PERIPHERAL RESISTANCE MEASUREMENT IN THE ASSESSMENT OF
RUNOFF IN FEMORODISTAL BYPASS GRAFTING

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Peripheral Resistance Measurement in the Assessment of Runoff in Femorodistal Bypass Grafting

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Vascular reconstruction beyond the inguinal ligament is a well established technique but the results are poor compared with more proximal reconstructions. The state of the vessels distal to the site of graft insertion is a major factor in determining the outcome. Arteriography, the main means of assessment of this runoff, is subjective and unreliable. Using the analogy to Ohm’s law a quantitative assessment of runoff has been made by calculation of peripheral resistance from measurement of pressure created by a known flow of blood infused into the vessel under study.

Resistance was measured in two groups of dogs, and in three groups of patients undergoing amputation, femorotibial or femoropopliteal reconstruction. Both constant pressure and constant flow measurements were applied with blood, saline and Dextran.

The dog work showed that resistance fell with increasing flow, so that to make comparisons between individuals necessitated measurement at a fixed flow. Results were very reproducible despite the varying sizes of the animals. The concentric cannula technique for pressure measurement was shown to be more accurate than direct stab or sidearm measurement. The constant pressure technique, whilst correlating well with the constant flow technique, was cumbersome and impractical. Saline and Dextran were both suitable for resistance measurement but neither carried any specific advantages over blood.

Resistance in the amputation, femorotibial and femoropopliteal groups correlated with; severity of disease defined by type of operation; level of graft insertion in the leg; and runoff defined by a comprehensive assessment of the arteriogram. Resistance was significantly higher in failed grafts than patent grafts up to six months after operation, and a cutoff level of resistance of 1200mPRU was a highly significant predictor of outcome. Similar results were achieved after drug induced vasodilatation.

Resistance measurement has proved a useful predictor of outcome in femorodistal reconstruction.
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STATISTICS

Except where stated in the text, all comparisons in this thesis have been tested using the single tailed Mann Whitney U test. Calculations have been made on a BBC microcomputer using a 'University Software' statistics package called Unistat. P values have been obtained from 'Nonparametric Statistics for the behavioural sciences' by Sidney Siegal (McGraw-Hill Kagakusha Ltd).
CHAPTER 1

INTRODUCTION

The introduction of intraluminal valve disrupters which led to the introduction of in situ femorodistal grafting has meant that vascular surgeons have become able to bypass more distal blocks in the femoral and popliteal arteries than was previously realistically possible using the reversed vein.

With this new freedom came the problem of assessing the runoff distal to the site of graft insertion. The available runoff plays an important role in determining outcome in femorodistal reconstruction. The conventional method for its assessment has been arteriography but there is evidence that it is inadequate when assessing more distal disease. Assuming that the runoff is an important factor in influencing the patency of the graft another method of assessment of runoff would seem to be required.

Quantitative measurement of runoff is an attractive proposition for three reasons. Firstly it might permit more precise definition of runoff. Secondly it might allow comparisons to be made between patients making for a more logical treatment regimen for any one individual. Thirdly it might allow more meaningful
PERIPHERAL RESISTANCE MEASUREMENT

comparisons to be made between the results of different centres.

The aims of this thesis have been to investigate the usefulness of an objective measurement of distal runoff in patients prior to reconstructive surgery. Resistance measurement has the potential to quantify runoff in the distal vascular tree and can be measured using the analogy to Ohm's law.

There are inherent difficulties in the accurate determination of flow, but pressure can be accurately measured quite easily. In this thesis resistance has been calculated by infusion of blood at a known flow rate with accurate measurement of the resulting pressure generated in the distal vasculature.

The first three chapters of the thesis review the general management of peripheral vascular disease, the role of flow and pressure measurement in the prognosis of vascular reconstruction, and previous work on peripheral resistance measurement. In Chapter 5 a pilot study of resistance measurement in the dog has been undertaken in order to assess its feasibility and reproducibility. In Chapter 6 a small group of patients having amputation have been studied using the same criteria. In Chapter 7 the method of pressure measurement is assessed, the type of infusion fluid is studied, and comparisons are made between constant
pressure and constant flow measurement of resistance. In Chapter 8 which is divided into six sections patients undergoing either femorotibial or femoropopliteal reconstruction have been studied in some detail employing modifications of the method derived from Chapter 7. A summary of the results and important conclusions are found in Chapter 9.

ACKNOWLEDGEMENTS

Although the author was responsible for the vast majority of the work in this thesis it would not have been possible without considerable technical assistance. The Department of Medical Physics at the Leicester Royal Infirmary and in particular Steven Bentley and Mike Asher were responsible for the accurate recording of all the data. Each spent many hours making measurements both in the operating theatre and during the animal experiments. Dr David Evans gave much appreciated advice and some assistance with the statistics. I am indebted to Professor Bell for allowing me to study his patients and for all his encouragement throughout my time in the Department of Surgery in Leicester.
Peripheral vascular disease is a common problem with a prevalence in the United States estimated to be 2-3% in men aged 45-60, and 1% in women aged 50-65 (Kannel, Wolf, Verter and McNamara 1970). There were 156,000 deaths due to ischaemic heart disease, 67,000 deaths due to cerebrovascular disease, and 15,000 deaths due to peripheral arterial disease in 1983 (OPCS 1983). Women lag behind men by approximately 10 years. In 1983 approximately 17,000 reconstructive operations were performed on arteries with a male to female ratio of 2:1. There were 14,900 amputations. Of these 2170 were primary below knee amputations and 3210 were above knee. (DHSS 1983).

Atheroma

Peripheral vascular disease is the clinical manifestation of atheroma, a condition in which the arterial wall becomes thickened and calcified and plaques of fat, platelets and thrombus are deposited in the intimal layer resulting in narrowing of the vessel. A number of theories exist to explain the
mechanism of atheroma formation (French 1971, Kao, Wissler and Dzoga 1968, Benditt 1977 and Baumgartner 1974). All arteries are affected by this process to a greater or lesser extent, but medium sized arteries of the coronary and cerebral circulation are particularly at risk resulting in the high mortality mentioned above.

**RISK FACTORS**

Known exacerbating risk factors include smoking, diet, ageing, male sex, hypertension, raised blood cholesterol, diabetes mellitus, and a strong family history (Hughson, Mann and Garrod 1978a). There is strong evidence that smoking is implicated in the aetiology of atheroma. The risk of developing atheroma is fifteen times higher in males and seven times higher in females who smoke (Hughson, Mann, Tibbs and Woods 1978b) than in those who do not. It is estimated that 25% of the deaths each year due to cardiovascular disease are associated with smoking. Post mortem studies reveal a significantly higher proportion of patients with severe atheroma among smokers (46%) than non-smokers (15%) (Auerbach, Hammond and Garfinkel 1965). The Framingham study (Kannel and Shurtleff 1973) reported cigarette smoking to be an independent factor in the aetiology of intermittent claudication.
The association between diabetes mellitus and peripheral vascular disease has been known for some time (Brandman and Redisch 1953). The diabetic patient has more distal vessel involvement (Strandness, Priest and Gibbons 1964) and usually more extensive vascular calcification. It has been suggested that there are extensive arteriovenous fistulae in the microcirculation with increased velocity of blood flow and shunting (Scarpello, Martin and Ward 1980, Edmonds, Wilton, Roberts et al 1980 and Ward 1982). The normal ischaemic changes of an arteriopath are accentuated by the peripheral neuropathy of diabetics (Watkins 1982).

SYMPTOMATOLOGY

The severity of symptoms from the atheroma bears little relation to the extent of the disease. Quite severe disease may result in minimal symptoms particularly when the disease has progressed slowly over many years. This is because collateral vessels enlarge and bypass stenotic segments, so that when the main vessel eventually thromboses there is a good collateral supply established which protects the distal circulation. Collateral vessel growth is thought largely to be due to the pressure gradient around the block (John and Warren 1961) though release of vasoconstrictor
tones in the collateral vessels (Edwards, Cohen and Marshall 1959) and accumulation of metabolites may play a part. Conversely an acute arterial thrombosis in an otherwise almost normal limb, as may occur with embolism, can result in severe ischaemia owing to the lack of collaterals.

In its mildest form peripheral vascular disease presents as a superficial femoral occlusion with intermittent claudication causing pain in the calf during exercise. The pain is characteristically tight and cramplike and is always relieved by rest. Aorto-iliac disease with internal iliac occlusion may result in the Leriche syndrome with impotence and buttock pain on walking. The natural history of intermittent claudication depends partly on the risk factors. If the patient stops smoking and takes regular exercise the condition often runs a benign course over many years either remaining static or improving (Quick and Cotton 1982; Juergens, Barker and Hines 1960; and Mathieson, Larsen, and Wulff 1970). If this simple advice is ignored then the disease and symptoms may progress so that the claudication distance shortens and the patient eventually develops pain at rest. Coupled with this rest pain is the risk of developing gangrene in the digits. At this stage the limb is threatened and if feasible, reconstructive surgery is indicated.
PERIPHERAL RESISTANCE MEASUREMENT  Ch. 2

(Bell, Charlesworth, DePalma et al 1982). If not then major amputation may be needed.

This process of atherosclerosis is fortunately patchy, characteristically affecting one or more of three main sites; the aorto-iliac segment, the femoropopliteal segment, and the distal tibial vessel segment. It is unusual for the disease to be confined to one site, and not uncommon for all sites to be affected together.

INVESTIGATIONS

Investigation of patients with peripheral arterial disease begins with a simple assessment of the risk factors. Diabetes and the hyperlipidaemias are diagnosed biochemically. Hypertension and ischaemic heart disease are diagnosed by accurate blood pressure measurement (Kirkendall, Burton, Epstein et al 1967), ECG and chest X-ray. Non-invasive investigations specific to the arterial disease may also be performed. Doppler examination may be used to look for patent smaller arteries (Roedersheimer, Feins and Green 1981) and at the quality of larger arteries. The ankle/brachial pressure index indicates the severity of the disease (Yao, Hobbs and Irvine 1969 and Heintz, Bone, Slaymaker et al 1978) and can be used...
together with post exercise measurements of the same ratio (Nicolaides 1978 and Chamberlain, Housley and Macpherson 1975) to monitor its progress. Non-invasive estimates of blood flow into the limb may be made with the plethysmograph (Whitney 1953 and Linhart, Dejdar, Hlavova et al 1974), isotope clearance techniques (Angelides and Nicolaides 1980 and Hurlow, Chandler, Hardman et al 1978), xeroarteriography (Kramann 1979) and ultrasound measurement of Doppler shift (Gill 1985). The results of plethysmography have proved difficult to reproduce (Nielsen, Bell and Lassen 1973). Doppler waveform analysis from the femoral artery has been used to characterise stenosis in the aortoiliac segment by performing principal component analysis, transfer function analysis and by calculating the pulsatility index (Evans, Macpherson, Bentley et al 1981; Desmorais and Johnston 1981; Archie and Feldman 1982; Macpherson, Evans and Bell 1984; and Campbell, Cole, Skidmore et al 1984).

MANAGEMENT

Medical management of patients with claudication predominates over surgical management. A large number of drugs have been advocated. Among these are antilipaemic drugs, antiplatelet drugs, prostaglandins,
anticoagulants, vasodilators, rheological agents, and metabolic enhancers. Boobis and Bell (1982) in their review of the subject suggest that none of these drugs alone is of much use but that alteration of the platelet/vessel wall interaction holds out the best hope of progress.

Although not all cases can be treated by reconstructive surgery, the degree of success when this is performed is related to the site reconstructed. Proximal reconstruction has a very good graft survival rate with typical five and ten year cumulative patency rates of 85% and 66% respectively (Malone, Moore and Goldstone 1975). The results of femoropopliteal grafting are summarised in Figure 1 and those for femorotibial grafting in Figure 2. Unfortunately patients who are at most risk of gangrene and rest pain tend to have severe distal disease requiring distal reconstruction for which the results are least good.
## FEMOROPopliteAL GRAFTs - SAPHENous VEIN

<table>
<thead>
<tr>
<th>Author</th>
<th>Date</th>
<th>Number</th>
<th>Patency % (5 year)</th>
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<tr>
<td><strong>Mixed claudication and salvage</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Myhre</td>
<td>1977</td>
<td>154</td>
<td>60</td>
</tr>
<tr>
<td>DeWeese</td>
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<td>113</td>
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<tr>
<td>Szilagy</td>
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<td>464</td>
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<td>Baddeley</td>
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<td>185</td>
<td>62</td>
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<td>1972</td>
<td>74</td>
<td>64</td>
</tr>
<tr>
<td>Cranley</td>
<td>1981</td>
<td>416</td>
<td>72</td>
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<tr>
<td><strong>Salvage only</strong></td>
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<tr>
<td>Naji</td>
<td>1978</td>
<td>100</td>
<td>66</td>
</tr>
<tr>
<td>Reichle</td>
<td>1979</td>
<td>310</td>
<td>60</td>
</tr>
<tr>
<td>Veith</td>
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**Figure 1**
PERIPHERAL RESISTANCE MEASUREMENT

FEMOROTIBIAL GRAFTS

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<td>164</td>
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<tr>
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<td>17</td>
<td>LSV</td>
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<td>204</td>
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<td>32</td>
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<td>81</td>
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<td>52</td>
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<tr>
<td>Bernhard</td>
<td>1972</td>
<td>41</td>
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* All peroneal reconstructions

Figure 2
**SURGICAL MANAGEMENT**

Despite the availability of large numbers of investigations the decision to attempt reconstructive surgery remains a clinical one, based on clinical assessment of the severity of the disease at the time, and the likely outcome of withholding surgery. Having made the decision to operate, the patient is normally subjected to invasive investigation. Arteriography is an essential adjunct to routine reconstruction though it may be omitted in some acute situations. It serves three purposes. Firstly, it defines the state of the proximal vascular tree (the inflow). Secondly, it shows the femoropopliteal segment although this can usually be assessed clinically and non-invasively. And finally, in expert hands, it may show the distal runoff beyond the knee into the foot. In the assessment of any one artery it provides information on whether or not the vessel is patent at all, and if so on its calibre, runoff, number of stenoses and their position, and on two dimensional arteriography the severity of the stenosis.

In the proximal aorto-iliac segment the operation required is usually obvious and arteriography merely confirms the clinical assessment. Because the results of reconstructive surgery in this region are so good
minor irregularities in the aorta or distally in the femoropopliteal segment can be ignored since they are unlikely to alter the outcome significantly.

In the femoropopliteal segment, however, where a failed operation may lead to amputation if the operation is being performed for critical ischaemia, and where the ensuing amputation may be at a higher level than if the patient had been subjected to primary amputation (Sethia, Berry, and Morrison 1986), the quality of the runoff is more important. The outcome of grafting to this level has been shown to correlate with the number of vessels communicating directly with the popliteal artery and then down into the foot (Dewese and Rob 1977; Koontz and Stansel 1972; Cutler, Thompson, Kleinsasser et al 1976; and Naji, Chu, Mccombs et al 1978). Stenoses affecting the runoff at this level are more important in determining outcome but it is usually possible to make a reasonable subjective assessment of the runoff from the arteriogram.

Assessment of the distal arterial tree is much less certain. The quality of the films is less good because there is considerable dilution of contrast before it reaches the region of interest. This can be improved by using reactive hyperaemia as described by Kahn, Boyer, Moran et al (1968) and Feins, Roedersheimer, Baumstark et al (1981). The addition of
ultrasonic detection of the arrival of contrast in the periphery by James and Galloway (1971) and Soulen, Tyson, Reichle et al (1973) has further improved the film quality. Shearman, Gwynn, Curran et al 1986 have suggested that it is possible to assess the popliteal segment noninvasively and Roedersheimer, Feins and Green (1981) have shown that the presence of a patent pedal arch can be accurately assessed by ultrasound alone.

The outcome of vascular replacement to the distal tibial or peroneal arteries at ankle level is significantly worse than that achieved with the femoropopliteal replacements (Figure 2). The potential runoff at this distal level is strictly limited. To be forced to graft to ankle level implies the absence of patent vessels higher up in the calf or at popliteal level. The runoff is therefore limited to the foot, supplying mainly skin and bone. The resultant flow as shown by Harris and Campbell (1983), is rarely in excess of 75ml/min and this is unlikely to be sufficient to maintain graft patency.

**OUTCOME**

The outcome of reconstructive vascular surgery depends upon several factors. Local factors include the quality of the runoff, the state of the inflow vessels (Charlesworth, Harris, Cave et al 1975), the size
(Koontz and Stansel 1972) and type of graft used for the bypass, and the site and angle of insertion of the distal end of the graft (Klimach, Underwood and Charlesworth 1984). Whilst synthetic materials are quite satisfactory for proximal reconstructions it is generally held that autogenous vein, either reversed or in situ, is best for distal reconstruction (Bergan, Yao, Flinn et al 1982 and Hall 1962). When the vein is not available, umbilical vein and polytetrafluoroethylene grafts have been used but with lower success rates (Bergan, Yao, Flinn et al 1982; Klimach, Underwood and Charlesworth 1984, and Charlesworth, Brewster, Darling et al 1985). Indirect factors include the seniority of the surgeon performing the operation, the general condition of the patient, the presence of diabetes, or heart disease, perioperative hypotension, and blood loss. Late indirect factors include progression of disease, continued smoking (Myers, King, Scott et al 1978), diabetes, the development of pseudointimal hyperplasia (Beard and Fairgrieve 1986), treatment with anti-platelet drugs (Goldman, Hall, Dykes et al 1983) or Warfarin (Kretschmer, Wenzl, Wagner et al 1986), and the use of a graft which crosses the knee joint.
CONCLUSION

Femorodistal reconstructive surgery has now been performed for over twenty years. The results of these operations are inferior to those achieved in the more proximal reconstructions. It is generally accepted that vascular reconstruction is always preferable to amputation (Bell 1985), and therefore vascular surgeons are obliged to continue searching for methods which separate those patients in whom a graft will succeed from those in whom it will fail. The outcome of vascular reconstructive surgery is obviously multifactorial and one of the more important factors must be the state of the distal circulation at the time of surgery. The remainder of this thesis examines methods of assessing the distal circulation prior to reconstruction with the aim of separating a group of patients in whom reconstruction is hopeless from one in whom it might be expected to succeed.
Kolin (1936) and Wetterer (1937) independently developed flowmeters based on Faraday's Law of electromagnetic induction. The square wave electromagnetic flowmeter principle was introduced in 1955 by Denison and Hall. In the early 1960's the clinical use of electromagnetic flowmeters increased so that it became possible to measure flow accurately after reconstructive surgery. Early measurements were made in patients undergoing varicose vein surgery where it was possible to mobilise the femoral artery at the same time (Schenk, Menno, Anderson et al 1960). Flow was shown to increase with vasodilators, lumbar sympathectomy and X-ray contrast media injected intra-arterially. The accuracy of early machines was fair (Golding and Cannon 1966 and Dedichen 1974) but it was pointed out that poor fit of the probe to the vessel and atheroma could increase the error considerably. The importance of measurement of augmented flow with papaverine was stressed with the mean increase in flow being approximately 100%. Golding and Cannon also suggested that pressure measurement without concomitant flow measurement was of limited value in the assessment.
of success of reconstructive surgery.

The normal flow in the common femoral artery has been shown to be 239 ml/min. In the superficial femoral artery flow was 134 ml/min and in the profunda artery 104 ml/min (Vanttinen 1975). Similar flows have been observed by Lewis, Psaila, Davies et al (1986) using a Duplex scanner. The papaverine response in the normal femoral segment was an increase in flow of 250%. The prognostic potential of flow measurement was described by Little, Shiel, Loenthal et al (1968). After femoropopliteal grafting flow of less than 60 ml/min was associated with a 80% chance of early graft failure whilst flow greater than 60 ml/min was associated with 80% patency in the first three months. Cappelen and Hall (1967) had a 10% failure rate with flow greater than 100 ml/min and a 50% failure rate with flow less than 100 ml/min. Terry, Allen and Taylor (1972), Sonnenfeld, and Cronestrand (1980), and Dedichen (1976) achieved similar results. Roberts and Cotton (1977) found no significant difference in flow after profundaplasty between those with successful outcome (107ml/min) and failures (78 ml/min). There were significant differences in flow velocity and it was suggested that this might be a more useful measurement. Scheinin and Inberg (1968) suggested that if there was not a significant increase in blood flow after the
administration of papaverine after vascular reconstruction then there was probably a technical error in the anastomosis. Immediate lumbar sympathectomy was shown to be of benefit if the reconstruction was otherwise deemed inadequate. Dedichen (1973) looked simultaneously at graft flow and pressure gradient across either an implanted graft or the endarterectomised segment of a femoral artery. He encountered similar results to Terry, Allen and Taylor and Cappelen and Hall and found only very small pressure gradients along the femoral segment or graft. He suggested that the resistance of the graft was minimal compared with the resistance distal to the reconstruction and that distal disease was the primary cause of early graft failure. In a further paper Dedichen (1975) noted that after reconstruction the flow increase due to papaverine was greater than that following five minutes of tourniquet occlusion of the leg confirming the usefulness of papaverine to induce maximal flow.

Pressure measurement alone is of limited use in the prediction of outcome of femorodistal reconstruction. Ankle/brachial pressure index measurement provides a rough idea of the severity of disease but is of no use as a predictor of outcome after surgery. Agerskov, Paris, Tonnesen et al (1983)
measured popliteal artery pressure by direct cannulation and compared it with indirect measurement of ankle pressure. The popliteal/ankle pressure difference did not correlate with outcome but did correlate with eventual ankle pressure six months after grafting. Crawford, Blaisdell, Morris et al (1963) measured pressure either side of a carotid bifurcation stenosis and noted that when the area reduction was in excess of 50% there was a significant reduction in distal pressure which could be reversed by surgery. In a similar study on the aortofemoral segment Weismann and Upson (1963) showed that decrease in femoral pulse assessed by palpation alone was inaccurate, that femoral pressure was decreased by iliac stenotic disease and that vascular replacement abolished the pressure gradient. Garrett, Slaymaker, Heintz et al (1977) showed that if the increase in ankle/brachial pressure index after aortoiliac reconstruction was <0.1 the clinical outcome was unsatisfactory. Similar results have been observed in patients undergoing femoropopliteal reconstruction (Lewis 1974 and Wood, Bishara and Darke 1985). Wood also assessed the technical adequacy of surgery with the same technique. Mannick, Jackson and Coffman (1966) suggested that if popliteal artery pressure could be raised above 75 mmHg by bypass grafting claudication would be abolished even in the
presence of severe distal disease. Dedichen (1976) studied the pressure gradient before and after reconstruction of both the aortoiliac and femoropopliteal segments and demonstrated almost complete abolition of the gradient after surgery. When a successful bypass was performed the ensuing gradient was slightly less than that measured when there was primary graft failure but the difference was not great enough to be used in a predictive way.

In their paper Evans, Quin and Bell (1980) emphasise the need to consider the results of pressure measurements in the light of the simultaneous changes which might be occurring in flow. It is also suggested that to be meaningful pressure measurement should be made at constant flow and preferably by direct cannulation of the artery being studied.

Impedance is an expression of the total opposition to blood flow in an artery and includes the effects of elasticity, inertia, reflection, and viscosity in the vessels beyond the point of measurement. Impedance measurement in normal dogs (O'Rourke and Taylor 1966) and humans (McDonald 1974) has been well described. Results were consistent and reproducible. Farrar, Malindzak and Johnson (1978) described the changes in impedance that occurred when a stenosis was introduced into the circulation both in an
experimental animal and in the human with atherosclerosis and noted that it provided a measure of the severity of disease. Cave, Walker and Naylor (1976) measured impedance at the time of, and three months after femoropopliteal grafting and showed significant differences in the successful group. Law, Graham, Cotton et al (1983) were able to substantiate these results in the aortoiliac group but not in the femoropopliteal group although the same trend existed. Impedance measurement alone has not been used to determine the outcome prospectively in patients undergoing femoropopliteal reconstruction.

CONCLUSION

Impedance and pressure measurement have not proved useful alone in determining the outcome after femorodistal reconstruction. The evidence for impedance is controversial and more work is required. Pressure measurement might be useful for deciding whether the reconstruction performed is technically adequate, and for the longterm follow-up of patients following vascular reconstruction. Flow measurement alone does seem to correlate with the outcome of reconstructive surgery and can also be used to assess the technical adequacy of the procedure. Of the three methods of assessment flow seems the most promising but none
appears to be the complete answer.
The concept of peripheral resistance owes much to the work of Poiseuille (1799-1869), a physicist as well as a physician who originally intended his studies to be of the flow properties of blood. He was however unable to anticoagulate it and so turned to study the flow of pure liquids in rigid glass tubes. The Poiseuille equation states that pressure drop is directly proportional to the length of the pipe, to the rate of flow, and to the viscosity and inversely proportional to the fourth power of the radius.

\[ Q = \frac{(P_1 - P_2)R^4}{8\eta L} \]

Where:
- \( Q \) = Flow
- \( P \) = Pressure
- \( R \) = Radius
- \( L \) = Length
- \( \eta \) = Viscosity

The Poiseuille equation

The equation relates flow and pressure of a Newtonian fluid in a cylindrical tube. A Newtonian fluid was defined by rotating a rod in a fluid bath. He noted that 'the resistance which arises from the defect of slipperiness of the parts of the liquid other things being equal is proportional to the velocity with which the parts of the liquid are separated from one another'. The hypothesis emphasized that there were lamellae of
fluid slipping on one another at different velocities. There is thus a velocity gradient in a direction perpendicular to the surface, the gradient being known as the rate of shear.

\[ T = \frac{d\nu}{dr} \]

\[ T = \text{Stress} \]

\[ \frac{d\nu}{dr} = \text{Velocity gradient} \]

\[ r = \text{Distance from the axis} \]

Rate of shear

If the flow is steadily increased then the resistance to flow eventually increases quite sharply and the Poiseuille equation then no longer applies. At this time flow ceases to be streamlined and laminar and becomes turbulent. This critical point is dependant on the diameter of the tube, the mean velocity of flow, the density, and the viscosity of the liquid. It is expressed as the dimensionless quantity known as the Reynolds number.

\[ Re = \frac{VDp}{\nu} \]

\[ V = \text{Average velocity} \]

\[ D = \text{Diameter} \]

\[ p = \text{density} \]

Reynolds number

When applied to the circulation certain assumptions have to be made regarding the Poiseuille equation.

1. The fluid is homogeneous. If the Diameter is large then the blood despite containing particles (red cells) behaves like a Newtonian fluid.
2. The viscosity is the same at all shear rates. When the vessel diameter is small there is an apparent change in viscosity owing to the presence of the red cells.

3. The liquid velocity immediately adjacent to the wall is zero. This is the case with blood and all other liquids, although it was felt that if the vessel was not wettable there might be some slip.

4. The flow is laminar. In large vessels with no disease this is probably true, but when the vessel is small or diseased Reynolds number is certainly exceeded and turbulence ensues.

5. The flow is steady. If the velocity of flow is altered the pressure gradient imparts some kinetic energy to the liquid and Poiseuille's equation does not apply. It does not therefore apply to pulsatile flow.

6. The tube is long compared to the region being studied.

7. The tube is rigid and diameter does not vary with internal pressure. Large arteries are elastic and flow is therefore not solely dependant on the pressure gradient. Smaller vessels and capillaries behave like rigid tubes and Poiseuille's equation applies.

It can be seen from the above conditions that the human circulation approximates only very roughly to the Poiseuille equation, and that further application of the equation must necessarily introduce errors.
The concept of an analogy to Ohm's Law for the measurement of peripheral resistance has been used in this thesis.

\[ V = IR \]

\( V \) = Potential difference
\( I \) = Current
\( R \) = Resistance

\[ P1-P2 = QR \]

\( P1 \) = Arterial pressure
\( P2 \) = Venous pressure
\( Q \) = flow
\( R \) = Resistance

Resistance is expressed in PRU (peripheral resistance units), where

\[ 1 \text{PRU} \text{=} 1\text{mmHg pressure drop} / 1\text{ ml/min flow} \]
\[ 1 \text{PRU} = 1000\text{mPRU} \]

Measurement of impedance implies a measurement of resistance under pulsatile flow conditions. Resistance measurement is performed at constant flow and reconsideration of conditions for the application of Poiseuille's equation shows that more of the conditions are met under these circumstances.

Whittaker and Winton (1933) summarised the previous work on blood viscosity and used an isolated dog hindlimb preparation in their own studies. It was noted that if the perfusing solution was changed from blood to Ringers solution then flow increased by approximately three times at the same pressure. For both blood and Ringers solution it was found that there was a linear relationship between pressure and flow and that at all but the lowest flow rates the Poiseuille equation
The haematocrit of the infused blood was also varied and it was noted that for a given pressure the flow achieved was inversely proportional to the haematocrit. The relationship between apparent viscosity and haematocrit was linear up to a haematocrit of 0.50, but viscosity increased steeply above this level. Although not deliberately the case, these experiments were performed at maximal vasodilatation by virtue of having an isolated hindlimb preparation.

In contrast, Pappenheimer and Maes (1942) studied a perfused dog hindlimb preparation at varying degrees of vasoconstriction. It was shown that blood flow was not proportional to the perfusing pressure. Vasoconstriction at low perfusion pressure resulted in a non-linear relationship between flow and pressure. Only when the pressure reached 100 mmHg was there an approximately linear relationship. There was no change in resistance with pressure when perfusing with Ringer's solution, and it was concluded that the change in resistance brought about by vasoconstriction was the result of a change in the apparent viscosity of the blood as well as of a change in the dimensions of the blood vessels. It was also shown that there was a wide variation in resistance between dogs measured at any one pressure with similar degrees of vasoconstriction suggesting that there was a variable number of perfused
vascular elements present. These two papers suggest that measurement of resistance at maximal flow might exclude errors induced by a change in apparent viscosity when vasoconstriction is present.

Green, Lewis, Nickerson et al (1945) measured resistance in three vascular beds: the skin of the thigh, quadriceps, and gastrocnemius and soleus of the dog. The definition of peripheral resistance units was coined and unlike their predecessors found a non-linear relationship between pressure and flow. The curve was sigmoid in shape. However, they agreed that at high flow there was a linear relationship between pressure and flow. The probable explanation for the non-linear part of the curve lies in the fact that the critical opening pressure is not reached until quite high pressures are attained. Thus at low flow rates the resistance is higher than expected.

Pappenheimer and Soto-Rivera (1948) by performing dog and cat isolated hindlimb preparation experiments were able to show that resistance increased greatly as flow was reduced by reducing the perfusion pressure.

Hanson and Johnson (1962) studied arterial and venous resistance in an isolated auto-perfused canine hindlimb and described three types of resistance/pressure curves. Resistance was shown to either increase steadily, decrease steadily, or
initially increase and subsequently decrease as pressure was reduced. These variations were not adequately explained by the authors and were at odds with the findings of Pappenheimer and Soto-Rivera (1948).

Vetto and Dunphy (1964) were the first to put peripheral resistance measurement to use in humans. Disappointed by the high failure rate of femoropopliteal reconstructions they measured peripheral resistance as a prognostic indicator in the popliteal artery prior to reconstructive surgery. Cold bank blood was pumped into the popliteal artery at a known flow rate and pressure generated in the artery was measured with a separate cannula. Resistance was calculated in dyne-sec cm^-2. Six patients were studied and there was a reasonable correlation between early outcome and resistance. It is not clear however if all the measurements were made at the same flow rate and if so what that flow rate was.

Conrad and Green (1964) studied digital vascular resistance in a group of fourteen patients with vasospastic diseases and eleven asymptomatic medical students as controls. Digital blood flow was estimated with an airfilled plethysmograph and pressure was estimated using the plethysmograph cuff. It was shown that in normals the resistance was moderately high in the resting state but reduced to about one third after administration of alcohol. Resistance in the patients
was markedly elevated at rest and fell with alcohol though not to normal levels. The most striking finding was the extreme 'normal' variation in resistance in the control subjects - a factor of 27 times at rest and six times after alcohol.

Weale, Taylor and Rothwell-Jackson (1964a) measured resistance in two groups of patients. Controls had their femoral arteries exposed for cytotoxic drug administration for management of their malignant melanoma or were having aneurysm repair. Study patients had popliteal artery resistance measured prior to femoropopliteal arterial reconstructive surgery. The technique (Weale 1964b) was a constant pressure one with readings being taken in the physiological range. Results showed that resistance at groin level was significantly lower than that measured in the popliteal artery (P=0.012) Mann-Whitney U test. It was noted that resistance was higher when the perfusing pressure was low and it was suggested that this was a manifestation of the collateral circulation.

Folse (1965a and 1965b) measured femoral resistance in 26 patients with femoropopliteal occlusion using a dye dilution technique to measure flow. Measurements were made both at rest and after exercise. Mean results for all the patients were presented and showed the resistance to be low at rest but to fall with
Delin and Ekestrom (1965) measured resistance in patients before and after surgery for occlusive vascular disease. In each case resistance fell after surgery but the resistance was not measured at the same flow rate and under these circumstances comparison of resistance values is not possible.

Mundth, Darling, Moran et al (1969) measured resistance in patients undergoing femoropopliteal vein grafting before and after reconstruction. Arteriography did not correlate well with resistance measurement, but neither was there any correlation between resistance and patency. As with Delin and Ekestrom (1965) resistance was measured at different flow rates making interpretation of results difficult.

Bliss (1971) in an excellent paper measured resistance in 23 patients undergoing femoropopliteal grafting. By his technique he was able to maintain a continuous infusion of the patients own blood into the popliteal artery prior to reconstruction. Using a concentric cannula of his own design he was able to measure pressure in the popliteal artery at the same time as infusing. Resistance was measured at a number of flow rates and before and after papaverine. He showed that resistance varied tremendously from patient to patient under the same conditions. Resistance fell and
sometimes increased with increasing perfusion pressure and flow, and the shape of the pressure/flow curve varied considerably. Papaverine increased the variation measured - a finding at odds with those of Conrad and Green (1964). In general, resistance fell with increasing flow and pressure and reached a steady level at flows in excess of 200ml/min. He suggested that at these flow levels it should be possible to make comparisons of resistance between two subjects. He concluded by saying that the resistance was made up from vasomotor tone and 'fixed arterial resistance' caused by stenoses and blocks, and that if an estimate of fixed arterial resistance was required then steps must be taken to minimise the vasomotor tone by giving a peripheral vasodilator.

In a further paper Bliss (1973) showed that resistance correlated well with runoff defined arteriographically but could not show any correlation between resistance and graft patency. These measurements were however made postoperatively and at a number of different flow rates from 128-230ml/min, making comparison between patients impossible.

Barner, Kaminski, Codd et al (1974) measured resistance in 74 patients after completion of femoropopliteal reconstruction. No difference in resistance between subsequently patent and occluded
grafts either at basal or peak augmented flow rates was noted. Neither could they show any difference in relation to the number of vessels patent to ankle level.

Sonnenfeld, Cronestrand, and Nowak (1979) and Sonnenfeld, Cronestrand, Von Euler et al (1981) measured resistance after femoropopliteal reconstruction in eleven patients. Blood transfusion immediately after reconstruction resulted in a reduction of peripheral resistance as did the administration of papaverine. It was concluded that the transfusion effect was secondary to hypovolaemia.

Serise, Le Heron, Janvier et al (1982) measured resistance in 22 patients undergoing femoropopliteal grafting. Saline was injected at 30ml/min in each case. A technical error was found in one of 17 patients with a resistance of < 3.0 PRU whose graft occluded early. When the resistance was > 4.0 PRU there were 4/5 early thromboses, and when the resistance was > 5.0 PRU every graft failed.

Menzoian, La Morte and Cantelmo (1985) performed resistance measurements in five dogs and 23 humans undergoing femoropopliteal reconstruction. A Harvard pump was used to perfuse the artery under study at known flow rates and pressure was recorded via a sidearm catheter. Resistance was measured at a number of predetermined flow rates. Blood was used for perfusion
in the dogs and saline was used in the human experiments. In both dogs and humans there was a significant change in resistance as flow increased from 50-200 ml/min. There was considerable variation in resistance from patient to patient. Preoperative arteriograms were awarded a score from 1-4 according to the severity of the disease and there was a very poor correlation between this score and the resistance.

SUMMARY

There is comparatively little work in the literature on the use of peripheral resistance measurement in the assessment of patients undergoing reconstructive vascular surgery. Early work showed that resistance depended on the viscosity of the perfusing solution (Whittaker 1933). It was shown that the relationship between pressure and flow was non-linear (Pappenheimer 1942; Green 1945) but that at high flow rates the relationship was approximately linear. There were considerable differences of opinion as to the shape of the pressure/flow curves (Hanson 1962; Pappenheimer 1948; Weale 1964a; Bliss 1971). The majority accept that the resistance falls with increasing flow and pressure (Green 1945; Pappenheimer 1948; Conrad 1964; Weale 1964). The need for maximal flow conditions for the measurement
of resistance remains contentious with Whittaker (1933); Conrad (1964); Folse (1965); and Sonnenfeld (1979 and 1981) in favour, but with Bliss (1971) and Barner (1974) unable to show any advantages. In the early studies on patients neither flow nor pressure were fixed (Vetto 1964; Delin 1965; Mundth 1969; Bliss 1973) and since there is a non-linear relationship between pressure and flow direct comparison between patients can only be made when the flow or pressure are fixed (Bliss 1973; Serise 1982; Menzoian 1985). Arteriography has been shown to correlate only poorly with resistance (Mundth 1969; Barner 1974; Menzoian 1985), but to correlate well by Bliss (1973). Probably the principal reason why resistance measurement has not become popular is that it has failed to correlate with graft patency (Bliss 1973; Mundth 1969; Barner 1974). In each of these papers resistance was measured at different flow rates and one may speculate that the poor correlation may in part be due to this fact.
CHAPTER 5

ANIMAL EXPERIMENT 1

Resistance measurement in an animal model

It has been shown in the preceding chapters that neither pressure nor flow alone is able to predict graft outcome. Resistance measurement theoretically might be useful because of its ability to quantify runoff, radiological assessment of which has been shown to be unreliable.

Because of the difficulties eluded to in Chapter 4 a series of dog experiments have been performed the aims of which were to:

(a) Discover a simple reliable method by which peripheral resistance might be measured.
(b) Investigate the reliability of the technique with particular reference to the reproducibility of the results.
(c) Investigate the relationship between pressure and flow over a range of flows in an animal model.

METHOD

Dogs have been used in this study. Resistance has been measured in the superficial femoral artery of the
right hindlimb.

**ANAESTHETIC**

Each animal was given a general anaesthetic. Induction was achieved in each case with Thiopentone and was maintained with nitrous oxide and oxygen and an infusion of intravenous Hypnorm. Ventilation was performed by the administration of the gases by closed circuit ventilation connected to an appropriate endotracheal tube. At the end of each experiment the animal was destroyed by the administration of a large intravenous dose of barbiturate. During the procedure pulse, systemic blood pressure and central venous pressure were monitored by continuous recording on a chart recorder. In order to standardise the anaesthetic as far as possible, both during a single procedure and between different dogs, arterial blood gases were estimated at intervals during the experiment. Systemic pressure was measured by placing a 20 gauge plastic cannula into one of the lateral branches of the aorta. The tip of the cannula was positioned at the aortic orifice of the branch. The branch itself was ligated distal to the site of cannulation. The cannula was connected by a 100cm length of manometer tubing to a pressure transducer and thence via an appropriate
amplifier and filter system to a chart recorder. Central venous pressure was measured using a size 20 Longdwell catheter placed via a stab in the left jugular vein into the superior vena cava. The cannula was sewn to the skin to prevent its displacement. The cannula was connected in the same way as the systemic pressure cannula to the chart recorder. ECG was monitored continuously with leads connected to electrodes appropriately placed on the chest. Urine output was monitored by direct puncture and catheterisation of the bladder. Intravenous fluids were given through a cannula placed in a front leg vein. Enough fluid was given to maintain urine output and central venous pressure at physiological levels.

THE MODEL

Once anaesthetised the dog was placed on its back on the operating table and its legs were strapped out. Sandbags were placed alongside the body to prevent it from tipping over and to help prevent heat loss. The dog was laid on a warming blanket. A rectal temperature probe was connected to the electric blanket and the thermostat set to 38°C.

A single long incision was made extending from the xiphisternum above to the stifle distally. In the abdomen the incision was made in the midline down to a
point marked by a line perpendicular to the inguinal ligament passing through the emerging femoral artery. The incision was continued along this line and then along the course of the femoral artery.

The hindlimb was rendered ischaemic by the technique described by Johansen and Bernstein (1979). The terminal aorta, both internal iliac arteries, and the last ipsilateral lumbar artery were all ligated. All branches of the external iliac artery and superficial femoral artery from the origin on the aorta to a point in the distal thigh were ligated and divided. The superficial femoral artery itself was then ligated in the proximal part of the thigh completing the devascularisation of the limb.

Venous pressure was measured with a 20 gauge cannula. This was sited in a sidebranch of the femoral vein at groin level its tip just emerging into the femoral vein itself. The cannula was connected to a pressure transducer and then the chart recorder with a manometer line. Arterial pressure was measured by a similar cannula sited in a sidebranch of the superficial femoral artery distally in the thigh.

Blood was withdrawn into two 50ml plastic disposable syringes. 500 units of Heparin had previously been added to each syringe to prevent the blood from clotting. These syringes were then mounted onto a
Harvard pump (Fig. 3). Each syringe was connected to the other by a short manometer line and a 3-way tap. The two were then connected to the infusing cannula by another longer manometer line.

The infusing cannula was placed in the superficial femoral artery immediately distal to the site of its ligation and was snugged in place with a silastic sling. The completed model is shown in Fig. 4.

**MEASUREMENT**

Resistance was measured in the superficial femoral artery before it was ligated. Flow was measured with an electromagnetic flow probe placed around the superficial femoral artery.

After ligation of the superficial femoral artery arterial and venous pressure were measured at a series of five different flow rates - 9.5, 19.1, 38.2, 76.4, and 190ml/min. Measurement was begun at the lowest flow rate and the flow was only increased when the arterial pressure had reached a plateau. When each of the flows had been tried once, the experiment was repeated with a further two syringes of blood after a delay of at least 20 minutes.

All pressures were measured with Elcomatic EM751 pressure transducers and recorded on a Gould 2800S.
Two 50 ml syringes are mounted on the Harvard pump.

**Figure 3**
The completed dissection of the animal model

Figure 4
PERIPHERAL RESISTANCE MEASUREMENT

Pressure ink direct writing recorder. Flow was measured with a Carolina 601D electromagnetic flowmeter using CF200 series flow probes. All parameters were recorded on a Racal 14DS multichannel instrumentation tape-recorder.

RESULTS

Before any measurements were made the accuracy of the Harvard pump was checked. There was no significant slowing in flow over a wide range of physiological resistances.

Details of the ten dogs used in this experiment are shown in Figure 5. Resistance was measured before ligation of the superficial femoral artery when the limb was still supplied with blood and was not yet ischaemic. Results for each dog are shown in Figure 6. The post-ischaemia resistance for each of the flow rates for all ten dogs is tabulated in Tables 1-5 in the Appendix (pages A2-6). Mean resistance for the two runs is shown in Figure 7. Prior to the introduction of ischaemia it will be noted that the range of flows into the hindlimb is 72-310ml/min, and that the resistance varies between 220-879 mPRU. The correlation between flow and resistance at this stage was good ($r = -0.9033$).
After the introduction of ischaemia the resistance fell in each case in comparison with the pre-ischaemia value. Direct comparison is not possible but reference to Figures 6 and 7 shows this to be the case at approximately equivalent flow rates. Figure 8 plots the mean resistance with standard error against flow for each of the dogs. It can be seen that resistance falls as flow increases.

<table>
<thead>
<tr>
<th>Number</th>
<th>Sex</th>
<th>Weight (Kg)</th>
<th>Fem art Diameter (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>28</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
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<td>4.5</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>28</td>
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</tr>
<tr>
<td>4</td>
<td>F</td>
<td>29</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
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</tr>
<tr>
<td>10</td>
<td>F</td>
<td>23</td>
<td>4</td>
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Figure 5
### RESISTANCE PRIOR TO ISCHAEMIA

<table>
<thead>
<tr>
<th>Dog</th>
<th>Q (ml/min)</th>
<th>AP (mmHg)</th>
<th>V (mmHg)</th>
<th>Res (mPRU)</th>
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<tr>
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<td>2</td>
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<td>80</td>
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<td>362</td>
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<td>8</td>
<td>72</td>
<td>69</td>
<td>5.7</td>
<td>879</td>
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<td>130</td>
<td>74</td>
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<tr>
<td>10</td>
<td>310</td>
<td>76</td>
<td>7.8</td>
<td>220</td>
</tr>
</tbody>
</table>

Q - Flow ml/min  
AP - Arterial pressure mmHg  
V - Venous pressure mmHg  
Res - Resistance mPRU  

**Figure 6**

### RESISTANCE AFTER ISCHAEMIA

| Flow ml/min | Dog  
<table>
<thead>
<tr>
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<tbody>
<tr>
<td></td>
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<td>797</td>
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<td>10</td>
<td>749.5</td>
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</table>

**Figure 7**
Mean resistance + SE vs. flow for the ten dogs.
Resistance falls with increasing flow.

Figure 8
DISCUSSION

These results reveal a number of features in relation to the measurement of resistance. Firstly there is a non-linear relationship between flow and pressure. At low rates of flow the pressure is relatively higher than at high rates. The reason for this is unclear. When starting an infusion, many of the capillaries distally are closed and a certain amount of energy is required to open them. Until this critical closing pressure is overcome pressure rises without any flow. As flow increases the viscosity becomes relatively lower as axial streaming of the red cells increases.

In order to make a comparison between the resistance of different individuals it is desirable to measure resistance on a flat part of the resistance/flow curve. Reference to Figure 8 shows that above a flow of 76ml/min the resistance/flow relationship is approximately linear, that the curve gradient is minimised, and that it should be possible to measure resistance accurately at this level. The non-linear relationship between pressure and flow shows that it is difficult to compare the pre-ischaemia resistance values with those made after ischaemia. In this case it is possible to approximate what the resistance would have been at any given flow rate and note that after
ischaemia it is certainly lower. However if any truly valid observations are to be made regarding resistance and its comparison between individuals it clearly has to be measured at either fixed flow or fixed pressure. The work of Vetto and Dunphy (1964); Delin and Ekestrom (1965); Mundth, Darling, Moran et al (1969); and Bliss (1973) was performed at a variety of different flow rates and therefore no comparisons should have been made.

Figure 8 also shows that despite the wide variation in size between the dogs there is remarkable similarity in the resistance measured for each one. This suggests that the investigation is reproducible.

Technically the measurement of resistance was straightforward. There was no problem getting blood out for the infusion, and the measurement of pressure distal to the infusing cannula was easy using the cannula in the sidebranch.
SUMMARY

These results suggest that it should be possible to measure resistance in humans and to use it as a technique for quantifying the runoff. Resistance needs to be measured at one flow rate to make the results between individuals comparable. In the next chapter a pilot study using the technique defined in dogs has been used in humans undergoing amputation.
CHAPTER 6

AMPUTATION RESISTANCE

 INTRODUCTION

The aim of the first human work on resistance measurement was to see whether the results achieved with the initial animal experiments could be reproduced in the human. It was felt that a small pilot study should be performed in humans in a situation where all the resistance measurements should be similar and where the potential risk to the patient from excessively rapid infusion could be minimised. A group of patients undergoing amputation was therefore studied.

METHOD

A group of patients undergoing lower limb amputation either above or below knee were included in this study. All the operations were performed under a general anaesthetic. Blood for infusion by the Harvard pump (Figure. 3) was withdrawn into two 50ml plastic disposable syringes. 500 units of Heparin had previously been added to each of the syringes to prevent the blood from clotting. A 21 gauge cannula was placed in the
femoral vein at groin level to measure venous pressure. It was connected by a manometer line to a pressure transducer and thence to a pressure amplifier and chart recorder. Arterial pressure could not be measured by the same technique as in the initial dog experiments and therefore was measured using a 27 gauge cannula which was inserted directly into the artery under study 1 cm distal to the tip of the infusing cannula. The largest cannula which could be easily inserted into the artery was used for the blood perfusion. At ankle level this was typically a 20 gauge cannula, but at knee level a 18 gauge cannula was used. The infusing cannula was connected by a manometer line to the syringes mounted on the Harvard pump. Pressure was then measured at the same series of flows that had been used in the dog experiments - namely 9.5, 19.1, 38.2, 76.4, and 190 ml/min. At each flow the infusion was maintained until the pressure was constant, and the flow was then increased. After the measurements were completed an arteriogram was performed and the amputation was completed.

**Patients**

A series of twelve patients was studied. Their details are shown in Figure 9. One patient (No 4) had
resistance measured twice in separate vessels. Five of
the patients were diabetic, seven were smokers, four
were ex-smokers, and one had never smoked. Five had
ulceration in the foot, seven had gangrene, four of
these had both ulcers and gangrene. Three patients had
had previous cerebrovascular accidents, two had had
myocardial infarction, and five had coexisting
hypertension. Two had had previous reconstructive
surgery one profundaplasty (No 8) and one
femoropopliteal bypass (No 9). Four above knee
amputations and eight below knee amputations were
performed. Arteriograms were available for only eight of
the patients. Resistance was measured at the ankle in
ten cases and above knee in three.
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<th>MI</th>
<th>BP''</th>
<th>DM</th>
<th>Pr</th>
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<th>Ulc</th>
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<td>X</td>
<td>*</td>
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<td></td>
</tr>
</tbody>
</table>

* Present  
- Absent  
X - Ex smoker  
DM - Diabetes mellitus  
Pr - Previous surgery  
XR - Xrays available  
CVA - Stroke  
MI - Myocardial infarct  
BP'' - Hypertension  
Sm - Smoker  
Ulc - Ulcers  
Gan - Gangrene

Figure 9
RESULTS

An attempt was made to measure resistance at each of the flow rates. The results achieved are shown in Table 1 in the appendix (pages B2-3), and are summarised in Figure 10. For patients 2, 3 and 4 pressures are not available at high flow rates.

**AMPUTATION SUMMARY**

<table>
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<tr>
<th>Name</th>
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<th>9.5</th>
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<td>2830</td>
<td>1600</td>
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<td>4000</td>
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<td>314</td>
<td>222</td>
<td>110</td>
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</table>

Mean: 11960 8351 2654 2092 759
SE: 2927 1922 628 617 218

**Figure 10**

Each of these patients started with very high resistances even at the lowest flows. Single readings were unavailable for patients 9, 10, 11, and 12 for technical reasons. As in the previous experiment the
Resistance vs. flow for 12 amputees.
There is a wide range of resistance but it falls with increasing flow.

Figure 11
Mean resistance + SE for 12 amputees.

As in the first animal experiment (Fig 9) resistance falls with increasing flow.

**Figure 12**
resistance fell as the flow increased in every case. This is demonstrated in Figures 11 and 12. Figure 11 plots resistance against flow for each individual and Figure 12 plots the mean and standard error of resistance against flow. The resistance measurement at 9.5 ml/min in patient 8 has been omitted from the graphs since it was obviously lower than would have been expected from the other values, and is assumed to be due to a technical error.

The results of arteriography have been included where an intraoperative arteriogram was possible and are shown in Figure 13. Each arteriogram was analysed by number of patent vessels in the calf, whether the pedal arch was intact, whether the pedal arch was present at all, and by a subjective assessment of the whole runoff. The runoff was assessed as good, moderate, poor, or terrible. In assessing the number of patent vessels in the calf, any vessel whether fully patent or patent only in small part was considered patent for the purposes of the study. A points system has been used to assess the arteriogram. One point is awarded for each occluded vessel in the calf. The overall runoff has been scored as follows: Terrible = 4, Poor = 3, Moderate = 2, Good = 1. Comparing resistance at 19.1 ml/min with the arteriogram score the correlation coefficient was 0.308 P = N/S (N=6). At 38.2
ml/min and 76.4ml/min the correlation coefficient was 0.223 P = N/S (N=5) (Spearman rank correlation test). The numbers are obviously small but there was no significant correlation between runoff defined arteriographically in this way and resistance.
### Amputations

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<th>Calf vessel</th>
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<th>Overall runoff</th>
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<td>Poor</td>
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<td>Poor</td>
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<td>AT/PT</td>
<td>N</td>
<td>Y</td>
<td>Mod</td>
<td>Poor</td>
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<td>-</td>
</tr>
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<td>-</td>
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<tr>
<td>8</td>
<td>B/K Ank</td>
<td>AT</td>
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<td>Poor</td>
<td>Poor</td>
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<tr>
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<td>AT</td>
<td>N</td>
<td>Y</td>
<td>Poor</td>
<td>Poor</td>
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</table>

A/K - Above knee  
B/K - Below knee  
Ank - Ankle level  
PT - Posterior tibial artery  
AT - Anterior tibial artery  
PN - Peroneal artery  
N - No  
Y - Yes  
- - No data available

**Figure 13**
DISCUSSION

As in the pilot dog study the resistance has been shown to fall with increasing flow. The range of resistance values observed however was much greater in the amputation group than in the dog group. This is not surprising given the severity of the disease in the patients. In every case except one the absolute value of resistance was far in excess of the values derived for the dog. The patient with low resistance (No 11) had resistance measured at above knee level, and had excellent runoff. His gangrene was very extensive, and the aetiology of his disease was probably a mixture of Buerger's disease, self inflicted damage, and frostbite, which explains why his resistance was so low compared with the rest of the group. Despite this the graphs of resistance vs. flow were of similar shape for both the amputees and the dogs suggesting that even in the presence of severe disease in the humans the distal vascular tree behaves in a similar way.

Only one set of measurements was made for each patient. None of the patients was fit, and it was felt that the anaesthetic should be kept as short as possible. The method was much more time consuming than in the dog model. This was largely due to the technical difficulty of measuring pressure in very small vessels.
severely involved with atheroma. The pressure measuring cannula was hand held and therefore prone to dislodgement from the vessel. It was important to try and maintain an angle of the opening of the needle of 90 degrees to the direction of flow within the vessel. This was to avoid the error induced due to streaming.

Clearly in this series of experiments grossly unphysiological pressures were generated in the distal artery. Had the intention been to reconstruct rather than to amputate it is possible that damage might have occurred in the distal circulation. This poses a potential problem in the method with regard to application of the investigation in clinical practice.

No problems were encountered using blood as the infusing fluid from the point of view of the patient. There was no fall in systemic blood pressure when it was withdrawn. Filling the syringes with blood was however awkward. There was not access to to a large vessel and blood had to be withdrawn by stab from the femoral artery transcutaneously. Filling time was slow and not infrequently messy. The longer filling took, the cooler the blood in the syringes became and the greater the degree of separation of the blood into red cells and plasma. Clearly it might be anticipated that this will be less of a problem in patients undergoing reconstructive surgery when the groin will be open and
there will be direct access to the femoral artery.

The 50 ml plastic syringes when full of blood tended to buckle when the pump was first switched on making it difficult to get a continuous and consistent flow at the beginning of each session. This was exacerbated in the amputation experiment by the high resistance encountered. To be viable clinically, stronger or larger syringes would be required.

In the initial dog study measurement of arterial pressure distal to the infusing cannula was no problem because a sidebranch of the main artery was used. In the amputation group however needling the artery directly was probably the single most difficult problem to overcome. The needle tended either to pass through the back of the vessel or fall back into the wall of the vessel at the front. In a small vessel the potential for damage of the intima is considerable. An alternative method for measurement of pressure is required.
CONCLUSION

This pilot study of resistance measurement in humans undergoing amputation has shown that resistance measurement in human distal arteries is feasible, and that results show a similar pattern to that achieved in the healthy canine femoral artery. There were some problems with the method; firstly pressure measurement was precarious using the needle method; secondly use of blood as the infusing fluid was timeconsuming to organise; and thirdly it was possible to generate very high pressures in the artery distally.
Chapter 5 has shown that it is feasible to measure resistance in an animal model with good reproducibility. The pilot human study on patients undergoing amputation confirmed that the method worked satisfactorily and that the resistance/flow graphs were similar though for a wider range of values than the dogs.

The technique for measurement of resistance is however cumbersome. It adds at least another 30 minutes to the time of the procedure and for this reason alone is unlikely to be useful in clinical practice in its present form. There were four main problems.

1. It took too long to fill the syringes for the infusion. By the time they were filled the blood was cooling and separating.

2. The method for pressure measurement was unsatisfactory because of the possibility of the needle damaging the vessel, and because it was difficult to keep the needle in the vessel lumen.

3. The syringes tended to buckle when full when the
pump was first switched on.

4. The technical backup required in theatre is considerable, expensive and unlikely to be available routinely to most surgeons.

The aim of this second study on dogs was to address the above problems, and see whether it might be possible to measure resistance in any other way.

Dardik, Ibrahim, Sussman et al (1981) suggested that the 'feel' of the syringe when injecting contrast for the arteriogram gave an indication of the distal disease. They were basically using a constant pressure method for the assessment of resistance noting how long it took for the contrast to be injected. In theory there is no reason why resistance cannot be measured by a constant pressure method. To be useful the same pressure would need to be used on every occasion so that comparisons could be made. One aspect of this experiment therefore was to employ a constant pressure infusion. Flow has been measured by timing the injection of known volumes of the infusion solution. If accurate this method would provide a cheaper alternative method of measurement of resistance which might then be more available clinically.

The problem of damage to the artery by the pressure measuring needle has been studied by measuring pressure through a concentric cannula and through a
sidearm and comparing these with the stab method.

In order to try and save time in the measurement of resistance other infusion solutions have been used in addition to blood. Normal saline and Dextran are readily available and represent solutions with viscosity both higher and lower than blood.

**METHOD**

Four dogs were used in this study. Resistance was measured in two vessels of different calibre. As previously, the superficial femoral artery provided one runoff distally to the foot. A medium sized muscular branch of the superficial femoral artery immediately distal to the inguinal ligament was used for the other.

**ANAESTHETIC**

As before each animal was given a general anaesthetic. It was induced with thiopentone and was maintained with nitrous oxide, oxygen, and halothane. Ventilation was again performed by closed circuit administration of the gases through a Manley ventilator. At the end of the experiment the dogs were destroyed by the administration of a large dose of intravenous barbiturate. Fluids were given through a cannula in the
cephalic vein to maintain the central venous pressure at approximately 5mmHg. Little extra fluid was actually required because so much was given as a part of the experiments. During the procedure pulse, central venous pressure and visceral blood pressure were recorded continuously on a chart recorder. Arterial blood gases were also checked at intervals in an attempt to maintain a stable preparation. Visceral blood pressure was measured by cannulation of a branch of the superior mesenteric artery. The cannula was connected by means of a manometer line to a pressure amplifier and thence to a chart recorder. Central venous pressure was measured through a 15cm cannula inserted into the left anterior jugular vein. This too was connected via a pressure amplifier to the chart recorder. ECG was monitored by leads attached to the chest of the animal connected to an appropriate amplifier, displayed on a monitor and as pulse rate on the chart recorder. Urine output was monitored by catheterisation and collection of the urine in a graduated flask.

**THE MODEL**

Once anaesthetised the dog was placed on its back on the operating table and its legs were strapped out. As before sandbags were placed along the trunk to
PERIPHERAL RESISTANCE MEASUREMENT Ch. 7

prevent it from twisting over and the warming blanket was set to 38 degrees centigrade. A single incision was made extending from 7cm below the xiphisternum in the midline down the midline to the the point marked by a line perpendicular to the inguinal ligament passing through the femoral artery. The incision was then taken along this line and into the upper part of the thigh. The hindlimb was then rendered ischaemic by the technique of Johansen and Bernstein (1979). However proximally the main trunk of the external iliac and superficial femoral arteries were left unligated. Distally ligation was carried approximately 12cm down the thigh to just beyond the origin of the saphenous artery. A single posterior muscular branch, which was consistently present and positioned about 1cm distal to the inguinal ligament was left unligated. This provided one of the two runoffs down which resistance would be measured. A sidebranch of this muscular branch was cannulated with a 20 gauge cannula. This was for the 'needle' stab pressure measurement. The cannula was connected to the chart recorder by a manometer line, pressure transducer and pressure amplifier. Distally in the thigh the saphenous artery was similarly cannulated and connected to the chart recorder. All branches in the thigh proximal to the saphenous artery were ligated. The second runoff was the main superficial femoral artery
Figure 14.

Twenty gauge cannulae have been placed in the femoral artery at inguinal ligament and midthigh position.
whose pressure was being measured by the cannula in the saphenous artery as shown in Figure 14.

The infusion was performed by the Harvard pump but the 50ml plastic disposable syringes were exchanged for two 100ml glass syringes (Fisons). The syringes were not heparinised. Instead the dog was heparinised systemically. During the course of the experiment the syringes were refilled with blood approximately twelve times. It was felt that there would be difficulties with control of blood clotting towards the end of the experiment if the syringes were heparinised each time they were refilled. Each dog was therefore given heparin by continuous infusion through a cannula sited in the right anterior jugular vein. The dose given was 200 units by bolus injection at the start of the experiment followed by an infusion of 500 units/hour. Using this regimen, which was derived empirically on a weight basis from the human infusion dose of 30,000 units/day, there was no obvious problem clinically with either over or under anticoagulation.

The infusion cannula was also altered to accommodate pressure measurement by concentric and sidearm techniques. The cannula used for the infusion was a 14 gauge Cathlon type. Connected immediately to it was a 'Y' adaptor (Vygon) with Luer type connectors. One limb of the 'Y' was closed with a plastic cap, in the
Figure 15

The completed concentric cannula ready for use.
centre of which was a rubber diaphragm. Through this diaphragm was placed a 20 gauge epidural catheter. The catheter passed down the main infusing cannula and was cut to length so that 1.5cm of it projected beyond the tip of the main cannula (Figure 15). A 14 gauge cannula was used to accommodate the epidural catheter without excessive narrowing of the main channel. The other limb of the 'Y' was connected directly to a 3-way tap. One limb of the 3-way tap was connected to the syringes on the harvard pump with a manometer line. The other limb, the sidearm pressure, was connected to a pressure transducer and thence to the chart recorder. Once assembled the cannula was inserted into the superficial femoral artery approximately midway between the two runoffs and facing distally.
The experiment was undertaken in three parts. When each part had been completed once, the whole routine was repeated.

1. In order to use the sidearm method for measuring pressure it is necessary to know the resistance of the cannula distal to it. Ideally it should be constant. The resistance of the infusing cannula was measured by connecting up the component parts of the cannula and connecting it to a syringe filled with blood. The pump was then set to 45ml/min and run with the cannula open to the air. Pressure was measured in the sidearm. The resistance was then calculated from this pressure and the preset flow from the pump. The resistance was measured at three further flow rates slightly different from the previous experiments; 83, 117, and 153 ml/min. Having completed the resistance measurement with blood the procedure was repeated using first saline and then Dextran.

2. Resistance was measured as in the initial dog study. Blood was infused into the superficial femoral artery at four flow rates; 45, 83, 117, and 153 ml/min. Firstly the distal runoff was clamped so that resistance
was measured in the proximal runoff. Then when this had been completed at each of the flow rates the proximal runoff was clamped and the measurements were repeated in the distal runoff. This procedure was then performed for saline and Dextran. All of the solutions were maintained at 38 degrees centigrade.

3. All measurements of resistance were made by measuring pressure simultaneously by the 'stab', concentric and sidearm techniques. The accuracy of the sidearm and concentric cannula techniques could then be compared with the 'Stab' technique.

4. Resistance was measured using a constant pressure infusion. A hand held 100ml glass syringe filled with blood was connected to the infusing cannula. Infusion was commenced and recording of the flow was begun when a steady pressure had been achieved in the 'stab' pressure line. A timed infusion of known volume was then performed so that the flow could be calculated. At least three recordings of resistance were made in this way in each of the runoffs and with each of the solutions. An attempt was made to use the same pressures each time so that the results could be compared.

Between measurements the superficial femoral
artery was unclamped so that blood could come into the
limb through the external iliac artery and prevent the
limb from becoming ischaemic. This first set of
measurements were therefore made 'at rest'. After
completion of the first set of measurements, the
external iliac artery was then clamped permanently.
After an hour all the measurements were repeated with
the assumption that the peripheral vasculature was
maximally dilated due to the ischaemic interval.
RESULTS

1. CANNULA RESISTANCE

The resistance between the sidearm and the tip of the infusing cannula has been calculated for each of the infusing solutions at four flow rates - 45, 83, 117, and 153ml/min. The results are shown in Table 1 in the Appendix (page C3) and Figure 16. For each cannula and for each solution except Dog 13 (blood) there was a small steady parallel rise in resistance with increasing flow. The absolute values were greatest for Dextran and smallest for saline. Combining the resistances at all four flow rates and allowing for the fact that there was a wide range of resistances, resistance measured with blood was significantly greater than saline in Dog 12 (p<0.05), and Dog 14 (p<0.05). Similarly Dextran resistance was greater than saline in Dog 12 (p<0.05) and Dog 13 (p<0.05). In one case Dextran resistance was significantly greater than blood - Dog 12 (p<0.05). There were striking differences between dogs however with a range of resistance at 45ml/min of between 266mPRU and 444mPRU for blood, 166mPRU to 400mPRU for saline and 366mPRU to 555mPRU for Dextran. These differences were repeated at each of the flow rates.
Cannula resistance for the four dogs has been plotted against flow for each of the infusion solutions. Resistance increases with flow, and with the viscosity of the infusing fluid. There is wide variation.

Figure 16
DISCUSSION

The resistance of the cannula was 100-700mPRU which indicated that despite using a large cannula its resistance was still moderately high.

To be useful in practice a sidearm technique of pressure measurement requires that the resistance of the cannula between the sidearm and the patient is always the same and preferably minimal. If it is not then the resistance of the cannula must be calculated each time it is used. These results show a wide variation in resistance measured for each of the solutions and that the resistance actually increases slightly with increasing flow. It is very unlikely that in clinical practice it would be possible to calibrate a cannula each time resistance was measured. The differences in resistance measured are presumably due to small differences in the diameter of the 14 gauge cannula and the epidural catheter down the middle. Differences in resistance with blood could be accounted for by differences in haematocrit but this is not the case for the saline or Dextran. The resistance of the cannula could have been reduced by removing the concentric epidural catheter. Measurements were not made under these circumstances, but irrespective of this possibility the cannula would still have presented some
resistance. On the basis of these observations it would seem that a sidearm measurement of pressure is not viable, and that the same changes occur with each of the infusion solutions.
2. SIDEARM CONCENTRIC AND 'STAB' RESISTANCE

In each of the experiments pressure was measured simultaneously by the three methods. Results of these simultaneous pressure measurements are shown in Tables 2, 3, and 4 in the appendix (pages C4-6). There were 63 sets of measurements for the blood, 59 for saline and 61 for Dextran. Mean pressure measured by the sidearm was significantly greater than that measured by the 'stab' for all of the solutions; blood t=2.63 p<0.005; saline t=2.148 p<0.05; and Dextran t=2.699 p<0.005 (Paired t test). There was no significant difference between the mean pressures measured by the concentric cannula and 'stab'. There was excellent correlation between concentric pressure and 'stab' pressure.

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<td>Saline</td>
<td>0.9976</td>
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<tr>
<td>Dextran</td>
<td>0.991</td>
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Concentric vs. 'stab' pressure

However when comparing the sidearm with the 'stab' the correlation was much less good.
Concentric and sidearm pressure vs. 'stab' pressure.
The best correlation is found between the concentric and 'stab' methods.

Figure 17

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### PERIPHERAL RESISTANCE MEASUREMENT

#### Ch. 7

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#### Sidearm vs. 'stab' resistance

The above results are shown in graph form in Figure 17.

When combining the measurements from the three solutions together the results are similar.

#### Concentric vs. Stab

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#### Sidearm vs. stab

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<td>18.25</td>
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These results are shown in Figures 18 and 19. The difference between the means is highly significant for the sidearm vs. 'stab'; t=4.27 p=0.0001.
There is good correlation between the concentric pressure and the 'stab' pressure.

Figure 18
There is poor correlation between the sidearm pressure and the 'stab' pressure.

Figure 19
DISCUSSION

The important finding from these results is that there is no difference between the concentric and 'stab' pressure measurements but that both of these are significantly different from the sidearm measurement. This means that in clinical practice it will be acceptable to use a concentric cannula for pressure measurement which will make the procedure for patients much quicker, and easier. There were no technical problems in the dog using the concentric cannula, and provided that the human popliteal artery is sufficiently large there should be no problems in the human. When studying an artery at ankle level a size 14 cannula may be too large and under these circumstances it will be necessary to continue with direct needling of the vessel with a 27 gauge cannula to measure pressure and to infuse through a smaller cannula.
3. RESISTANCE - BLOOD, SALINE AND DEXTRAN

In this and subsequent experiments pressure recorded from the concentric cannula has been used to calculate the resistance. Raw data of resistance measured is shown in Tables 5, 6, and 7 in the Appendix (pages C7-9). The upper runoff has a higher resistance than the lower runoff for all solutions. If the results for each flow rate from each of the dogs are grouped together then for Dextran, the differences in resistance between upper and lower runoffs before ischaemia are significant as follows: upper runoff p<0.05 at 45, 83, and 117ml/min (there were no measurements made at 153 ml/min for dogs 11 and 12). For saline and blood the differences are also significant at 45, 83, and 117ml/min for both the upper and lower runoffs (p<0.05).

In each case for the smaller upper runoff the resistance falls as the flow increases as in the previous experiment. In the larger runoff however the resistance remained approximately the same over the range of flows tested. These results are shown in Figures 20, 21, and 22, where mean resistance ± standard error are plotted against flow.

The resistances measured after the ligation of the external iliac artery are shown on the same figures. For both runoffs the shape of the resistance/flow curve...
Pumped infusion of blood

Resistance vs. flow for blood. Resistance is higher in the smaller runoff and falls in both with increasing flow. Ischaemia does not significantly alter resistance.

Figure 20
Pumped infusion of saline

Resistance vs. flow for saline. Resistance is higher in the smaller runoff and falls in both with increasing flow.

Figure 21
Resistance vs. flow for Dextran. Resistance is higher in the smaller upper runoff and falls with increasing flow. The resistance was lower after ischaemia in the upper runoff.

**Figure 22**
is much the same and for blood and Dextran the resistance is slightly lower. For saline there was a small rise in resistance after the introduction of ischaemia for both runoffs. From the graphs it can be seen that the best separation of resistance between the two runoffs is provided by the blood, although there were also statistically significant differences in the case of both saline and Dextran.

Resistance was measured before ischaemia in the upper runoff at 83ml/min combining the measurements from each of the dogs. Resistance measured with Dextran was higher than for blood (mean 1768 mPRU SE 282 vs. 1483 mPRU SE 143) but not significantly so. There were significant differences between blood and saline (mean 1483 mPRU SE 143 vs. 701 mPRU SE 106; p<0.05) and between Dextran and saline (mean 1768 mPRU SE 282 vs. 701 mPRU SE 106; p<0.05). Similar results are found for the lower runoff before ischaemia (p<0.05) but again the differences between blood and Dextran were not significant. After the introduction of ischaemia there were no significant differences for either runoff, but for the larger runoff the resistance measured with Dextran was again highest and that measured by saline the lowest.

Considering resistance at any one flow rate then for the smaller upper runoff the introduction of
ischaemia only reduced resistance for Dextran but for saline and blood there was no significant difference. For the larger runoff introduction of ischaemia made very little difference. Papaverine has previously been shown to be a more potent vasodilator than induction of ischaemia by tourniquet (Dedichen and Myhre 1975) but use of papaverine in this experiment would not have been possible because of the large numbers of observations to be made.
DISCUSSION

From this experiment it can be seen that each of the solutions can separate the two runoffs from each other. Looking at the graphs suggests that the Dextran and blood produce a wider separation than the saline. This may prove important in clinical practice where as wide a separation as possible would be useful.

It is surprising that resistance does not fall with increasing flow for the physically larger lower runoff as it does for the smaller runoff. It may be that the pressures generated by the available flow in the larger runoff are in fact unphysiologically low and this may explain the differences.

There seems to have been no significant fall in resistance following ligation of the external iliac artery in either of the runoffs, and in fact for saline the resistance actually rose for both runoffs. This is most obvious in the larger runoff and could be explained on the basis of resistance measurement at unphysiologically low flow rates. Also it is possible that despite trying to avoid ischaemia during the early part of the experiment the runoffs were in fact ischaemic and already vasodilated. Alternatively the saline or Dextran may have affected resistance directly, or the dogs may have been becoming haemodynamically unstable after a long anaesthetic.
The results of using the different infusing solutions were predictable. Dextran being more viscous than blood or saline produced the highest resistance values. Saline being the least viscous produced the lowest resistances. The important property of the infusing solution is that it provides the widest possible separation by resistance of different runoffs. Because of its low viscosity saline is least suitable in this respect. The dogs tolerated rapid infusion of Dextran poorly with the onset of muscle fasciculation in the leg distally. Whilst this is unlikely to occur in humans the additional advantages of Dextran over blood would not justify its further use.
4. CONSTANT PRESSURE RESISTANCE MEASUREMENT

Results of constant pressure measurements are shown in Tables 8, 9, and 10 in the appendix (pages C10-12). The results are displayed graphically in Figures 23, 24, 25, 26, 27, and 28. An attempt was made to measure resistance at the same pressure for each dog and for both runoffs. For the lower runoff with the larger lumen however it was impossible with the handheld syringe to generate a pressure above 78mmHg except in 12 out of 72 cases (8 with Dextran). Flows at 75mm Hg were typically in excess of 300ml/min (range 150-720 ml/min). Similarly for the smaller upper runoff it was very difficult to get the pressure below 100mmHg (only 8/72 cases). Flow at 100 mmHg was typically 75ml/min (range 21-225 ml/min). From the Figures 24, 26, and 28 it is clear that unlike the constant flow infusions there was no clear pattern for the lower runoff in the relationship between pressure and resistance. For the upper runoff however where the pressures generated were more uniform the characteristic pattern of falling resistance with increasing pressure was observed. Comparisons involving pooling of data of all four dogs was not possible because resistance was measured at a selection of different pressures. As before resistance was higher when calculated for blood and Dextran than
PERIPHERAL RESISTANCE MEASUREMENT

Resistance falls with increasing pressure. Ischaemia does not significantly alter resistance.

**Figure 23**
Resistance was very low in each of the dogs. There was no significant relationship between pressure and resistance in this runoff.

**Figure 24**
Resistance falls with increasing pressure. The effects of ischaemia are unpredictable.

**Figure 25**
Manual infusion of saline - Lower runoff

There was no relationship between pressure and resistance. A combination of low distal resistance and the low viscosity of saline may account for this.

Figure 26
Manual infusion of Dextran - Upper runoff

Resistance falls with increasing flow. Ischaemia has no consistent effect on resistance.

Figure 27
There was no significant relationship between resistance and flow before or after ischaemia.

Figure 28
it was for saline. After the induction of ischaemia the resistance did not fall uniformly and in some cases rose to higher levels. This was true for both runoffs and for all three infusing solutions.

The only real comparison which could be made was between the constant pressure and constant flow data. Where flow generated by the constant pressure technique was close to the flow used in the constant flow measurements (within 10%) a comparison of resistances has been made. There were 26 suitable measurements. The correlation coefficient between them was 0.9267. The gradient of the regression line was 0.746 and the intercept 236.6. These results are shown in Table 11 in the Appendix (page C13) and in Figure 29.
Constant pressure vs. constant flow estimate of resistance. Correlation between methods is good.

**Figure 29**
DISCUSSION

The correlation data between the constant flow and constant pressure measurements of resistance is acceptable indicating that resistance could be measured by this technique. However in practice it was not possible, given the two runoff resistances provided by this dog model, to measure resistance at a single pressure.
There were four main aims to this chapter. The first was to see whether it was possible to use a solution other than blood for infusion. This would simplify matters considerably by speeding up the preparation. Saline proved to be unsuitable because, as a result of its low viscosity, all measured resistances were low and it failed to adequately separate the two runoffs. Dextran showed some promise producing greater separation than blood presumably because of its greater viscosity. However further experiments with Dextran in humans would need to be undertaken with caution given the worrying incidence of muscle fasciculation in the dog model.

The easiest method of pressure measurement would undoubtedly be to employ a sidearm. However the resistance between the sidearm pressure transducer and the tip of the infusing cannula was so variable that it would have been necessary to recalibrate the cannula for each measurement of resistance. In addition the relationship between resistance and flow was not constant, resistance increasing with increasing flow, so that calibration for each flow rate would also be required. There were no such differences between the concentric method and the 'stab' method, and therefore
in the rest of this thesis the 'stab' method has been replaced by the concentric method.

The problem of the buckling syringes was solved easily by replacing them with more durable glass syringes.

Infusing the solution by hand at constant pressure is an attractive alternative to the use of the pump being cheaper. Where flows were similar to those achieved by the pump there was good correlation between resistances measured by the two methods. One of the problems with the experimental model was that the larger of the two runoffs was too large and that the flows generated in it were unphysiologically low. For the constant pressure method of resistance measurement this was important because there is a limit to how rapidly it is possible to inject blood or Dextran through a 100 ml syringe. Although therefore constant pressure resistance measurement did not work in this instance it might be more successful in humans where the vessels are more uniform in size.
CHAPTER 8

FEMOROTIBIAL AND FEMOROPPLITEAL RESISTANCE

INTRODUCTION

The aim of this next chapter is to determine whether the changes applied in the second dog experiment are applicable to the human. The 'stab' method of resistance measurement has been replaced by the concentric method. Blood continues to be used as the infusion solution and, because they were done at about the same time as the second dog experiments, saline was used in a small number of cases to compare with blood. A constant flow technique is used to measure resistance.

The chapter has been divided into six sections. Each relates to resistance measured in patients undergoing either femoropopliteal or femorotibial reconstruction. The first section examines the technique of measurement. The second examines and compares resistance measured in the two groups above with the original group of amputees. The third section examines the place of papaverine induced vasodilation in measurement of resistance in the femoropopliteal group. The fourth section compares resistance measurement with radiological runoff. The fifth section relates
resistance to patency in both the femoropopliteal and femorotibial groups, and the sixth section studies the influence of site of graft insertion.

AIMS

The main aim was to apply the technique with its modifications to a further set of patients to ascertain whether resistance measurement might be useful as a predictive test in patients undergoing femorodistal reconstructive procedures.

PATIENTS

Two groups of patients undergoing reconstructive surgery have been studied in detail. The first group were all undergoing femorotibial reconstruction to a single vessel beyond the popliteal trifurcation. The details of these patients are shown in Figure 30. The mean age of the group was 68.15. There were seven females in the group. Eight had hypertension, four had had at least one myocardial infarction, and three more had angina. There were nine diabetics, one on diet control, six on oral therapy and two on insulin. All but five were either smokers or ex-smokers, and the non-smokers included two diabetics. Eight of the patients had undergone previous vascular surgery
including one who had already had an ipsilateral femoropopliteal graft. All patients had rest pain and critical ischaemia and thirteen had either ulcers or gangrene.

The operative details of the group are summarised in Figure 31. There were five femoro-posterior tibial grafts, three femoro-peroneal grafts and twelve femoro-anterior tibial grafts. All but two of the group had an adjunctive arteriovenous fistula placed at the level of graft insertion to increase flow down the leg (Ibrahim, Sussman, Dardik et al 1980). All but three of the procedures were performed with a distal anastomosis at the level of the ankle. The remaining three were performed at midcalf level. All of the operations except
### PERIPHERAL RESISTANCE MEASUREMENT

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1. Popliteal embolectomy
2. Phenol block
3. Lumbar sympathectomy
4. Femoropopliteal graft
5. Profundaplasty

- BP° - Hypertension
- MI - Myocardial infarct
- CVA - Stroke
- DM - Diabetes mellitus
- XSm - Ex smoker
- PrS - Previous surgery
- Gang - Gangrene
- Ang - Angina
- D - Diet control

For further definition of labels see page 117.

**Figure 30**
one were performed by a single Consultant surgeon, the remaining operation being performed by the author. Six patients had a simultaneous ipsilateral amputation of toes or part of the foot. Four patients required at least one embolectomy in the immediate postoperative period. The majority of the procedures were performed with prosthetic grafts. There were nine umbilical vein grafts, five in situ saphenous vein grafts and seven composite umbilical and saphenous vein grafts. The composite vein grafts were used because of the difficulty in performing the distal anastomosis between umbilical vein and the front of an arteriovenous fistula and to reduce the cost of the procedure by reducing the length of umbilical vein required. The saphenous vein was placed distal to the umbilical vein to facilitate this anastomosis.
### FEMOROTIBIAL GRAFTS - OPERATIVE DETAILS

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**F-PT** - Femoro-posterior tibial graft  
**F-AT** - Femoro-anterior tibial graft  
**F-PN** - Femoro-peroneal graft  
**I-PT** - Ilio-posterior tibial graft  

**M/C** - Mid calf  
**ISVG** - In situ saphenous vein graft  
**UVG** - Umbilical vein graft  
**UVG+SVG** - Composite umbilical and saphenous vein graft  
**UVG+BVG** - Composite umbilical and basilic vein graft

Con - Consultant surgeon  
SReg - Senior registrar surgeon  
* - Present  
- - Absent

---

**Figure 31**

Page 113
The second group were all undergoing femoropopliteal grafting. The patient details are summarised in Figure 32. Forty patients were included and they underwent a total of 44 operations. The mean age at operation was 64.04. Ten of the patients were hypertensive at the time of surgery, three had had a myocardial infarction, and two had had a previous stroke. Seven patients were diabetic, one with diet control, two on insulin and four on oral therapy. There were five non smokers, the rest being either active smokers (twenty one) or ex-smokers (fourteen). Thirteen patients had undergone previous vascular surgery. Sixteen patients had either ulcers or gangrene and the rest had either disabling claudication or rest pain.

The operative details of the group are shown in Figure 33. There were ten above knee and thirty four below knee reconstructions. Below the knee there were sixteen grafts placed on the popliteal artery above the origin of the anterior tibial artery, seven placed on the tibio-peroneal trunk, five to the tibio-peroneal trunk straddling into the posterior tibial artery, one on the tibio-peroneal trunk straddling into the peroneal artery, two to the posterior tibial artery immediately distal to its origin and three to the peroneal artery immediately distal to its origin. There were six pure umbilical vein grafts, four composite umbilical and
saphenous vein grafts, twelve polytetrafluoroethylene
grafts, two reversed saphenous vein grafts, and twenty
in-situ saphenous vein grafts. Fourteen of the grafts
were performed by a consultant surgeon and the rest were
performed by the author. There were ten additional
procedures performed including six local amputations
within the foot, three simultaneous aortic bifurcation
grafts, and an iliac angioplasty. Eleven of the patients
required an embolectomy in the immediate postoperative
period. Five of the grafts were sewn to dacron from a
previous aortic bifurcation graft and one graft took
origin from the external iliac artery.
### FEMOROPOPLITEAL GRAFTS - PATIENT DETAILS

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**Figure 32 (1)**

Cont...
**PERIPHERAL RESISTANCE MEASUREMENT**  
*Ch. 8.1*

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6 - Aortic bifurcation graft  
7 - Amputation of toes  
8 - Carotid endarterectomy  
9 - Contralateral femoropopliteal graft

For a detailed definition of labels see page 111

**Figure 32 (2)**
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**Figure 33 (1)**

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<td>SR</td>
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F-PT - Femoro-posterior tibial graft  
F-AT - Femoro-anterior tibial graft  
F-PN - Femoro-peroneal graft  
I-PT - Ilio-posterior tibial graft  
D-TPT - Dacron-tibioperoneal trunk  
M/C - Mid calf  
ISVG - In situ saphenous vein graft  
UVG - Umbilical vein graft  
UVG+SVG - Composite umbilical and saphenous vein graft  
RSVG - Reversed saphenous vein graft  
Iliac Ang - Iliac angioplasty  
ABG - Aortic bifurcation graft  
Amp - Amputation  
Con - Consultant surgeon  
SR - Senior registrar surgeon  
B/K - Below knee graft insertion  
A/K - Above knee graft insertion  

Figure 33 (2)
In each case the artery to be reconstructed was first mobilised and controlled with silicone rubber slings. In every case an arteriogram was performed using the largest cannula compatible with the size of the vessel under study. This was done to confirm or expand upon the findings of the preoperative arteriogram. An inflow study was performed with measurement of femoral/aortic pressure gradient before and after papaverine injection (Sako 1966 and Quin, Evans and Bell 1975). If this investigation indicated the presence of proximal disease proximal reconstruction was performed prior to distal reconstruction. Next 100ml of blood was withdrawn from the common femoral artery into two previously heparinised glass syringes and these were mounted onto the Harvard pump. For the femorotibial grafts the artery under study was then cannulated with a size 20 Cathlon cannula. For the femoropopliteal grafts the popliteal artery was cannulated with the composite double lumen cannula previously described.

Chronologically most of the femorotibial grafts were performed before most of the femoropopliteal grafts. In the early stages a smaller Harvard pump was in use and the flows generated were slightly different from those measured latterly. For most of the
femorotibial and for several of the early
femoropopliteal grafts resistance was measured at 9.5,
19.1, 38.2, 76.4, and 190 ml/min. When the new pump
became available resistance was measured at 45, 81, 117,
and 153 ml/min. From patient 37 onwards pressure was
only measured at 81 ml/min. The low rates of infusion in
the early experiments were abandoned because the
pressure generated by the low infusion rate was often
insufficient to raise the pressure above the prevailing
collateral pressure. This would clearly render any
resistance measurement meaningless. In the
femoropopliteal group resistance was measured both
before and after the administration of papaverine. This
was not done in the femorotibial group and reflects the
fact that most of the grafts were performed before the
femoropopliteal grafts. Venous pressure was measured in
every case in the femoral vein by a separate needle
cannulation.

In a small group of femoropopliteal grafts
pressure was measured simultaneously by the concentric
cannula and by the sidearm technique to confirm the
findings noted in the animal experiments.

After grafting, pressure and flow in the graft
itself were recorded both before and after the
administration of papaverine so that the resulting
resistance could be compared with the resistance
measured prior to grafting.

**FOLLOW UP**

After the operation all patients in the femoropopliteal group and the majority of the patients in the femorotibial group were followed up either until the graft occluded or until the February 1st 1986. The minimum follow up time was eight months though all but two grafts had been performed more than 13 months previously. Three of the femorotibial group had been referred from distant centres and were followed up by the referring Surgeon locally. Details of outcome were obtained by telephone enquiry. Where there was any doubt about continuing patency a combination of ankle pressure measurement and Duplex scanning was used to resolve the question.
RESULTS

The results of these experiments will be presented and discussed under a number of headings. At the end of the Chapter the results will be summarised.

METHOD OF PRESSURE MEASUREMENT

In ten patients undergoing femoropopliteal grafting sidearm and concentric cannula measurements of pressure have been made both before and after papaverine. These measurements of pressure have been made with both blood and saline. The results of this experiment are shown in Tables 1-3 in the Appendix (pages D3-5). Resistance has been calculated by both of the methods and the ratio of concentric resistance to sidearm resistance has been calculated.

1. Blood. The results show that in each case the concentric resistance is lower than the sidearm resistance. The ratio between the two methods however varies widely between 0.28 and 0.815. The same findings are true after papaverine where the ratio is between 0.13 and 0.52. Prior to papaverine there is an acceptable correlation between the two methods $r=0.9411$ (Figure 34). Interestingly however the same correlation after papaverine is very poor $r=0.1480$
Concentric vs. Sidearm resistance measurement

Correlation between the sidearm and concentric measurements of resistance before papaverine is good.

*Figure 34*
Concentric vs. Sidearm resistance measurement

Correlation between the sidearm and concentric measurements of resistance after papaverine is poor.

Figure 35
Similarly the correlation between resistances measured before and after papaverine but by the same method is poor (for the concentric cannula r=0.1672 (Figure 36) and for the sidearm r=0.8348 (Figure 37). The mean difference in resistance between the two methods before papaverine was 714 mPRU (SE 46). After papaverine the mean difference was 819 mPRU (SE 79).

2. Saline. For saline there were only measurements available for six patients (Table 3 in the Appendix on page D5). As with the blood, the resistance measured by the concentric cannula was lower than that measured by the sidearm method. The ratio of the two resistances on any one occasion was as wide as it was for the blood measurements 0.28-0.84. The correlation between the two methods was poor prior to papaverine r=0.7086, and there were no results in the saline group after papaverine. The resistance measured with blood was higher than that measured with saline and the correlation between the resistances measured with the two different fluids was poor r=0.5690 for the concentric cannula and r=0.8829 for the sidearm. The mean difference in resistance measured by the two methods where comparison between fluids was available was 633mPRU (SE 66) for blood and 380 mPRU (SE 78) for saline.
Resistance pre and post papaverine - concentric cannula

There is poor correlation between resistances measured before and after papaverine by the same method.

**Figure 36**

Page 127
Resistance pre and post papaverine - sidearm cannula

There is poor correlation between resistances measured before and after papaverine by the sidearm cannula.

Figure 37

Page 128
DISCUSSION

If the two methods of pressure measurement were interchangeable the ratio or resistances measured should have been the same. In this small series there was wide variation. This is probably due to variations in the size of the component parts of the concentric cannula. Small variations in the length and diameter of either the cannula or the epidural catheter threaded through it or in the internal dimensions of the three way tap allowing attachment of the sidearm will effect the resistance measured in the sidearm. The results with saline indicate no advantage in its use since the variation between methods is as wide as for blood. It is interesting to note that the mean difference in resistance between methods with saline is approximately half that found with blood. This is a clear manifestation of the effect of the higher viscosity of blood compared with saline resulting in a proportionately higher sidearm pressure recording with blood than with saline. The difference is significant (t-test p<0.02).
Section 2

RESISTANCE AND OPERATION - PRE-PAPYVERINE

INTRODUCTION

With the addition of the femorotibial and femoropopliteal groups to the amputation group of patients there are three distinct groups of patients available for study. In this section the resistance measured for the three groups is compared. There has been no attempt to divide the patients into subgroups and the comparison has been made at all the available flow rates. Eight patients have been excluded. In the femorotibial group patients 11, 12, and 20 have been left out because resistance was not measured at ankle level as it was for the rest and it was felt that this would bias the results. In the amputation group patients 5, 6, and 11 have been excluded because resistance was measured in the above knee popliteal artery. In the femoropopliteal group patients 6 and 14 were excluded because the results were technically unsatisfactory at the time of measurement. In both there was significant leakage of blood around the cannula during the infusion resulting in a lower result than would have been expected.
AMPUTATION

The results for this group have already been described in Chapter 6. The main results are shown again in Figure 38. In this group resistance has been measured at five flow rates; 9.5, 19.1, 38.2, 76.4, and 190 ml/min. The significant differences between the resistances measured at the five flow rates is also summarised in Figure 38.

PESFORTIBIAL GROUP

The results for this group are shown in Table 4 in the Appendix (pages D6-8). It will be noted that in this group the flows at which resistance has been measured change approximately half way through the series. This coincided with the acquisition of a new Harvard pump which had slightly different flow ranges from the old one. The new range of flows was 45, 81, 117, and 153 ml/min. The results from Table 4 in the Appendix have been summarised by flow rate in Figure 39. In the following results levels of significance refer to resistances measured at higher flow rates for each individual flow. Resistance at 9.5 ml/min was significantly higher than that
### PERIPHERAL RESISTANCE MEASUREMENT

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<td>1910</td>
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| Mean | 11960| 8351 | 2654 | 2092 | 759        |
| SE   | 2927 | 1922 | 628  | 617  | 218        |

--- p<0.001 ---

----- p<0.01 -----

----- p<0.01 -----

^- p<0.05 -

**Figure 30**

---

Page 132
measured at 45 ml/min p<0.001, 81 ml/min p<0.001, 117 ml/min p<0.001, and 153 ml/min p<0.001. Resistance at 9.5 ml/min was lower than that measured at 19.1 ml/min. Resistance at 19.1 ml/min was significantly higher than resistance measured at all the other flow rates except 38 ml/min; at 45 ml/min, 81 ml/min, 117 ml/min and 153 ml/min p<0.001; at 76 ml/min p<0.01. Resistance at 38.2 ml/min was significantly greater than resistance at 45 ml/min, 81 ml/min, 117 ml/min and 153 ml/min p<0.001. At 45 ml/min resistance was significantly less than that measured at 76 ml/min p<0.001 and 117 ml/min p=0.009. At the other flow rates there were no significant differences. At 76 ml/min resistance was significantly greater than at 81 ml/min, and at 117 ml/min p<0.001; it was also greater than at 153 ml/min p<0.01. At 81 ml/min there were no differences with higher flow rates. Similarly there was no difference between resistances at 117 ml/min and 153 ml/min. These results are summarised in Figure 40. It will be noted that in Figure 41 the resistances at 38.2 ml/min have been combined with those at 45 ml/min as have the resistances at 76.4 ml/min and 81 ml/min. This has been done since the resistances have been measured at similar flow rates. However in the femorotibial group there are significant differences between the resistances measured individually and those that have been grouped together.
### FEMOROTIBIAL GROUP - SUMMARY OF RESISTANCE

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**Flow** 76 81 76/81 117 153 ml/min

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</table>

**Figure 39**

Page 134
Resistance at 38/45 ml/min is significantly higher than at 45 ml/min alone $p<0.001$ but not significantly different from that measured at 38.2 ml/min. Similarly resistance at 76/81 ml/min is significantly greater than resistance at 81 ml/min alone $p<0.025$ but not significantly different from the resistance at 76.4 ml/min.
Resistance falls with increasing flow.

Resistance at 45 and 81 ml/min is significantly lower than at 38 and 45 ml/min.

**Figure 40**
Femorotibial grafts - Mean resistance ± SE vs. flow

38/45 ml/min and 76/81 ml/min combined. After an initial rise resistance falls significantly with increasing flow.

Figure 41
DISCUSSION

As with the amputation group the resistance measured in the femorotibial group falls with increasing flow rates. The measurements are complicated by the change in flow rates that occurred half way through this group. The new flow rates were chosen partly through necessity having acquired the new pump and partly because it had become clear that resistance measured at the very low flow rates was both excessively high and unreliable. 45 ml/min was as close as it was possible to get to 38 ml/min and 81 ml/min was as close as it was possible to get to 76 ml/min. The extra flow rate at 117 ml/min was chosen to fill the gap between 81 ml/min and 153 ml/min. The differences in resistance between 38 and 45 ml/min and between 76 and 81 ml/min are significant but in spite of this the two groups of flows have been grouped together.
FEMOROPOPLITEAL GROUP

The results for the femoropopliteal group are shown in Table 5 in the Appendix (pages D9-13) and are summarised in Figure 42. As with the femorotibial group some of the patients have had resistance measured at the earlier set of flows. The majority however have been measured with the new pump. Patients 37, 38, 39, and 40 have had resistance measured only at a single flow rate - 81 ml/min. The resistance fell with increasing flow rates, and the mean resistances are plotted on Figure 43. The resistance measured at 9.5 ml/min was significantly greater than that measured at any other flow rate; 38 ml/min p=0.0084, 45 ml/min p=0.0016, 76 ml/min p=0.0001, 81 ml/min p=0.0003, 117 ml/min p=0.00003, 153 ml/min p=0.00003. At 38.2 ml/min resistance was again higher than at higher flow rates; 76 ml/min N/S, 81 ml/min p=0.008, 117 ml/min p=0.0003, and 153 ml/min p=0.00007. At 45 ml/min resistance was higher than at 76 ml/min p<0.05, 81 ml/min p=0.001, 117 ml/min p<0.00003, and 153 ml/min p<0.00003. Resistance at 76 ml/min was higher than resistance at 153 ml/min p=0.0089, at 117 ml/min there was no significant difference p=0.0823. Resistance at 81 ml/min was significantly higher than at 117 ml/min p=0.0139, and at 153 ml/min p=0.0005. Resistance at 117 ml/min was not
PERIPHERAL RESISTANCE MEASUREMENT

FEMOROPOPLITEAL GROUP - SUMMARY OF RESISTANCE

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| Mean  | 2489 | 1565 | 1383| 1434  | 1068     |
| SE    | 346  | 258  | 113 | 107   | 176      |

*Figure 42 (1)*
### Femoropopliteal Group - Summary of Resistance

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*Figure 42 (2)*
Femoropopliteal grafts - Mean resistance ± SE vs. flow

Resistance falls progressively with increasing flow. There are significant differences in resistances measured between adjacent flows.

Figure 43
significantly different from resistance at 153 ml/min. When the results at 38 ml/min and 45 ml/min were combined there was no significant difference between the combined resistance and resistance measured at either flow singly. Similarly combined resistance at 76 ml/min and 81 ml/min was not significantly different to that measured at either of the flow rates singly.
The same decrease in resistance has been shown with increasing flow for this group as the two preceding groups. In this group the change in flow rates has had less effect on the results, since there is no significant difference between the combined and single resistance measurements. It is therefore reasonable to perform further comparisons using the combined figures. Resistance has been shown to fall with increasing flow in a remarkably consistent way in dogs, and in patients undergoing amputation, femorotibial and femoropopliteal grafting. In each situation the resistance falls rapidly at low flow rates and tends to level out from 80 ml/min. For this reason, and to simplify and speed up the procedure in theatre, resistance has only been measured at 81 ml/min latterly in the femoropopliteal group. It is probable that a flow of >100 ml/min would be more desirable but since the majority of the early studies have been performed most frequently at 76, 81, or 83 ml/min this rate was chosen.
INTERGROUP COMPARISON

Using the raw data obtained from the three groups it is possible to draw comparisons between them.

1. **9.5 ml/min.** The resistance of the amputation group was greater than the femorotibial group which was in turn greater than the femoropopliteal group; \( p < 0.01 \) and \( p = \text{NS} \) respectively.

2. **19.1 ml/min.** There was only data available for the amputation and femorotibial groups. Whilst the resistance of the femorotibial group was lower than the resistance of the amputation group; mean 5788 mPRU SE 1127 vs. mean 8862 mPRU SE 2276 the difference was not significant.

3. **38.2 ml/min.** The resistance of the femorotibial group was actually higher than that of the amputation group but the difference was not significant; mean 4106 mPRU SE 823 vs. mean 3123 mPRU SE 808. Both the femorotibial and amputation groups had significantly higher resistance than the femoropopliteal group; \( p < 0.001 \) and \( p < 0.025 \) respectively (mean resistance of femoropopliteal group 1565 mPRU SE 258).

4. **45 ml/min.** There was no data for the amputation group but the resistance of the femorotibial group (mean 812 SE 227) was significantly lower than the femoropopliteal group (mean 1363 mPRU SE 113);
P=0.03.

(5) **Combined 38.2 and 45 ml/min.** The combined group resistances were only available for the femorotibial and femoropopliteal groups where the resistance of the former (Mean 3075 mPRU SE 666) was significantly higher than the latter (Mean 1434 mPRU SE 107); p<0.005.

(6) **76.4 ml/min.** The femorotibial resistance was higher than the amputation group and again there was no significant difference (mean 2516 mPRu SE 257 vs. mean 2121 mPRU SE 701). Both of these groups had significantly higher resistance than the femoropopliteal group (Mean 1068 mPRU SE 176); P<0.001 and P=0.025 respectively.

(7) **81 ml/min.** At this flow measurements were available for the two reconstruction groups. Resistance of the femorotibial group (Mean 816 SE 80) was slightly but not significantly lower than the femoropopliteal group (Mean 956 mPRU SE 71).

(8) **Combined 76.4 and 81 ml/min.** For the combined groups the femorotibial (Mean 1983 mPRU SE 295) resistance was significantly higher than the femoropopliteal resistance (Mean 986 mPRU SE 68); P<0.0003.

(9) **117 ml/min.** Measurements at this flow rate were not available for the amputation group. The
resistance of the femoropopliteal group (Mean 761 mPRU SE 68) was slightly higher than the resistance of the femorotibial group (Mean 696 mPRU SE 69) but the differences were not significant.

(10) 153 ml/min. Again at this flow figures were only available for the femoropopliteal and femorotibial groups. Femoropopliteal resistance (Mean 673 SE 68) was lower than femorotibial resistance (Mean 901 SE 289) but the differences were not significant.

The results at 38/45 ml/min, 76/81 ml/min, 117 ml/min, and 153 ml/min are shown in graph form in Figure 44.
Resistance vs. flow - pre papaverine - Three groups

At 38/45 and 76/81 ml/min femoropopliteal resistance is significantly lower than in either of the other groups.

Figure 44
Comparing the three groups it is clear that the resistances measured at the extremes of flow are not able to separate the three groups. At 9.5, 19.1, 117, and 153 ml/min there were no significant differences. The reason for this is not clear. At low flow rates the pressure generated by the infusion is often not significantly higher than the preceding collateral pressure (Tables 4 and 5 in the Appendix (pages D6-13). Ideally infusion pressure will be considerably greater than collateral pressure. If this is not the case then the resistance measured must inevitably be inaccurate. At the highest flow rates again the resistances become similar. There are two possible explanations for this. Firstly it may be that there are inadequate numbers of observations at the high flow rates. Secondly it might be that when the flow rate is unphysiologically high all the blood vessels in the limb distal to the infusion become maximally dilated and that normally closed or very small vessels open up to accommodate the enhanced flow. If this were the case resistance would reflect the end arterial resistance made up by the arteriolar bed. This resistance is likely to be the same irrespective of the severity of the disease present and would depend upon the bulk of tissue
being supplied by the artery under study. At 38 - 81 ml/min however it is possible to separate the femoropopliteal from the two other groups both of which have a significantly higher resistance. At 117 ml/min the resistance of the femoropopliteal group was higher than the femorotibial group. The numbers in the femorotibial group were small but this alone is not enough to account for this finding. The most likely explanation is that the femoropopliteal group had a higher resistance as a result of having poorer runoff relative to the femorotibial group. Resistance will be compared with runoff later in this chapter. It is interesting that the resistance of the femorotibial and amputation groups is the same. This indicates that the severity of disease in the two groups is similar, and the results achieved in the femorotibial group (Figure 51) would support this suggestion. The conflicting results achieved at 38/45 ml/min and 76/81 ml/min are hard to explain, particularly the fact that the femoropopliteal resistance is significantly higher than the femorotibial resistance at 45 ml/min. The pooling of results for the two flow rates is inevitably a compromise but in future the combined results will continue to be quoted.

In conclusion resistance is higher where the disease is more severe, but the flow rate at which
resistance is measured is important to permit this
differentiation. In the data presented the available
runoff was very variable and this might be reflected in
some of the anomalous results. In subsequent sections
data analysis will concentrate upon the findings at
38/45 ml/min and 76/81 ml/min.
POST PAPAVERINE RESISTANCE

INTRODUCTION

It has been suggested extensively in the literature that all haemodynamic measurement in peripheral vascular surgery should be performed under conditions of maximal vasodilatation. This it is argued will remove the error induced by having a partially vasoconstricted vascular tree and will allow comparisons to be made between patients. For the majority of the patients in the femoropopliteal group but excluding the first six, resistance has first been measured under resting conditions, and then under maximal vasodilatation induced by intra-arterial papaverine. No such measurements were made in the femorotibial or amputation groups. Resistance has been measured at the combined flow of 76/81 ml/min, 117 ml/min and 153 ml/min. In each case the resistance was first measured at 76/81 ml/min and the lowest pressure reached after injection of papaverine was recorded. When the pressure had reached its trough at 76/81 ml/min the flow was changed.

The aim of this section was to examine the post papaverine resistances and to compare them with the
RESULTS

The results are shown in Table 6 in the Appendix (pages D14-16) and are summarised in Figure 45. The differences between the resistances at the three flow rates both pre and post papaverine are shown below. Resistance at 76/81 ml/min was higher than at 117 or 153 ml/min but there was no significant difference between 117 and 153 ml/min. At each flow rate resistance pre papaverine was significantly higher than post papaverine.

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<th>117 SE</th>
<th>153 SE ml/min</th>
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<td>986 68</td>
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<td>673 68</td>
</tr>
<tr>
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<tr>
<td>Post pap</td>
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<td>457 102</td>
</tr>
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</table>

'-- p<0.01' --'

'-------- p<0.02 --------'

'-- N/S --'
**PERIPHERAL RESISTANCE MEASUREMENT**

*Ch. 8.3*

---

**FEMOROPOPLITEAL GROUP - POST-PAPAVERINE RESISTANCE**

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Mean 597 402 457
SE 66 70 102

Figure 45
As has previously been shown the resistance in general decreases as the flow increases. However there was no difference between the resistance measured at 117 ml/min and 153 ml/min. This lack of difference is artefactual and is due to the properties of papaverine. The duration of action of the papaverine is short so that by the time the pressure has reached its trough for the first flow rate the papaverine effect was already wearing off. This has the effect of artificially lowering resistance measured at the early flow rates in relation to the later readings, and explains why the resistance measured at 117 ml/min is lower than that measured at 153 ml/min. If the post-papaverine results are to be used for subsequent analysis then repeated injections of papaverine will be required. The comparison between pre and post-papaverine resistances shows that even though the papaverine was wearing off the resistance was still lower than prior to its administration. For each flow rate the difference was significant. For subsequent sections of this chapter the post-papaverine results will only be examined at 76/81 ml/min since this was the flow which was always measured first in the sequence of flow rates.
PERIPHERAL RESISTANCE MEASUREMENT  Ch.8.4

Section 4

RESISTANCE AND RADIOLOGICAL RUNOFF

INTRODUCTION

In this section a detailed examination of resistance in relation to radiological runoff will be made. One would expect from the previous sections, which have shown that resistance correlates with the severity of disease defined by the type of operation, that the resistance should correlate with radiological runoff. The runoff has been studied in two ways. The first method is that which is usually used in reports in the journals (Koontz and Stansel 1972) to separate groups of patients by the severity of disease. The patients are split up according to the number of vessels patent in the calf. This method is inaccurate because it is usually not clear whether the vessel must be fully patent from top to bottom into the foot, whether a short segment of patent vessel in the calf counts as patent, whether connection to the foot by collaterals counts as a patent vessel, or how important is full connection to the popliteal artery. In most patients some part of all three vessels is patent below the knee on intraoperative arteriography, but these patients are
not usually considered to have three vessel runoff. The second method of assessment takes into account these problems by defining runoff in a more comprehensive way. Each vessel below the knee is scored according to the degree of narrowing in it: 1= normal; 2= mild atheroma; 3= severe atheroma; and 4= blocked. The popliteal artery above the anastomosis is also scored to give some idea of how good the proximal runoff is. The popliteal artery has been scored with the same scoring system as used for the individual calf vessels. The anastomosis between graft and artery is also scored; 1= excellent; 2= mildly narrowed; and 3= severely narrow. Finally the number of vessels patent to the ankle has been noted; 1= 3 vessels patent; 2= 2 vessels patent; 3= 1 vessel patent. In both the first and second methods the patency of individual vessels in the calf has been counted as present if the vessel is patent no matter how narrow it may be.

**METHOD**

Using the above methods of scoring the runoff has been objectively defined for each of the patients in the femoropopliteal group. The maximum score possible for the first method is three with a minimum of zero whilst for the second the maximum score was 23 with a minimum of 6. The resulting score has been compared with the
resistance measured at 38/45 ml/min, 76/81 ml/min, 117 ml/min, and 153 ml/min.

RESULTS

The main results are summarised in Figure 46. In this table patient (Pat No), comprehensive runoff (CRO), simple runoff score (RO), and resistance at the specified flow rates, have been given. The last two columns of resistance values are the measurements after papaverine. Figure 48 shows the raw data for the comprehensive runoff score.

The combined results are detailed in Figure 47. Correlation using the Spearman Rank Correlation test is shown together with level of significance for each column. As can be seen the correlation is poor using the simple estimate of runoff but significant using the comprehensive runoff score. Interestingly the correlation between the two methods of evaluation of the arteriogram is fair $r = 0.8844$. At 81 ml/min it is probable that the poor correlation with simple runoff score is partly artefactual and due to the number of tied scores.

The results have also been analysed by listing resistance by flow rate split up according to the runoff. For the simple runoff (RO) this is by number of
vessels patent to the foot. For the comprehensive runoff the patients have been arbitrarily divided into three groups. Group one had a score of 6-11, group two had a score of 12-16, and group three had a score of 17-23.

The results for the RO group are summarised in Figure 49. Before papaverine there were no significant differences between the adjacent groups except at 45, 81, and 153 ml/min the resistance for three vessel runoff (score one) was significantly lower than that for the single vessel group (score three) (p<0.05). After papaverine there were significant differences in resistance between adjacent groups with one exception.

The results for the CRO group are summarised in Figure 50. With the exception of one measurement there were no significant differences at all. The mean resistance did however generally increase with increasing severity of disease. The post-papaverine results in this case also showed no significant differences.
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*Figure 46*
PERIPHERAL RESISTANCE MEASUREMENT  

**PERIPROPOPLITEAL GROUP - RESISTANCE VS. RUNOFF**

Correlation between RO, CRO, and Resistance

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All tests - Spearman Rank correlation test

*Figure 47*
## Peripherial Resistance Measurement

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*Figure 48*
### Peripheral Resistance Measurement

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<th>Name</th>
<th>Pop</th>
<th>At</th>
<th>Pn</th>
<th>Anast</th>
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<th>Resistance to Ankle Vessels</th>
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<td>4</td>
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</tr>
</tbody>
</table>

**Score**

1 - Normal  
2 - Mild  
3 - Severe  
4 - Blocked

**Patent**

At least 4 inches

**Anast**

1 - Excellent  
2 - Narrowed  
3 - Badly narrowed

**Popliteal**

1 - Good  
2 - Moderate  
3 - Poor  
4 - Blocked

**TPT** - Tibioperoneal trunk

**Pop** - Popliteal artery  
**AK** - Above knee  
**BK** - Below knee

*Figure 48*
### Femoropopliteal Group - Resistance vs. Runoff

Conventional assessment - Arteriogram score

<table>
<thead>
<tr>
<th>Vessels</th>
<th>One P</th>
<th>Two P</th>
<th>Three P (1 vs. 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pre papaverine</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>45 ml/min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Res</td>
<td>1225 N/S</td>
<td>1470 N/S</td>
<td>1704 &lt;0.05</td>
</tr>
<tr>
<td>SE</td>
<td>104</td>
<td>357</td>
<td>211</td>
</tr>
<tr>
<td>No.</td>
<td>11</td>
<td>7</td>
<td>13</td>
</tr>
<tr>
<td>81 ml/min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Res</td>
<td>813 N/S</td>
<td>988 N/S</td>
<td>1193 &lt;0.025</td>
</tr>
<tr>
<td>SE</td>
<td>76</td>
<td>152</td>
<td>133</td>
</tr>
<tr>
<td>No.</td>
<td>10</td>
<td>11</td>
<td>14</td>
</tr>
<tr>
<td>117 ml/min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Res</td>
<td>630 N/S</td>
<td>844 N/S</td>
<td>781 N/S</td>
</tr>
<tr>
<td>SE</td>
<td>64</td>
<td>251</td>
<td>104</td>
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<tr>
<td>No.</td>
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<td>5</td>
<td>7</td>
</tr>
<tr>
<td>153 ml/min</td>
<td></td>
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<td>828 N/S</td>
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<td>9</td>
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<td>81 ml/min</td>
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<tr>
<td>Mean Res</td>
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<td>688 0.047</td>
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<tr>
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<td>151</td>
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<tr>
<td>No.</td>
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<td>10</td>
<td>7</td>
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<tr>
<td>117 ml/min</td>
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<td></td>
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<tr>
<td>Mean Res</td>
<td>302 &lt;0.05</td>
<td>657 0.04</td>
<td>313 &lt;0.05</td>
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**Figure 49**
PERIPHERAL RESISTANCE MEASUREMENT  Ch. 8.4

FEMOROPOPLITEAL GROUP - RESISTANCE VS. RUNOFF

Comprehensive runoff score

<table>
<thead>
<tr>
<th></th>
<th>6-11 P</th>
<th>12-16 P</th>
<th>17-23 P</th>
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<td>Pre papaverine</td>
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<tr>
<td>45 ml/min</td>
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<td></td>
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</tr>
<tr>
<td>81 ml/min</td>
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<td>1014</td>
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<tr>
<td>117 ml/min</td>
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<td></td>
</tr>
<tr>
<td>Mean Res</td>
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<td>N/S</td>
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</tr>
<tr>
<td>153 ml/min</td>
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<tr>
<td>Post papaverine</td>
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</tr>
<tr>
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<tr>
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<td>636</td>
<td>657</td>
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<td>SE</td>
<td>81</td>
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<td>197</td>
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<tr>
<td>No.</td>
<td>7</td>
<td>10</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>117 ml/min</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Mean Res</td>
<td>315</td>
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<td>No.</td>
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<td>5</td>
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</table>

Figure 50
DISCUSSION

Of the two methods used to assess the runoff arteriographically the comprehensive method is, not surprisingly, better than the conventional method. When the mean resistance was calculated according to the number of patent vessels in the calf using the conventional score there was a trend towards higher resistance with fewer vessels patent at each flow rate though this was not significant in each case. The same trend was seen with the three groups divided up by the comprehensive runoff score but the results were less convincing. This is presumably because of the way the cut off points were chosen. Whilst it would have been reassuring to find a good correlation between runoff and resistance it is not surprising that it has not been the case. The assessment of runoff does not take into account the actual size of the vessels, or the number and quality of collateral vessels. Correlation with patency is the key measurement by which the two methods must be assessed.
PERIPHERAL RESISTANCE MEASUREMENT Ch.8.5

Section 5

RESISTANCE AND GRAFT PATENCY

INTRODUCTION

The most important part of this thesis is to discover whether resistance measurement is able to predict the likely outcome of a bypass operation. In this fifth section patency has been assessed and compared with the resistance measured preoperatively. The results are available for both the femorotibial and femoropopliteal groups. The minimum follow up period is eight months though only three grafts had a follow up of less than one year. Presentation of the results is not simple because a considerable number of the grafts remain patent. The small numbers in the post-papaverine group make analysis impossible though the results are presented for completeness.

RESULTS

As a group the femorodistal grafts remained patent for a median of only 1.0 months. Femoropopliteal graft patency was more difficult to assess because a proportion of the grafts were still patent at the time
of writing. The mean patency time of those grafts which had occluded was 5.89 months. If the whole group was included then mean patency was greater than 10.4 months. By whichever method femoropopliteal patency was assessed it was significantly better than the femorotibial group; p<0.00003 for the entire femoropopliteal group and p<0.007 for the occluded femoropopliteal group. These differences will obviously increase with time.

1. FEMOROTIBIAL GROUP

For the femorotibial group patency rates are summarised in Figure 51. None of these grafts except one remained patent for more than a few months. The minimum follow up period was four months. Resistance of those grafts surviving less than one month has been compared with those patent in excess of one month and the results are shown in Figure 52. There were no significant differences between the groups at any of the three flow rates measured.
PERIPHERAL RESISTANCE MEASUREMENT  Ch. 8.5

**FEMOROTIBIAL GRAFTS - GRAFT PATENCY (Months)**

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<th>PATENCY</th>
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<td>02</td>
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</tr>
<tr>
<td>03</td>
<td>4.5</td>
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<tr>
<td>04</td>
<td>0.5</td>
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<tr>
<td>05</td>
<td>1.5</td>
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<td>06</td>
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</tr>
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<td>4 **</td>
</tr>
<tr>
<td>20</td>
<td>4</td>
</tr>
</tbody>
</table>

* - Indicates graft still patent at time of writing
** - Indicates patient died with a functioning graft

*Figure 51*
### FEMOROTIBIAL GRAFTS - PATENCY

**Pre Papaverine**

<table>
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<tr>
<th>Flow (ml/min)</th>
<th>&lt; One month</th>
<th>&gt; One month</th>
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<td>45</td>
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</table>

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</tbody>
</table>

There were no significant differences in resistance at any of the flow rates.

**Figure 52**
DISCUSSION

The results in this group are uniformly poor. All but three of the patients went on to amputation immediately after the graft failed, and as has already been shown the resistance in this group is no different to that measured in the amputation group. It is not surprising that there were no significant differences in this situation. Analysis of the results over a longer period was not possible for obvious reasons, and one may conclude that based on these results there is no justification doing the operation in patients with such severe disease.
2. **FEMOROPOPLITEAL GROUP**

For the femoropopliteal group the graft patency rates are summarised in Figure 53. Three patients with four grafts died with patent grafts, and sixteen grafts in fourteen patients were still patent at the time of writing. At one month, three months, six months, and twelve months resistance in patients with patent grafts has been compared in those with blocked grafts. Patients dying with a patent graft have been excluded.

**Pre-papaverine**

a. **One month.** The majority of grafts were patent (87.5%) and the resistances are shown in Figure 54. Mean and standard error are shown at the bottom of each column. At each flow rate the patent grafts had a significantly lower resistance than the blocked grafts. At 45ml/min $p<0.01$; at 81ml/min $p<0.01$; and at 117ml/min $p<0.02$.

b. **Three months.** More of the grafts had occluded (83% patent) but the differences were still significant at each of the flow rates (Figure 55); at 45ml/min $p<0.005$; at 81ml/min $p<0.005$; at 117ml/min $p<0.02$; and at 153ml/min $p<0.005$.

c. **Six months.** 67.5% of the grafts were still patent. The resistances are shown in Figure 56. At 81 and 153ml/min there were significant differences between the
### Femoropopliteal Grafts - Graft Patency

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<th>Patency</th>
<th>Name</th>
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<th>Name</th>
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* - Still patent at time of writing
** - Died with a functioning graft
**FEMOROPLITEAL GROUP - RESISTANCE AT ONE MONTH**

**PRE PAPAVERINE**

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At each flow rate patent grafts had a significantly lower resistance than occluded grafts.

**Figure 54**
## Periophoral Resistance Measurement

### Femoropopliteal Group - Resistance at Three Months

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**Mean**

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At each flow rate patent grafts had a significantly lower resistance than occluded grafts.

*Figure 55*
At 81 and 153 ml/min patent grafts had significantly lower resistance than occluded grafts.

**Figure 56**
PERIPHERAL RESISTANCE MEASUREMENT  Ch.8.5

FEMOROPOPLITEAL GROUP - RESISTANCE AT TWELVE MONTHS

PRE PAPaverINE

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Mean 1581 1065 853 491 1336 938 693 564
SE 186 122 141 141 111 68 61 48

There were no significant differences in resistance at twelve months at any of the flow rates.

Figure 57
two groups (p<0.02 and p<0.025 respectively) but at 117 ml/min there was no significant difference. At 45 ml/min the difference approached significance (p=0.0594).

d. Twelve months. There were approximately equal proportions of patent and occluded grafts and the resistances are shown in Figure 57. There were no significant differences between the two groups at this stage at any of the flow rates, and at 153 ml/min the resistance in the patent group was higher than the occluded group.

To be most useful it should be possible to choose a level of resistance below which a graft would have a reasonable chance of success and above which an alternative procedure would be more appropriate. Patency time has been studied above and below four critical resistance levels, 800, 1000, 1200, and 1500 mPRU. Resistance at 81 ml/min has been chosen because overall this flow has produced the most encouraging results to date. The results are shown in Figure 58. There were significant differences in patency at 1000 (p<0.05), 1200 (p<0.05), and 1500 mPRU (p<0.01), but not at 800 mPRU. All grafts were included in this analysis except those in which there had been death with patency. If the grafts still patent were excluded then there were still
### FEMOROPopliteal Group - Patency by Resistance Level

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| M   | 9.78 | 9.97 | 10.85 | 8.65 | 10.63 | 8.18 | 10.5  | 6.83 |
| SR  | 1.46 | 1.98 | 1.13  | 2.75 | 1.26  | 3.49 | 1.41  | 6.4  |

**Figure 58**

Page 179
significant differences at the resistance levels already documented; at 1000 mPRU $p=0.01$; at 1200 mPRU $p<0.025$; and at 1500 mPRU $p<0.01$ (Figure 59).

**POST-PAPAVERINE**

Resistance was measured in each case at 81 ml/min prior to its measurement at the other flow rates. A similar correlation between resistance and patency has been calculated after papaverine as has been calculated for the correlation prior to papaverine. At each time interval patent grafts had a significantly lower resistance than occluded grafts; at one month $p<0.005$; at three months $p<0.001$; at six months $p<0.05$; and at twelve months $p<0.01$ (Figure 60). When comparing patency rates for a given resistance cut off level different resistance levels were chosen; 400, 500, and 700 mPRU. Patients with a resistance less than 400 mPRU had a significantly longer patency than those with a resistance greater than 400 mPRU $p<0.05$. The same was true at 500 mPRU $p<0.01$ and 700 mPRU $p=0.001$ (Figure 61). If the grafts remaining patent were excluded then the differences were no longer significant at 400 mPRU but remained so at 500 mPRU $p=0.01$ and 700 mPRU $p<0.01$ (Figure 62).
PERIPHERAL RESISTANCE MEASUREMENT

**FEMOROPOPITEAL GROUP - PATENCY BY RESISTANCE LEVEL**

*PRE PAPYRERINE - 81 ML/MIN - Excluding still patent grafts*

Patency in months

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Mean: 6.66 7.28 8.16 6.03 7.46 6.33 7.13 6.83
SE: 0.96 2.39 1.21 2.82 1.16 4.03 1.00 6.39

**Figure 59**
### Femoro-Popliteal Group - Resistance in Months

**Post Papaverine - 81 ml/min - All cases**

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<th>&lt;3/12</th>
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</table>

| Mean | 1225 | 450 | 1037 | 431 | 778 | 441 | 718 | 390 |
| SE  | 326  | 30  | 236  | 29  | 173 | 34  | 134 | 43  |

At each time interval resistance in patent grafts was significantly lower than in the occluded grafts.

**Figure 60**
## Femoropopliteal Group – Patency by Resistance Level

### Post Papaverine - 81 mL/min - All cases

#### Patency in months

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Mean: 12.58, 7.2, 12.43, 5.73, 10.8, 0.5  
SE: 2.17, 1.56, 1.69, 1.73, 1.33, 0.38

Figure 61
### Femoropopliteal Group - Patency by Resistance Level

**Post PAPaverine - 81 mL/min** - Excluding still patent grafts

Patency in months

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**Figure 62**
DISCUSSION

There are inherent difficulties in comparing graft patency in two groups of patients when 36% of the grafts remain patent at the time of analysis. For this reason it was not possible to look at a straight correlation between resistance and patency. Clearly the longer a graft remains patent the more potential factors there are likely to lead to its occlusion. Pseudointimal hyperplasia (Beard and Fairgrieve 1986), progression of disease distally, continued smoking (Myers, King, Scott et al 1978), graft degeneration (Layer, King and Jamieson 1984), repeated kinking of the graft as it traverses the knee joint, or inadequate inflow (Charlesworth, Harris, Cave et al 1975) are all factors which affect graft patency to an increasing extent with time. The most significant differences in patency which are due to the runoff resistance at the time of grafting will therefore be felt to the greatest extent in the early postoperative period. Few grafts were available for analysis with a potential patency of more than 18 months but all grafts had a minimum follow up of eight months. At one and three months both before and after papaverine there were the most significant differences in resistance between patent and occluded grafts. Only in the post papaverine group were the
differences significant at one year. The majority of
graft failures occur in the first twelve months
(Cutler, Thompson, Kleinsasser et al 1976), and it
would seem that resistance measurement is able to detect
this group. After papaverine the comparison between
patent and non-patent grafts has only been made at
81 ml/min. As has previously been described, this was
because the effect of papaverine was transient and the
resistances measured at 117, and 153 ml/min were
therefore not at maximal enhancement and essentially
inaccurate. To be useful clinically the method should be
able to differentiate grafts into patent and occluded
groups by a cut off resistance level. Three of the four
pre-papaverine resistance levels and all three
post-papaverine resistance levels were able to
demonstrate significant differences in patency. There
was however overlap between the groups such that the
differences might only be useful clinically when using a
comparatively high cut off level which suffers from
making the test less discriminating.
INTRODUCTION

It is known that femoropopliteal reconstructions to the above knee popliteal artery have a longer patency than those placed beyond the knee. It might be expected that the resistance of the popliteal artery above the knee would be lower than that measured beyond the knee since the potential runoff is greater. In this group of forty four grafts there were ten placed above knee. In this section the resistance of this group has been compared with the rest and with the ensuing patency. All measurements have been made before the administration of papaverine.

RESULTS

Resistance has been measured at four flow rates; 45, 81, 117, and 153 ml/min. In each case all results for the above knee group have been grouped together regardless of arteriographic runoff. In the below knee group data has been presented in two ways. Firstly all the results have been put together in a single group,
Mean resistance - pre papaverine - femoropopliteal grafts

Significant differences in resistance only occur when comparing above knee and single vessel runoff groups.

Figure 63
and secondly data for single vessel runoff cases has been looked at separately. The results are shown in full in Table 7 and 8 in the Appendix (pages D17-18), and in Figure 63 where mean resistance is indicated by the horizontal bar. It can be seen that there were no differences between the two groups when all the below knee cases were included. However when only the single runoff cases were compared with the above knee group the differences were significant at all four flow rates; p=0.05 at 45 ml/min; p<0.05 at 81 ml/min; p<0.05 at 117 ml/min; and p<0.05 at 153 ml/min. There were no differences between the above knee group and the two and three vessel runoff below knee group. The mean patency of the above knee group was 15.4 months (SE 1.91) and this was significantly longer than the below knee group 8.78 months (SE 1.59) p<0.005. Both groups contained patent grafts at the time of writing; the above knee group with 7/10 and the below knee group with 6/30.
DISCUSSION

Contrary to what might be expected these results indicate that there is no significant resistance advantage to grafting above knee except when the runoff below knee was very poor. In this series as in others (Charlesworth, Brewster, Darling et al 1985) the patency of above knee procedures was superior to that achieved below knee. It is possible that the use of artificial grafts might account for this difference but similar proportions of the above knee (6/10) and below knee (18/34) procedures were performed with artificial grafts suggesting that this is not in fact the case. There must be some inherent problem with grafts that have to cross a joint which results in their premature occlusion which has yet to be defined. Recent research suggests that for artificial grafts this factor might be the kinking which occurs at knee level when the knee is flexed.
Resistance has been measured in three groups of patients, and a total of 77 limbs have been studied. At any one flow rate patients having femoropopliteal reconstruction had lower resistance than those having either amputation or femorotibial reconstruction. Interestingly there were no real differences between the two latter groups indicating the severity of disease in the femorotibial group. Indeed the results in the femorotibial group would suggest that they should have undergone primary amputation.

Within the femoropopliteal group resistance measurement was only able to separate all above knee grafts as a group from single vessel below knee grafts. Two and three vessel runoff grafts below knee did not have significantly different resistance levels. This is perhaps surprising given the differences in clinical outcome, even though the length of popliteal artery separating the two sites is only 10 cm.

The comparison between concentric and sidearm methods of resistance measurement confirmed that to use the simple sidearm method would require recalibration on each occasion.

Saline was used in a small group of patients in parallel with blood to measure resistance. The
correlation between it and blood was poor and as in the
dog experiments saline failed to separate different
runoffs as well as blood.

The comparison between resistance and runoff in
the three operative groups showed that at low flow rates
resistance was not a good predictor of runoff. At high
flow rates there were only small numbers but again the
discriminatory power of resistance was lost. There
appeared to be a narrow window where resistance
measurement was accurate. Previous work has suggested
that a minimum flow of between 60 ml/min (Little,
Shiel, Loewenthal et al 1968) and 100 ml/min (Cappelen
and Hall 1967) is required to maintain longterm graft
patency. Resistance measured at a flow somewhere in this
range would therefore seem to be desirable. At the end
of the study resistance was measured at the single flow
rate of 81 ml/min. Within the femoropopliteal group the
resistance was shown to correlate with a comprehensive
assessment of runoff but not simply with the number of
vessels patent in the calf.

In the femoropopliteal group where the highest
number of results was available there was good
correlation between patency and resistance both before
and after papaverine. Resistance was however only a
significant predictor upto nine months after grafting.
It is not clear whether this was due to small numbers or
because of disease progression. Employing a cutoff resistance also resulted in a significant prediction of outcome at several of the flow rates tested.

To be useful, an assessment of runoff must allow the surgeon to make decisions as to whether reconstructive surgery is possible or whether he should proceed directly to amputation. The cut off levels shown in Figure 58 indicate that a level of resistance in excess of 1200 mPRU is generally associated with a very short graft patency and this may represent the area where resistance measurement might be most useful.
Peripheral resistance measurement has been shown in the preceding chapters to correlate with disease severity in three groups of patients with widely differing types of disease. In a group of dogs with no vascular disease the resistance measured in each of the individuals was very similar, suggesting that the method was reproducible. Within any one of the groups of patients resistance correlated well with the comprehensive assessment of runoff defined arteriographically and would support the findings of Bliss (1973).

Resistance has been shown not to be constant but to vary with flow, being lower the higher the flow at which it is measured. This implies the need to measure resistance at a single flow rate in order to make comparisons between individuals, a fact not apparently noted by previous authors (Vetto and Dunphy 1964, Delin and Ekeström 1965, Mundth, Darling, Moran et al 1969, and Bliss 1973). The relationship between resistance and severity of disease is, however, approximately constant.
over a range of flows except when these are either very low or very high (Pappenheimer and Maes 1942 and Green, Lewis, Nickerson et al 1945).

Resistance measurement has also been shown to correlate with outcome in the femoropopliteal group, where higher resistance values were associated with shorter patency. Unlike previous authors, particularly Bliss (1973); Mundth, Darling, Moran et al (1969); and Barner, Kaminski, Codd et al (1974) it has been shown that if resistance at 81 ml/min is over 1200 mPRU the chances of prolonged graft patency are small. The fact that comparisons have been made at constant flow may account for these differences.

Despite trying three infusion solutions none had any significant advantage over blood. Saline was distinctly inferior because its low viscosity resulted in poor separation between different resistance loads. Dextran was more suitable having a viscosity similar to that of blood but it caused muscle fasciculation in the dog and by adding extra expense to the procedure carried no other significant advantages.

The role of papaverine is not clear from these experiments. Because of its short duration of maximal action its use is only suitable for resistance measurement at one flow rate. It resulted in a reduction in resistance peripherally in almost every case, but
the relationship to pre-papaverine measurements was not constant. Post-papaverine measurements, like the pre-papaverine measurements, correlated with outcome and therefore either set of measurements could have been used.

The early experiments required large quantities of blood so that resistance could be measured at a range of flow rates. As a result it has been shown that both low and high flow rates were unsuitable for resistance measurement and that the best separation of resistances was achieved at 81 ml/min. It can be concluded that it is possible to measure resistance at one flow rate and that this should be at approximately 80-120 ml/min. This means that less blood is required at each session speeding and simplifying the procedure.

Providing a suitable yardstick by which to judge resistance measurement is not easy. Arteriography, traditionally held to be the gold standard, has been shown to correlate with resistance when a comprehensive assessment of the arteriogram was made. The simple method of counting the number of patent vessels in the calf was not sufficient. The majority of surgeons do not make such a comprehensive assessment and almost all reports in the literature of graft patency are based on simple runoff. Resistance measurement must therefore stand or fall on its ability to be as good as
or better than arteriography in defining the outcome.

Resistance measurement might be expected to have influence over outcome for a limited period because other factors will have an increasing influence the longer the life of the graft. These will affect the predictive power of both resistance measurement and arteriography. This study has suggested that resistance exerts its main influence in the first year of a grafts life, though numbers for comparison beyond one year are small.

Resistance measurement, unlike arteriography cannot be used to detect technical errors on the part of the surgeon except where these are gross. Some early failures in this series were certainly due to technical problems but because all the measurements have been included results are less significant than they might have been. It is not uncommon for authors reporting the results of reconstructive surgery to omit failures that occur in the first 30 days as technical failures. This manoeuvre undoubtedly favours arteriography as a means of judging results in these papers since apparently favourable pre reconstruction films would have been associated with early occlusion. No such exclusions were made in this work.

Even if both resistance measurement and arteriography were equally able to predict outcome there
would still be an advantage to using resistance measurement. In the first place direct comparison between patients in any one centre or between different centres becomes possible. The principle advantage of this is that standardisation of reporting of results might be achieved. Secondly sensible treatment regimens might be produced. It might be possible to save the patient, who will inevitably finish with an amputation within a few months, from expensive and time consuming efforts at vascular reconstruction. Similarly it might allow a borderline group to be identified in whom some procedure other than simple femoropopliteal reconstruction should be tried. Such alternatives include the use of adjunctive arteriovenous fistula, multiple sequential grafts or adjunctive extended profundaplasty.

The postoperative flow measurements in the graft have not been included. Because these were generally far in excess of the flows used to measure resistance, comparison and correlation between the two methods of prognosis prediction was not possible.

Though it would be easier to measure the pressure using the sidearm technique it has been shown to be inaccurate in practice both in the animal and human situation. The concentric cannula is undoubtedly easier to use and produces cleaner data than the direct needle.
The direct needle also carries the risk of damage to the atheromatous lining of the artery. Commercially available double lumen cannulae are currently undergoing evaluation to streamline the method further.
FUTURE PROSPECTS

At the moment measurement of resistance is still rather cumbersome. Trained Medical Physics personnel are required in theatre and their equipment takes up a lot of space. With a Department of Trade grant I am currently building a portable module containing pump, pressure amplifier, and single channel chart recorder. This, it is hoped, will be within the price range of many vascular surgeons so that the longterm goal of comparisons of outcome between centres by resistance measurement may become a reality.

As with any research project more work is required both to clarify this project and in new areas. The new module will run at 100 ml/min, and a new set of standard resistance levels will need to be found. Resistance measurement after papaverine which has not been emphasised in this thesis, needs to be compared with non-papaverine measurement of resistance at a single flow rate. Resistance measurement in other areas, particularly the femoral artery, might be useful. The problem of management of combined segment disease - aortoiliac and femoropopliteal - remains unresolved. Resistance measurement at groin level might make it possible to answer the question of whether aortoiliac reconstruction alone or a combination of the two is
required. A new project addressing this question is in progress.

As usual in research, providing an answer to one question, rather than being an end in itself, merely leaves one pondering the answers to many more.
APPENDIX

Section A

In this section of the Appendix the raw data for the first animal experiments is shown. Against each flow arterial and venous pressure are tabulated with the resultant resistance. In each case two sets of measurements have been performed and these are shown as Run 1 and Run 2. Flow is measured in ml/min, pressure is measured in mmHg and resistance is measured in mPRU.
## PERIPHERAL RESISTANCE MEASUREMENT

### App. A

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### Table 1

Appendix A2
### PERIPHERAL RESISTANCE MEASUREMENT

#### APPENDIX A

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**Table 5**

Appendix A6
APPENDIX

Section B

In this section the raw results of the amputation group are listed. Patients are numbered 1-12. In the first column (COLL) collateral pressure is shown in mmHg. For each flow arterial and venous pressure and the calculated resistance are shown. Flow is measured in ml/min, pressure in mmHg and resistance in mPRU. Patient 4 had pressure measured in both the anterior tibial (AT) and posterior tibial (PT) arteries. All measurements were made without Papaverine.
## PERIPHERAL RESISTANCE MEASUREMENT

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*Table 1*
In this section raw data for the second animal experiments are tabulated. Page C3 is concerned with the calibration of the sidearm cannula resistance. For each of the dogs numbered 11 - 14 resistance has been measured at four flow rates (Q). Pressure (P) and the consequent resistance (Res) are tabulated for each of the infusing solutions.

In the second section, pages C4 - C6, raw data concerning the comparison between different methods of pressure measurement are listed for each of the infusing fluids in turn. Two columns of concentric (Conc), sidearm (Side), and Stab pressure are shown each measured in mmHg.

In the third section, pages C7 - C9, raw data for the constant flow infusions are shown. Under each flow arterial (P), and venous (V) pressure, and resistance (Res) are shown. Results are detailed for each of the two runoffs both before and after ischaemia.

In the fourth section, pages C10 - C12, raw data for the constant pressure infusions are shown. Tables are divided by presence or absence of ischaemia and by runoff. Under each dog, pressure (P), flow (Q), venous pressure (V) and resistance are tabulated.
In the final section, page C13, a comparison between constant pressure and constant flow measurement of resistance is made. For each dog where measurements are available the first three columns refer to constant pressure measurements - Const P, flow and Res, - and the final column shows the corresponding constant flow measurement of resistance.

Flow in each of these Tables is measured in ml/min, pressure in mmHg and resistance in mPRU.
## DOG EXPERIMENT 2

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- **Q** Flow ml/min
- **P** Pressure mmHg
- **Res** Resistance mPRU

Table 1

Appendix C3
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## DOG EXPERIMENT 2

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## Dog Experiment 2

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## PERIPHERAL RESISTANCE MEASUREMENT

### APP.C

---

**DOG EXPERIMENT 2**

**DEXTAN BY PUMP**

**Upper runoff - Pre ischaemia**

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**Table 7**

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Appendix C9
### DOG EXPERIMENT 2

**MANUAL INFUSION BLOOD**

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**Table 8**

Appendix C10
## PERIPHERAL RESISTANCE MEASUREMENT

### DOG EXPERIMENT 2

#### MANUAL INFUSION SALINE

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**Table 9**
### PERIPHERAL RESISTANCE MEASUREMENT

**Appendix C**

**DOG EXPERIMENT 2**

**MANUAL INFUSION DEXTRAN**

Pre Ischaemia

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Appendix C12
## DOG EXPERIMENT 2

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*Table 11*
APPENDIX

Section D

In this section raw data from the femoropopliteal and femorotibial groups are listed. The first section, pages D3 - D5, contains the results of the comparison between concentric and sidearm measurement of resistance. For each infusion fluid, and at each flow rate, pressure by the two methods (Conc) and (Side) are listed with venous pressure (V), and resistance by the stab (Res 1) and sidearm (Res 2) methods. Measurements before and after Papaverine were available for both fluids.

In the second section, pages D6 - D13, is the raw data of pressure and resistance for both the groups. For each patient, collateral pressure (Coll), flow (Q), arterial pressure (P), venous pressure (V), and resistance (Res) are tabulated.

In the next section, pages D14 - D16, post papaverine results for the femoropopliteal group are listed in the same way as for the previous section.

The final section, pages D17 - D18, contains the
PERIPHERAL RESISTANCE MEASUREMENT  App.D

raw data of resistance in the femoropopliteal group above and below knee. All measurements were taken prior to papaverine. In the first Table all above knee measurements of resistance were grouped together by flow rate. The second Table lists both below knee measurements of resistance for single vessel runoff and all cases together.
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#### Femoropopliteal Grafts Concentric and Sidearm

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**Post Papaverine**
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### Femoropopliteal Group - Resistance Above Knee

**Pre Papaverine**

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**Table 7**
PERIPHERAL RESISTANCE MEASUREMENT

APPENDIX D

TABLE 8

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| Mean   | 1687          | 1455          | 1151           | 989            | 924            | 753            | 880            | 703            |
| SE     | 216           | 131           | 131            | 79             | 156            | 80             | 174            | 87             |
| N      | 13            | 27            | 15             | 31             | 7              | 17             | 8              | 19             |

Table 8

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