to vary inversely with the distance from the heart. The reason for the relative success of femoral grafts is not clear, but the high proportion of autografts used in the femoral veins (proportionally much more than any other site) may have favourably influenced this observation.

Autograft veins appear to be the best material to use for vein replacement although authors using Teflon report results almost as good. It is of interest in this respect that the results with Dacron grafts like those with allografts are far inferior, although the reported experience with fresh allografts is more promising.

Methods of improving graft patency at any site can be grouped into several categories according to the general method used. One of the more successful of these is to increase the rigidity of the plastic graft inserted either by external support or treatment with such compounds as Toluene di-isocyanate. The superiority of Teflon over

Dacron as a graft material might be explained in terms of the relative rigidity of the former compound when made up for prosthetic grafts. That venous prosthetic grafts should be relatively rigid to be successful is not surprising when the low intraluminal pressure and the collapsibility of the vein walls is compared with the very different situation in arteries. One of the ways in which an arteriovenous fistula may enhance the patency rate of venous grafts is by increasing the intraluminal pressure thus making the graft wall more rigid. Improvement in patency rates is more noticeable when synthetic grafts are used. The rigidity of the proposed graft is most important unless an autograft vein is used and on the whole the more rigid the graft material the more successful it is. For anything more than short term patency, the porosity of the graft is also of vital importance, as tissue in-growth through the interstities of the graft and the adherence of the fibrous neo-intima are vital for long term patency.

The porosity of the synthetic grafts in common use today is less than 50 ml of water per minute per square centimetre under standardised conditions (Wesolowski 1961), and for vein grafts, where the intraluminal pressure is one hundredth part that of arterial pressure, a graft of high porosity could be used safely. There is a need therefore to develop a synthetic graft of high porosity and high rigidity for use in the venous system. Usually these two requirements of high porosity and rigidity of the graft material are at variance with one another and a compromise situation must be reached. At the present time woven Teflon or Toluene di-isocyanate treated knitted Dacron grafts are the best available but both of these fall far short of the ideal requirements.

From the foregoing comments made in this discussion, the reader will be aware that several separate problems remain unsolved in the

field of experimental venous grafting. It is only by concentration of experimental effort on the separate problems associated with graft failure that the successful use of venous grafting in clinical practice will be achieved.

INTRODUCTION AND AIMS OF THE INVESTIGATION

Experimental work in the field of venous grafting has been directed towards defining the factors which influence graft patency. It is not clear from the experimental literature reviewed so far whether an arteriovenous fistula is helpful in enhancing the patency of all types of graft, although the majority of papers suggest that it is beneficial.

Although most authors who have used an arteriovenous fistula have commented on the increased blood flow so produced, none up to the present time have measured graft blood flow either in the presence or absence of an arteriovenous fistula, and subsequently related this flow to the patency of the venous graft. The present study was designed (1) to define the role of an arteriovenous fistula when used with tissue and then synthetic grafts, (2) to measure the blood flow at the graft site and make a quantitative assessment of the increase in blood flow produced by the fistula, relating this where possible to graft patency or intraluminal graft diameter.

The pelvic veins were chosen as the site for the experiment for two reasons (1) examination of the literature shows that venous grafts below the renal veins have a poor patency rate, so successful grafting in this area is more likely to be of significance, (2) grafts in the iliac veins allow a comparison between sides to be made. (An arteriovenous fistula on one side; the other being used as a control). This is obviously not possible in the inferior vena cava.

Autograft veins of comparable size cannot be used for replacement of large veins as they are just not available. Replacement of large veins is thus only possible with a synthetic replacement, an allograft or something similar. Bearing this in mind knitted Dacron and vitally

preserved allografts were investigated to see if they would provide an acceptable substitute in experimental animal. Dacron as a synthetic venous graft has not found favour in the literature and the small number of papers describing its use are not encouraging. This is surprising in view of its widespread application in arterial work and the present author thought that the use of Dacron in venous grafts should be investigated in greater depth.

In view of the difficulties of using autograft veins of comparable size the author investigated the use of vitally preserved allografts as a possible substitute.

Examination of the literature reviewed indicates that both fresh and vitally preserved allografts have an increased chance of success compared with dead allografts, and the author was able to use a technique of vital preservation of tissue developed by Al Janabi and her co-workers at the National Heart Hospital, London. This technique has been used with success in aortic valve replacement (Ross et al. 1972).

MATERIALS AND METHODS

CHOICE OF ANIMAL

It was decided during the planning phase of these experiments that a single strain of animals would be used if possible, as this would help to eliminate some of the biological variations inherent in the use of mongrels.

Female greyhounds were available in sufficient numbers and were of suitable size. They appeared to be a logical choice, and their suitability is enhanced for the following reasons:

(i) Being a homogeneous group their size and weight are relatively constant. The detailed anatomy and size of blood vessels is virtually identical in every dog. This made anaesthesia and operative technique much easier.

(ii) They are docile animals and are easy to handle for procedures like venepuncture and radiography.

(iii) The size and blood-flow characteristics of the pelvic vessels approximates to that of man. This may have some bearing on the relevance of the experiments to man.

(iv) Obstruction of the pelvic veins causes minimal morbidity to the animals (pain and oedema) so that they are not inconvenienced by pelvic vein thrombosis.

However, greyhounds do have disadvantages:

(i) They are large animals and consequently expensive to house and feed.

(ii) Being thin they are susceptible to pressure sores around bony prominences.

ANAESTHESIA

The same anaesthetic regimen was adopted as far as possible in all operative experiments, because it was realised that the choice of anaesthetic agent and its concentration materially affected blood flow at the graft site; halothane being particularly potent in this respect.

Dogs were starved over-night before operation, and one hour before anaesthesia they were weighed and pre-medicated with an intra-muscular injection of acetpromazine (1 mgm./kg.). Skin over the cephalic vein on one foreleg was shaved and a Mitchell intravenous needle inserted (all intravenous drugs and fluids were given by this route).

General anaesthesia was induced by a rapid infusion of 2% thiopentone sodium (10 mgm./kg.). As soon as the dog began to sag to the ground from the standing position, it was lifted onto the operating table and placed in a supine position. Once on the table there was sufficient muscular relaxation for the dog to be intubated with a Magill cuffed endotracheal tube. A closed circuit rebreathing apparatus, with a soda-lime absorber, was then connected to the dog and anaesthesia maintained with an oxygen/nitrous oxide mixture in the ratio of 1:2 at a flow rate of approximately 3 litres/min. This mixture was supplemented with halothane up to 2% from a Fluotec Vapourizer. Saline infusions were used in varying amounts throughout the operation (as detailed elsewhere). Anaesthesia was maintained satisfactorily for periods of up to 8 hours using this method and several animals received three such anaesthetics within a fortnight with no visible ill effects.

All dogs were closely observed after anaesthesia and the endotracheal tube left in situ until the animal physically resented its

presence and was swallowing spontaneously; at this stage the tube was deflated and removed. Most animals were able to respond to their names and make purposeful movements within one hour after operation and several managed to walk back to their kennels unaided.

Dogs were killed at the conclusion of each phase of the experiments by an intravenous injection of concentrated pentobarbitone sodium solution.

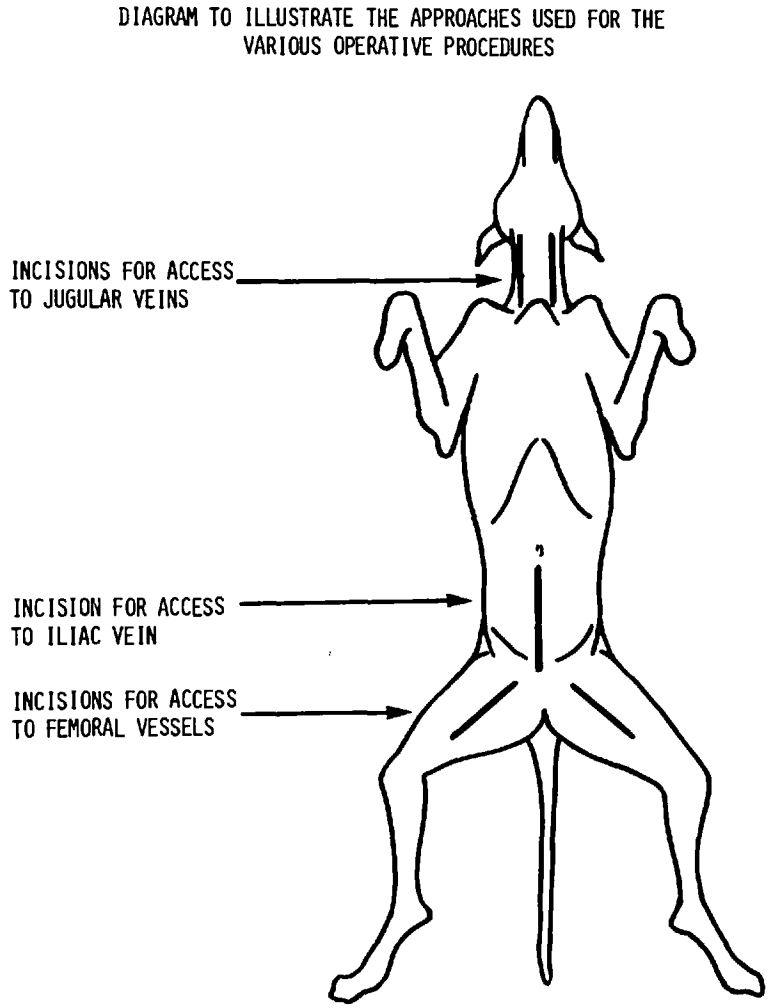

Fig. 1.1. POSITION OF ANIMAL FOR SURGICAL PROCEDURES. THE OPERATIVE SITES ARE INDICATED

OPERATIVE TECHNIQUE

GENERAL:

All operative procedures were performed in a purpose-built veterinary operating theatre, using a full sterile technique. Most operations were conducted with two assistants, one of whom attended to the maintenance of anaesthesia and the other assisted the surgeon (in all dogs the operative procedures described have been personally performed by the author).

For all procedures the dogs were placed in the supine position as indicated in Fig. 1.1 suitably supported by sand-bags, with the hind legs extended. The skin was shaved for a wide area around the operation site and then cleansed with aqueous chlorhexidine solution. Skin sterilisation was obtained with a 10% povidone iodine solution before isolation of the operation site with sterile towels.

ILIAC VEIN GRAFTS:

The approach to the iliac veins was made via a lower mid-line incision, about 20 cms. long (see Fig. 1.1) care being taken to avoid the bladder. The intestines and uterus were protected with packs and the iliac veins on both sides exposed by incision of the pelvic peritoneum. The common, internal and external iliac veins were isolated between atraumatic occlusion clamps and the appropriate grafting manoeuvre carried out in the common iliac vein.

When the grafts had been inserted the pelvic peritoneum was replaced over the grafts and iliac veins, but not sutured.

The anterior abdominal wall was closed in three layers; peritoneum-continuous chromic cat-gut; linea abla-interrupted silk thread; skin-continuous polyglycolic acid (P.G.A.) polymer fibre.

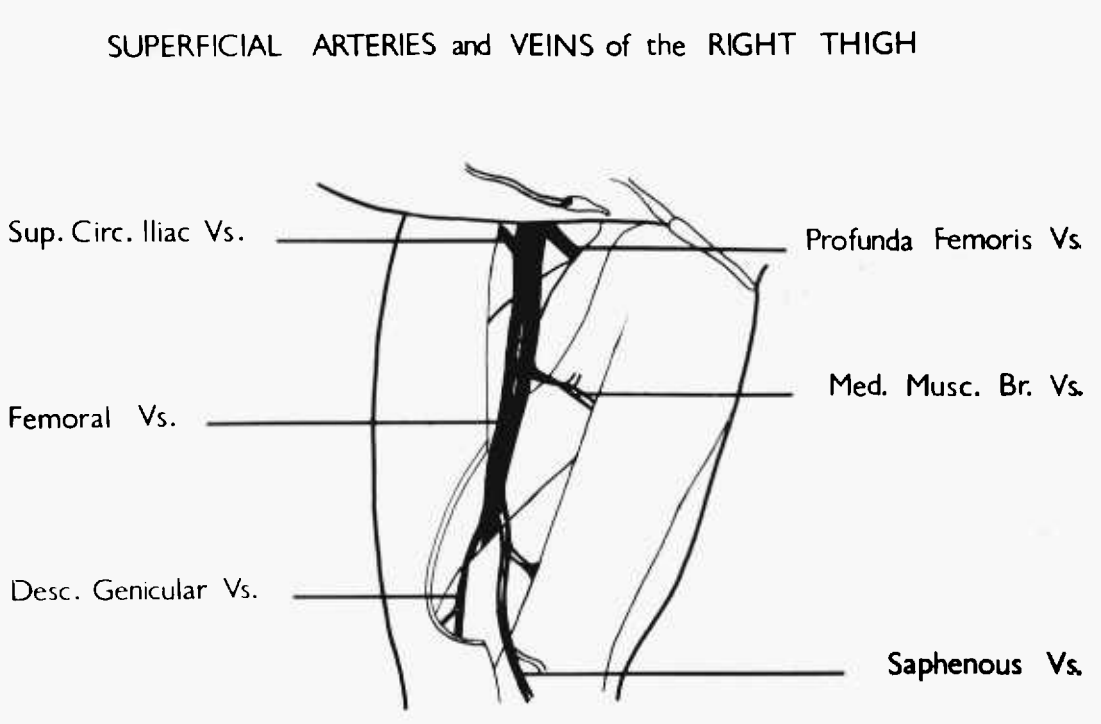

Fig. 1.2. THE VESSELS OF THE RIGHT THIGH

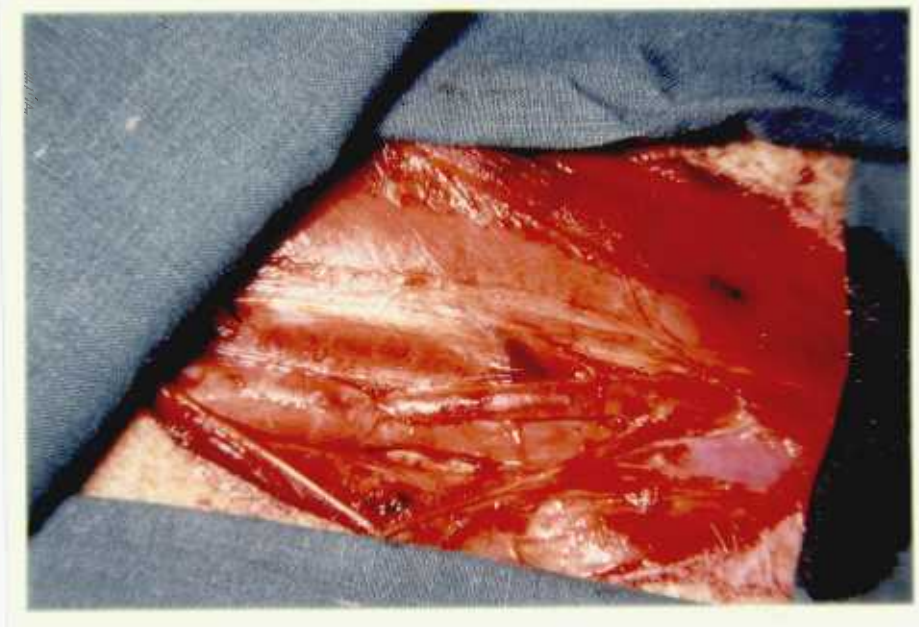

Fig. 1.3. THE FEMORAL ARTERIO-VENOUS FISTULA

ARTERIOVENOUS FISTULA:

The femoral vessels were exposed by a vertical incision begun over the inguinal ligament and extended some 15 cms. down the thigh. The femoral sheath was opened giving immediate access to the femoral vessels. The femoral artery was ligated about 5 cms. beyond the medial muscular branch artery (Fig. 1.2) and divided proximally. The proximal cut end of the artery was then anastomosed end-to-side to the adjacent femoral vein using No 60 P.T.F.E. coated polyester sutures. The anastomosis was performed in two parts, anterior and posterior, with two trans-diameter stay sutures and the completed anastomosis is shown in Fig. 1.3. Wound closure was in two layers; fascia and femoral sheath-using continuous chromic cat-gut; skin-using continuous P.G.A. polymer fibre.

CLOSURE OF ARTERIOVENOUS FISTULA:

The groin wound was re-opened and the site of the arteriovenous fistula isolated. The arterial part of the fistula was then ligated flush with the femoral vein and the artery cut and allowed to retract away. The wound was again closed in layers with chromic cat-gut and P.G.A. polymer sutures.

EXCISION OF THE VALVED VEIN GRAFTS:

A vertical incision about 10 cms. long was made over the external jugular vein from the root of the neck towards the angle of the jaw. Approximately 5 cms. of the vein was isolated from surrounding structures and stripped of all adventitia, and tributaries were ligated with fine silk thread (Fig. 1.4). A 2.5 cms. segment of the vein bearing a competent valve in its centre was excised and the proximal end of the vein identified with a 60 silk suture. The cut ends of the remaining jugular vein were ligated with silk and the wound closed in layers with chromic cat-gut to the fascia and P.G.A. polymer sutures to the

(Fig. 1.4 overleaf)

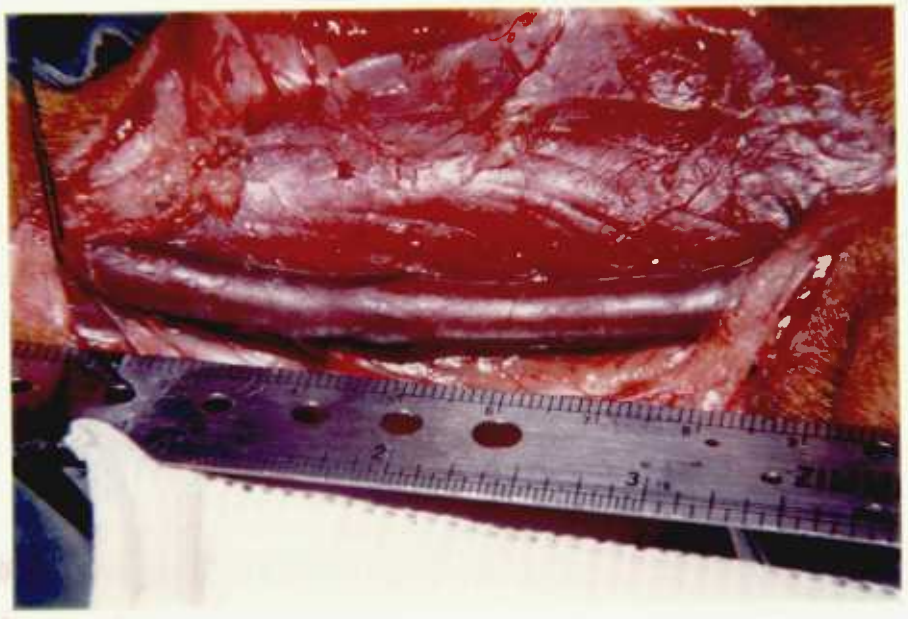

Fig. 1.4. THE EXTERNAL JUGULAR VEIN SHOWING THE VALVE, IN SITU.

skin. An identical procedure was then carried out on the opposite side of the neck, excising another 2.5 cms. valved segment of vein.

The excised portions of jugular vein were then placed in a sterile container already holding 20 ml of a Tissue Culture medium, see page 45. After not more than two hours the veins and their containers were stored at a constant temperature of 4°C.

The grafts were usually stored for about a week, and were taken out of storage immediately prior to the grafting procedure.

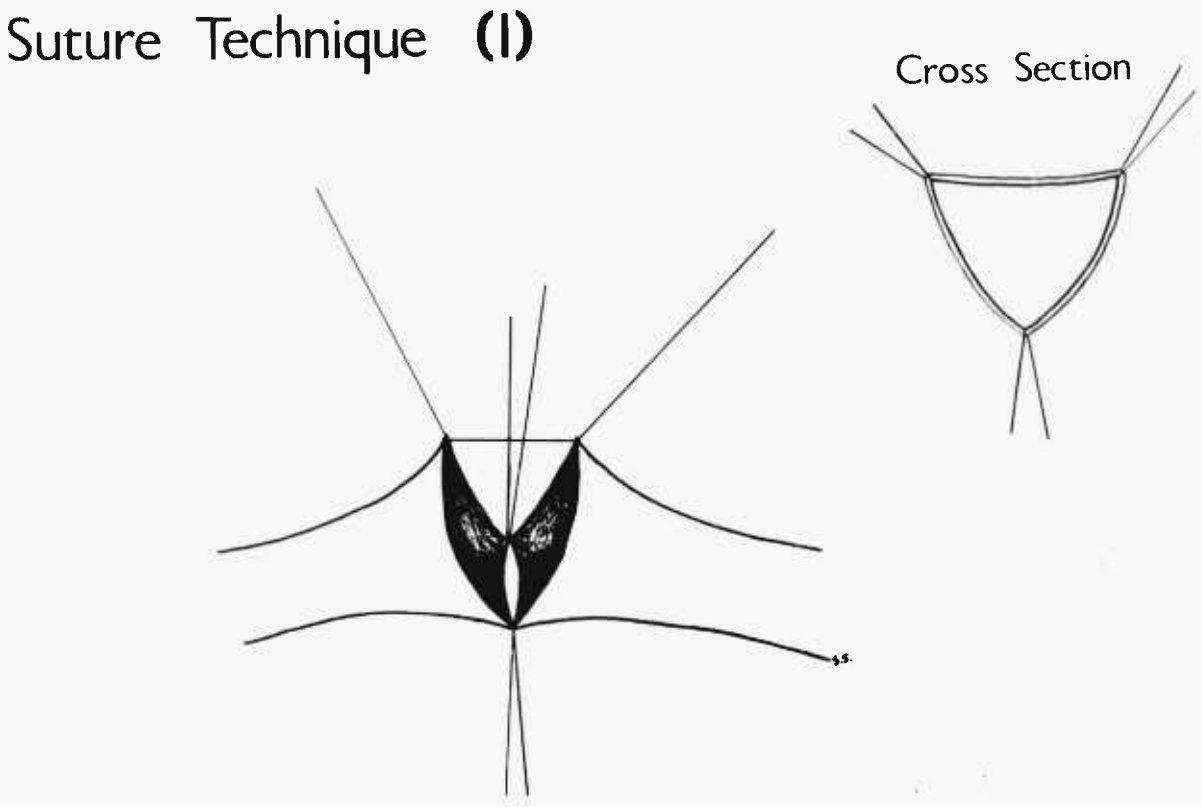

Fig. 1.5. SUTURE TECHNIQUE. INITIAL STAGES SHOWING TRIANGULAR SUTURES

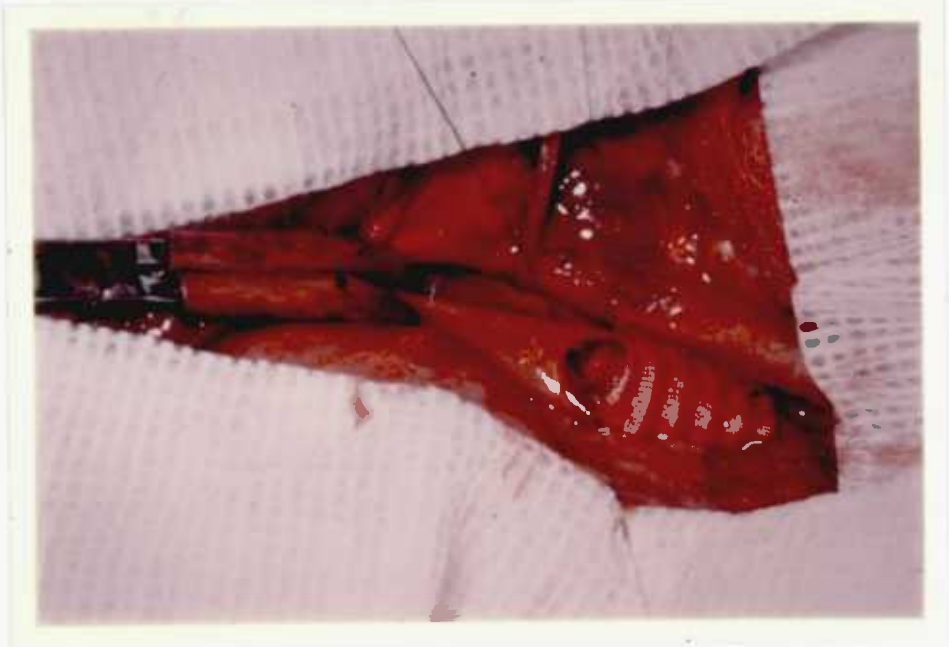

Fig. 1.6. INSERTION OF DACRON PROSTHESIS INITIAL STAGE

TECHNIQUE OF VEIN ANASTOMOSIS

Since Carrel's initial experience in blood vessel anastomosis, most authors have been emphatic about the importance of technique in venous anastomosis; this is well illustrated in Cerino and his co-workers' paper, which summarizes the important points in technique (Cerino et al. 1964). In his review Haimovici and his colleagues state that there is little margin for error in venous replacement and emphasise the importance of precise, meticulous, careful technique to ensure success (Haimovici et al. 1970). With these comments in mind the author was at some pains to develop a method before applying it to the experimental animal. This primary work was done on cadavers.

The following points of technique are considered important:

(i) All adventitia must be removed from around the anastomosis site, and for a distance of 3-4 mms. away from the free edges, for not only does the adventitia tend to snag the suture material but also it may become inverted through the suture holes into the vein lumen, interfering with the free running of the suture and predisposing to thrombosis.

(ii) It is important that the venous tissue is not allowed to dry out; irrigation with heparinised blood or peritoneal exudate from time to time will prevent this. Irrigation with saline should be avoided as this damages the venous endothelium. (Unpublished data.)

(iii) Direct handling of the intima must be avoided and the finest dissecting forceps used for handling the vein, which should be grasped by the media and adventitia only. Stay sutures are used to oppose the free edges of the anastomosis which may then be sutured with minimal use of dissecting forceps. (Fig. 1.5 and Fig. 1.6.)

(iv) Suture materials should be as fine as possible consistent with the operator's skill. In this study No. 60 suture materials were

Suture Technique (2)

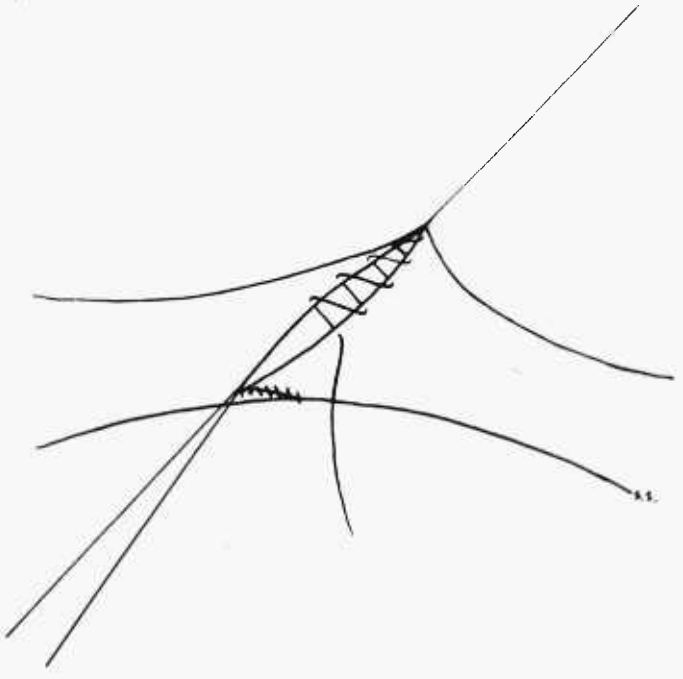

Fig. 1.7. SUTURE TECHNIQUE. FINAL STAGE.

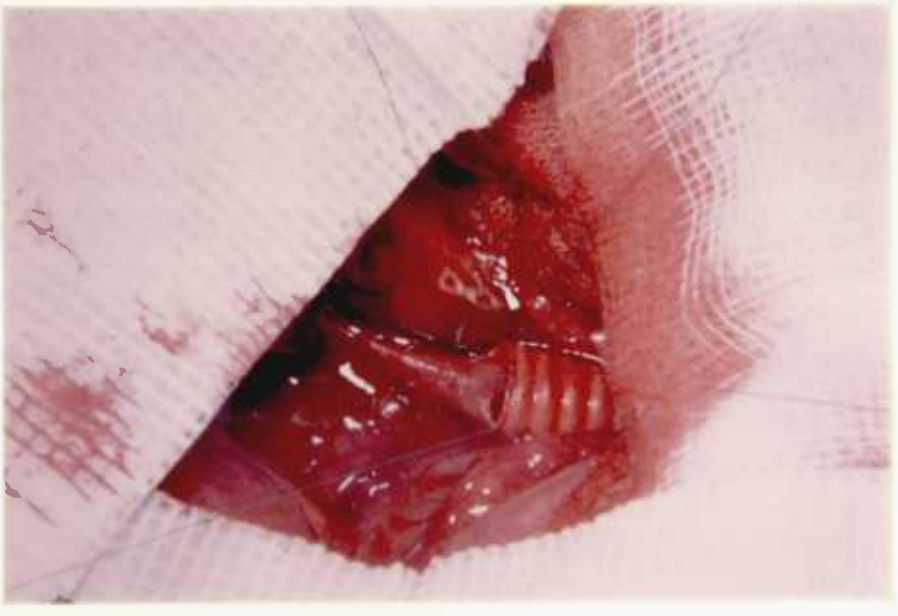

Fig. 1.8. INSERTION OF THE DACRON PROSTHESIS.
COMPLETION OF THE ANASTOMOSIS.

used (P.T.F.E. coated polyester fibre and braided silk), although No. 70 sutures could be used on peripheral veins.

(v) Stay sutures are used initially to oppose the anastomosis, three sutures being placed equidistant around the circumference of the vessel. (Fig. 1.6.) Tension of two of the stay sutures aligns the tissues to be joined and tends to dilate the vein. The anastomosis is made easier if one such suture is placed on the posterior part of the circumference farthest away from the operator.

Sauvage and Wesolowski (1954) compared biangular and triangular stay sutures for vein anastomosis and found no difference between them, in terms of patency. The author found triangulation sutures easier to manipulate and this is why they were used.

The anastomosis proceeds in three parts, with a continuous stitch, the sutures being placed 2-3 mm. apart, about 1 mm. from the free edge. (Figs. 1.7 and 1.8). It is important to use only enough tension to keep the vein opposed as too much tension with a continuous suture tends to constrict the anastomosis.

(vi) As with arterial anastomosis the graft should be under slight tension when in position for if there is laxity of the graft, kinking may occur under the low pressure conditions of blood flow, with consequent thrombosis.

(vii) At the end of the grafting procedure the peritoneum is replaced over the graft but not sutured in place, as tension of the parietal peritoneum over the vein may again cause kinking and thrombosis.

MEASUREMENT OF BLOOD FLOW

THEORY AND BASIC PRINCIPLES

An electromagnetic blood flow-meter was first described by Kolin (1936). This method provides an attractive, indirect way of measuring blood volume in intact vessels.

The principle of operation is based upon the laws of electromagnetic induction. These may be described as the generation of an electromagnetic force (e.m.f.) in a conductor when it is cut by a magnetic flux; the magnitude of the e.m.f. being proportional to the rate at which the conductor cuts or is cut by, the magnetic flux.

Blood flowing in arteries or veins is a moving conductor. The magnetic flux is provided by a probe placed around the vessel, which also provides the electrodes to pick up the generated e.m.f. The volume flow rate may then be related to the cross-sectional area of the vessel as follows:

$$E = \frac{4 B Q}{D}$$

E voltage generated or e.m.f.

B magnetic flux

Q volume flow rate

D diameter of the vessel.

Therefore a true volume flow reading requires a knowledge of the vessel diameter. This is provided by having a rigid probe head which closely fits the vessel, thereby giving a fixed measurement diameter. Subsequent electronic processing allows an output proportional to the volume flow through that particular probe. The above represents an idealized situation; in practice some problems and limitations occur and these may be considered under four headings:

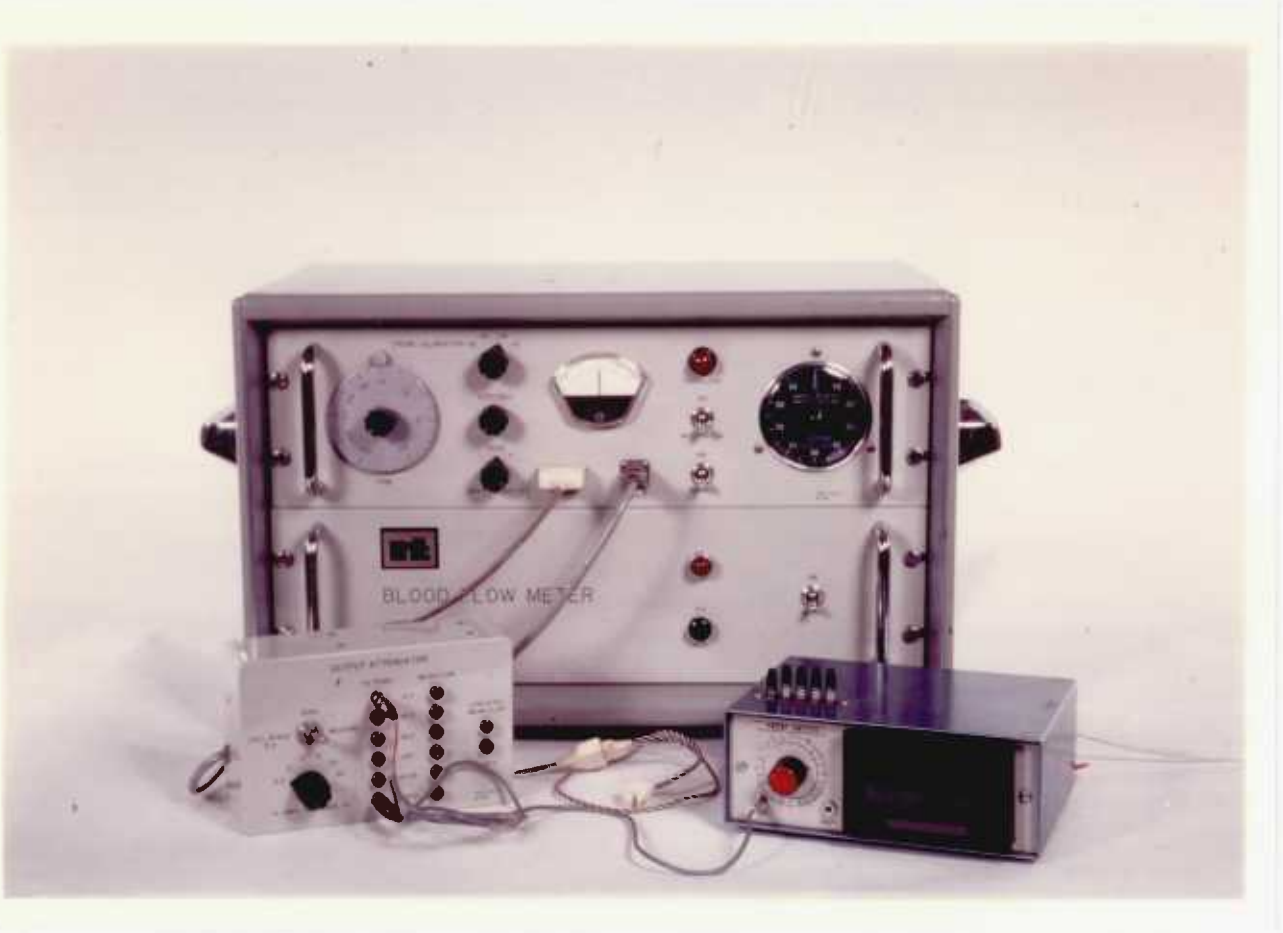

Fig. 1.9. THE NYCOTRON 372 BLOOD FLOW METER. THE OUTPUT ATTENUATOR AND DIGITAL DISPLAY OF BLOOD FLOW ARE IN THE FOREGROUND.

(a) .Knowledge of the physical properties of the blood and its vessel.

(b) Design of a suitable transducer.

(c) The transducer/tissue interface.

(d) The design of the recording system.

Further problems stem from these considerations, namely:

(i) Blood flow must be axisymmetrical.

(ii) The conductivity of the vessel wall should be the same as that of the blood.

(iii) The magnetic flux should be uniform across the flowing blood.

(iv) Extraneous signals due to currents energizing the coils which produce the magnetic flux must be minimized.

(v) Alteration of the blood haematocrit value alters the conductivity of the fluid and hence the e.m.f.

Several other problems related to the probe design and electronic processing cause difficulties. These are discussed in a paper by Wyatt (1966).

FLOWMETER AND ITS USE:

The flowmeter used for these experiments was a Nycotron 372. (Fig. 1.9). This is a square-wave flowmeter i.e. the magnetic flux is produced by coils energized by a square-wave current. The induced e.m.f. produced by the blood flow is "gated" in that the e.m.f. induced by energizing the coils is not recorded.

An output attenuator and variable frequency response instrument were provided by the makers. This allowed the frequency response to be varied from 0.3 cycles/second, described as mean flow, through 3, 6, 12, 25 and 50 cycles/second. (Fig. 1.9).

Typical Blood Flow Recording with Calibration Markers

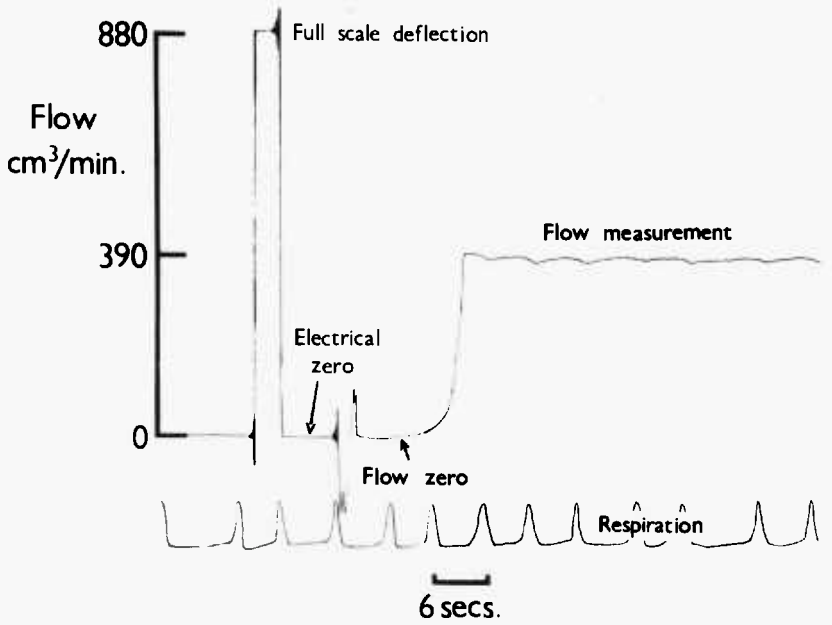

Fig. 1.10. CHART PAPER RECORDING OF IN SITU CALIBRATION OF THE FLOW METER AND A TYPICAL FISTULA FLOW MEASUREMENT.

NYCOTRON FLOWMETER (See Fig. 1.9.)

The Nycotron flowmeter was provided with the following features:

(a) Coarse calibration control, ranging from x 2, through x 4 and x 8, to x 16.

(b) Time calibration control.

(c) Zeroing potentiometer.

(d) Polarity reversing switch.

(e) Volume integrator, manually operated, providing electro-mechanical integration of the flow signal.

(f) Blood flow overload light.

During blood flow recording, the coarse calibration control was adjusted as dictated by the flow levels, i.e. when overloading occurred on one range the control was switched to a higher range level. The fine calibration control was not adjusted at any time.

Zero blood flow was determined mechanically and at an electrical zero adjusted by means of a balance potentiometer. (See Fig. 1.10).

The integrator was used only during calibration of the probe.

The output signal was generally recorded as a mean flow rate but a recording at 12 cycles/second was made on chart paper when permanent records were required.

CALIBRATION:

In vitro calibrations were initially carried out. However in comparison with in vivo calibrations, it was found that the latter were accurate to within $\pm$ 5% and in vivo calibrations were not routinely employed for day to day measurements.

The calibration procedures were designed to investigate the response of the system to some of the physiological variables likely to be encountered. Those selected were the haematocrit, the vessel wall conductivity and the flow profile. Also calibration was performed to

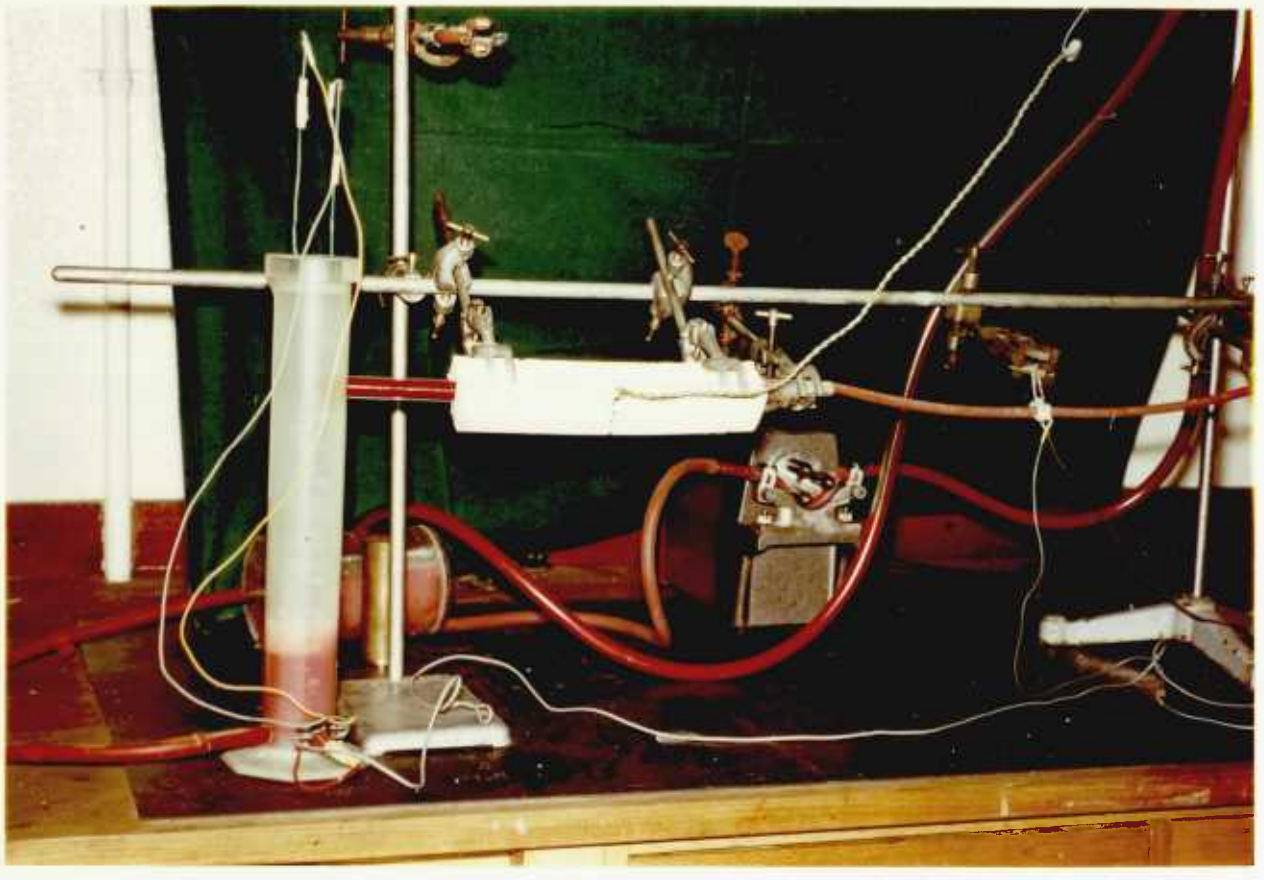

Fig. 1.11 APPARATUS FOR IN VITRO CALIBRATION OF BLOOD FLOW PROBES. ILLUSTRATED ARE: (i) THE VARIABLE OUTPUT PUMP. (ii) MEASURING CYLINDER FOR ELECTRONICALLY TIMED COLLECTION. (iii) BLOOD FLOW METER PROBE EMBEDDED IN SILICONE RUBBER.

determine the limitations of the frequency response, linearity of the response, drift and sensitivity of the equipment.

A model was built in the laboratory for in vitro calibration of blood flow; Fig. 1.11, inherent in the design was the ability to simulate the variables mentioned.

The pump (illustrated in Fig. 1.11) allowed flow variation between zero and 2 litre/minute, with a frequency response variable of about twenty Hertz. The steady-flow variations were of similar order, achieved by a screw clamp on the output of the reservoir (not shown in Fig. 1.11). Attempts were made to reduce turbulence in the recording part of the system by siting the measuring probe in the middle of a long straight piece of tubing (approximately x 50 diameters away from a curve). Turbulence was also reduced by the use of silicone rubber piping, avoidance of internal irregularities in the tubes and matching of the probe/silicone tube junction. The model was designed to allow recycling of the flow medium so that only an initial priming was required.

EFFECT OF BLOOD HAEMATOCRIT:

Outdated human blood for transfusion was used. This was either diluted with isotonic saline or allowed to sediment in order to alter the haematocrit. The response of the system was then determined within the range 0% to 50% haematocrit; the latter being measured on a Goulter Analyser Model S.

The results showed that the system was remarkably insensitive to haematocrit, within the range 5% to 40%. The variation recorded being about ±2% within those extremes. (Bashford. Personal Communication).

EFFECT OF VESSEL WALL CONDUCTIVITY

Using excised arteries and veins from dogs, conductivity was investigated in comparison with the ideal case, i.e. no vessel wall.

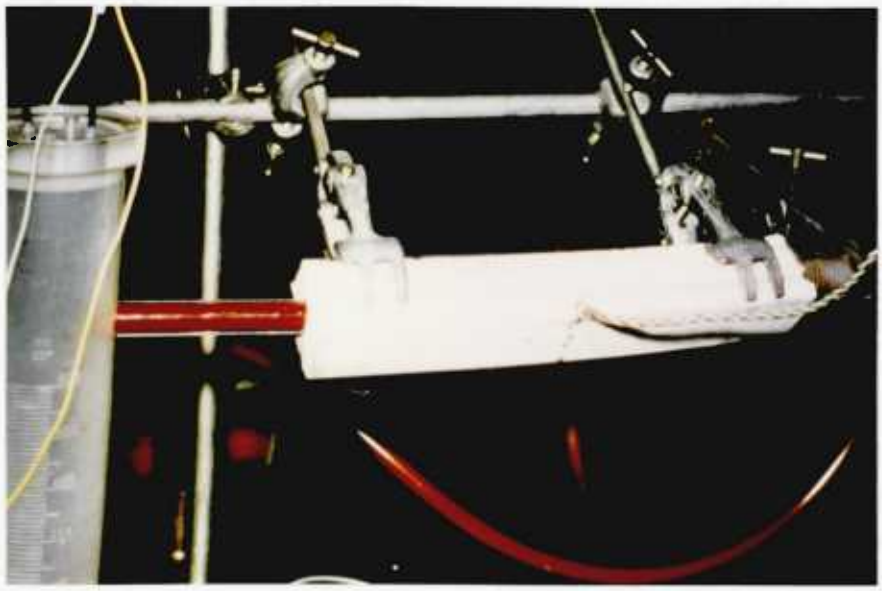

Fig. 1.12. DETAIL FROM Fig. 1.11. THE BLOOD FLOW PROBE EMBEDDED IN SILICONE RUBBER AND THE OUTFLOW TO THE ELECTRONIC MEASURING DEVICE.

This was obtained by encasing the probe in a silicone rubber mould. (Fig. 1.12.) With the samples available a difference of up to 5% was observed; the readings in the blood vessels giving the larger flows. (Bashford. Personal Communication.)

INSTRUMENTATION VARIABLES:

The linearity of the probes and associated electronics was determined by using the electronically timed collection procedure. (Fig. 1.11.) After passing through the probe the blood was collected in a measuring cylinder, the outflow of which was clamped during the collection period. The level detecting probes were adjusted to trigger the clock and flow integrator on and then off after a specific volume had been collected. The volume of fluid collected between the levels of the two probes was then measured using an accurate measuring cylinder. This volume was usually 250 mls., and was calibrated to an accuracy of 1 ml.

The electronic clock and flow integrator recordings were visualized on a digital display and the clock was calibrated to an accuracy of 0.1 second. Since the maximum flow rate was 2 litre/minute, the minimum recording time was about 10 seconds.

Care was taken to ensure a true mechanical zero by distal clamping of the outlet tube from the measuring site. The dead space of tubing containing fluid between the probe and the measuring instrument was full before and after recording and did not reduce the accuracy of the test. The mean flow was calculated from the time taken to collect a known volume. This flow was then compared with the mean flow recorded instantaneously on the Nycotron instrument digital display. As a further check the volume integrator on the blood flow machine was also used.

Comparison of the results showed that for both pulsatile and

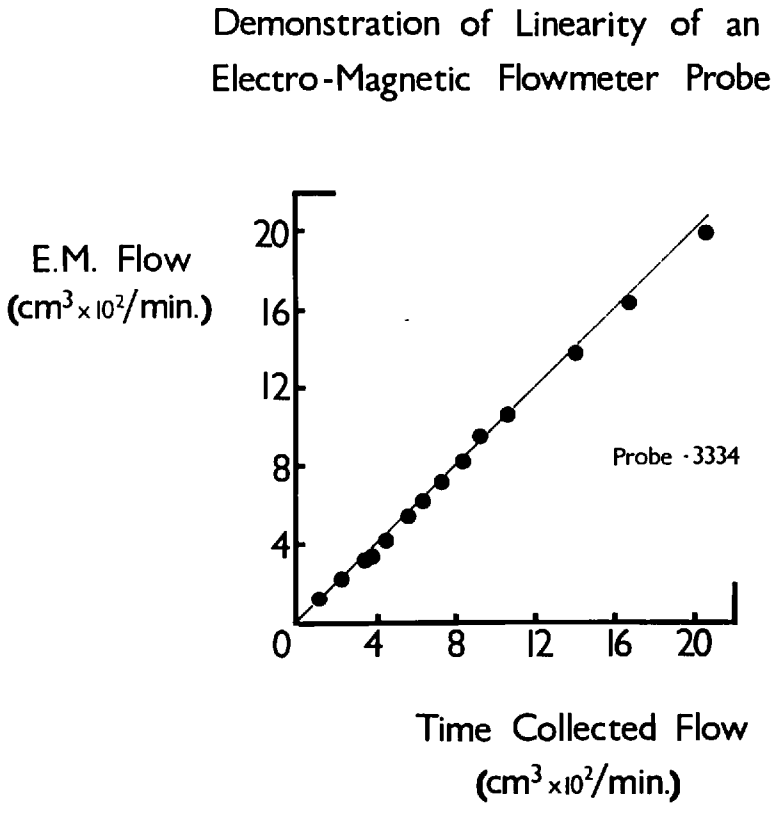

Fig. 1.13. SEE ALSO APPENDIX A.

even flows the system did not significantly depart from true linearity over a range of flows from 0 to 1.5 litres/min. (Fig. 1.13.) However, above this flow level variation in response (generally a decrease) was noticeable. When flow visualization was performed (using an injection of coloured dye via a fine needle, upstream of the probe) it could be seen that the flow profile became turbulent above a rate of 1.5 litres/min. It was concluded that the asymmetrical flow profile was responsible for the discrepancy.

The frequency response of the electromagnetic probe was investigated in comparison with a Doppler ultrasound probe. Using this method of comparison, no significant difference between the recorded traces from both systems could be seen, if the outputs of each were attenuated to provide the same level of signal.

USE OF THE ELECTROMAGNETIC FLOWMETER IN PRACTICE:

Use of the Nycotron flowmeter and its probes requires care and precision to obtain consistent and accurate results.

The initial problem encountered was that of sterilizing the probes (probes were damaged by steam autoclaving). A small ethylene oxide batch-sterilizing plant was built and used for sterilizing all the delicate electronic apparatus. The
electrodes in the probes require to be scrupulously clean for satisfactory use, blood and debris must be washed off immediately after use. From time to time the probes were cleansed with a cloth soaked in ethyl alcohol solution and then the electrodes gently rubbed with emery cloth, rinsed with distilled water and dried.

Before use the probe was placed in a bowl of saline to demonstrate the correct function of the system; inability to obtain a zero flow reading in this situation leads to re-appraisal of the probe's cleanliness and/or fault finding within the Nycotron apparatus. If

the machine indicates an overload which cannot be corrected electronically, this indicates a general fault within the flowmeter or output attenuator. If the probe fault is minor or the probe is a bad fit around the vessel, it may be found that the zero flow reading cannot be adjusted either side of the flow zero. Another probe should be chosen so that it is a snug fit around the vessel.

Overload simulation will also occur if a source of R.F. is nearby, the diathermy machine being a common culprit. (It should be noted also that the diathermy machine can be earthed through the probe electrodes, so the diathermy should not be used with the probe in place or the graft may be damaged by the diathermy current.)

It is important that the probe be held rigidly in position at right angles to the long axis of the vessel. This is possible with arteries merely by the tight fit of the probe and the intra-luminal pressure. Veins, however, do not contain these pressures and the probe easily twists or slips off the vessel.

To assist the surgeon to recognise the correct positioning of the probe a readily visible digital display of blood flow was constructed, this display allowing simple switching in of pre-calibrated probes to give a direct read-out of flow. (See Fig. 1.9.)

It was anticipated that un-physiological flow patterns would occur due to the presence of an arteriovenous fistula, and steps were taken to avoid errors due to turbulent blood flow. The sensitivity of the probes was investigated by Shercliff (1962). He produced a value for the sensitivity of the flowmeter, to flow at any given point in the cross-sectional area of the vessel. This value was described as the weight function, and a map can be produced of this for the cross-sectional area of the monitored blood flow. The major effects to be demonstrated are there is an increase in sensitivity (or over-

estimation of flow) if this flow is concentrated in the region of the electrodes. The converse of this applies if flow decreases in the region of the electrodes. It is often impossible to know when effects like this are occurring unless two readings are taken at the same site. After the first, the probe is rotated through 90°, if these two readings vary by more than ±5% they were discarded, and readings taken at another site close by.

Flow readings were not taken until 15 minutes after completion of the fistula, since flow monitoring showed that this was the time required for the flow to stabilise.

The sites of flow measurement and their timing are detailed in the sections dealing with the experimental results.

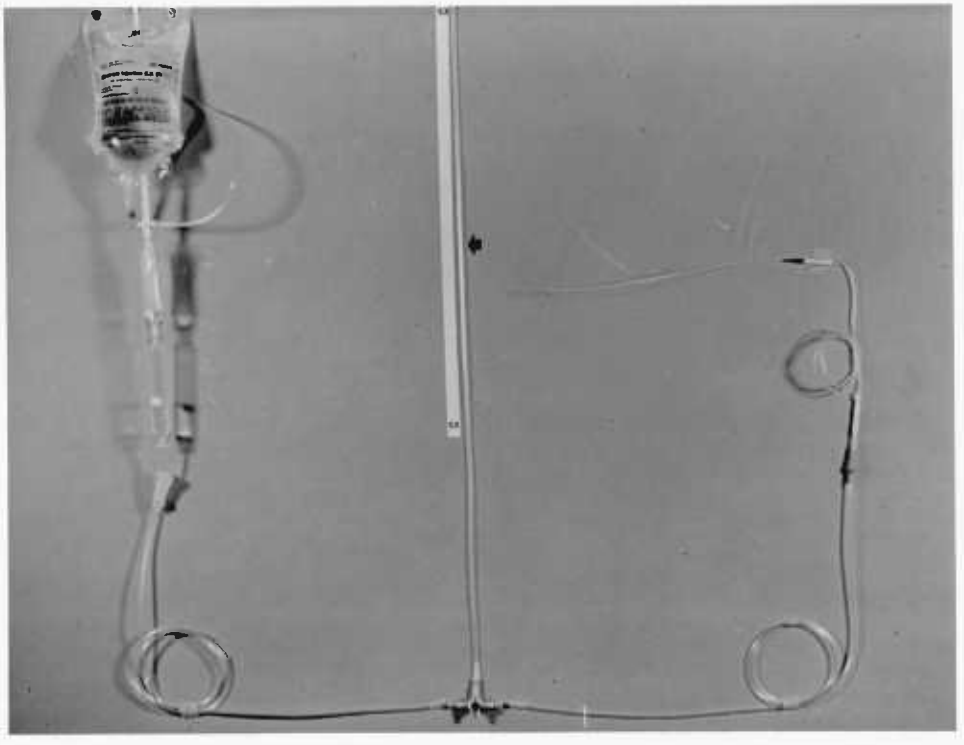

Fig. 1.14. APPARATUS USED FOR MEASURING VENOUS PRESSURE WITHIN THE ILIAC VEINS.

MEASUREMENT OF VENOUS PRESSURE

Attention has been drawn to the significance of intra-luminal pressure in venous grafting by Haimoici and his colleagues in their review, and it was decided to measure venous pressure at the graft site in conjunction with blood flow to see if there was any correlation between them (Haimovici et al. 1970).

METHOD:

Venous pressure was measured with a saline manometer, as shown in the photograph opposite. (Fig. 1.14.) A large bore cannula (Portex 6 F.G. 24" long) was inserted into a tributary of the saphenous vein on the side of the arteriovenous fistula and threaded proximally until it lay in the common iliac vein. The saline in the cannula was in direct continuity with the fluid in the saline manometer, and readings were taken when a rise and fall of the fluid meniscus, phasic with respiration, was observed in the calibrated tubing. This reading was the mean of the extremes of amplitude of the meniscus, and was made with the reference to the dog's right atrium. (This point, 5cm. below the level of the sternum with the dog horizontal, was taken as having zero pressure.)

Readings were taken after grafting and 15 minutes after construction of the arteriovenous fistula.

In two further experiments pressure was measured in the I.V.C. concurrently with blood flow.

RESULTS:

Pressure measurements were conducted only in the first series of grafts, i.e. the isotopic autografts. The results are shown

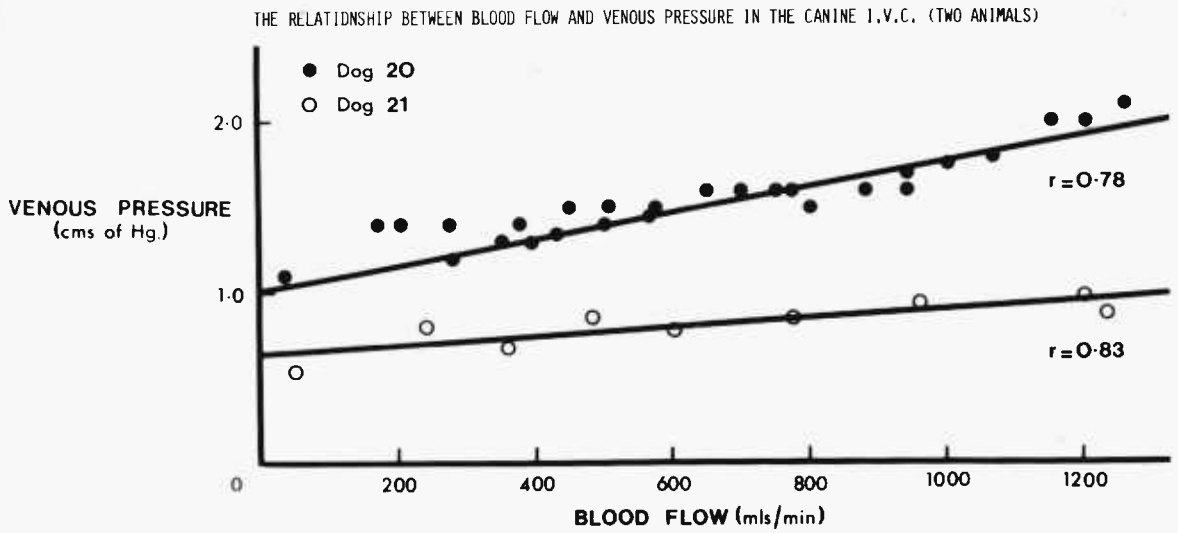

Fig. 1.15. SEE ALSO APPENDIX B.

r : CORRELATION COEFFICIENT.

graphically in Fig. 2.5 on page 53. (See also Appendix B). There appeared to be little correlation between the venous pressure and blood flow as measured in the group of dogs as a whole. The reason for this is thought to be that at a given rate of blood flow the venous pressure varies considerably from dog to dog due to such factors as heart rate, right ventricular filling pressure and ventricular stroke volume, so as relationship was not established and the investigation discontinued. However, if the relationship between venous pressure and blood flow is investigated in a single animal there is a correlation, as shown from the graph. (Fig. 1.15). Venous pressure is a relatively insensitive parameter as measured by this method, for on occasions the same pressure was recorded as the flow varied by up to 300 mls./min. It was decided on account of this inaccuracy of the method and the variability between animals to abandon this mode of measurement.

VENOGRAPHY

The majority of experimental workers in canine venous grafting have used venography as the principal method of assessing the state of the grafted segment, the paper by Cerino and his associates may be cited as an example (Cerino et al. 1964). Stenosis and occlusion due to thrombosis may cause few signs in the dog because of the rapid establishment of an effective collateral circulation. For this reason it was considered essential to visualise the graft site by venography in the immediate post-operative period and in subsequent weeks. Continuous observation is necessary as recanalisation may occur in thrombosed segments of the venous system and early graft failure may not be appreciated if venography is performed several weeks after grafting. This point is explained by Dale (1963).

In the series of isotopic autografts, Doppler directional ultra-sound was used in conjunction with venography, as access to x-ray equipment was limited. Ultra-sound was unsatisfactory as the results obtained did not relate well with the venographic findings, so improved x-ray equipment and facilities were sought and obtained and in dogs subsequent to number 6, venography was employed as routine.

METHOD:

The dogs were sedated with a mixture of narcoleptic agent and tranquilliser in a pre-mixed form (Immobilon), for details see below. This agent was found to be ideal for venography as it rendered the dogs analgesic and virtually motionless save for slow respirations. As cardiac output is markedly reduced with this drug it was easy to visualise large segments of the venous system with small volumes of contrast material.

An intravenous injection of etorphine hydrochloride (0.004 mgm./Kg.) and methotrimeprazine (1 mgm./Kg.) was given via the cephalic vein. Some five minutes later when the drugs had taken full effect and the dog was stuporose, it was placed on the x-ray table lying on its side, the leg to be examined below. The upper hind limb then was abducted and extended out of the way whilst the femoral vein was entered percutaneously in the distal thigh, using a 19 gauge infusion-set needle. Blood was aspirated initially to check the position of the needle and then 20 ml. of a 45% solution of sodium diazotrote was rapidly injected. When three quarters of the volume had been injected an x-ray film of the pelvic and thigh veins was exposed. The plate was then developed and if satisfactory the injection needle was withdrawn from the femoral vein and pressure applied until bleeding ceased. Patency of the needle was maintained by intermittent injections of a small volume of saline.

The dog was turned over and venography repeated on the opposite leg, in an identical fashion.

Care was taken to position all dogs in an identical way for pelvic venography as measurements of the graft diameter were taken subsequently in each animal.

Following successful venography the effect of the narcoleptic agent was reversed by an intravenous injection of diprenorphine hydrochloride (0.016 mgm./Kg.) and within two to three minutes the dogs were able to walk back to their kennels unaided.

Venography utilizing the above technique was used regularly on a weekly (or occasionally on a twice weekly) basis with apparently no ill effects to the animals concerned, and was found to be entirely satisfactory. Dogs were studied at intervals throughout

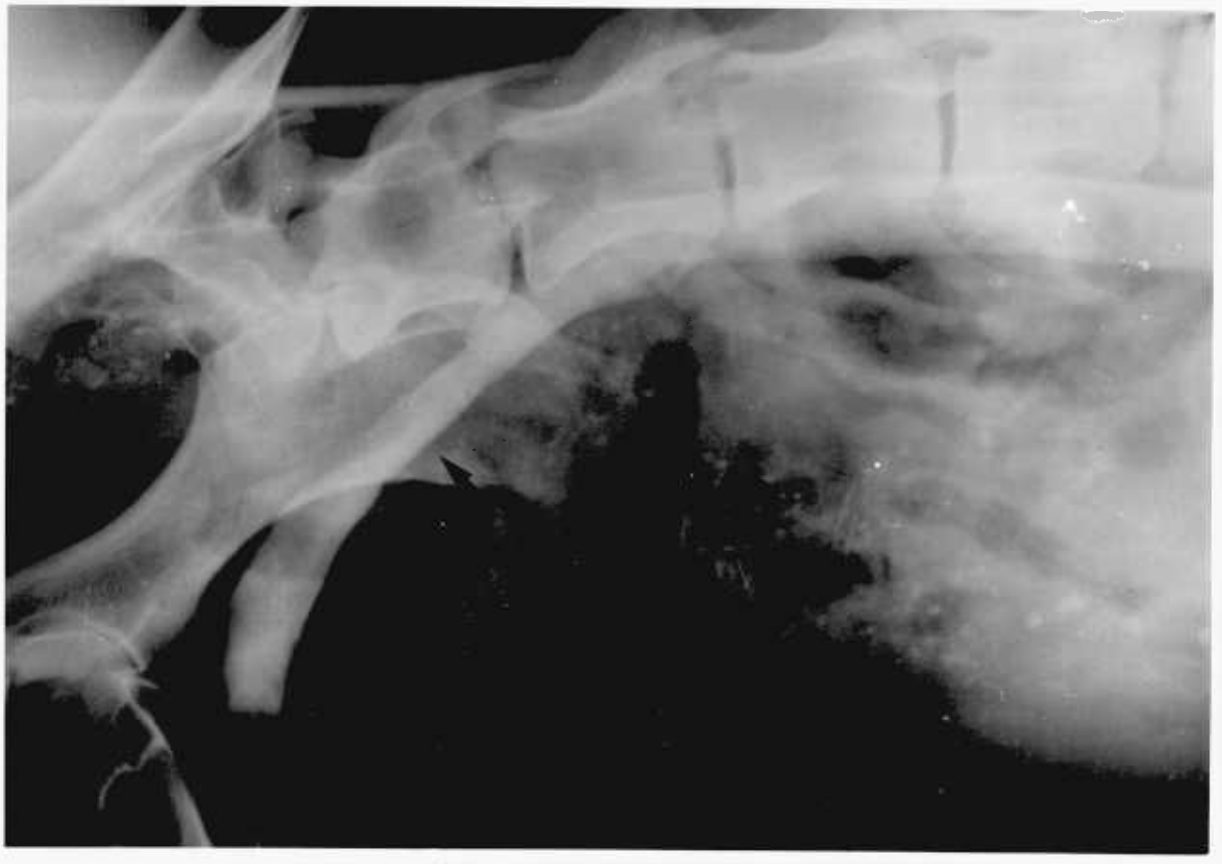

Fig. 1.16. PATENT ILIAC VEIN GRAFT (GRAFT INDICATED BY THE ARROW).

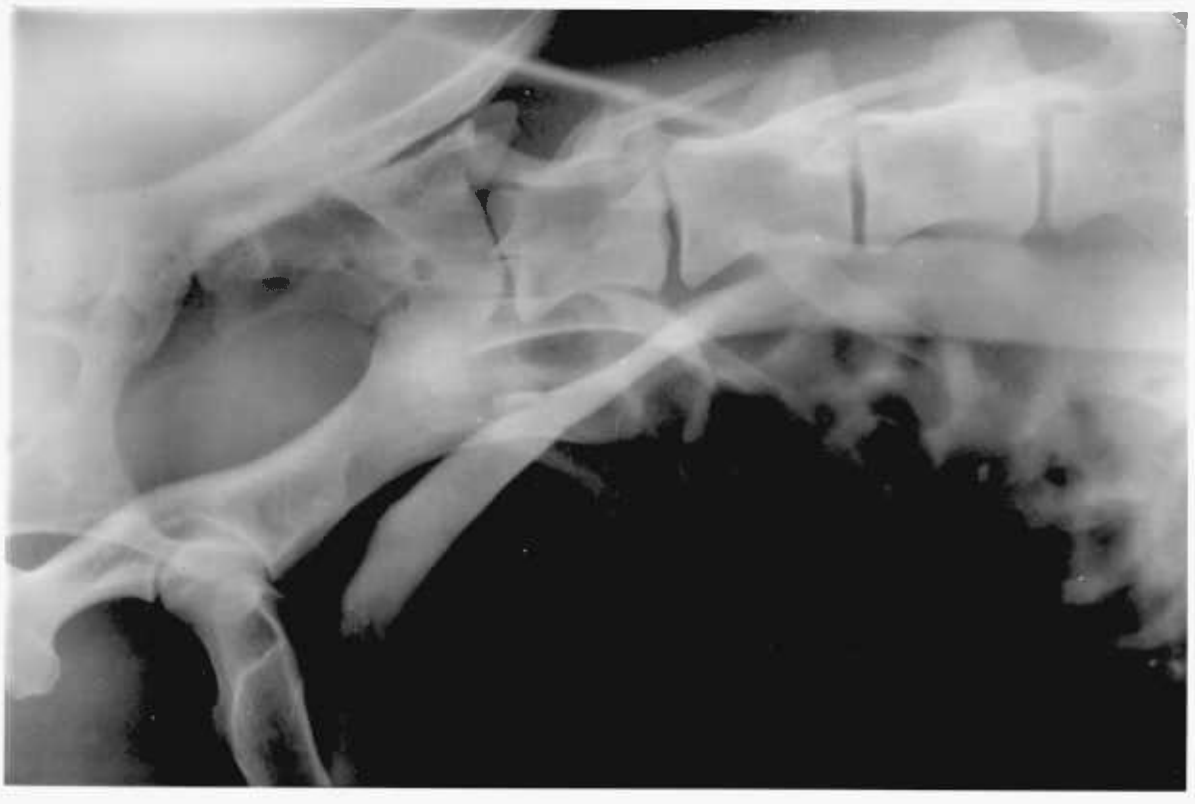

Fig. 1.17. ILIAC VEIN GRAFT SHOWING STENOSIS.

the experiment although most venograms were performed during the initial month and then at longer intervals during the succeeding months, until death.

The iliac vein grafts, as visualised by venography, were measured directly from the x-ray film, making due allowance for magnification, the diameter (in millimetres) recorded being that of the narrowest part of the graft.

The magnification on the x-ray film was calculated by comparing the distance between the x-ray machine anode and the table on which the dog was lying, and the distance between the dog and x-ray cassette. The former was 30" and the latter 3". This gives a magnification factor of $\frac{30+3}{30}$ or x 1.1

As well as direct measurements grafts were also classified as patent, (Fig. 1.16) occluded or stenosed (the latter being arbitrarily defined as narrowing of the diameter equal to or less than 1/3 of the original). (Fig. 1.17). These results are recorded in the appropriate sections.

RETROGRADE VENOGRAPHY:

Preserved autografts and allografts. Dogs 28 - 39.

It was not possible to demonstrate valvular function using the conventional antegrade venographic technique in these animals, and a method of retrograde venography was employed.

The animals were anaesthetised and placed in the supine position with the hind legs extended. (See Fig. 1.1). The abdomen was opened through a mid-line incision and the right circumflex iliac vein cannulated (6 F.G. Portex cannula 24" long) (Fig. 1.18). The cannual was passed distally till it lay in the proximal I.V.C. and about 20 ml. of a 45% sodium diazotrote solution injected. The

(Fig. 1.18 overleaf)

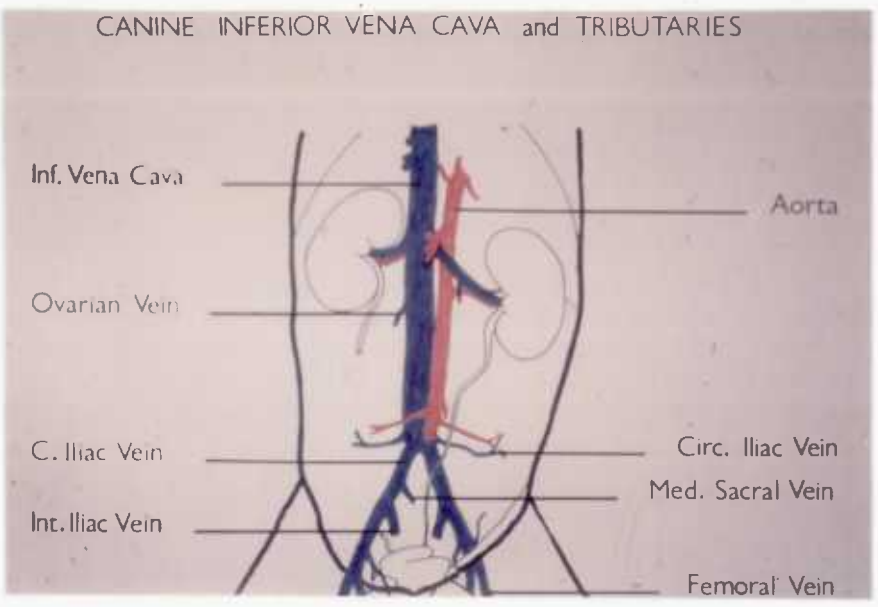

Fig. 1.18.

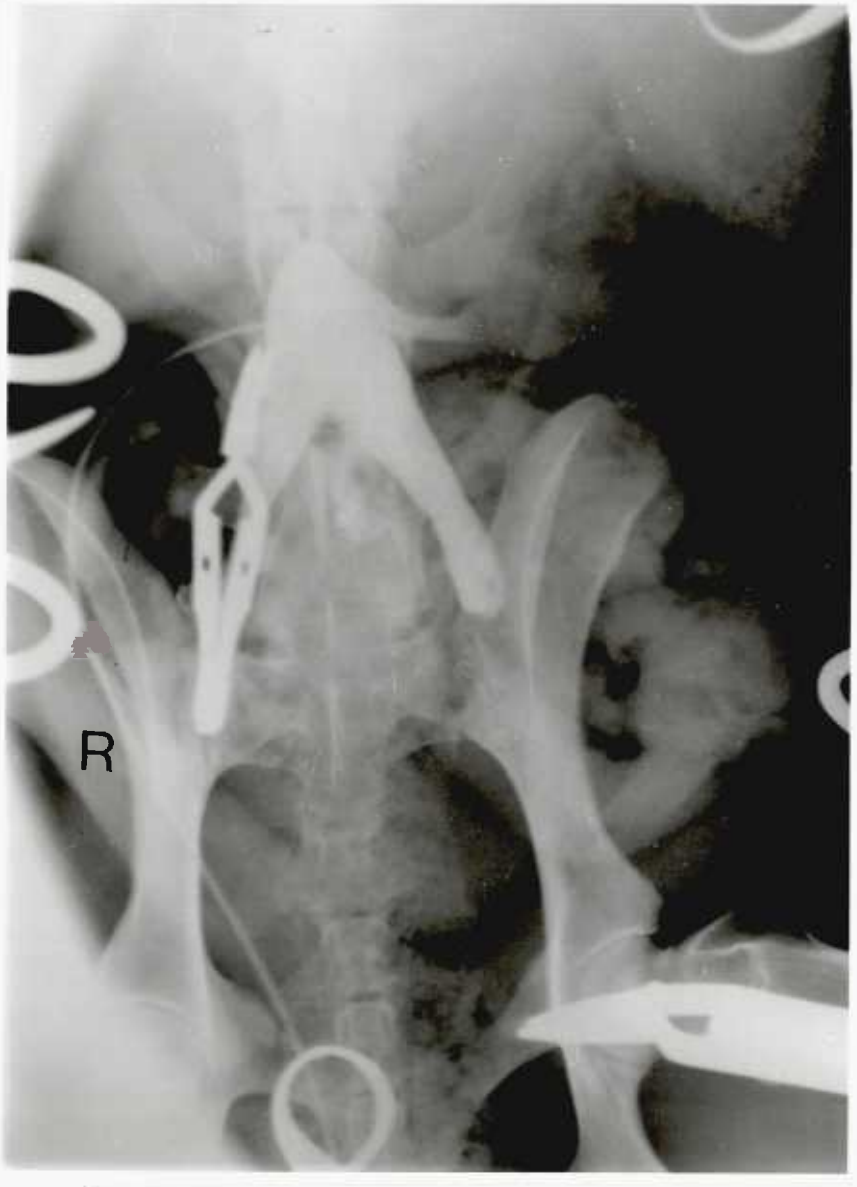

Fig. 1.19. RETROGRADE VENOGRAM. THE CONTRAST IS ARRESTED AT THE SITE OF THE VENOUS VALVE ON THE LEFT.

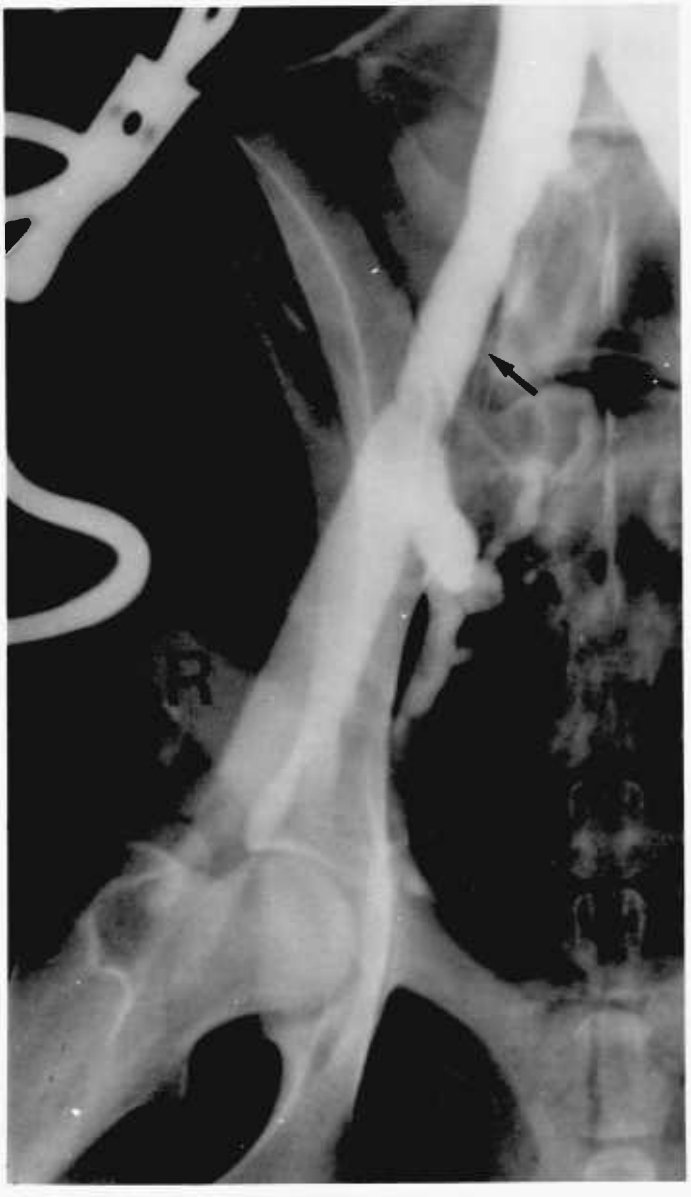

Fig. 1.19a. RETROGRADE VENOGRAM. THE CONTRAST FLOWS PAST THE SITE OF THE ALLOGRAFT VEIN. (THE VEIN GRAFT IS INDICATED WITH AN ARROW).

I.V.C. was temporarily occluded during the injection so that the contrast flowed into the ilio-femoral systems in order to demonstrate valvular function in the vein grafts. Fig. 1.19 illustrates the flow of contrast arrested at the level of the valves in the graft on the left hand side (adequate flow was not obtained into the right iliac system on this occasion). On repeating the injection with saline instead of contrast material the valves in the grafted segment could be seen to function in response to the retrograde flow.

Fig. 1.19a demonstrates the retrograde filling of the ilio-femoral systems and related tributaries, in the absence of valvular function. (See page 62 et seq.)

The results of this retrograde venography, which was performed in seven dogs, are tabulated and discussed in the chapter on Preserved Autografts and allografts.

(Fig. 1.19a overleaf)

COMPOSITION OF TISSUE CULTURE MEDIUM

STERILE DISTILLED WATER	80 ml
TC 199 SOLUTION	10 ml
PRE HEATED CALF SERUM Nº. 1	8 ml
SODIUM BICARBONATE SOLUTION (4.4%)	2 ml
TOTAL VOLUME	100 ml

Fig. 1.20

STORAGE TIME (DAYS) FOR PRESERVED AUTOGRAFTS AND ALLOGRAFTS.

DOG	AUTOGRAFT	ALLOGRAFT
27	4	11
28	18	7
29	15	7
30	4	4
31	3	3
32	5	7
33	4	4
34	5	12
35	1	4
39	7	1
Average:	7.3 days	5.8 days

Fig. 1.21.

PRESERVED VEIN GRAFTS

In view of the difficulties of collecting and storing donor veins under conditions of sterility, it was thought that vital preservation of veins by tissue culture methods may be a method of solving the problem. Valved segments of external jugular veins were collected at a small initial operation, stored for a period and subsequently inserted into the iliac veins. After discussion with Al Janabi and others the method used by Ross for preservation of aortic valve grafts was selected (personal communication). This is described in the paper by Al Janabi and Ross (1973).

METHOD OF STORAGE:

The tissue culture medium was made up under aseptic conditions in batches of 100 ml. according to the formula given in Fig. 1.20. Before use 4 mls. of the solution was discarded and a further 4 mls. of a solution of Benzyl Penicillin (concentration 75 mgms. per ml.) and Streptomycin (concentration 250 mgms. per ml.) were added. Twenty millilitre aliquots were prepared in sterile glass containers and stored at 4°C until required.

The excised portions of jugular veins were placed in the containers, stored at a constant temperature of 4°C. The tissue culture medium was changed every 48 hours under sterile conditions until the grafts were required. Table 1 (Fig. 1.21) gives the details of the length of time for which each graft was stored, the average time being about one week.

ASSESSMENT OF VIABILITY:

Autoradiography was used to determine the viability of the

preserved vein and this has been shown to be a useful method of assessing cellular metabolism (Boyd 1955, Gude 1968).

Viability of the jugular grafts was inferred from parallel studies on other jugular veins, using the same batches of tissue culture medium and the same method of storing, as the grafts could not be used for viability assays. The method of assessing viability utilises R.N.A. activity within the ribosomes as a measure of cell viability. If tritiated Leucine (^{3}H Leucine) is incubated with active cells, it is concentrated on the ribosomes, where it is incorporated into polypeptide chains, and is thus a measure of protein synthesis (Gough 1966). Using autoradiography techniques, it is possible to detect radioactivity within the ribosomes on photographic emulsion plates applied over the tissue, as the ^{3}H Leucine undergoes radioactive decay.

METHOD:

Vitally preserved portions of excised jugular veins were placed in 5 ml. of tissue culture fluid containing 0.1 ml. of ^{3}H Leucine solution (activity 250 microcuries per 0.5 ml.), and incubated at 37°C for 20 hours. After this they were washed in tissue culture fluid for 5 minutes to remove excess ^{3}H labelling and then placed in formal saline for fixation.

Paraffin sections were cut at 8μ thickness in the usual way, and the tissue slices mounted on glass slides. A thin film of emulsion (Kodak AR10 stripping plate) was placed over the sections, allowed to dry and then kept in light-proof boxes for 3 weeks incubation. The emulsion covered sections were then developed (Kodak D-19 developer) and fixed (Kodak metafix) in the routine way. Sections were stained with haematoxylin and examined for perinuclear granules, indicating

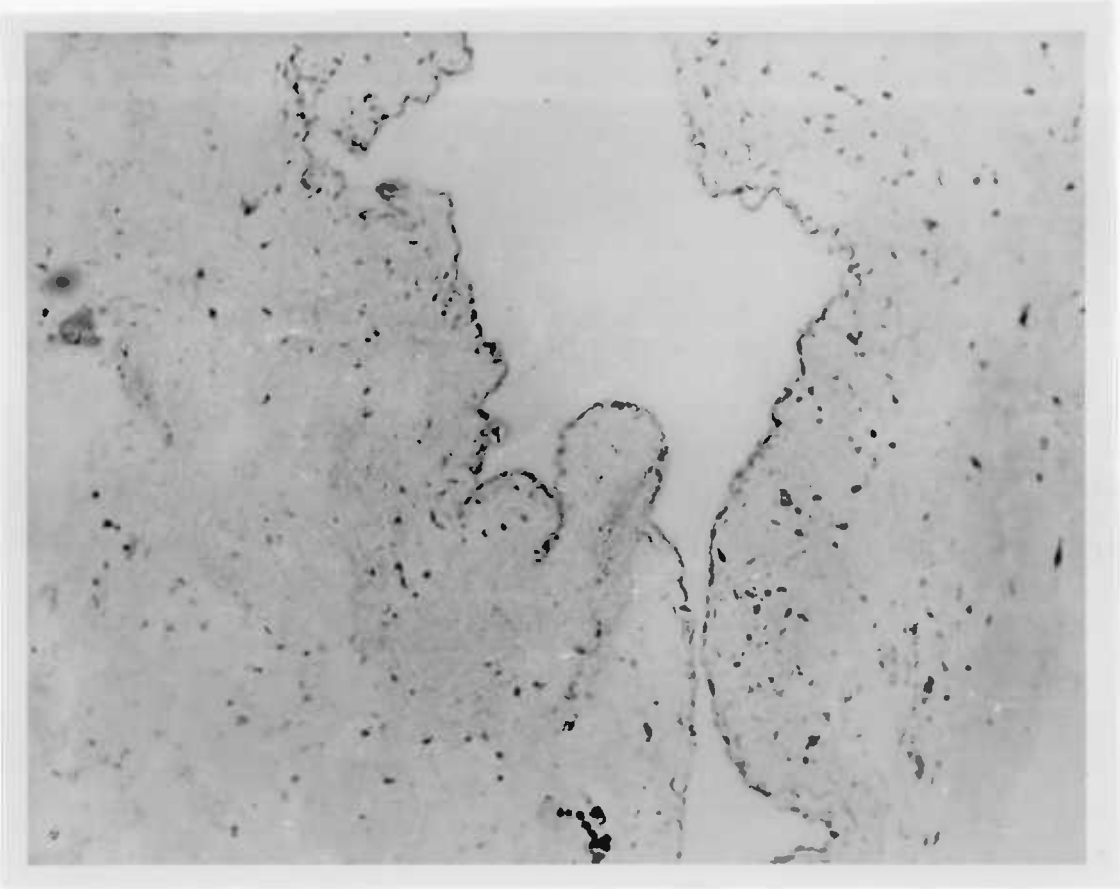

Fig. 1.22. SECTION OF VEIN WALL (HAEMATOXYLIN). THE RADIOACTIVE LABELLING FROM THE RIBOSOMES CAUSES THE VENOUS ENDOTHELIUM TO APPEAR DENSELY STAINED.

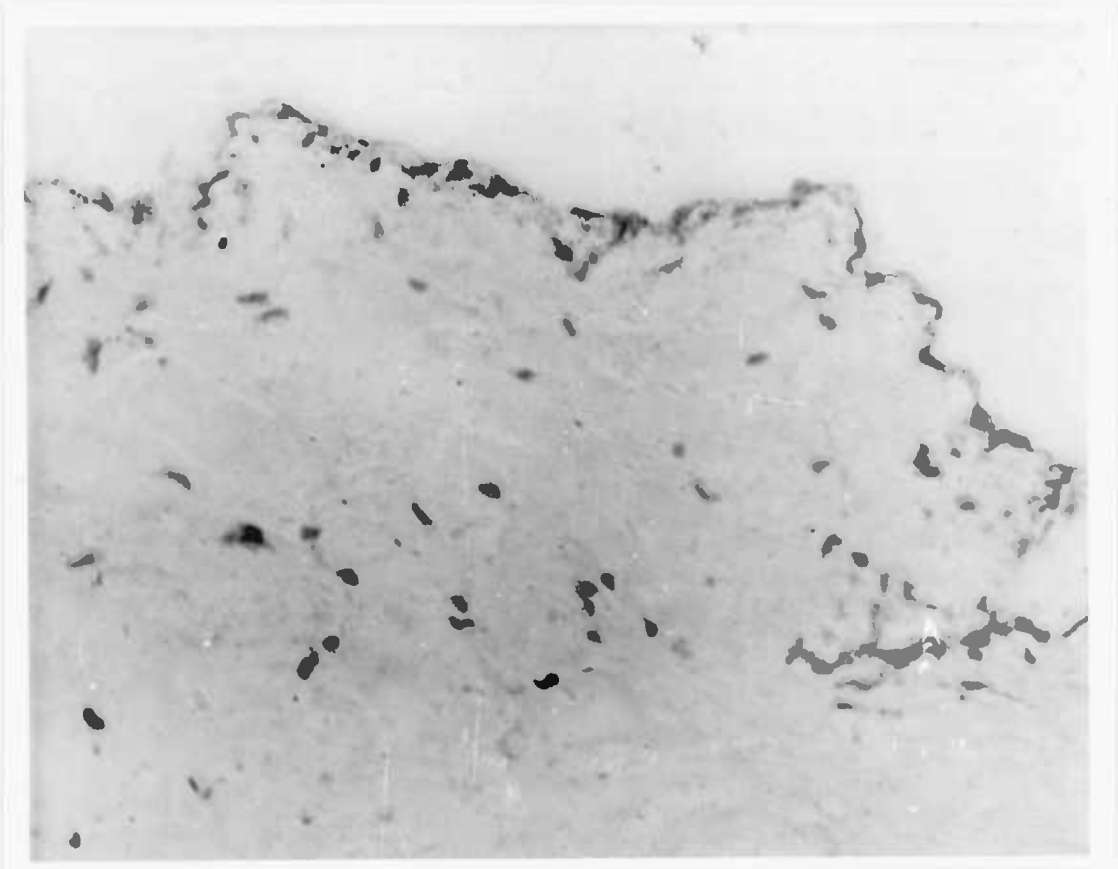

Fig. 1.22(a) HIGH POWER VIEW OF Fig. 1.22. THE INDIVIDUAL GRANULES MAY BE DISTINGUISHED.

ribosomal labelling with ^{3}H Leucine. Fig. 1.22, and Fig. 1.22a.

The veins were examined, (i) immediately upon removal from the dogs, (ii) after one week, (iii) two weeks and (iv) three weeks storage in tissue culture fluid at 4°C.

Three separate veins were sectioned and examined microscopically for the presence and number of intra-cellular granules in each part of the experiment. Fifty endothelial cells were counted in each section, a total of 150 cells.

RESULTS: (See Appendix C)

The average number of granules per cell in respect to time stored in tissue culture fluid is illustrated in Figure 1.23. If the granule count on day one is taken as unity, it may be seen that there is roughly half this activity after one week and one fifteenth of the original activity after a fortnight. The diminution of activity is roughly exponential with respect to time.

DISCUSSION:

Three grafts (two autografts and one allograft) stored in tissue culture medium for more than one week all functioned satisfactorily when grafted into the host animal and one of these grafts (dog 28 autograft) had functioning valves.

It would appear that ^{3}H Leucine labelling of the tissue as a measure of cellular viability is perhaps too sensitive when applied to veins stored at 4°C without added oxygen. Oxidative phosphorylation is an essential precursor of protein synthesis and the latter will not take place under anaerobic conditions. It is therefore not surprising that ribosomal activity is reduced after several weeks storage in tissue culture fluid whilst the viability of the

(Fig. 1.23 overleaf)

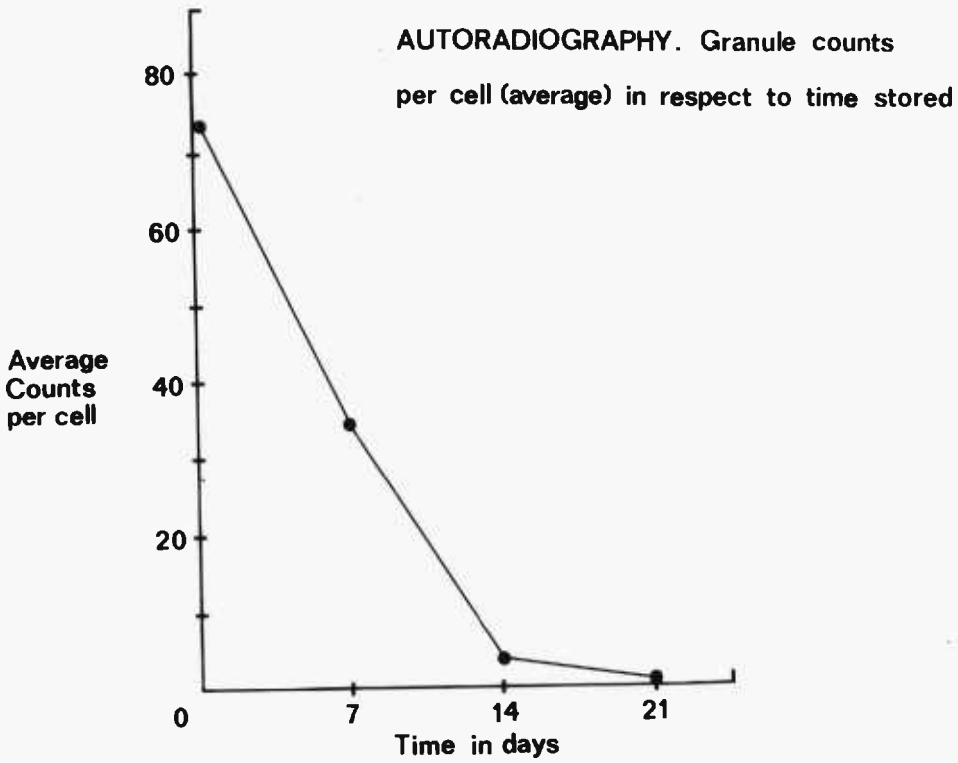
AUTORADIOGRAPHY. Granule counts
per cell (average) in respect to time stored
Average
Counts
per cell
80
60
40
20
0
7
14
21
Time in days

Fig. 1.23

of the venous tissue remains satisfactory.

ILIAC VEIN GRAFTS

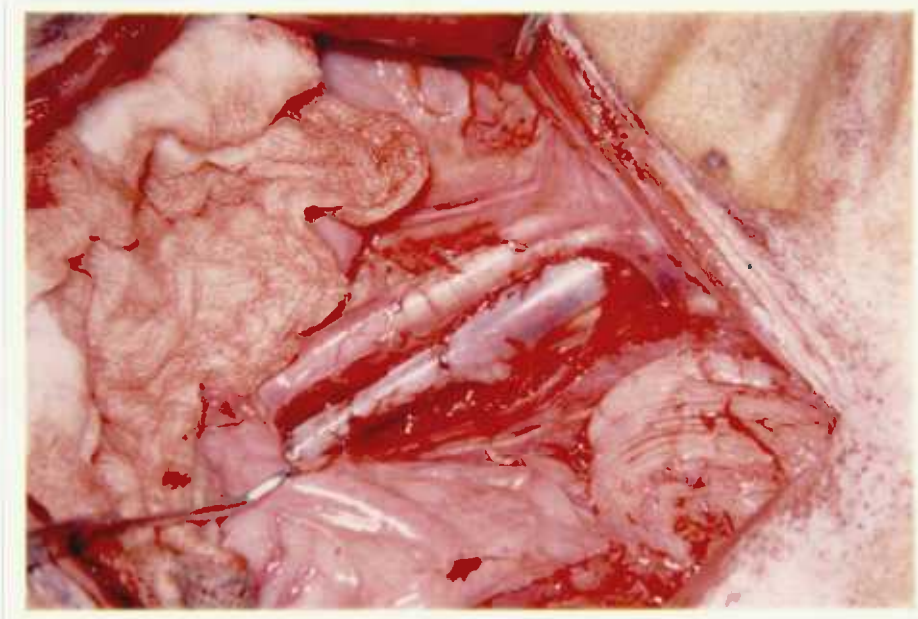

Fig. 2.1. ISOTOPIC AUTOGRAFT IN SITU. THE ILIAC ARTERY IS IMMEDIATELY ABOVE.

ISOTOPIC VEIN GRAFTS

INTRODUCTION:

The first part of this study was to establish the feasibility of venous grafting in this experimental model and additionally to develop a technique of vein anastomosis appropriate for the delicate vein tissues, which was satisfactory in practice. As well as this, the experiment was designed to compare:

(i) The effect of an arteriovenous fistula on the patency rate after isotopic venous grafting.

(ii) The effect of two different suture materials on patency.

METHOD:

Ten adult greyhounds, average weight 19.7 kg. (Range 14-21 Kg.) were used for this study. With the anaesthetic and operative technique described on pages 24 et seq., 2.5 cms. segments of each common iliac vein were excised and replaced isotopically, (Fig. 2.1) the procedure being carried out on both veins. After completion of the second venous graft a femoral arteriovenous fistula was constructed on one side (see also page 27.). Six of these fistulas were constructed on the right hand side of the animal and four on the left, in an attempt to eliminate any bias associated with anatomical variation and hence blood flow, although none was detected at operation or subsequently (see page 72).

Two types of suture material were used for the graft anastomosis, No. 60 P.T.F.E. coated polyester fibre and No. 60 braided silk, the latter being lubricated with liquid paraffin. The choice of side was randomly allocated for the polyester fibre by spinning a coin before each operation. The silk suture was then used on the

opposite side. An infusion of 0.9% sodium chloride continued for the duration of the operation via a cannula placed in the cephalic vein, the average volume infused being 670 ml. The average duration of the procedure was 5.3 hours. Blood loss was estimated in conjunction with the amount collected in the vacuum suction apparatus and varied between 100 and 300 ml, the average blood loss being 175 ml.

In seven dogs the arteriovenous fistula was closed at a subsequent operation (see page 27). The interim period varying from 16 to 41 days (average 23 days). The duration of this operation was about 40 minutes, and the blood loss in each case negligible.

Six surviving dogs were studied for a further period following the second operation ranging from 46 to 76 days from the original procedure (average 61 days), at the end of this time the dogs were killed and the grafts examined.

BLLOD FLOW RECORDINGS: APPENDIX D.

Blood flow was measured at the following points:

(i) In both iliac veins after mobilisation of the parietal peritoneum,

(ii) and again twenty minutes after completion of the arteriovenous fistula.

(iii) On the arterial part of the fistula at the end of the first operation,

(iv) and again before closure of the fistula at the second operation.

The N. 372 blood flow recorder was used in every case (see pages 33 and 36 et seq.)

Results after Isotopic Autograft Replacement

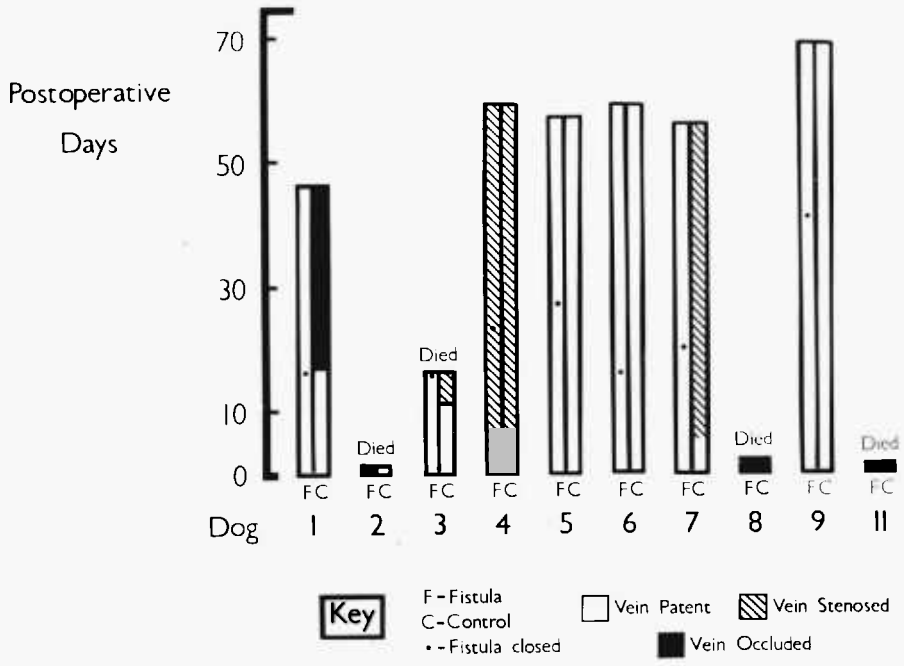

Fig. 2.2

TABLE 1.

FINAL STATE OF ISOTOPIC AUTOGRAFTS (10 DOGS)

	PATENT	STENOSED	OCCLUDED
CONTROL	4	3	3
A/V FISTULA	6	1	3

	PATENT	STENOSED	OCCLUDED
SILK	5	3	2
P.T.F.E. POLYESTER	5	1	4

TOTAL NUMBER OF GRAFTS 20
(Stenosed - $\frac{1}{3}$ original diameter)

Fig. 2.3

TABLE 2.

VENOUS PRESSURE RECORDINGS: APPENDIX E

Venous pressure was measured in the common iliac vein on the side of the fistula before venous grafting, and again after completion of the arteriovenous fistula. (See pages 39-40).

VENOGRAPHY:

X-ray studies were somewhat haphazard in the first six dogs, as already discussed in the section on venography, and comparative studies were not possible as the films were often taken in different planes. However, on the basis of several casual x-ray films and post-morten studies it was possible to allocate the grafts to one of the three groups previously described, i.e. patent, stenosed or occluded.

RESULTS:

Table 1 (Fig. 2.2) gives a summary of the findings in this first group of dogs. Three of the ten animals died within forty-eight hours of the first operation (dogs 2, 8 and 11), a fourth dog died at the second operation (dog 3) as the fistula was being closed, sixteen days after successful grafting.

Table 2 (Fig. 2.3) shows the final state of the vein grafts at death and it can be seen that there is no significant difference ($P > 0.2$) between the graft failure rate in the control or fistula groups. Similarly the choice of suture material does not affect the graft patency rate at a significant level ($P > 0.2$). This is in accordance with the results of Phelan and his co-workers who reached a similar conclusion (Phelan et al. 1958).

Overall there were ten grafts fully patent and a further four stenosed, out of a total of twenty grafts. Five of the failures

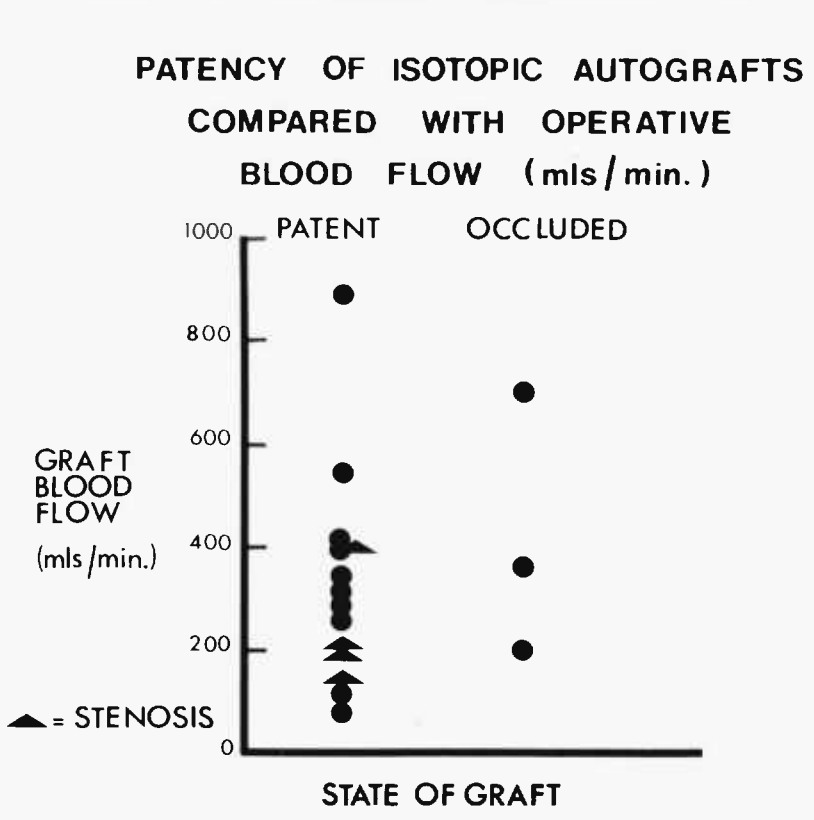
PATENCY OF ISOTOPIC AUTOGRAFTS
COMPARED WITH OPERATIVE
BLOOD FLOW (mls/min.)
PATENT
OCCLUDED
1000
800
600
400
200
0
GRAFT
BLOOD
FLOW
(mls/min.)
= STENOSIS
STATE OF GRAFT

Fig. 2.4

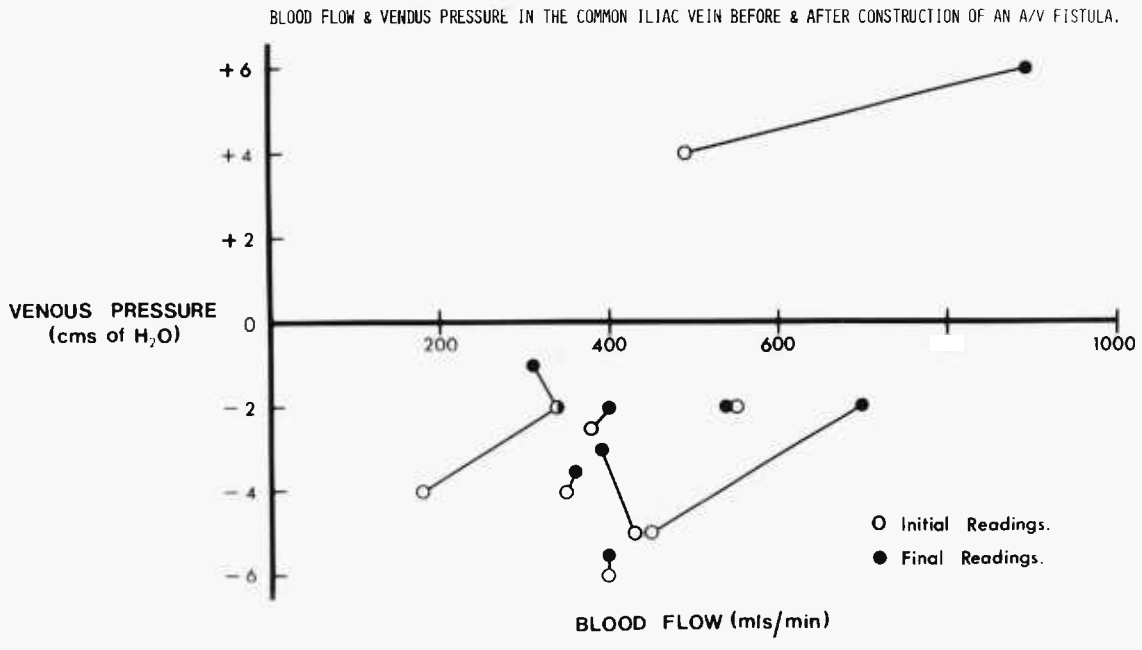
BLOOD FLOW & VENOUS PRESSURE IN THE COMMON ILIAC VEIN BEFORE & AFTER CONSTRUCTION OF AN A/V FISTULA.
+6
+4
+2
0
−2
−4
−6
VENOUS PRESSURE
(cms of H2O)
200
400
600
1000
O Initial Readings.
● Final Readings.
BLOOD FLOW (mls/min)

Fig. 2.5.

occurred in the dogs which died soon after operation.

Blood flow readings are detailed in Appendix C. The histogram which relates graft blood flow to the state of the graft at the animal's death derives from these figures, Fig. 2.4 and shows the wide range of operative blood flow in both the grafts which stayed open and in those which subsequently occluded. Three grafts which occluded are not represented in the histogram, as the graft blood flow was not recorded. This finding tends to confirm the impression that increasing the operative graft blood flow by means of an arteriovenous fistula has no effect on the patency rate of venous autografts.

Venous pressure measurements were conducted only in this first series of grafts, and the results are detailed in Appendix E. Figure 2.5 shows the graph relating graft blood flow to the venous pressure in that graft measured at the same time. The first reading taken at the beginning of the operation, and the second after completion of the arteriovenous fistula. Venous pressure was measured only on the side of the fistula. In four of the dogs studied there was no real change, and in a further two there was a fall in blood flow at the end of the operation associated with a rise in venous pressure seen, and this was not consistent with these animals. From the results of this albeit small experiment it was concluded that there was little relationship between graft blood flow and pressure and venous pressure measurements were discontinued in subsequent experiments.

HISTOLOGY:

The graft site and related areas were examined in all ten animals at death. As previously mentioned dogs 2, 8 and 11 died within forty-eight hours of operation. In dogs 8 and 11 the grafts on both sides

were totally occluded by fresh thrombus and emboli were observed in the pulmonary arteries; the site of the arteriovenous fistula was patent in both animals. The graft on the control side was widely patent in dog 2, whereas the fistula site and its adjacent graft were occluded. Although the lungs were not examined in this animal, the presumptive cause of death on clinical grounds was that of pulmonary embolism.

Dog 3 and dog 7 had patent grafts on the side of the fistula and adjacent valves in the external iliac vein were normal on macroscopic inspection. Grafts on the control side however appeared narrow although patent and webs were observed within the graft lumen particularly near the anastomosis site, indicating previous thrombosis and subsequent organisation (Edwards and Edwards 1937). Dog 3 died from the combined effects of anaesthesia and blood loss at the second operation.

Dogs 5, 6 and 9 had patent grafts on both sides, there being no evidence of past thrombosis macroscopically, and all three dogs had normal valves in the adjacent veins. In dogs 5 and 9 there was thrombosis and organisation on the vein wall at the site of the previous arteriovenous fistula.

Dog 1 had a patent graft on the side of the fistula, and a thrombosed graft on the opposite side.

Both grafts in Dog 4 were narrowed and septa were noted within the graft lumen, indicative of past thrombosis and organisation.

Microscopical examination of the patent grafts confirmed the presence of normal vein wall within the graft, however sub-endothelial fibrosis was marked around the anastomosis sites and epithelialisation of the suture tracks was frequently observed.

Normal valves were often observed in the adjacent veins when graft thrombosis was absent.

DISCUSSION:

This pilot study illustrates well the difficulties involved in the assimilation of a new technique. In the ten animals involved, four died in the perioperative period, an indication of the difficulties involved in anaesthetising dogs and then operating on them for about 5 hours. One half of the grafts in the series were occluded or stenosed - an unacceptable percentage in any clinical series, but illustrative of the "learning phase' in vein grafting. This is better appreciated when the results are compared with those of the third series of vein grafts.

The arteriovenous fistula appears to have no effect on the patency of the isotopic autografts, when considered overall (in terms of patency) or when considered in terms of increased blood flow through the vein grafts.

These findings are in agreement with those of Smith and Schisgall (1963) who found that the presence of an arteriovenous fistula had no effect on the patency rate of canine autografts. Levin and his colleagues were able to demonstrate a significant beneficial effect of an arteriovenous fistula in a series larger than most (Levin et al. 1971), although the animals were only studied for three days. This is not sufficient time for all the failures to occur.

Three other papers report a small, but statistically insignificant advantage on using a fistula with autografts (Scheinin and Jude 1964, Steinman et al. 1966, Johnson and Eiseman 1969).

It would appear that the case for improving the patency of

autografts by using an arteriovenous fistula remains unproven.

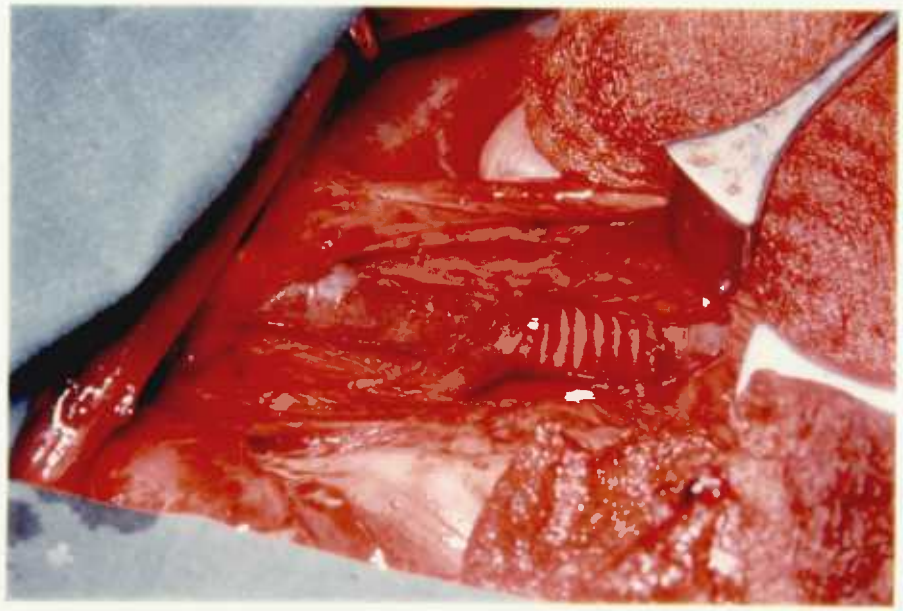

Fig. 3.1. DACRON GRAFT IN THE COMMON ILIAC VEIN.

DACRON GRAFTS

INTRODUCTION:

In a second series of experiments the established technique of venous grafting was applied to synthetic grafts, and an experiment was designed to compare the effect of an arteriovenous fistula on the patency rate of Dacron grafts placed within the iliac veins. Again it was hoped to compare the effect of using silk or polyester fibre suture materials with the Dacron grafts, but the silk proved unsuitable for use with knitted Dacron, as in the 60 size its tensile strength was inadequate.

METHOD:

Fifteen adult greyhounds of average weight 21.2 Kg. (range 13-25 Kg.) underwent iliac grafting procedures using the anaesthetic and operative techniques described previously. (See pages 24 and 26). Knitted, crimped, 1.5 cm., Dacron grafts of internal diameter 1.0 cm. were inserted bilaterally in the common iliac veins (Fig. 3.1) and on one side a femoral arteriovenous fistula constructed. Eight fistulas were on the right hand side of the animal and seven on the left.

The average duration of operation was 4.7 hours and each dog received 500 ml. of 0.9% saline during this time. Average blood loss was 110 ml.

Thirteen dogs survived the first procedure and in ten of these the arteriovenous fistula was closed at a subsequent operation; the interim period varying from 14 to 37 days (average 23 days). The duration of this operation was about forty minutes and the blood loss negligible.

The thirteen surviving dogs were studied for an average of 115 days (range 13 - 408 days) from the original grafting procedure and at the end of this period the dogs were killed and the grafts examined.

BLOOD FLOW RECORDINGS: APPENDIX E.

Blood flow measurements were taken with the Nycotron 372 equipment as described on page 36. Blood flow was measured at the following points:

(i) In both iliac veins at the conclusion of the first operation.

(ii) On the side of the arteriovenous fistula, in the common iliac vein, with the fistula clamped and unclamped.

(iii) On the arterial part of the fistula at the end of the first procedure,

(iv) and again at the second operation prior to the closure of the fistula.

VENOGRAPHY:

Bilateral ilio-femoral venograms were performed in all dogs as described in the section on venography. These venograms were performed on the second post-operative day and then twice weekly for a month. At the end of this period they were performed at more irregular intervals, usually every three to four weeks, until sacrifice.

RESULTS:

Two animals, dogs 14 and 15, died from the effects of halothane overdosage towards the end of the first operative procedure, the cause being traced to a faulty vapouriser. As the grafting procedures

Results after Dacron Graft Replacement

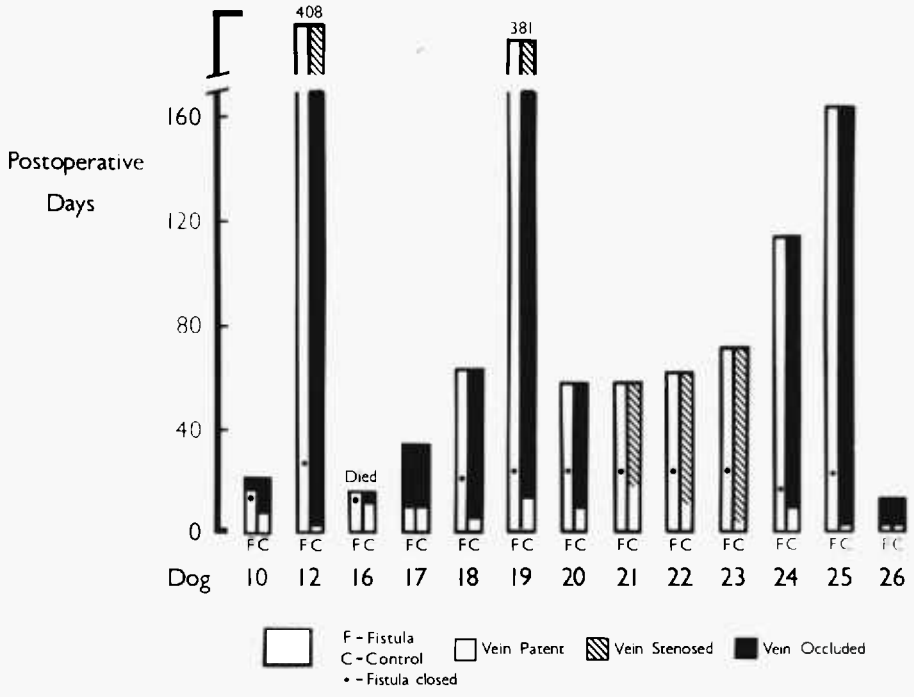

Fig. 3.2.

TABLE 1

FINAL STATE OF DACRON GRAFTS (13 DOGS)

	PATENT	STENOSED	OCCLUDED
CONTROL	0	3	10
A/V FISTULA	10	0	3

TOTAL NUMBER OF GRAFTS 26
(Stenosed - $\frac{1}{3}$ original diameter)

Fig. 3.3.

TABLE 2

were unfinished, the animals have been excluded from the results.

Table 1, Fig. 3.2 gives a summary of the findings in this series of animals. Dog 16 died on the thirteenth post-operative day with graft occlusion and a pulmonary embolus, and the arteriovenous fistula was not closed in this animal. All the other dogs survived until the end of the experiment. Two animals were observed for over a year to assess the long term effects of the Dacron grafts. It is interesting to note that partial recanalisation of the thrombosed grafts occurred in these two animals.

Table 2, Fig. 3.3 shows the final state of the Dacron grafts on the animal's death. Comparison of the results between the fully patent grafts and the stenosed and occluded ones, including the latter two together, shows that there is a significant difference ($P < 0.005$) between the control and arteriovenous fistula groups, using the Chi^2 test with the Yates correction for small numbers.

Blood flow readings are detailed in Appendix F. The table relating blood flow to the state of the graft at death derives from these, Fig. 3.4, and shows that fourteen out of the sixteen unsuccessful grafts (stenosed or occluded) were associated with a graft blood flow of less than 200 ml./min. at operation. Expressed in a different way, the average blood flow of the unsuccessful grafts was 126 ml./min., whereas that of the fully patent grafts was 382 ml./min., a three fold difference.

The minimum diameter of the grafts as visualised on the first post-operative venogram was recorded for each dog, and this was related to the appropriate graft blood flow as measured at operation. (See Appendix G.)

In the graph overleaf, Fig. 3.5, there appears to be a

(Fig. 3.4 overleaf)

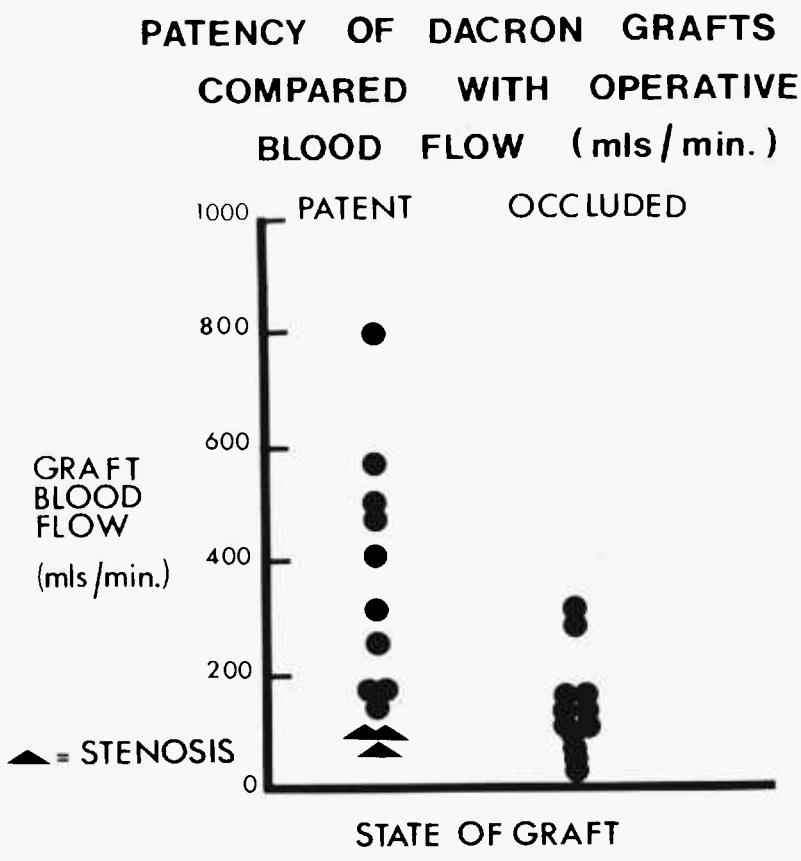

Fig. 3.4 SEE ALSO APPENDIX C.

The Relationship between Per-Operative Graft Flow and Post-Operative Graft Diameter (Dacron Grafts)

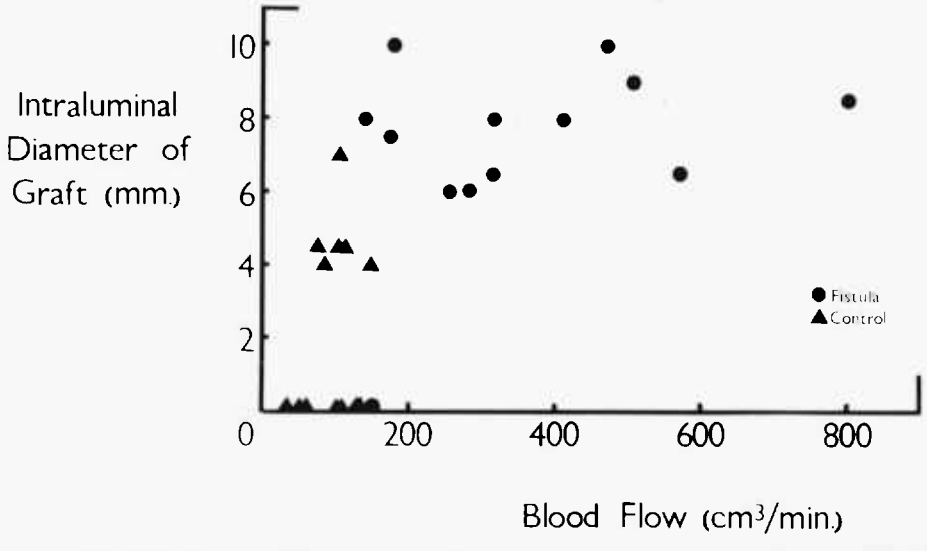

Fig. 3.5. SEE ALSO APPENDIX D.

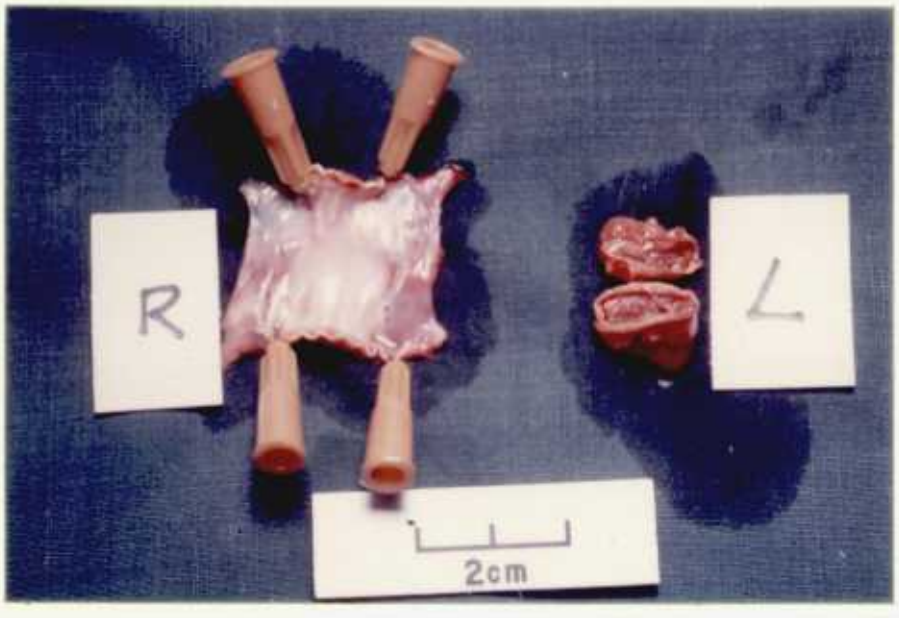

Fig. 3.6. DACRON GRAFTS REMOVED POST MORTEM. RIGHT SIDE: GRAFT COVERED WITH PSEUDOINTIMA. LEFT SIDE: GRAFT COLLAPSED AND OCCUPIED BY ORGANISED THROMBUS.

threshold value of about 150 ml./min., above which graft diameter is little influenced by blood flow. This threshold value separates two populations of co-ordinates related to the control and arteriovenous fistula groups. The former, as expected, were associated with low levels of blood flow in the graft and a marked reduction in intraluminal diameter; in the latter group there was no relationship between blood flow and graft diameter, the average intraluminal diameter in this group being over 70% of the original.

HISTOLOGY:

The graft site and related areas were examined in thirteen animals on their death. In five of these animals (dogs 16, 18, 20, 24 and 25) the graft site on the side of the arteriovenous fistula was widely patent with no evidence of previous thrombosis insofar as normal valves were seen in adjacent veins, and there were no intraluminal septa within the graft (Edwards and Edwards 1937). On the control side, however, there was complete occlusion of the graft by organised thrombus in every case. The photograph overleaf, Fig. 3.6, is representative. The specimen labelled "R" is from the fistula side, that labelled "L", and cut in cross-section, is from the control group.

In a further five animals (dogs 11, 19, 21, 22 and 23) the graft on the control side was distorted and stenosed by intraluminal septa, so that the lumen was virtually occluded; this effect was particularly marked in dogs 12 and 19. (Both of these animals were studied for over a year). Grafts on the side of the arteriovenous fistula were similar to those mentioned in the preceding paragraph. Microscopical examination of all these patent grafts was very similar, revealing continuity of the endothelium from the host vein

onto the lining of the graft. Beneath these cells there was a layer of mature collagenous fibrous tissue and then cellular granulation tissue enmeshed in the interstices of the Dacron graft.

In three animals (dogs 10, 17 and 26), the grafts on both sides were thrombosed, with complete occlusion of the lumen and some organisation of thrombus.

DISCUSSION:

There was only one death in this series due to graft failure and pulmonary embolism, a reflection of further experience with the grafting technique.

There appears to be a threshold value for graft blood flow, above which there is little effect on graft diameter. Below this threshold level there is a roughly linear relationship between flow and graft diameter, and this threshold demonstrates the effect and use of an arteriovenous fistula to enhance the graft patency.

Two authors who used Dacron grafts in the IVC, in association with an arteriovenous fistula reported good results (Todd et al. 1963, Steinman et al. 1966). These reports are more encouraging than those of other workers who did not use a fistula (Collins et al. 1960, Demetz et al. 1961). In the latter papers there were no successful grafts.

Of the four grafts studied for more than one hundred days, there was no late stenosis seen and the grafts remain widely patent: this gives further weight to the concept of the critical early period. In two of these animals who were studied for over a year, the control grafts which thrombosed early in the experiment subsequently recanalised; this is in accordance with the accepted statements on recanalisation by Dale (1963), although he only specifically mentions

recanalisation in tissue grafts.

PRESERVED AUTOGRAFTS AND ALLOGRAFTS

INTRODUCTION:

In a third series of experiments valved autografts and allografts were placed in the common iliac veins.

In the clinical situation two of the problems encountered in venous reconstruction are the provision of valved segments of veins, and the use of large calibre veins which are not already essential. This experiment was designed to assess the possibility of:

(i) grafting valved segments of veins, and,

(ii) to see if large calibre allografts could be successfully substituted for autografts where the use of the latter was impracticable. In addition, the effect of increasing the blood flow through the graft and the use of two different suture materials for anastomosis was also studied.

METHOD:

Ten adult greyhounds of average weight 20.4 Kg. (Range 14-25 Kg.) underwent bilateral excision of their jugular veins, as described on Page 28. Four jugular veins were obtained by similar procedures from two other dogs, not in this series, at the moment of death. The average duration of this operation was about 30 minutes and the blood loss negligible.

Neither jugular vein in dog 35 contained a valve, so the preserved autograft in this dog was grafted without one; however, the allograft did contain a valve.

Examining the effects of autografts and allografts, the arteriovenous fistula and two different suture materials (braided silk and P.T.F.E. coated polyester fibre) gives eight different combinations

ALLOCATION OF THE THREE PAIRS OF VARIABLES TO THE TEN DOGS.

LEFT - HAND SIDE			RIGHT - HAND SIDE			DOG			
A/V FISTULA	ALLOGRAFT	SILK	CONTROL	AUTOGRAFT	POLYESTER	27	31	35	39
A/V FISTULA	AUTOGRAFT	POLYESTER	CONTROL	ALLOGRAFT	SILK	28	32		
CONTROL	ALLOGRAFT	POLYESTER	A/V FISTULA	AUTOGRAFT	SILK	29	33		
CONTROL	AUTOGRAFT	SILK	A/V FISTULA	ALLOGRAFT	POLYESTER	30	34		

Fig. 4.1.

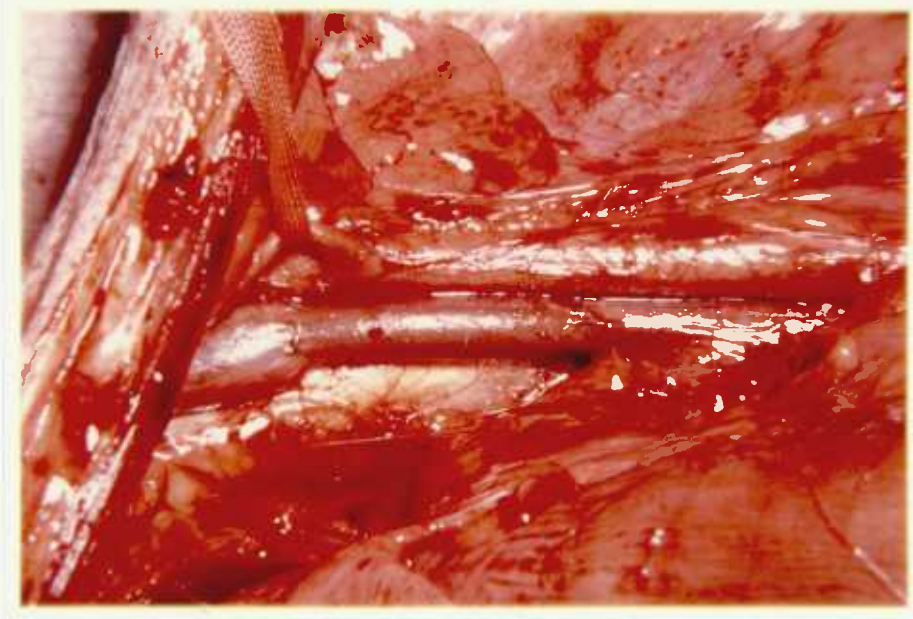

Fig. 4.2. PRESERVED TISSUE GRAFT IN SITU.

of the variables, if the effect of the different side of the dog is ignored. The allocation of variables at the second operation is illustrated in Fig. 4.1.

Several days later at a subsequent operation one autograft vein and another vitally preserved vein, i.e. an allograft, were grafted into the common iliac veins, Fig. 4.2. It was thus arranged that each dog had an autograft and an allograft. To accommodate these grafts a 2.0 cm. segment of iliac vein was excised. Six allografts and four autografts were on the same side as the arteriovenous fistula.

Each dog received 500 ml. of 0.9% sodium chloride solution during the operation, which lasted on average 4.2 hours. Blood loss was less than 100 ml in every dog.

All ten animals survived the first procedure and in eight of these the arteriovenous fistula was closed at a subsequent operation, the interim period varying from 18 to 47 days. (Average 30 days.) The duration of this operation was about 40 minutes and the blood loss again negligible.

The eight surviving dogs were studied for an average of 169 days (range 114 - 268 days) from the grafting procedure and at the end of this period the dogs were killed and the grafts examined.

In seven dogs a retrograde venogram was performed before death to assess the competence of the valves in the grafted segment. This is described more fully on Page 43.

BLOOD FLOW RECORDINGS: APPENDIX H

Blood flow was measured with the N.372 machine at the following points:

(i) In both iliac veins at the conclusion of the grafting

Results after Autograft and Allograft Replacement

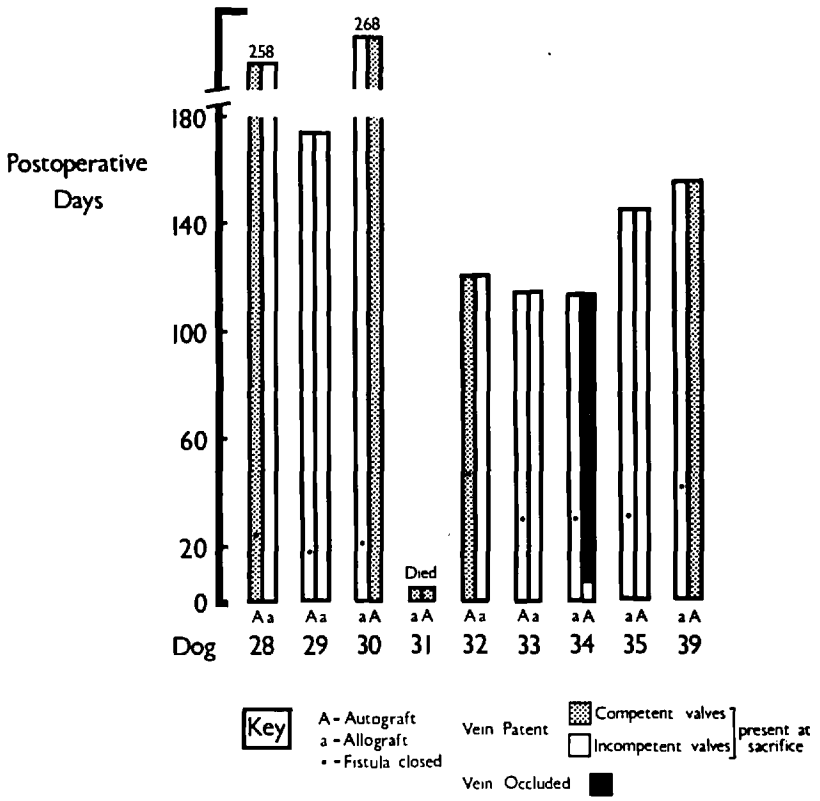

Fig. 4.3.

TABLE I.

procedure.

(ii) In the common iliac vein, on the side of the arterio-venous fistula, with the fistula clamped.

(iii) On the arterial part of the fistula at the end of the grafting procedure, and again

(iv) at the third operation prior to the closure of the fistula.

VENOGRAPHY: APPENDIX J

Bilateral ilio-femoral venograms were performed in all dogs as described in the section on venography. These venograms were performed on the second post-operative day and then twice weekly for a month. At the end of this period they were performed at more irregular intervals, usually every three to four weeks, until sacrifice.

RESULTS:

The first dog in the series, dog 27, inadvertently received vein grafts which had been stored in an unsuitable tissue culture medium. It was subsequently discovered that the pH of this medium was 4 instead of 7. As one of the objects of this experiment was to test the feasibility of vitally preserved grafts, this dog was excluded from the results.

The table opposite gives a summary of the findings in this series of animals (Fig. 4.3, Table 1.) Dog 31 was killed in a fight with some other animals on the fourth post-operative day, and the follow-up of this dog was considered inadequate to draw many conclusions, both grafts were patent however with normally functioning valves.

FINAL STATE OF PRESERVED ALLOGRAFTS AND AUTOGRAFTS (9 DOGS)

	PATENT	STENOSED	OCCLUDED
CONTROL	8	0	1
A/V FISTULA	9	0	0

	PATENT	STENOSED	OCCLUDED
SILK	8	0	1
P.T.F.E. POLYESTER	9	0	0

TOTAL NUMBER OF GRAFTS 18
(Stenosed - $\frac{1}{3}$ original diameter)

Fig. 4.4 TABLE I.

The Relationship between Per-Operative Graft Flow and Post-Operative Graft Diameter (Tissue Grafts)

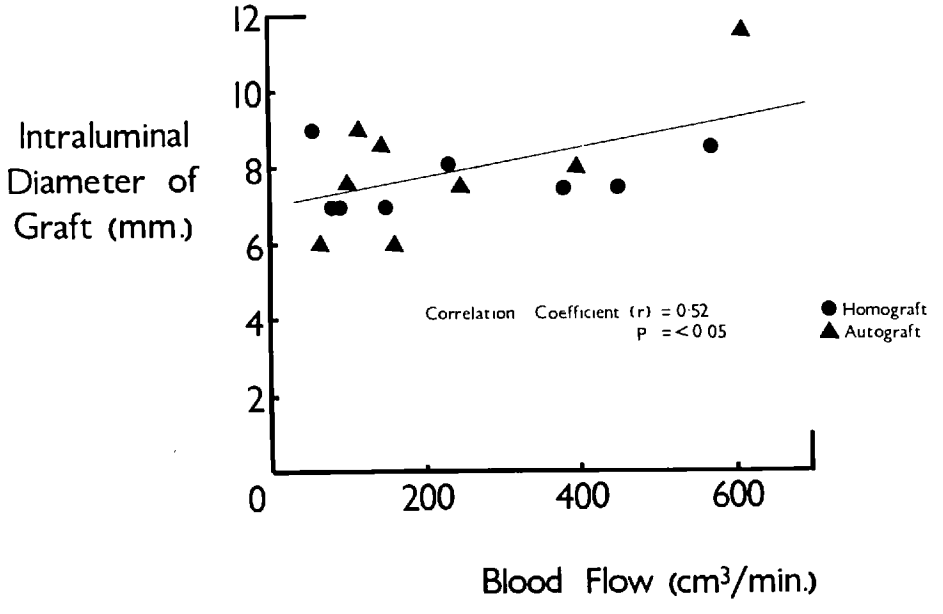

Fig. 4.5.

With the exception of the autograft in Dog 34, all the other grafts remained widely patent throughout the period studied.

The final state of the allografts and autografts at death is shown in Table 1, Fig. 4.4, as only one graft occluded in a series of eighteen, there is obviously no significant difference between either the control and fistula groups or the two types of suture materials.

Retrograde venography demonstrated competent valves in four of the autografts (dogs 28, 30, 34 and 39) out of a possible seven grafts. This finding was somewhat bizarre in the case of dog 34, where antegrade venography had suggested graft thrombosis. On direct inspection of the graft site however it could be seen that the occlusion had occurred a centimetre or so proximal (presumably at the site of vascular clamping during the insertion of the graft) and that the graft itself was patent, although narrow, with competent valves. From the functional point of view however this graft must be regarded as occluded.

For technical or other reasons the valves in the autograft of dog 32 could not be made to function on retrograde venography, although they subsequently appeared perfectly normal (see the section on Histology).

Valves were not visible on x-ray studies in any of the allografts studied for more than one week.

Blood flow readings are detailed in Appendix G. The graph relating post-operative vein diameter to operative graft blood flow is shown opposite, Fig. 4.5. It would appear that the operative blood flow has little effect on the graft diameter in the two groups, if considered as a whole or separately. The mean intraluminal diameter of the autograft group being 8.0 mm, and that of the allograft group

7.5 mm. Even at low blood flow rates, i.e. less than 200 ml./min., allografts remain patent, and there is therefore no evidence from this graph that an arteriovenous fistula materially affects graft diameter, over the range of flows studied.

HISTOLOGY:

The graft sites and related areas were examined in nine animals at the end of the experiment. In all cases the graft site was patent, although in dog 34 the site of vascular clamping proximal to the graft was occluded.

All the autografts except dog 35, where no valves were grafted, had valves present macroscopically. In six of these animals (dogs 28, 30, 31, 32, 34 and 39) the valve leaflets appeared normal, in dogs 29 and 33 the valves were tethered along their free edges by adhesions, either on one or both cusps, preventing their effective action. Microscopical examination confirmed the presence of normal valves and vein wall in each autograft.

Valves were seen in only one allograft (dog 31). In all the others, valves were completely absent on gross examination and on microscopy, although they were seen in the host veins adjacent to the graft site.

All the veins showed evidence of sub-endothelial fibrosis around the anastomosis site and endothelialisation of the suture tracks was frequently observed. Apart from the absence of valves in the allografts, both series of grafts showed an essentially similar picture. There was no evidence of immunological rejection. It was not possible to distinguish a histological cellular pattern in relation to the type of suture material used.

DISCUSSION:

The absence of graft occlusion in this series is gratifying and shows that veno-venous anastomosis is possible in the experimental situation at least with a degree of success acceptable in clinical practice. The presence of an arteriovenous fistula has no adverse effect on the patency of the autografts or allografts; this confirms the previous findings in the group of isotopic autografts.

The continuing patency of the fresh allografts albeit without valve function suggests that preserved allografts may have a clinical role in the replacement of essential veins where an autologous substitute is not readily available. It would appear from the series that autogenous veins must be used when functional valves are required as the autograft valves are the only ones to survive. These findings are in agreement with the work of McLachlin and his colleagues who recorded continuing valvular patency in canine autografts but not allografts (McLachlin et al. 1965), and contrasts with the experience of Waddell and his colleagues who were able to demonstrate valvular function in allografts three weeks after transplantation (Waddell et al. 1964). Two other papers have also established that if autografts remain continuously patent valvular function is maintained (Baird et al. 1964, De Weese and Niguidula 1960).

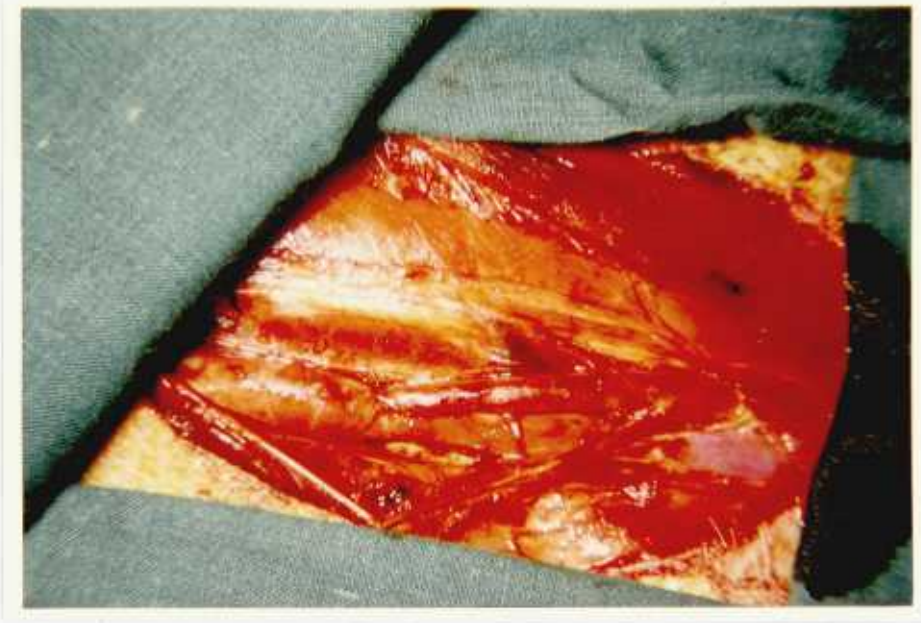

Fig. 5.1. FEMORAL ARTERIOVENOUS FISTULA. THE END OF THE FEMORAL ARTERY IS ANASTOMOSED TO THE SIDE OF THE FEMORAL VEIN.

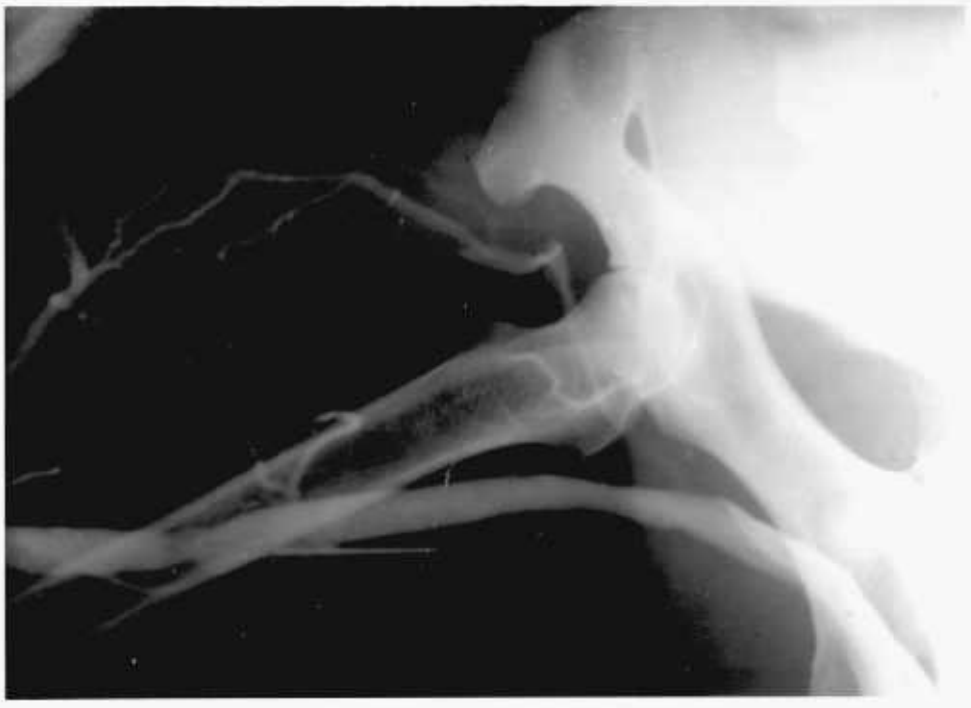

Fig. 5.2. X-RAY OF A FEMORAL ARTERIOVENOUS FISTULA. THE NEEDLE LIES IN THE FEMORAL ARTERY. MOST OF THE CONTRAST MATERIAL LIES IN THE FEMORAL AND ILIAC VEINS.

THE ARTERIOVENOUS FISTULA

An arteriovenous fistula can be defined as an abnormal connection between an artery and vein whose resistance is less than that offered by the capillary bed that connects them.

Arteriovenous fistulae have attracted the interest of physiologists and surgeons for many years. It was William Hunter who first described an arteriovenous aneurysm in 1757, and the physiology was intensively investigated and described by Holman (1937). Most reports in the literature relate to congenital fistulae or those acquired as a result of trauma, and it was not until more recently that interest in surgically produced arteriovenous fistulae was aroused with the introduction of the Brescia shunt used for haemodialysis (Brescia et al. 1966).

Fistulae constructed for these experiments were all between the superficial femoral vessels on either leg, the artery being divided obliquely some 10 cms. distal to the inguinal ligament and anastomosed obliquely end-to-side to the femoral vein. This is illustrated in Figs. 5.1 and 5.2.

On release of the vascular clamps after construction of the fistula, it was possible to palpate a distinct thrill over the femoral vein immediately distal to the fistula and on occasions turbulent mixing of the venous and arterial blood was visible through the vein wall. On auscultation of the vein distal to the fistula with an ultra-sound probe (Parkes directional Doppler 801.10 mHz signal) it was possible to detect grossly turbulent blood flow at the site of the fistula. Ten centimetres or so downstream on the venous side the flow again approximated to that of laminar on auscultation with the probe, although the velocity was considerably increased. In

COMMON ILIAC VEIN BLOOD FLOW COMPARED BETWEEN THE CONTROL AND A/V FISTULA SIDE (FISTULA TEMPORARILY OCCLUDED)

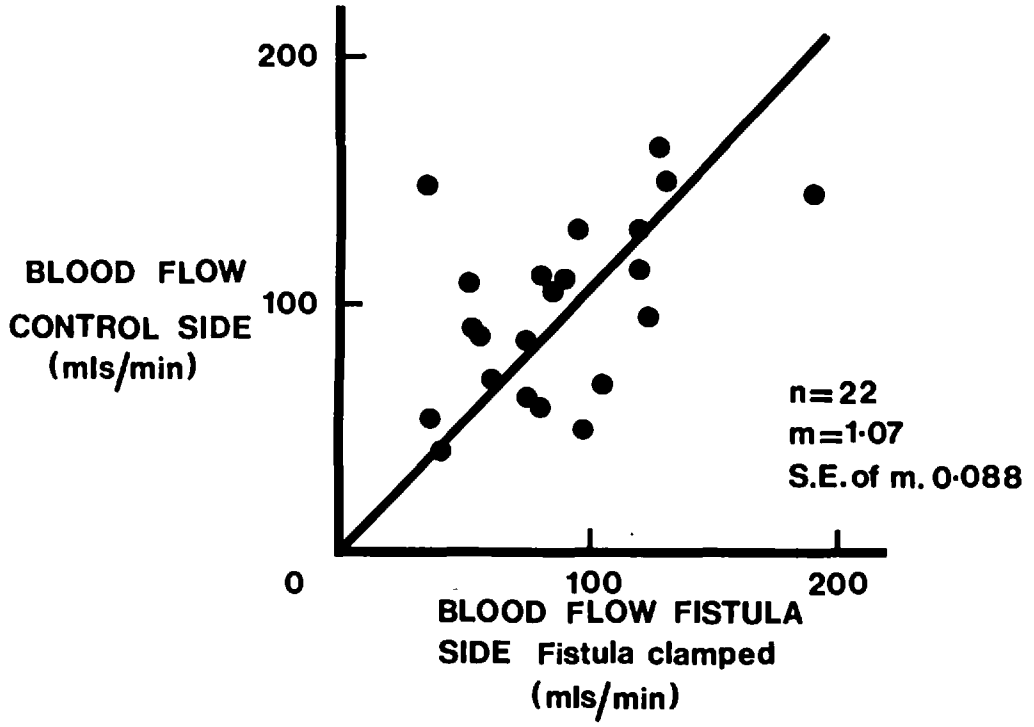

Fig. 5.3. KEY. n: NUMBER OF READINGS. m: SLOPE. S.E.: STANDARD ERROR.

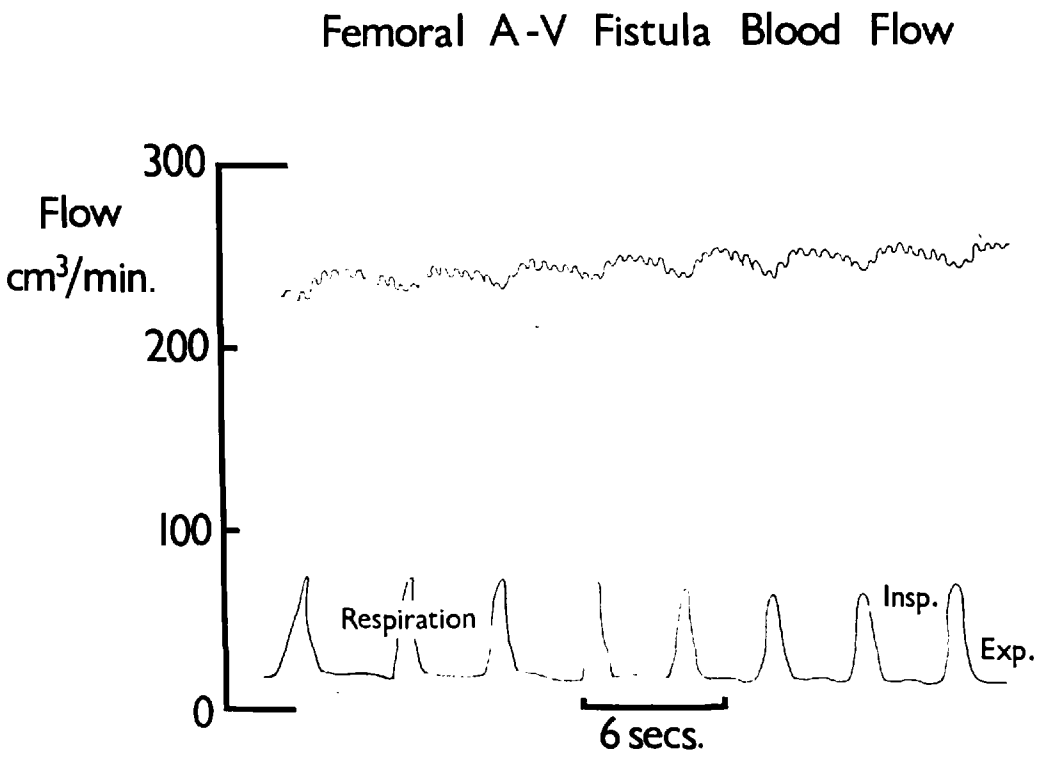

Fig. 5.4.

view of the large decrease in peripheral resistance caused by the femoral arteriovenous fistula, in conjunction with the division of a superficial femoral artery and its distal ligation, it was thought that there may have been some evidence of ischaemia in the distal part of the affected limb. Clinically, the dogs were able to walk normally when the fistula was established. There was no evidence of claudication in any animal. Inspection of the limb also revealed no abnormality.

These findings were borne out experimentally by comparing the iliac vein flows on each side when the arteriovenous fistula was momentarily clamped (Fig. 5.3). Over the lower range of blood flows (that is below 200 millilitres per minute) the two sides were comparable, but the average flow through the iliac veins on the side of the fistula was about 10% below that on the other side (see Appendix F and H.) This is in accordance with the theoretical reasoning which predicts that an arteriovenous fistula would lower the peripheral resistance in that limb so increasing the cardiac output. The increasing cardiac output is diverted through the fistula and the drop in the distal limb flow is in the region of 15% depending on the size of the fistula (Burton 1965).

Blood flow recordings were made over the arterial part of the fistula 15 minutes after its construction (Fig. 5.4). It was technically easier to record blood flow in the more rigid arterial vessel and its flow was approximately laminar as judged by ultrasound examination.

In 22 animals blood flow recordings were documentated immediately after construction of the fistula and before its closure about 3½ weeks later (see Appendix D, F and H), the longest period of study was 47 days. During this time there was an increase in the mean blood flow

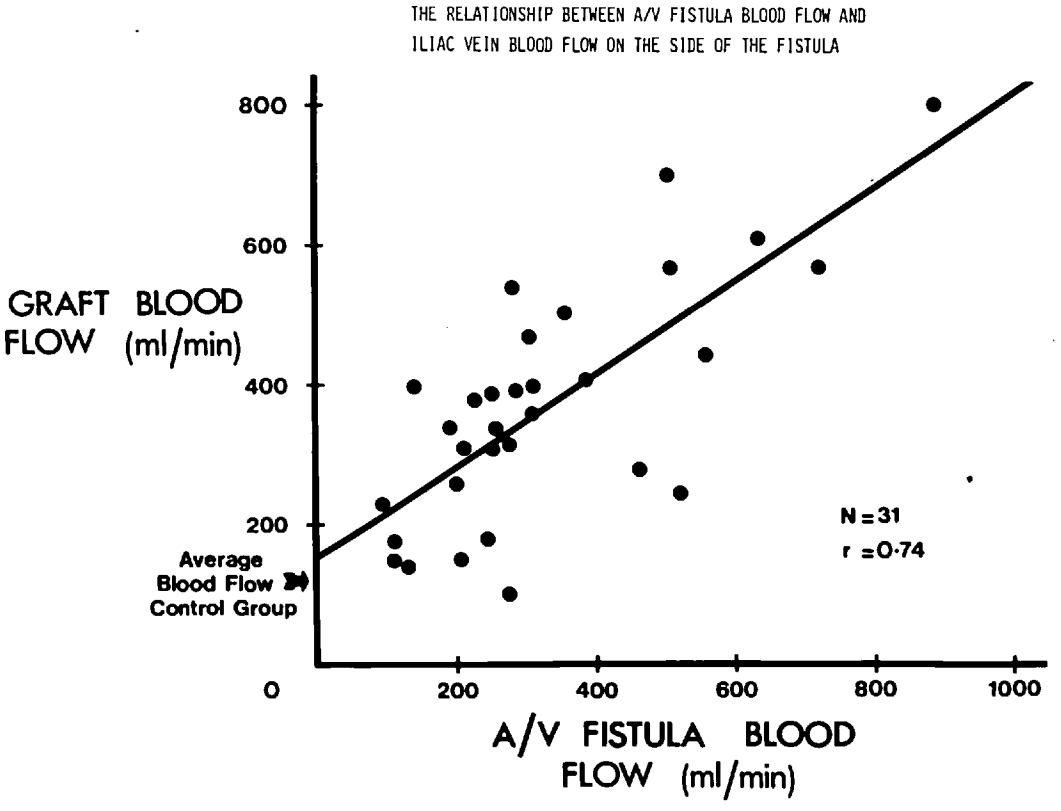

Fig. 5.5 SEE TEXT FOR FURTHER EXPLANATION.
KEY. N: NUMBER OF READINGS. r: CORRELATION COEFFICIENT.

through the fistula from 340 millilitres per minute (S.E. ±42) to 352 millilitres per minute (S.E.±56). These two groups of figures show considerable overlap when their standard errors are compared and there is no significant difference between them, i.e. there is no difference in the mean flow through the fistula from the beginning to the end of the periods studied. The readings for the mean fistula flow agree with the findings of Schenk and his colleagues who found a mean fistula flow of 390 mls./min. in eight femoral arteriovenous fistulae constructed in dogs (Schenk et al. 1957).

In view of the wide range of fistula blood flow produced, (95 millilitres per minute up to 880 millilitres per minute) at the time of the grafting procedure, it was decided to investigate the relationship between the graft blood flow (on the side of the A/V-fistula) and volume flow through the fistula (Fig. 5.5). There appears to be a linear relationship between the two variables over the flow rates indicated, and if the fistula flow (i.e. 50 millilitres per minute) corresponds well with the average graft blood flow (i.e. 122 millilitres per minute) as measured in the control group. The relationship is such that the effect of the fistula flow is not additive as might be expected, (i.e. the expected graft blood flow with a fistula flow of 200 mls. per minute might be 150+200 = 350 mls. per minute instead of 250 mls per minute, the value from the graph). This effect becomes more pronounced at high fistula flows, indicating that increasing amounts of blood from the fistula are being shunted away from the graft (the iliac veins) and are passing through other venous channels. This is presumably due to the large rise in venous pressure at the site of the fistula associated with the high flow rate,(see page 39).

If, in the presence of a femoral arteriovenous fistula, blood is

ILIAC VEIN BLOOD FLOW

DURING AND AFTER FISTULA OCCLUSION.

DOG	FISTULA FLOW	ILIAC VEIN BLOOD FLOW "CONTROL" SIDE		DIFFERENCE IN ILIAC VEIN BLOOD FLOW	
		FISTULA OCCLUDED	FISTULA PATENT	ABSOLUTE	PERCENTAGE
27	203	56	58	2	3.5
28	285	90	90	0	0
29	520	70	85	15	19.2
30	556	114	119	5	4.3
31	255	95	95	0	0
32	630	130	150	20	14.3
33	276	54	54	0	0

BLOOD FLOW IN mls/min. Mean Values.

Fig. 5.6.

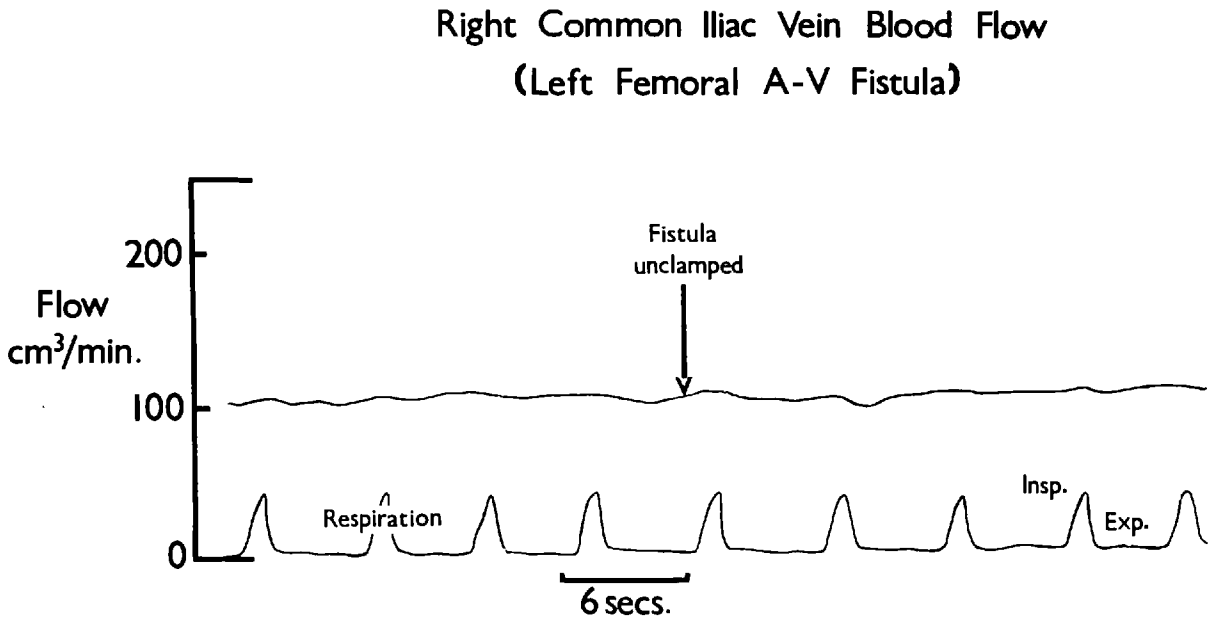

Fig. 5.7.

BLOOD FLOW IN THE COMMON ILIAC VEINS COMPARED, PRIOR TO VEIN GRAFTING.

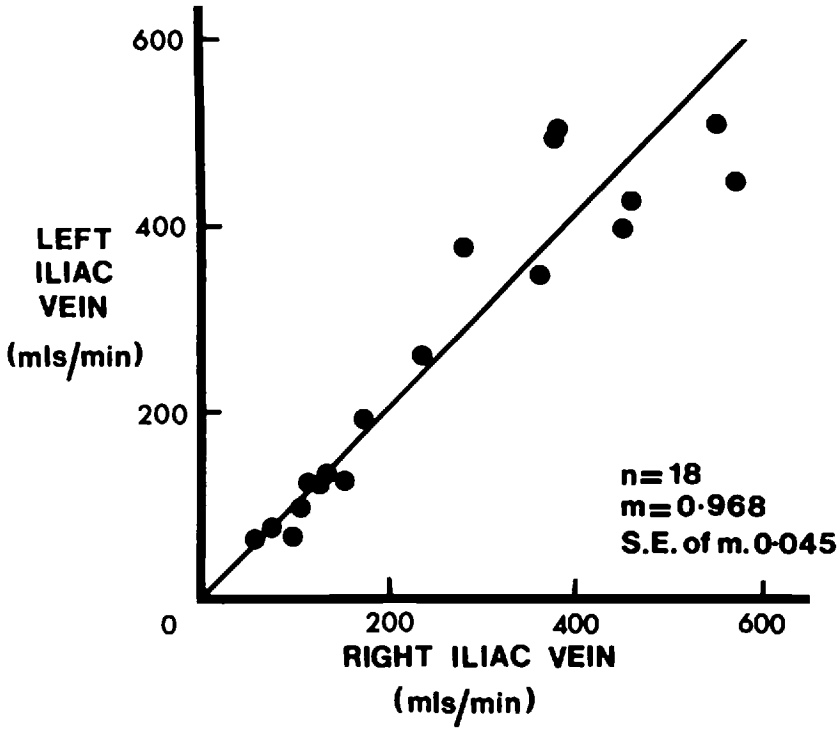

Fig. 5.8. KEY. n: NUMBER OF READINGS. m: SLOPE. S.E.: STANDARD ERROR.

redistributed through the venous channels other than in the ipsilateral iliac veins, the possibility exists in the experimental situation studied that blood was diverted through the iliac veins on the side opposite the fistula (that is the control side). To test this hypothesis the iliac vein flow on the control side was studied in 7 animals whilst the fistula was clamped and then released. (Fig. 5.5). In 5 of the animals, there was either no difference in flow or it was within the error of the blood flow measurement (i.e. $\pm$ 5%) (Fig. 5.6). In 2 animals (both of which had high fistula flows) there was an appreciable increase in the iliac vein flow on the control side following release of the occluded A/V fistula. This suggests that at high fistula flow rates at least, the effects which are discussed in a previous paragraph and illustrated in Figure 5.4, do occur. However, it is not possible to identify from the results of the graft experiments, patent grafts on the control side where there was a high fistula flow (greater than 400 mls per minute) so there is no evidence that the results are biased.

It is pertinent to ask whether the observations made on control graft blood flow (on page 50) could not be due to anatomical variation and discrepancies between flow on the two sides. Blood flow readings taken before the grafting procedures comparing the two sides are illustrated graphically (Fig. 5.8) and show that over a wide range of blood flow, common iliac veins have comparable flows. (Appendix D and elsewhere).

(Fig. 5.8. overleaf).

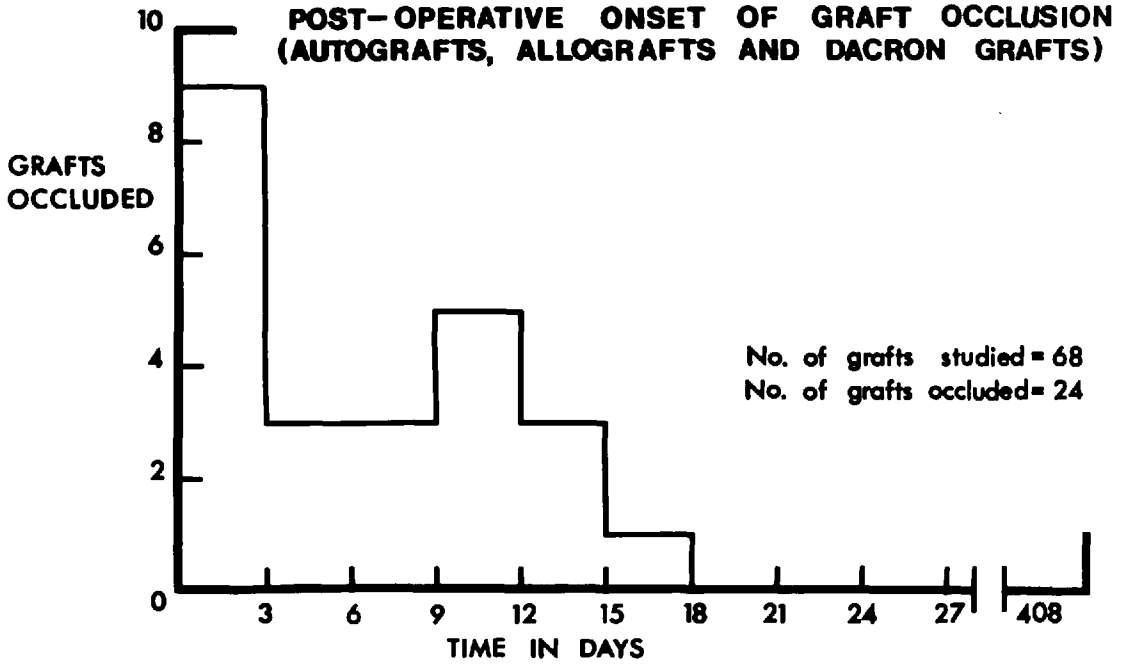
POST-OPERATIVE ONSET OF GRAFT OCCLUSION
(AUTOGRAFTS, ALLOGRAFTS AND DACRON GRAFTS)
GRAFTS OCCLUDED
10
8
6
4
2
0
No. of grafts studied = 68
No. of grafts occluded = 24
3
6
9
12
15
18
21
24
27
408
TIME IN DAYS

Fig. 6.1.

CRITICAL EARLY PERIOD

Moore and his co-workers first drew attention to the fact that late occlusion of venous grafts rarely occurs and that prolonged patency was likely if the graft remained open for more than a fortnight (Moore 1963). This has been called the critical early period by Haimovici and his colleagues who refers to one or two weeks after graft implantation in his review (Haimovici et al.1970).

Time of onset of graft occlusion was studied in the 17 animals in which it occurred. The series covers both tissue and Dacron grafts but two-thirds of the occluded grafts occurred in the Dacron group. The average onset of occlusion was 6.9 days and the time of graft occlusion for the series as a whole is expressed in the histogram (Fig. 6.1).

These results confirm the concept of a critical early period following graft replacement and are in agreement with the three week period generally suggested in the literature.

In the absence of any late graft occlusions in the series studied, it is interesting to speculate on the change within the graft that occurs during the first 3 weeks which subsequently confers long-term patency. This change must be associated with the lining of the graft as this is the only material in contact with the blood and it is presumably the establishment of a pseudointima over the anastomosis site (and Dacron) which inhibits graft thrombosis. This theory may explain why tissue grafts have a much greater success rate than synthetic grafts, as in the former the establishment of a pseudointima is presumably a much more rapid process and there is less time for the occlusive progress to occur. Certainly, pseudo-intima were seen covering the Dacron and anastomotic sites in all the patent

grafts studied histologically in the three series.

The phenomenon of the critical early period enables the use of adjuvant techniques to maintain graft patency to be planned for a definite period, after which they may be safely discontinued knowing that long-term graft patency will be unaffected.

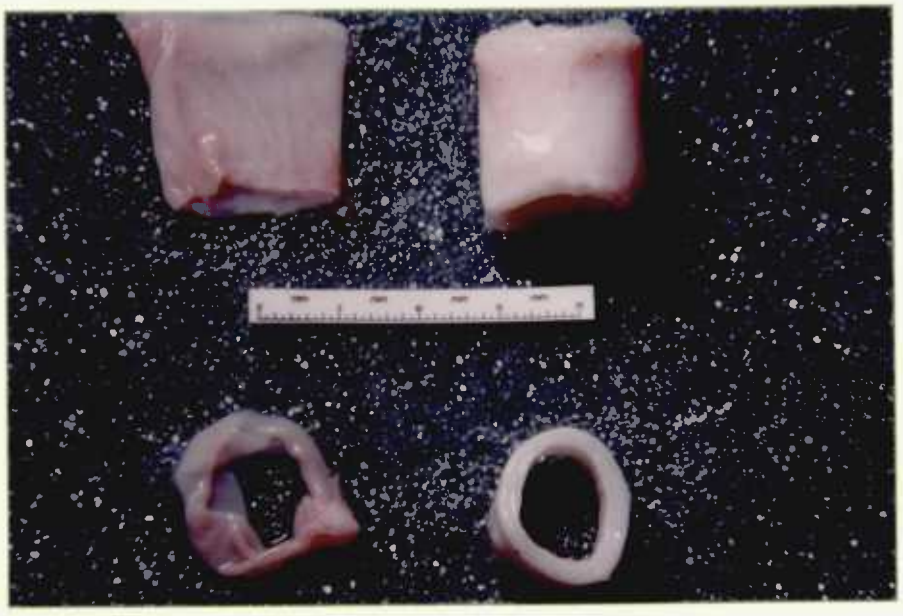

Fig. 7.1. I.V.C. IS ILLUSTRATED ON THE LEFT AORTA ON THE RIGHT.

GENERAL DISCUSSION

The author was initially attracted to this experimental work by the discrepancy between the fate of arterial and venous grafts. It may well be instructive to compare and contrast the relative differences in the fluid dynamics between the arterial and venous systems for a clue to the differences in the patency rates.

The flow rate through the aorta and I.V.C. in the dog are comparable at any given moment but the velocity of the flowing blood is about ten times slower in the I.V.C. At the same time the diameter of the I.V.C. is roughly twice that of the aorta.

The aortic blood pressure is over ten times higher than the pressure in the great veins, but the pressure differences (between the heart and the periphery) are more comparable. Together with this great difference in intraluminal blood pressure goes a marked difference in the rigidity or "stiffness" of the vessel walls to external compression. The aorta having its own natural "stiffness" to deformation enhanced by its intrinsic blood pressure. Neither of these factors operates within the great veins. Fig. 7.1.

Lastly, aortic blood flow is pulsatile whereas pressure in the venous system is phasic with respiration and only becomes pulsatile in the great vessels adjacent to the heart. It is difficult to see how this difference is of any significance with respect to the fate of venous grafts.

Discrepancies between the success of arterial and venous grafts may well be explained in relation to (i) the difference in blood velocities in the two systems, (ii) the intraluminal pressure differences between the two types of vessel and their consequent physical structure.

It is relevant at this point to speculate exactly how an arteriovenous fistula might enhance the patency of venous grafts and it is the author's proposal that it could do so in the two ways described in the previous paragraph, namely by increasing the velocity of blood through the graft and secondly by increasing the intra-mural tension of that graft and thus making it more rigid. Evidence for both of these proposals may be obtained from the literature on experimental venous grafts; Dale (1963) and Schenin and Jude (1964) both reported better results with S.V.C. grafts when the azygous vein was ligated, i.e. the S.V.C. flow was increased. Haimovici and his colleagues (1963) had more failures with their autogenous bypass grafts when the grafts were used as a collateral circulation, i.e. carried half the normal blood flow. Venous velocity increases as blood nears the heart and this may well explain the superiority of grafts placed in the S.V.C. and intra-thoracic I.V.C. compared with those placed more peripherally. This idea however, over-looks the success of femoral grafts (in a site of low venous velocity) although there may well be an alternative explanation. (See page 14).

In reports from the literature grafts made with rigid materials give consistently better results than those made with flimsy ones, and the same applies to grafts with external support. The degree of "stiffness" which is imparted to a graft by the presence of an arteriovenous fistula will depend on the size of that fistula, but in the author's experience the presence of an arteriovenous fistula always increased the stiffness of the graft (including tissue grafts) presumably by an increase in the intra-mural tension consequent on a rise in intra-luminal pressure.

If the foregoing speculations are correct, it would seem that an

arteriovenous fistula should be used in situations where there is a low venous velocity at the recipient site, or when the surgeon is unhappy about the quality of his technique and fears graft failure for this reason.

A P P E N D I C E S

APPENDIX A — CALIBRATION OF THE ELECTROMAGNETIC FLOWMETER PROBE - ASSESSMENT OF LINEARITY

PROBE 3334

MECHANICALLY COLLECTED FLOW	FLOW AS REGISTERED BY E.M. PROBE
50	49
115	117
202	202
332	323
437	425
550	540
625	620
715	715
820	820
925	940
1050	1060
1400	1385
1670	1640
2070	2000

Blood flow measured in ml./min.

For further explanation see page 35 et seq.

APPENDIX B — BLOOD FLOW AND VENOUS PRESSURE MEASUREMENTS IN THE I.V.C.

DOG 20		DOG 21	
BLOOD FLOW	VENOUS PRESSURE	BLOOD FLOW	VENOUS PRESSURE
35	11	50	5.5
170	14	240	8
205	14	360	6.75
275	14	480	8.5
280	12	600	7.75
350	13	775	8.5
375	14	960	9.5
395	13	1200	9.75
435	13.5	1235	8.75
450	15		
500	14		
505	15		
565	14.5		
575	15		
650	16		
700	16		
750	16		
775	16		
800	15		
880	16		
940	16		
940	17		
1000	17.5		
1065	18		
1150	20		
1200	20		
1255	21		

Blood flow ml./min. Mean values.

Venous pressure cm. of Hg.

APPENDIX C. VEIN AUTORADIOGRAPHY

Vein sections stored in tissue culture fluid. Average granule count per cell (fifty cells counted) on autoradiograph slide sections.

Storage time in tissue culture fluid	Slide Section "A"	Slide Section "B"	Slide Section "C"	Average value
NIL	74.4	77	68.6	$\frac{220}{3} = 73.3$
1 WEEK	36.8	31.8	35.8	$\frac{104.2}{3} = 34.7$
2 WEEKS	4.4	4.5	5.2	$\frac{14.1}{3} = 4.7$
3 WEEKS	0.9	0.6	1.1	$\frac{2.6}{3} = 0.9$

APPENDIX D. BLOOD FLOW RECORDINGS

DOG	FEMORAL A/V FISTULA		COMMON ILIAC VEIN			
	1st OPERATION	2nd OPERATION	AFTER MOBILISATION		AFTER ANASTOMOSIS	
			CONTROL SIDE	FISTULA	CONTROL SIDE	FISTULA
1	310^{R}	-	-	490^{R}	-	890^{R}
2	224^{L}	-	360	350^{L}	260	360^{L}
3	250^{R}	-	195	170^{R}	210	310^{R}
3	310^{L}	100^{L}	450	400^{L}	150	400^{L}
4	190^{R}	140^{R}	380	280^{R}	120	340^{R}
6	250^{L}	140^{L}	460	430^{L}	80	390^{L}
7	280^{R}	330^{R}	510	550^{R}	200	540^{R}
8	300^{L}	-	570	450^{L}	200	700^{L}
9	140^{R}	100^{R}	500	380^{R}	280	400^{R}
11	110^{R}	-	500	380^{R}	-	-

(i) Blood flow measured in ml./min. Mean values.

(ii) Letters adjacent to the figures in the table refer to the side on the experimental animal.

For further explanation see page 51 .

APPENDIX E. VENOUS PRESSURE RECORDINGS

DOG	BEFORE FISTULA CONSTRUCTION	AFTER FISTULA CONSTRUCTION
1	+4	+6
2	-4	-3.5
3	-2	-1
4	-6	-5.5
5	-4	-2
6	-5	-3
7	-2	-2
8	-5	-2
9	-2.5	-2
11	-3	-2.5

(i) Venous pressure measured in cm. of water.

For further explanation see page 39 and page 52.

APPENDIX F

BLOOD FLOW RECORDINGS

DOG	FEMORAL A/V FISTULA		COMMON ILIAC VEIN AFTER ANASTOMOSIS		
	1st OPERATION	2nd OPERATION	CONTROL SIDE	FISTULA SIDE	FISTULA SIDE FISTULA OCCLUDED
10	460^{R}	400^{R}	60	280^{R}	-
12	210^{R}	0^{R}	130	315^{R}	120^{R}
16	130^{R}	-	148	140^{R}	35^{R}
17	110^{L}	-	108	150^{L}	51^{L}
18	200^{R}	513^{R}	110	260^{R}	90^{R}
19	880^{L}	460^{L}	50	800^{L}	97^{L}
20	505^{L}	560^{L}	90	570^{L}	55^{L}
21	385^{R}	385^{R}	75	410^{R}	60^{R}
22	110^{L}	0^{L}	105	175^{L}	65^{L}
23	355^{L}	860^{L}	110	505^{L}	80^{1}
24	302^{L}	870^{L}	105	470^{L}	85^{L}
25	245^{R}	468^{R}	40	180^{R}	40^{R}
26	275^{R}	-	130	315^{R}	95^{R}

(i) Blood flow measured in ml./min. Mean values.

(ii) Letters adjacent to figures in the table refer to the side in the experimental animal.

For further explanation see page 53.

APPENDIX G. DIAMETER OF DACRON GRAFTS AS MEASURED ON THE FIRST POST-OPERATIVE VENOGRAM

DOG	GRAFT DIAMETER	
	CONTROL SIDE	FISTULA SIDE
10	0	6
12	0	8
16	4	8
17	0	0
18	0	6
19	0	8.5
20	4	6.5
21	4	8
22	7	7.5
23	4.5	9
24	4.5	10
25	0	10
26	0	6.5

Graft diameter measured in millimeters.

See page 58.

APPENDIX H. BLOOD FLOW RECORDINGS

DOG	FEMORAL A/V FISTULA		COMMON ILIAC VEIN AFTER ANASTOMOSIS		
	1st OPERATION	2nd OPERATION	CONTROL SIDE	FISTULA SIDE	FISTULA SIDE FISTULA OCCLUDED
27	203^{L}	-	58	150^{L}	80^{L}
28	285^{L}	570^{L}	90	395^{L}	53^{L}
29	520^{R}	680^{R}	85	245^{R}	74^{R}
30	556^{R}	235^{R}	114	445^{R}	120^{R}
31	255^{L}	-	95	338^{L}	123^{L}
32	-	630^{L}	150	610^{L}	135^{L}
33	276^{R}	525^{R}	54	100^{R}	35^{R}
34	225^{R}	0^{R}	163	380^{R}	128^{R}
35	713^{L}	290^{L}	145	570^{L}	190^{L}
39	95^{L}	123^{L}	62	230^{L}	75^{L}

(i) Blood flow measured in ml./min. Mean values.

(ii) Letters adjacent to the figures in the table, refer to the side in the experimental animal.

For futher explanation see page 64.

APPENDIX J. DIAMETER OF AUTOGRAFTS AND ALLOGRAFTS AS MEASURED ON THE FIRST POST-OPERATIVE VENOGRAM

DOG	GRAFT DIAMETER	
	CONTROL SIDE	FISTULA SIDE
28	7	8^{A}
29	7	7.5^{A}
30	9^{A}	7.5
32	7	11.5^{A}
33	9	7.5^{A}
34	6^{A}	7.5
35	8.5^{A}	8.5
39	6^{A}	8

(i) Graft diameter measured in millimetres.

(ii) Letters adjacent to the figures in the table refer to the graft being a preserved autograft.

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ILIO-FEMORAL THROMBECTOMY IN THE DOG. A STUDY OF THE EFFECTS OF STREPTOKINASE AND ARTERIOVENOUS FISTULA

INTRODUCTION:

Deep vein thrombosis in the lower limbs and its associated sequelae, continue to be an important clinical problem. The principal causes for concern in ilio-femoral thrombosis are the high incidence of pulmonary embolism, and the development of the post-phlebitic syndrome caused by the destruction of the venous valves (Edwards and Edwards 1937).

Enthusiasm for venous thrombectomy has never been marked in this country but it has been advocated for ilio-femoral or 'proximal segment' thrombosis by Mavor for at least two decades (Mavor and Galloway 1967).

Thrombectomy is a satisfactory method of clearing the ilio-femoral segment if the thrombotic process is less than one week old (Edwards et al 1970; Mavor 1971), but rethrombosis is often a problem if clearance is less than adequate. In Mavor's series re-thrombosis occurred in 32% when only partial clearance had been possible (Mavor and Galloway 1969).

REVIEW OF THE EXPERIMENTAL LITERATURE:

Experimental work on venous thrombectomy in the literature is sparse. Various authors, using the dog as a model, have attempted to find a successful way of treating thrombosis in major veins with the avowed intention of preventing pulmonary embolism and valvular destruction. In one early paper Mahorner and his colleagues (Mahorner 1957) were able to remove an inferior ven caval thrombosis in 65% of their experimental animals, compared with spontaneous lysis of the thrombus in 38% of their controls. The animals were assessed by venography for 72 days. This pioneer work contrasts with the

findings of Shiel and Sabiston (1963); all seven animals in their series had rethrombosis in their inferior vena cavae within three days, and Bradham (1964) had similar results in ten animals after femoral vein thrombectomy. Harjola and his coworkers state that thrombectomy is difficult and often incomplete if it is performed after several days, and in these circumstances it is usually followed by rethrombosis (Harjola et al 1969). They used an adjacent peripheral arteriovenous fistula as a method of preventing rethrombosis after thrombectomy. There were ten animals in their series and each acted as its own control; eight veins remained patent after thrombectomy in association with an arteriovenous fistula, compared with one in the control series. This demonstrates the efficacy of a fistula in the experimental animal but the authors did not go on to report any clinical cases.

There are two experimental series which have examined the effect of Heparin following femoral thrombectomy. In Bradham's series there were seven veins fully patent and a further nine stenosed in twenty limbs treated with Heparin for 24 hours (Bradham 1964). Thrombectomy was performed within 24 hours in this series which may explain his superior results compared with those of McLachlin and his coworkers (McLachlin 1970). In the latter paper thrombectomy was performed two days after an induced thrombosis and they were unable to demonstrate an effect from the administration of Heparin post-operatively.

More recently streptokinase has been used clinically in the treatment of deep vein thrombosis with complete lysis in 50-60% of cases, and partial lysis in about 25% (Hiemeyer 1967; Kakkar et al 1969; Mavor et al 1969; Olow et al 1976; and Robertson et al 1970). Mavor and his colleagues were specifically concerned with the

treatment of rethrombosis after ilio-femoral thrombectomy; the only clinical trial that has concentrated on this anatomical segment.

Karmody and his coworkers investigated the optimal method of using streptokinase in the experimental animal (Karmody et al 1971). In femoral vein thrombosis they found the highest rate of clot lysis with topical therapy using a high dosage regimen.

It appears from the literature that experimental thrombectomy has an unacceptably high rate of rethrombosis, particularly if the procedure is incomplete or used by itself. Heparin may be of additional benefit but other forms of therapy show more promise when used in conjunction with thrombectomy. The author was impressed with the reported effects of an arteriovenous fistula, and topical streptokinase in relation to thrombectomy (Harjola et al 1969; Karmody et al 1971). The experiments described below investigate the effect of these two forms of treatment in relation to ilio-femoral thrombectomy in the dog.

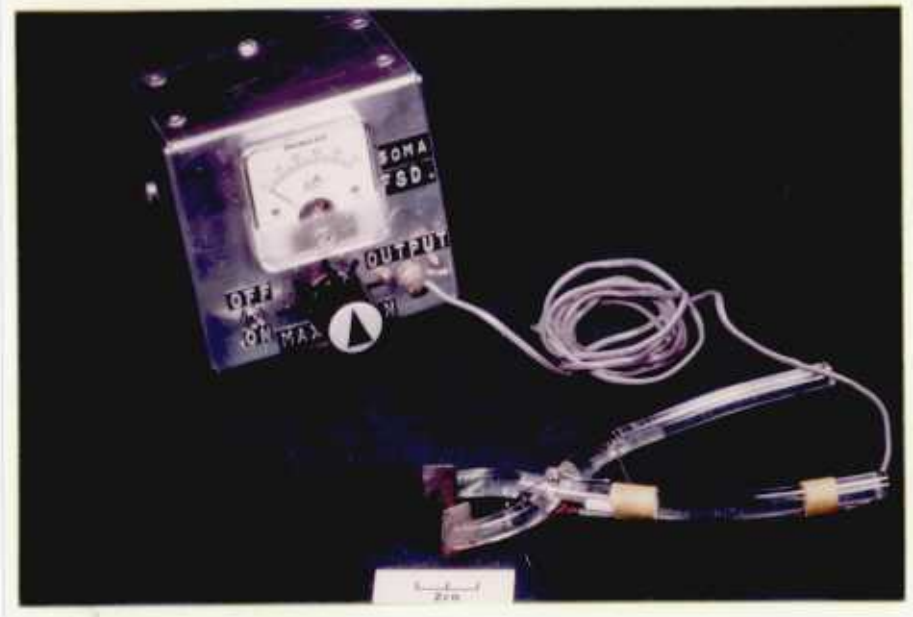


Fig. 1. APPARATUS FOR PRODUCING THROMBOSIS

(SEE TEXT)

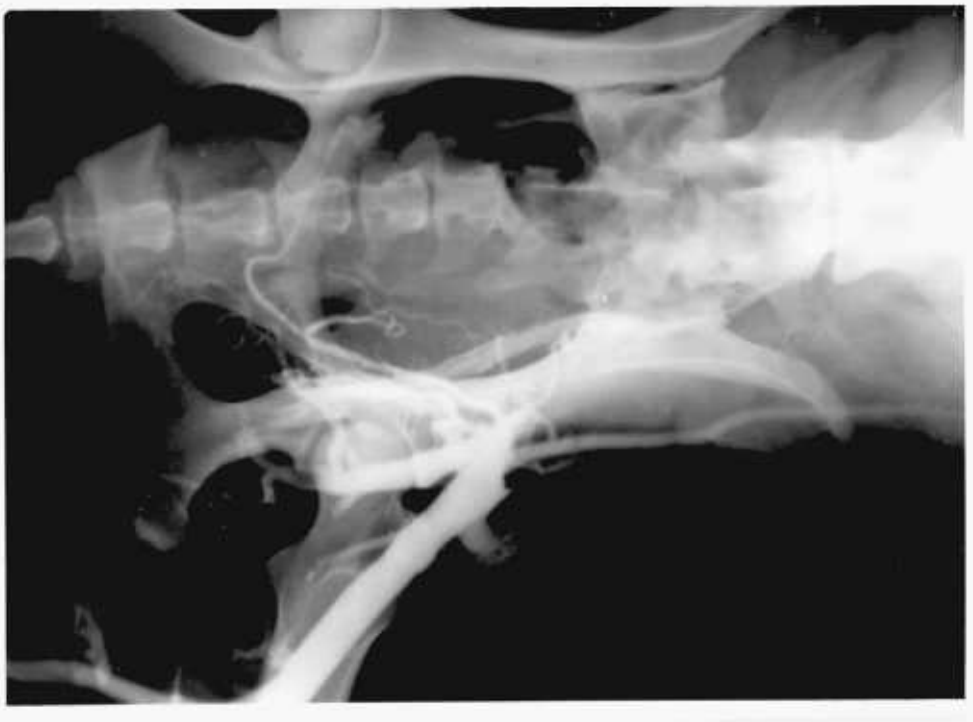


Fig. 2. ILIO-FEMORAL VENOGRAPHY. THERE IS OCCLUSION OF THE EXTERNAL ILIAC VEIN, AND RETROGRADE FILLING OF THE PROFUNDA FEMORIS VEIN.

MATERIALS AND METHODS:

Forty adult greyhounds were used for the study, six in the initial series, and thirty-four in the second involving thrombectomy. Their average weight was 24 kgs.

All forty dogs were treated in the same way initially. Anaesthesia was induced with thiopentone sodium and maintained with oxygen, nitrous oxide and halothane. The abdomen was opened through a lower mid-line incision, and the external iliac vein exposed and mobilised on one side, it was then occluded proximally flush with the inguinal ligament. An electric current was applied across the vein by means of two plates (1cm x 2cm) kept 2 mm apart; a forty milli-amp current being applied for ten minutes (Fig. 1.) This technique was derived from a similar method used by Bradham (1964). The apparatus was then removed and the abdomen closed. Sterile technique was used throughout.

The animals in the second series were re-anaesthetised two days later, and a venogram performed to assess the extent of thrombosis in the iliac vein (Fig. 2). Using a sterile technique the affected femoral vein was exposed and its tributaries temporarily occluded. A balloon catheter was passed into the common iliac vein through a femoral venotomy 1 cm long and a thrombectomy performed. This manoeuvre was carried out twice in each animal to ensure complete removal of the thrombus. The venotomy was closed with 6 0 P.T.F.E. coated polyester suture, and a further venogram performed to assess the completeness of thrombectomy.

The dogs in the second series were treated subsequently in one of three ways: (i) Control group. These animals received no further treatment, and were observed for a period of fourteen days.
(ii) Fistula group. These animals had an arteriovenous

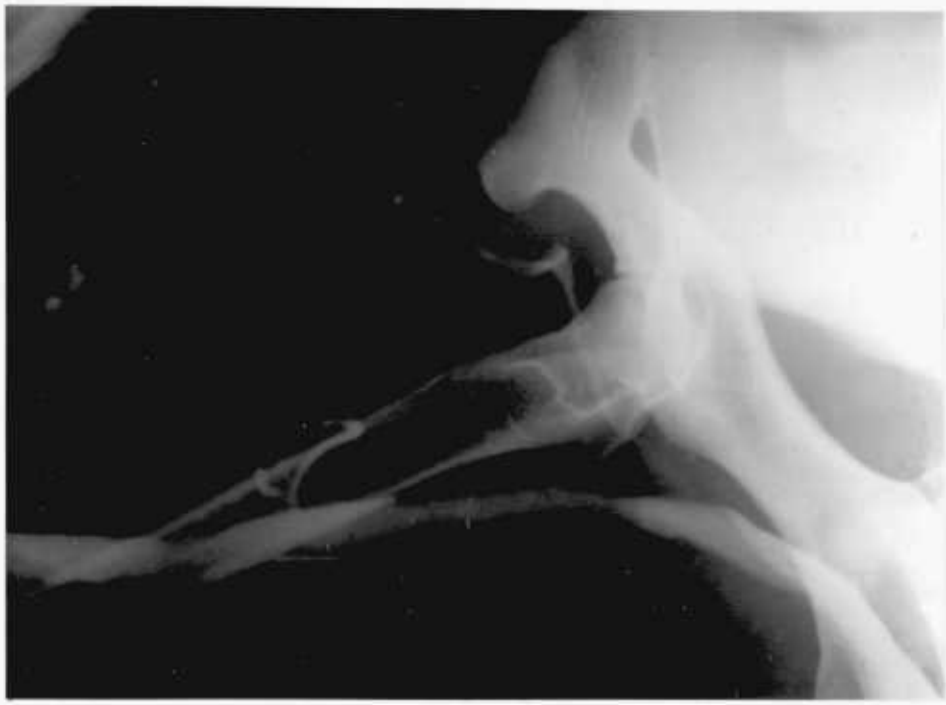


Fig. 3. X-RAY. THE INJECTION NEEDLE LIES IN THE FEMORAL ARTERY AND DISTAL TO THIS THE ARTERIOVENOUS FISTULA MAY BE SEEN. MOST OF THE CONTRAST MATERIAL LIES IN THE FEMORAL AND ILIAC VEINS.

fistula constructed between the femoral vessels, about 10 cms from the inguinal ligament (Fig. 3). The fistulas remained patent throughout the experiment. (iii) Streptokinase group. These animals had a streptokinase/human plasma infusion for twelve hours after thrombectomy. An intravenous cannula was introduced into a tributary of the saphenous vein, some 30 cms distant from the inguinal ligament, and the distal end of the cannula led via a subcutaneous tunnel to an infusion apparatus strapped on the dogs back. Towards the end of the operation 25,000 I.U. of streptokinase was infused to neutralise streptococcal antibodies, and when the dogs had been returned to their kennels, a solution containing 80,000 I.U. of streptokinase and 8 ml of fresh human plasma was infused over the next twelve hours. The cannulae were withdrawn at the end of the infusion.

VENOGRAPHY:

Venograms were performed (i) two days after the initial operation, (ii) after thrombectomy (where appropriate), (iii) four days after the initial operation and then (iv) every seventy-two hours for the next fourteen days, or until venous occlusion occurred.

BLOOD FLOW RECORDING:

Blood flow measurements were made on the exposed vessels using a Nycotron 372 Blood Flow Recorder. Two readings were made at each site and the average value was used.

Records were made at the following positions; (i) on both common iliac veins before the electro-coagulation procedure (nine animals only), (ii) on the exposed femoral vein following the thrombectomy procedure, and (iii) on the exposed femoral vein with the fistula flow established (where appropriate).

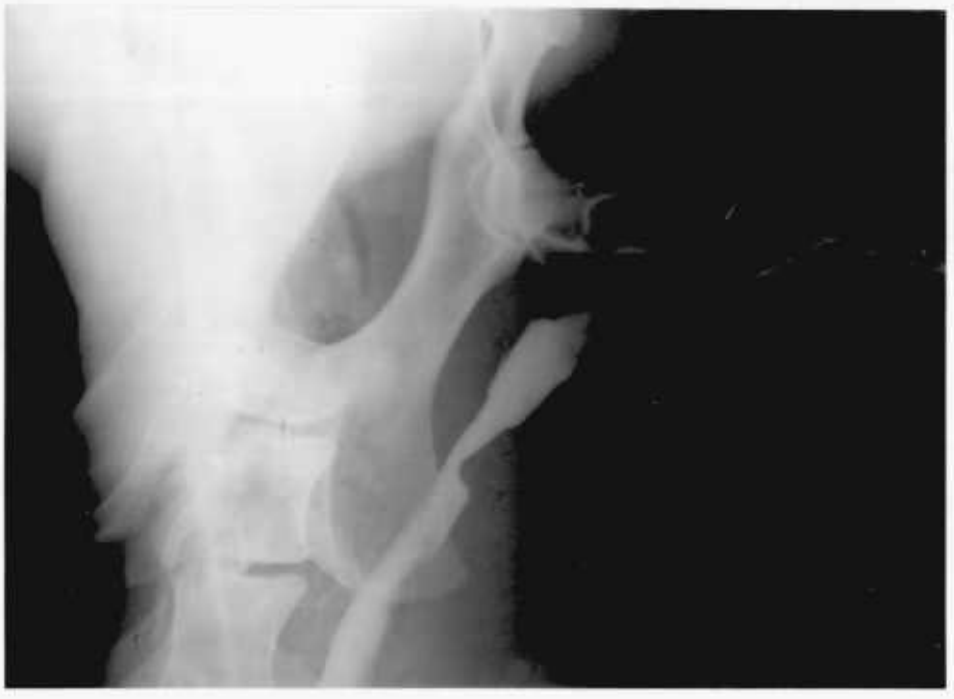


Fig. 4. ILIO-FEMORAL VENOGRAM.
THERE IS A STENOSIS IN THE EXTERNAL ILIAC VEIN.

TREATMENT	TOTAL	PATENT	THROMBOSED
NO THROMBECTOMY	6	2	3 OCCLUDED 1 STENOSED
THROMBECTOMY ONLY	11	2	4 OCCLUDED 5 STENOSED

Fig.5. Final State of Thrombectomy Segment

TREATMENT	TOTAL	PATENT	THROMBOSED
THROMBECTOMY ONLY	11	2	4 OCCLUDED 5 STENOSED
THROMBECTOMY AND AV/ FISTULA	10	10	0
THROMBECTOMY AND STREPTOKINASE	9	4	4 OCCLUDED 1 STENOSED

Fig. 6. Final State of Thrombectomy Segment

RESULTS:

Two animals died from blood loss when the iliac vein was ruptured during the thrombectomy procedure. Dog 61 died before the procedure was completed, and this animal has been excluded from the results. Dog 50 died about thirty-six hours after thrombectomy and available data from this animal has been included.

For technical reasons, three animals (dogs 68, 69 and 74) were excluded from the streptokinase series. The first had an infusion without human plasma, in the second the infusion apparatus became disconnected, and in the third the thrombus could not be removed with the balloon catheter and the vein remained occluded.

The final venogram for each animal was assessed and the thrombectomy segment classified as patent, occluded or stenosed (the latter was arbitrarily defined as a reduction in the vein diameter to less than one third of its original size Fig. 4). Fig. 5 compares the first series of dogs with those animals from the second series which had a subsequent thrombectomy only (Control group). There is no significant difference between these two groups at the end of the study ($P>0.2$). Fig. 6 compares the three treatment groups in the second series of dogs fourteen days after thrombectomy. Occlusion or stenosis due to rethrombosis occurred in the control and streptokinase treated groups only and they are comparable. Fourteen days after thrombectomy, there is a significant difference between the control and arteriovenous groups ($P<0.002$), but no significant difference between the control and the streptokinase groups ($P>0.2$).

The serial venograms were analysed further in both series of dogs and the minimum vein diameter at the thrombectomy site measured at various times during the experiment. This was compared with the

The Effect of Thrombectomy on Vein Diameter Following the Creation of a Thrombus in the External Iliac Vein

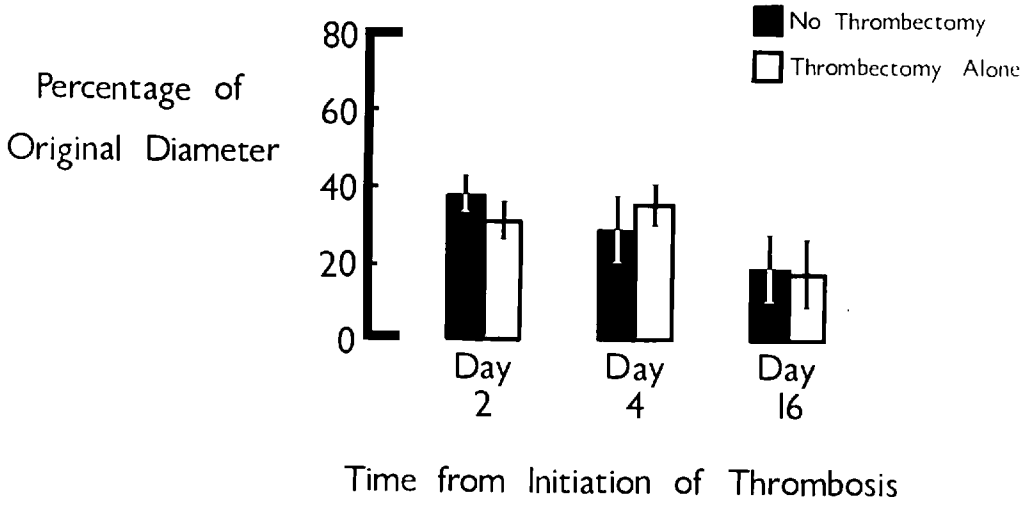


Fig. 7

Comparison of the Effect of Streptokinase or an Arterio-Venous Fistula on the Diameter of the External Iliac Vein after Thrombectomy

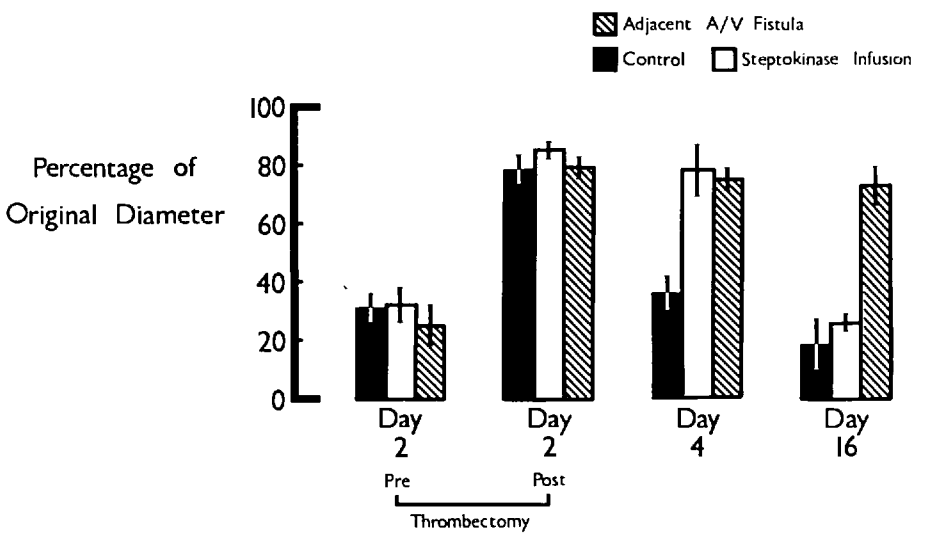


Fig. 8

original diameter of the external iliac vein (as measured on a venogram) and the results expressed as a fraction of the original diameter. i.e.

$$\frac{\text{Diameter after treatment}}{\text{Original diameter}}$$

The results expressed as a fraction of the original vein diameter are presented individually in tables I-IV for the four groups of dogs. Thrombectomy was performed on day 2 and follow-up venograms are recorded on day 4 and day 16. In table V the mean values of the vein diameters are presented in all the groups. They are expressed as percentages and should be studied in conjunction with the subsequent histograms.

The first histogram (Fig. 7) compares the animals in the first series with those in the second series who had thrombectomy alone. There is no significant difference between them which suggests that thrombectomy has no effect after 48 hours in this experimental model. Reduction in the average size of the vein lumen is progressive throughout the period studied.

The second histogram (Fig. 8) compares all the dogs in the second series which underwent thrombectomy. These animals are comparable before and after thrombectomy and the results show that a balloon catheter is able to clear a thrombosed vein satisfactorily. In the control group this effect lasts for less than 48 hours. In the two other groups the increased vein diameter is sustained for 48 hours with the additional treatments and in the case of the fistula group throughout the period of study. In the streptokinase group the effect of this drug is not apparent more than 48 hours after thrombectomy and the values return to the control level. It should be borne in mind though that the streptokinase infusion was

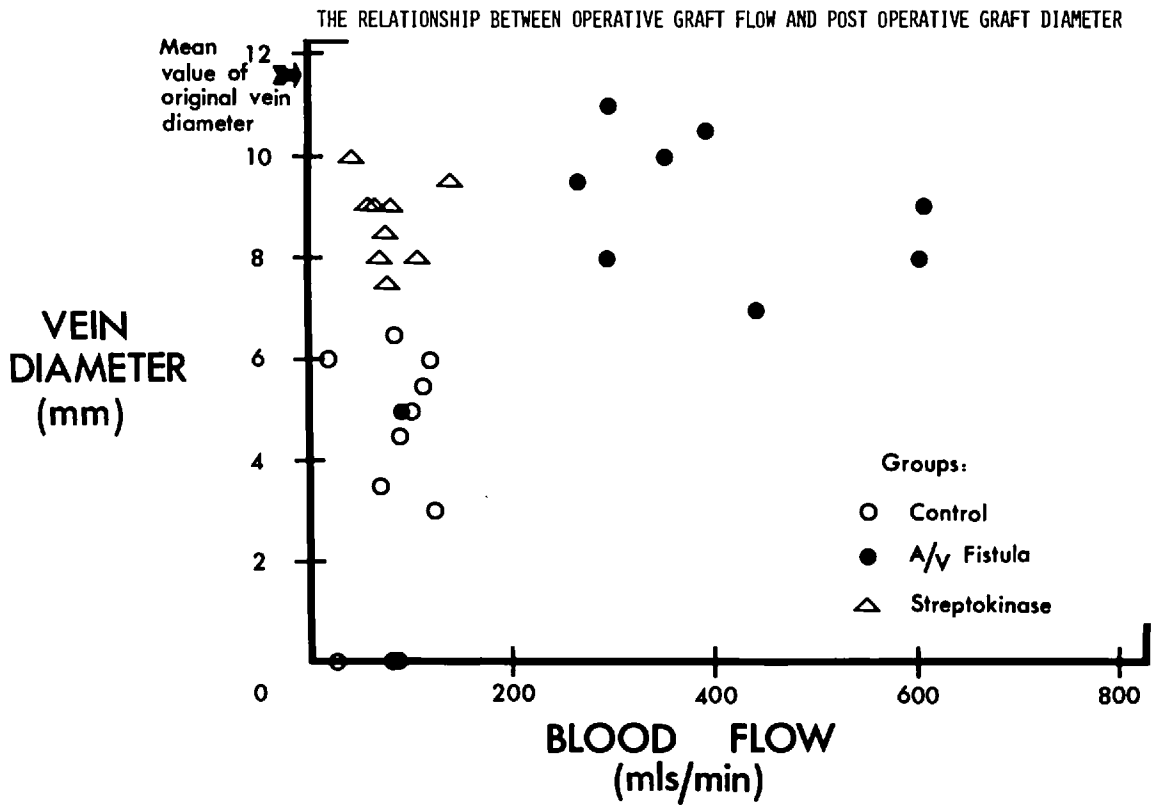

THE RELATIONSHIP BETWEEN OPERATIVE GRAFT FLOW AND POST OPERATIVE GRAFT DIAMETER
Mean value of original vein diameter
12
10
8
6
4
2
0
VEIN DIAMETER (mm)
200
400
600
800
BLOOD FLOW (mls/min)
Groups:
Control
A/V Fistula
Streptokinase

Fig. 9

maintained only for 12 hours, whereas the fistulas were patent for the duration of the study.

The minimum diameter of the thrombectomy segment on the first post-operative venogram was related to the femoral vein blood flow as measured at operation, in three groups of animals undergoing thrombectomy (Fig. 9), see also Appendix B. The co-ordinates fall into three distinct populations according to the different treatment groups. There is no difference between the blood flow in the control and streptokinase groups but the mean vein diameter is nearly doubled in the early post-operative period by the use of the latter drug.

There is a significant difference between the mean blood flow of the control and arteriovenous fistula groups (Control Av. 81.9 mls/min. S.D. $\pm$ 36. Arteriovenous fistula: Av. 370.7 mls/min. S.D. $\pm$ 163), and it is reasonable to attribute the increased blood flow as the cause of the increased vein diameter in the fistula group.

DISCUSSION:

Treatment of an iliac vein occlusion by venous thrombectomy in this experimental model has no effect on long term patency, and indeed 48 hours after thrombectomy the average size of the vein lumen is similar to those veins having no treatment at all. These findings are similar to those of Shiel and Sabiston (1963) and Bradham (1964), and confirm the clinical impression that venous thrombectomy alone is inadequate treatment.

However, this work does show that individually streptokinase or an arteriovenous fistula can maintain vein lumen size after thrombectomy, when the latter procedure by itself is inadequate. These findings support other experimental work in this field (Harjola et al 1969; Karmody et al 1971) and give the clinician confidence to extend this work to the clinical situation.

The practical difficulties of administering streptokinase topically for long periods in the experimental animal unfortunately limits the time that its effect may be studied. It would seem reasonable to sepculate that a topical infusion of streptokinase maintained for several days would have had a more sustained beneficial effect on the thrombectomy segment, and this is a feasible clinical procedure.

TABLE 1 Fraction of original vein diameter. Iliac vein thrombosis only (Initial series)

DOG	DAY 2	DAY 4	DAY 16
54	0.26	0	0
55	0.36	0.45	0.45
62	0.25	0.17	0.17
63	0.64	0.64	0.48
64	0.29	0.25	0.21
65	0.46	0.25	0
Mean value	0.38	0.29	0.19
Standard Error	0.05	0.09	0.09

TABLE 2 Fraction of original vein diameter. Thrombectomy only (control group)

DOG	DAY 2		DAY 4	DAY 16
	Pre-thrombectomy	Post-thrombectomy		
40	0.43	0.86	1.00	0.62
41	0	0.75	0	0
42	0.36	0.73	0.32	0.23
43	0.50	0.83	0	0
44	0.50	1.00	0.50	0.42
45	0.50	0.92	0.23	0
46	0.08	0.50	0.50	0.25
47	0.29	0.62	0	0
51	0.28	0.88	0.40	0.24
66	0.22	0.96	0.48	0.26
67	0.29	0.58	0.54	0
Mean value	0.31	0.78	0.36	0.18
Standard Error	0.05	0.05	0.09	0.06

TABLE 3 Fraction of original vein diameter. Thrombectomy and an arteriovenous fistula (Arteriovenous fistula group)

DOG	DAY 2		DAY 4	DAY 16
	Pre-thrombectomy	Post-thrombectomy		
48	0.37	0.67	0.42	0.71
49	0.58	0.83	0.67	0.75
50	0.28	0.92	-*	-*
52	0.17	0.92	0.58	0.58
53	0.17	0.58	0.92	1.00
56	0	0.78	0.91	0.78
57	0.45	0.91	0.91	0.73
58	0	0.96	0.82	0.55
59	0.45	0.73	0.82	0.77
60	0	0.61	0.70	0.70
Mean Value	0.25	0.79	0.75	0.73
Standard Error	0.07	0.04	0.06	0.04

*Dog died on Day 3

TABLE 4 Fraction of original vein diameter. Thrombectomy and a streptokinase infusion. (Streptokinase group.)

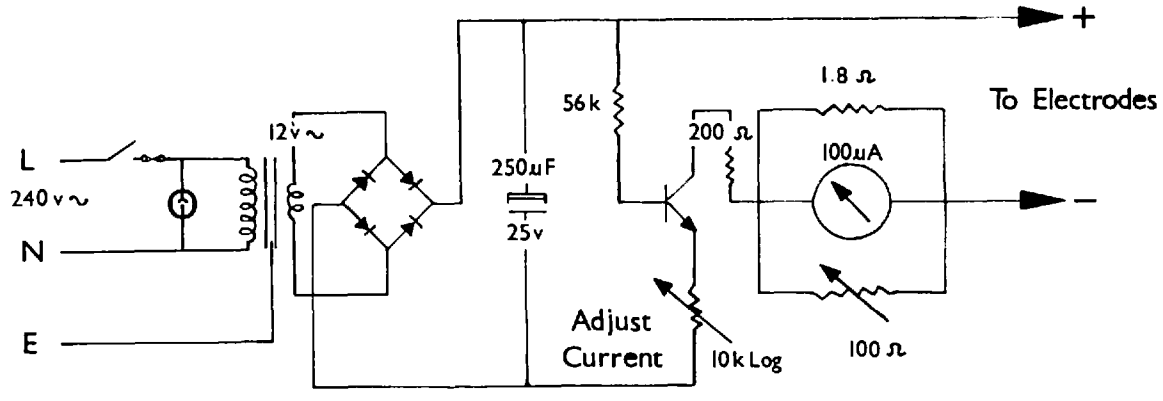
DOG	DAY 2		DAY 4	DAY 16
	Pre-thrombectomy	Post-thrombectomy		
70	0.25	0.83	0.63	0.63
71	0.50	0.63	0.75	0.50
72	0.52	0.87	0.78	0.52
73	0	0.83	0.70	0
75	0.26	0.78	0.74	0.17
76	0.38	1.00	0.95	0
77	0.59	0.86	0.73	0
78	0.23	0.95	0.86	0.55
79	0.19	0.95	0.86	0
Mean value	0.32	0.85	0.78	0.26
Standard Error	0.06	0.03	0.03	0.09

TABLE 5 Percentage of original vein diameter (normal vein 100%) Both series of dogs.

GROUP	DAY 2		DAY 4	DAY 16
	Pre-thrombectomy	Post-thrombectomy		
Creation of thrombosis only	38	-	29	19
Thrombectomy: Control	31	78	36	18
Thrombectomy: Fistula	25	79	75	73
Thrombectomy: Streptokinase	32	85	78	26

APPENDIX A

Circuit Diagram for Electro-Coagulation Device



APPENDIX B

DOG	GROUP	MEAN BLOOD FLOW			
		COMMON ILIAC VEIN		FEMORAL VEIN FOLLOWING THROMBECTOMY	FEMORAL VEIN WITH FISTULA
		LEFT	RIGHT		
40				82	
41				25	
42				70	
43				89	
44				120	
45	CONTROL			125	
46				20	
47				80	
51				93	
66		130	150	112	
67		70	95	85	
68		125	125	82	
69		265	235	89	
70		65	57	78	
71		133	133	77	
72		125	120	63	
73	STREPTOKINASE			107	
74				27	
75		98	105	75	
76		78	76	42	
77				70	
78				138	
79				63	
48				85	93
49				93	600
50				52	210
52				53	440
53	FISTULA			59	295
56				30	390
57				77	350
58				35	265
59				61	605
60				26	298

APPENDIX B

DOG	GROUP	MEAN BLOOD FLOW			
		COMMON ILIAC VEIN		FEMORAL VEIN FOLLOWING THROMBECTOMY	FEMORAL VEIN WITH FISTULA
		LEFT	RIGHT		
40				82	
41				25	
42				70	
43				89	
44				120	
45	CONTROL			125	
46				20	
47				80	
51				93	
66		130	150	112	
67		70	95	85	
68		125	125	82	
69		265	235	89	
70		65	57	78	
71		133	133	77	
72		125	120	63	
73	STREPTOKINASE			107	
74				27	
75		98	105	75	
76		78	76	42	
77				70	
78				138	
79				63	
48				85	93
49				93	600
50				52	210
52				53	440
53	FISTULA			59	295
56				30	390
57				77	350
58				35	265
59				61	605
60				26	298

APPENDIX C

DOG	GROUP	FEMORAL VEIN BLOOD FLOW	ILIAC VEIN POST-OPERATIVE DIAMETER
40		82	0
41		25	0
42		70	3.5
43		89	4.5
44	CONTROL	120	6
45		125	3
46		20	6
47		80	0
51		93	5
66		112	5.5
67		85	6.5
70		78	7.5
71		77	9
72		63	9
73		107	8
75	STREPTOKINASE	75	8.5
76		42	10
77		70	8
78		138	9.5
79		63	9
48		93	5
49		600	8
52		440	7
53	FISTULA	295	11
56		390	10.5
57		350	10
58		265	9.5
59		605	9
60		298	8

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