HAEMODYNAMIC STUDIES ON ARTERIAL STENOSES AND THE ASSESSMENT OF PERIPHERAL VASCULAR DISEASE

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ABSTRACT

Various methods of assessing peripheral vascular disease are studied by making measurements both on dogs, and patients with arterial disease. Theoretical and experimental models of blood flow in diseased arteries are reviewed. A new type of experimental inter-changeable stenosis is described; and the flow, pressure and Doppler ultrasound results from a number of dog experiments using the device are presented. The relationship between the pressure drop across a stenosis and the flow through it in-vivo is shown to differ from previously reported in-vitro values. The severity of a stenosis is shown to have little effect on peripheral resistance, and attention is drawn to the lack of concrete evidence in the literature suggesting that it does. A possible explanation for this finding is given. It is suggested that ultrasonic Doppler traces are influenced by the distal bed as well as by proximal stenoses. Experimental Doppler spectra are compared with spectra calculated from electromagnetic flow waveforms and found to be in good agreement. Measurements from over 150 vascular patients are presented, and the difficulty of determining the validity of these measurements discussed. The indirect pressure measurement method of assessing vascular disease is examined and shown to be of limited value. It is shown that an inflatable cuff can substantially alter the pressure distribution within an artery, and the possibility of worsening disease being reflected by a higher occlusive cuff pressure is introduced. It is shown that both Doppler ultrasonic velocity measurements and direct

arterial pressure measurements agree with the clinical assessment in extreme cases, but that in equivocal cases the two tests often disagree with each other. The difficulty of adjudicating between tests is reaffirmed and a new method of objective evaluation suggested. Finally the problems consequent upon the dynamic nature of the disease are mentioned.

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The thesis was typed speedily and accurately by Mrs. Val Crozier who cheerfully coped with a difficult manuscript.

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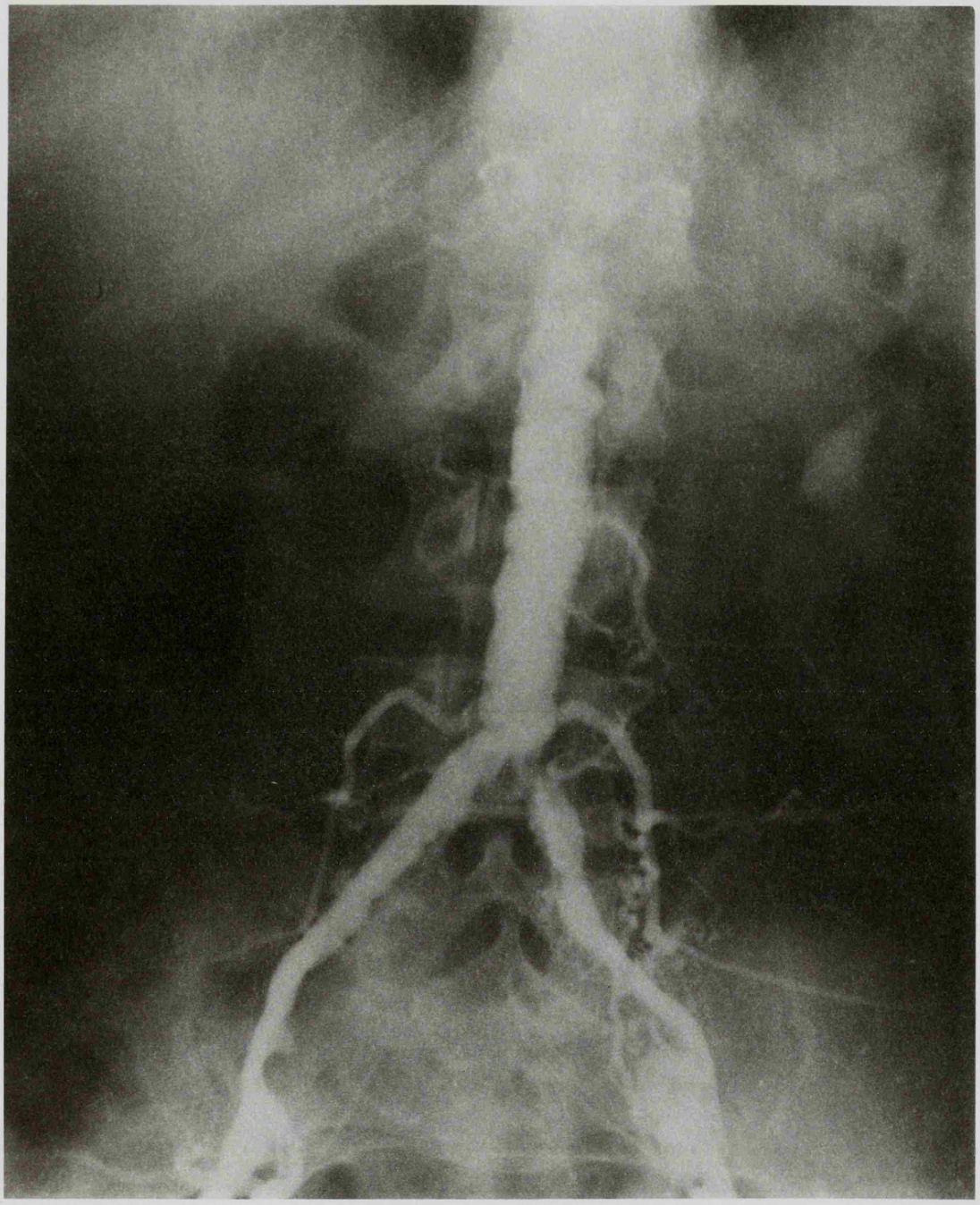


Arteriogram of badly diseased aorto-iliac segment. The aorta is irregular, the origin of the left common iliac artery badly stenosed and both internal iliacs are occluded. The right common and external iliacs are clearly diseased but may be able to provide enough inflow for a femoro-popliteal vein graft.

INTRODUCTION

There is a vast literature on the diagnosis of occlusive peripheral arterial disease. It suffers however from two major defects.

The objectives of diagnostic tests are confused and often seemingly irrelevant to the management of an individual patient. It is of some academic interest to have a test that will distinguish between patients with intermittent claudication, and those with rest pain; and indeed to have tests that will distinguish between groups of patients with different degrees of disease, but these are of no use whatever to the surgeon hoping to improve the patient's quality of life. In the first instance the patient can simply tell the surgeon of his symptoms, in the second it is the pathology of an individual patient that is in question, not that of a group.

The second defect is the lack of any definitive test with which others can be compared. This means any technique of assessment that is developed can only be evaluated properly by following up large groups of patients over a long period, a difficult task at the best of times. Arteriograms which are often used as a standard give only limited anatomical information, and very little functional information about diseased arteries (Frontispiece).

The purpose of this thesis is to examine in detail some of the diagnostic tests used for the assessment of peripheral arterial disease, and to consider what useful information can be derived from them. Useful, that is, in the sense of helping to answer questions about the treatment an individual

patient should receive.

It is impossible in a short study to follow sufficient patients over a long enough period of time to prove the efficacy or otherwise of a test (nor indeed is it always ethical to do so) and thus the approach has been to examine methods of assessment using theoretical and animal models, and then to make measurements on patients to help substantiate or refute the conclusions drawn from these models. This will not be perfect and the conclusions reached must in the final analysis be tested more fully on patients. A number of results from the animal experiments are interesting in their own right in that they are at variance with current thought.

This thesis is divided into four sections. The first, part A, consists of three chapters. Chapter one is a brief description of the symptoms, causes and treatment of peripheral arterial disease, Chapter two is a review of theoretical models of the arterial system and Chapter three a review of experimental models that have been used to investigate the behaviour of diseased arteries.

Section B is an account of experimental work carried out on dogs. Chapter four describes the experimental apparatus, Chapter five deals with the animal preparation, Chapter six with direct pressure and electro-magnetic flow measurements, whilst Chapter seven relates to ultrasonic Doppler measurements made on the same animal model.

Section C contains discussions of various techniques of assessment either in clinical use at present, or which may be of use in the future. The material presented in the first two sections, together with measurements made on

over one hundred and fifty patients with peripheral arterial disease are used to assess the scientific validity of these techniques. Measurements examined include cuff pressure measurements, direct pressure measurements and Doppler flow measurements.

Finally, Chapter eleven in Section D summarises the position and a suggestion is made as to how diagnostic techniques may be better evaluated.

The work contained in this thesis is essentially the work of the author, but any work in a multi-disciplinary field must of necessity involve close collaboration with colleagues in other specialities. I have already recorded, in the acknowledgements, my gratitude to my surgical colleagues, and some of the work presented in Chapters eight and nine has already been published in papers written jointly with them (Quin et al 1975, 1977). This work has however been expanded upon, and placed within a more meaningful framework.

S E C T I O N A

'This strange disease of modern life'

Matthew Arnold
The Scholar-Gipsy

CHAPTER ONE

OCCLUSIVE PERIPHERAL ARTERIAL DISEASE

Peripheral arterial disease is a general term used to describe both atheromatous changes in the arteries supplying blood to the lower limbs, and the ultimate results of these changes, that is to say vascular occlusion, and consequent ischaemic damage. The disease, however, usually only manifests itself in the later stages when the patient begins to experience pain whilst exercising and seeks medical advice.

1.1 Symptoms and Signs

Clinically there are three distinct degrees of occlusive (as opposed to aneurysmal) peripheral arterial disease; that of intermittent claudication, where the patient experiences pain during exercise, rest-pain in which the patient has pain even at rest, and finally gangrene. Although an individual patient's disease often follows these stages, intermittent claudication (IC) does not necessarily progress to rest-pain (RP) or gangrene, and indeed may improve spontaneously as other vascular beds, the so called collateral vessels, enlarge and allow blood to flow around rather than through diseased vessels. By the same token older patients sometimes suddenly occlude their arteries and the first sign of their long standing disease is the abrupt onset of ischaemia and gangrene.

In the first stage of the disease, that of intermittent claudication, both the blood flow and pressure of the patient at rest is comparatively normal, it is only when the patient exercises, and the leg muscles require more oxygen, and hence blood, that the diseased vessels are unable to cope satisfactorily

with the flow. The result is that anaerobic metabolic products accumulate in the tissues, and the patient experiences pain. If the patient then stops and rests, the demand from the tissues for oxygen decreases, the blood is able to clear the already accumulated metabolites, and after a short while the pain disappears. This then is the classical picture of a person with intermittent claudication - they walk perhaps 50 or 100 metres, are then forced by pain to stop, the pain recedes, and after a short period of time they are able to walk on, until once again they are forced by pain to stop.

The haemodynamic upset is more severe in patients with rest-pain, and even their resting blood pressure may be significantly reduced. The patient experiences pain whilst stationary, and there is little they can do to relieve it. The pain is typically worse at night, presumably due to their recumbent position, and prevents sleep. Severe rest-pain is indicative of imminent gangrene.

Gangrene is the ultimate stage of peripheral arterial disease. The diseased arteries are finally unable to supply enough blood even to keep the tissues viable. Gangrene almost always starts in the toes and proceeds proximally. Usually the gangrene is triggered off by a small traumatic event such as a cut or graze, and the vessels which have reached their capacity flow, are unable to supply the extra blood required to heal the damaged tissues.

Aneuryms, or localised dilations of the vessel wall, are a result of a weakening of the arterial wall. Although aneurysmal disease is classed together with obliterative disease under the general heading of peripheral arterial disease, the two seem to be of a somewhat different nature.

Most aneurysms are associated with atherosclerotic changes, but the relationship between the two is not absolutely clear, (Strandness and Summer 1975).

Aneurysms, particularly in the abdominal aorta may grow to very large sizes, and with increasing size become more susceptible to rupture (Klippel and Butcher 1966, Foster et al 1969), a potentially catastrophic event in a major artery. They are particularly interesting entities in that they only appear to form in places of localised trauma, or haemodynamic stress.

1.2 Atherosclerosis

As previously mentioned, it is only the final stages of arterial disease that are clinically apparent. If one accepts that in some way or another fatty streaks are a precursor of atheroma (and there are two schools of thought on the subject - Schwartz and Mitchell 1962, McGill et al 1963) then atherosclerosis begins in childhood, and progresses at different rates in different individuals and different arteries throughout life. Whatever their cause it is the fibrous plaques which begin to appear in the second and third decade of life (McGill et al 1963)that are the ultimate cause of the clinical disease. These 'raised lesions' are eloquently described by Woolf (1970).

> 'The lesions are considerably elevated above the surface of the surrounding intima and most of them consist essentially of a yellow lipid-rich basal pool covered by a connective tissue cap which varies in thickness from lesior to lesion. In some plaques this cap is the predominant element and gives the lesion a 'pearly'

white appearance. In others, the basal lipid accumulations may be of massive proportions and are separated from the vessel lumen only by a thin, easily ruptured sheet of fibromuscular tissue. All gradations between these extremes may be seen and, as complicating factors such as ulceration, thrombosis, calcification and haemorrhage may be superimposed, the lesions can appear markedly heterogeneous. The significance of the complication in the natural history of the raised lesion cannot be emphasized too strongly. From the point of view of an affected patient, atherosclerosis becomes of clinical importance only when lesions, or even a single lesion, encroach significantly on the vessel lumen. At first, the flow through the affected segment may merely be reduced but repetition of mural thrombosis or rupture of the plaque may ultimately occlude the vessel completely leading to crippling or fatal clinical disease.'

1.3 Distribution of Atheroma

Atheromatous changes affect every artery in the body to a greater or lesser extent; there are however, various sites which are particularly susceptible to the disease (Schwartz and Mitchell 1962). It is this fact in particular that has led to the belief that the geometry of the vessels is an important factor in the pathogenesis of atheroma. Some workers regard haemodynamic disturbances as being the primary cause of atherosclerosis, and suggest that the roles of other contributory atherogenic factors such as age, sex, diet, lipid metabolism, hormones, hypertension, stress etc., must be regarded as secondary or modifying influences (Texon 1963).

There are several theories on the haemodynamic factors that are responsible for atherogenesis. Wesolowski and co-workers (Wesolowski et al 1962,1965) believe that turbulance is the most significant factor, and suggest two mechanisms whereby it may lead to vascular lesions. One, investigated by Bruns et al (1959), is that high frequency vibrations, caused by the turbulance, damage the arterial wall sufficiently to lead to atheromatous lesions. The second, which is of particular interest because it is directly opposed to that of Texon et al, is that localised high pressure zones initiate the pathogenesis, either directly or through a mechanism of suppression of lipid secretion in the arterial wall.

The thesis upon which Texon's work is based is that it is localised low pressure areas that lead to the formation of atheromatous plaques. It does seem that his claim that - "the sites of predilection for atherosclerosis are found to be precisely the sites of relative reductions in lateral pressure", (Texon 1963) can be substantiated, but this is of course not proof that the relationship is one of cause and effect. The mechanism whereby low pressure areas give rise to atheromatous lesions is, according to Texon, one of suction on the arterial wall giving rise to a lifting of the endothelial layer. There is then a local reaction which produces a thickening of the intima due to proliferation of endothelial cells. The vessel is thus narrowed, the Venturi effect becomes greater, and a vicious circle is created. This explanation however seems unlikely because, as was pointed out by Gessner (1973), it is unlikely that the local pressure beneath the endothelium could exceed intraluminal pressure.

Other workers believe different factors again are responsible, for example D.L. Fry (Fry 1968,1969) who believes that abnormally high sheer stresses are the important factor, and C.S. Caro and co-workers (Caro et al 1969) who believe regions of reduced sheer stress are more susceptible to atheromatous disease.

The exact role of haemodynamic disturbance in atherogenesis is still very much open to question, but on present evidence it seems likely that it is a very significant factor. It is possible that it will be shown that all other atherogenic factors merely influence the ability of the vessels to respond to injury in such a way as to preserve their ability to transport blood.

1.4 Medical Treatment of Peripheral Arterial Disease

Medical treatment, unfortunately, seems to have little to offer at present in cases of established peripheral vascular disease. It is basically aimed at treating or removing factors that are known to speed up atherogenesis. These factors include hyperlipidemia, diabetes mellitus, hypertension, obesity and smoking.

Several types of drug are used, most of which have not had their efficacy proved, and some of which have been shown in carefully controlled trials to be worthless.

Probably the most useful drug at present is clofibrate ('Atromide S') which has the effect of lowering serum lipids, fibrinogen and viscosity, and has proved its worth in some types of patient (Dormandy & Goyle 1976). Anti-coagulants have their place in some types of disease where the major problem is one of recurrent emboli. Vasodilators, although still prescribed, are worse than useless in that they shunt

blood away from the areas where it is most needed (Strandness DE 1970, Coffman and Mannick 1972, DeBakey et al 1947, Kane 1970, Ruckley et al 1976). There is as yet little, if any evidence that drugs of the 'Parovin' type, which it is claimed increase oxygen utilization, are of any use (Barber 1977).

1.5 Surgical Treatment of Peripheral Arterial Disease

All surgical treatment is aimed at increasing the blood supply to the tissues. This may be achieved either by decreasing the peripheral resistance of the limb in question, or by bypassing or removing the block in the artery.

Reduction of peripheral resistance is achieved by destroying the sympathetic nervous system to the limb, by the operation known as sympathectomy. This operation has been shown to be worthless in the treatment of intermittent claudication (Shaw et al 1964, Quin et al 1974, Fyfe and Quin 1975), probably because the vessels supplying the ischaemic muscle are already fully dilated (Hoffman and Jepon 1968, Donald et al 1970). It may be of value in the treatment of rest-pain and gangrene as it increases flow to the cutaneous vessels (Wright and Cousins 1972), however it carries with it the attendant risk of shunting blood away from the most ischamic sites (Lassen et al 1968, May et al 1963). Furthermore, sympathectomy has a larger effect on blood flow through arteriovenous shunts, than it does on capillary flow (Scarpino and Delaney 1971, Delany and Scarpino 1973).

Endarterectomy, the operation that is performed to remove atheroma from the inside of diseased vessels was at one time popular, but its long term success rate in all but the largest vessels is now known to be poor. (DeBakey et al 1958, Edwards 1968).

By-pass grafting is now the usual treatment of choice in cases of severe peripheral arterial disease. Grafts for peripheral disease fall into two main categories:- aorto-iliac and femero-popliteal reconstruction. The former are carried out using man-made grafts, usually of woven or knitted Dacron or Teflon. These tubes are sewn into the arterial system above and below the lesion so as to bypass the affected part of the circulation. Generally speaking the implant follows the course of the arterial system, but in some circumstances the grafts are inserted to join parts of the arterial system that are not normally connected directly. Axillo-femoral, (Blaisdell and Hall 1963, Mannick et al 1970, Moore et al 1971) and femero-femoral 'Cross-over grafts' (McCaugham and Kelvin 1960, Vetto 1962, 1966, Sumner and Strandness 1972, Brief et al 1972) are examples of these.

Femero-popliteal reconstructions are usually carried out using the patients own long saphenous vein. This is dissected out through the same incisions that are made to approach the artery. After suitable preparations the vein is sewn in 'upside down' (so that the valves do not interfere with flow) around the site of the block (Jackson and Abel 1972, Horton 1974, Kaminski et al 1973, Linton and Darling 1962).

There are three ways of anastomosing a graft into a blood vessel; 'end-to-end', 'end-to-side', and 'side-to-side'. Side-to-side anastomoses are of little relevance to peripheral arterial disease, but each of the other two grafting techniques has its haemodynamic advantages. End-to-side anastomoses have the virtue that any remaining circulation along the diseased vessel can continue in the event of the graft failing, whilst end-to-end anastomoses tend to produce less disturbed flow (Schultz et al 1967), and are also more

likely to remain patent as they carry more blood than the corresponding end-to-side graft.

1.6 Failure of Surgical Treatment

Unhappily the failure rate of reconstructive surgery, especially below the inguinal ligament, is high (Baddeley et al 1970, Douglas et al 1973, Miller 1974). This is particularly unfortunate, as the situation following the acute occlusion of a graft is often worse than that which existed before surgery. This is so for two reasons. Following bypass surgery, the collateral vessels that had previously enlarged to permit flow around the stenosis or block regress (Jacobson 1957, Longenecker 1960), and a vessel that was only stenosed prior to surgery will often be tied off during surgery to permit an end-to-end anastomosis to be made.

Collaterals have time to develop during the 'normal' disease process as this is relatively slow, and as the pressure drop across an atheromatous lesion increases, so the collaterals become larger. However, if a graft occludes it is usually due, at least in part, to clotting in the graft, an acute event.

An example of the desirability of ligating stenosed vessels in some situations is provided by the femero-femoral cross-over graft as it is performed to relieve intermittent claudication. If the diseased side is anastomosed end-to-side (the other side must clearly be joined in this way to permit flow to the good leg also), then at rest there would be virtually no pressure drop across the graft, and little or no flow through it. As a result of this the graft would almost inevitably clot.

There are at least five reasons why grafts are thought to fail, (Edwards et al 1966, Koontz and Stansel 1972, Greenstein and Mannick 1966), these are poor 'run-in' as a result of there being disease proximal to the site of the graft, poor 'run-off' which is due to disease distal to the graft, poor surgical technique (the graft may be twisted, or some of the intima may be partially stripped from the wall of a vessel during suturing), advancing disease, and the use of an incorrect size of graft. This last mentioned fault probably occurs more often during vein grafts when the surgeon has very little choice as to what size the graft will be. If the graft is too small a large pressure drop develops across it, if it is too large the flow through it is sluggish, and both these events appear to lead to occlusion. As yet the role that each of these factors plays is not well documented.

It is hoped that the results of this study will increase the understanding of haemodynamic changes which occur in peripheral arterial disease and thus help the surgeon to assess the disease more accurately, and that this in turn will improve the success rate of reconstructive vascular surgery.

CHAPTER TWO

THEORETICAL MODELS OF BLOOD FLOW IN ARTERIES

There are numerous theoretical models of blood flow in arteries, ranging from the naive to the impractically complex. Only a limited number can be mentioned in a discussion such as this, and thus a measure of selection has been employed. The models discussed here are those which give an insight into arterial blood flow, and those that will be of use in the analysis of experimental results, and in the discussion of the assessment of vascular disease.

2.1 Pulsatile Laminar Flow in Normal Arteries

There are a large group of models which treat blood flow as a laminar flow phenomena. These will be considered, as they are probably the most useful model of blood flow in non-diseased or slightly diseased arteries, and they give an insight into the movement of blood within the arteries.

Twenty one such models have been enumerated by R.H. Cox (1969) in his useful review. The vast majority of these deal with the axisymmetric motion of a viscous, non-compressible, Newtonian liquid through straight isotropic compressible tubes. The best known of these models are those of J.R. Womersley (1955, 1957a, 1957b, 1958a, 1958b) partly because of their completeness and partly because D.A. McDonald has used them extensively in his popular monograph on blood flow in arteries (1960, 1974). It is the models of Womersley that will be discussed here. They may be divided up according to the type of wall assumed in each case. These

are a) rigid, b) free elastic, c) constrained elastic, and d) visco-elastic.

2.1.1 Rigid Tube Model

As pointed out by Womersley (1957a) the flow of a viscous liquid in a long straight circular tube under the influence of a periodic pressure gradient seems first to have been investigated by Richardson and Tyler (1929). The exact equation of motion may be written

$$\frac{\partial w}{\partial r} = \frac{1}{\rho}\frac{\partial p}{\partial z} + \nu\left(\frac{\partial^2 w}{\partial r^2} + \frac{1}{r}\frac{\partial w}{\partial r}\right) \qquad 2.1$$

when w is the velocity along the tube at radial co-ordinate r, ν the kinematic viscosity, ρ the density of the liquid, z an axial co-ordinate and $\partial p/\partial z$ the pressure gradient.

The solution to this equation for a pressure gradient

$$\frac{\partial p}{\partial z} = M \cos (nt - \phi)$$

may be written

$$w = \frac{MR^2}{\mu}\frac{M_o'}{a^2}\sin (nt - \phi + \varepsilon_o') \qquad 2.2$$

where M_o' and ε_o' are both functions of y and a, y being the non-dimensional radial co-ordinate r/R, and a the important non-dimensional parameter $R(n/\nu)^{\frac{1}{2}}$. which characterises the motion of the liquid. The functions M_o' and ε_o' are further discussed in Appendix One where it can be seen they are related to complex Bessel functions in a and y.

The volumetric flow Q, can be obtained by integrating equation 2.2 across the tube. This yields

$$Q = \frac{\pi R^4 M}{\mu} \frac{M'_{10}}{a^2} \sin (nt - \phi + \varepsilon'_{10}) \qquad 2.3$$

where M'_{10} and ε'_{10} are functions of a alone. This too is discussed further in Appendix One.

2.1.2. Free Elastic Tube Model

Clearly a rigid walled model of the artery is in many cases of little use for predicting the behaviour of blood flow in arteries. More particularly it will predict no longitudinal or radial movement of the artery wall, and the apparent velocity of a pressure wave within the artery will be infinite.

The analysis of flow in an elastic tube is considerably more complex than that in a rigid tube, but it may be shown (Womersley 1955, 1957) that the average velocity of fluid across the tube is given by

$$\bar{w} = \frac{MR^2}{\mu} \frac{M''_{10}}{a^2} \sin (nt - \phi + \varepsilon''_{10}) \qquad 2.4$$

where M''_{10} and ε''_{10} are functions of a, Poisson's ratio σ and k the ratio of wall thickness to the radius of the tube = h/R, (these functions are discussed further in Appendix One). Equation 2.4 has been written for average velocity, rather than for volumetric flow, as the tube is elastic and will obviously change in diameter throughout the cycle. Volumetric flow can be calculated from

$$Q(t) = \bar{w} \pi R^2 (1 + \xi/R) \qquad 2.5$$

where ξ is the radial displacement of the tube wall. If there is no reflected pressure wave then this factor has the particularly simple form of

$$\xi/R = \bar{w}/2C_o \qquad 2.6$$

C_o being the wave velocity. From this it follows that

$$Q(t) = \bar{w} \Pi R^2 (1 + \bar{w}/2C_o) \qquad 2.7$$

If the expression contains a reflected wave, then ξ/R is given by

$$\frac{\xi(t)}{R} = \frac{P}{2\rho_o C_o^2} (1-\alpha^2) \frac{x}{2} (1+\eta F_o) \qquad 2.8$$

where P is pressure, ρ_o the density of the liquid and x, η and F_{10} are functions of α, σ and k as defined in Appendix One. This equation is of little practical use for calculating flows, but as Womersley (1957) points out the phase of the complex quantity $\frac{1}{2}x(1+\eta F_o)$ is positive for all finite values of k, so that the variation in diameter always leads pressure, though never by more than a few degrees.

The velocity of wave propagation in a thin walled elastic tube containing an inviscous liquid has been long known, and is called the Moens-Korteweg (M.K.) velocity after the work of Moens (1878) and Korteweg (1878).

$$C_o = \left(\frac{Eh}{2R\rho}\right)^{\frac{1}{2}} \qquad 2.9$$

where E is Young's modulus, h the wall thickness and ρ the density of the liquid in the tube. This equation has been modified by Bergel (1960) to allow for a thick-walled tube, and his corrected velocity may be approximated by

$$C = \left(\frac{Eh}{2R\rho(1-\sigma^2)}\right)^{\frac{1}{2}} \qquad 2.10$$

Womersley in his 1957 monograph allowed for both the wall thickness, and for the viscosity of the fluid by introducing a complex wave velocity such that

$$\frac{C_o}{C} = X - iY = \left\{(1-\sigma^2)^{\frac{1}{2}} \frac{x}{2}\right\}^{\frac{1}{2}} \qquad 2.11$$

Thus the phase velocity C_1 may be written,

$$C_1 = \frac{C_o}{X} = \left(\frac{Eh}{2R\rho}\right)^{\frac{1}{2}} / \mathrm{Re}\left\{(1-\sigma^2)^{\frac{1}{2}} \frac{x}{2}\right\}^{\frac{1}{2}} \qquad 2.12$$

Furthermore, the attenuation coefficient may be found from the imaginary part of 2.11 and is given by

$$a = \frac{nY}{C_o} = \frac{n}{C_o} \mathrm{Im}\left\{(1-\sigma^2)^{\frac{1}{2}} \frac{x}{2}\right\}^{\frac{1}{2}} \qquad 2.13$$

Finally the attenuation per wavelength may be found from

$$A = \exp(-2\Pi Y/X) \qquad 2.14$$

The quantities C/C_o and A have been plotted as a function of α by Womersley in his 1957 monograph.

2.1.3. Constrained Elastic Tube Model

Womersley has examined the effect of adding additional mass, elastic constraint and internal viscous damping to the vessel wall, and has shown that the equations take the same form as those for the perfectly elastic wall, but that the constant k, which represented the thickness of the wall must be replaced by a new constant k' given by

$$k' = \left(\frac{1+h_1 R_1 \rho_1}{h\ r\ \rho}\right) \cdot \left(1 - \frac{m^2}{n^2}\right) \qquad 2.15$$

where m is the natural frequency of the longitudinal constraint, h_1, ρ_1 and R_1 are the thickness, density and radius of the added mass and h, ρ and R those of the unconstrained vessel. Unfortunately there is no way of evaluating k' at present and Womersley has examined the effect of changing this quantity within the range $0.4 > k' > -\infty$. An interesting fact which emerges is that as the constraint increases, i.e: as k' tends to minus infinity so M''_{10} tends to M'_{10} and ε''_{10} tends to ε'_{10}. Two further relationships may be derived for the case of limiting constraint

$$\frac{C_o}{C} = \left(\frac{1-\sigma^2}{M'_{10}}\right)^{\frac{1}{2}} \exp\left(-i\,\varepsilon'_{10}/2\right) \qquad 2.16$$

and

$$\xi/R = (1-\sigma^2)P/2\rho\ C_o^2 \qquad 2.17$$

2.1.4. Visco-elastic Tube Model

Finally Womersley (1957) examined the modifications that would be required to his theory to take into account the internal damping within the wall of the vessel. This required the postulation of a complex elastic modulus and a complex Poissons ratio, such that

$$E_c = E(1+in\Delta E) \qquad 2.18$$

$$\sigma_c = \sigma(1+in\Delta\sigma) \qquad 2.19$$

Womersley was then able to show that the equation for the complex wave velocity in a visco elastic tube can be written

$$\frac{C_o}{C} = \left(\frac{1-\sigma^2}{M'_{10}}\right)^{\frac{1}{2}} \exp\left(-i\varepsilon'_{10}/2\right)\left\{1-in\left(\frac{\Delta E}{2}+\frac{\Delta\sigma}{3}\right)\right\} \quad 2.20$$

The quantity $n(\Delta E/2 + \Delta\sigma/3)$ has been determined experimentally by McDonald and Gessner (1968) for both blood and Kreb's solution in perfused carotid arteries, and appears to change little with frequency, its value being about 0.2.

2.1.5 Further Sophistication

Two further interesting aspects of blood flow that Womersley has examined are the effect on flow and pulse velocity of a liquid whose viscosity varies with frequency (Womersley 1958b), and of a thin boundary layer of liquid with low viscosity (Womersley 1957b).

2.2 The Application of Pulsatile Laminar Models of Blood Flow to diseased arteries

There is of course the question of how applicable the pulsatile laminar model is, even to normal blood flow in normal arteries. Any theory can only be as good as the assumptions upon which it is based. Womersley's model assumes a long straight parallel sided tube, containing a homogeneous Newtonian fluid that is excited in a strictly periodic manner. None of those assumptions are correct, however, they are sufficiently realistic for the theory to make reasonable predictions of blood flow from blood pressure gradients (McDonald 1974). Clearly any extension

of Womersley's theory to diseased arteries depends on the flow remaining laminar. The question of under what circumstances pulsatile flow becomes non-laminar has not been fully answered. It appears, perhaps contrary to expectation, that pulsatile flow in long straight tubes remains laminar to a higher Reynolds number than steady flow in the same tube (Sarpkaya 1966, Yellin E.L. 1966), but in a pathological situation there will be discontinuities of one sort or another in the arterial lumen that will give rise to eddies. Goldstein (1938) states that for steady laminar flow to be maintained in the presence of a sharp-edged projection of height ε in a pipe of diameter D

$$\varepsilon/D < 2/(Re)^{\frac{1}{2}} \qquad 2.21$$

Therefore even if ε/D is only 0.2, a relatively small encroachment in an atheromatous vessel, and if the Reynolds number exceeds 100, the flow will become turbulent. If this calculation is even approximately valid for pulsatile flow, it is clear that pulsatile laminar theory may not be applied to the diseased circulation. It is of passing interest to note that Womersley in his 1957 monograph did deal with the effects of rigid inserts in the artery, as well as with reducing the local cross-sectional area, but these calculations were in order to predict the effect of applying various electromagnetic flow probes to the vessel wall, and dealt only with the effect of very mild constrictions on reflected waves.

2.3 Steady Flow Through Narrowings in the Arterial System

The opening sentence of the first edition of D.A. McDonald's book "Blood Flow in Arteries" (1960) was

'the most obvious feature of (blood flow in arteries) is that it is pulsatile'. Any complete model of blood flow in arteries must take account of this pulsatility, but it is useful, because pulsatile flow in diseased arteries is so complex, to first consider steady flow through arterial narrowings.

2.3.1. Interaction between mean and pulsatile flow components

Before embarking on a discussion of steady flow and pressure it is as well to note that if, as is usually the case in diseased arteries, the system is non-linear then the mean components of flow and pressure cannot be separated from the pulsatile components and treated in isolation. This can be readily shown if the pressure drop across a simple model of a stenosis is considered. Let the pressure drop across the stenosis be of the non-linear form

$$P = AQ + BQ^2 \qquad 2.22$$

where Q is flow, and A and B are constants. In general any periodic flow may be written

$$Q(t) = \sum_{m=o}^{\infty} Qa_m \cos mnt + Qb_m \sin mnt \qquad 2.23$$

where Qa_m and Qb_m are Fourier coefficients, mn is the angular frequency of the m^{th} harmonic and t is the time. Substituting equation 2.23 into 2.22, the mean pressure drop may be written

$$\overline{\Delta P} = AQa_o + \frac{B}{T_o}\int^{T} \sum_{r=o}^{\infty} \sum_{m=o}^{\infty} (Qa_r \cos rnt\, Qa_m \cos mnt$$

$$+ Qb_r \sin rnt.\, Qb_m \sin mnt + Qa_r \cos rnt.\, Qa_m \sin mnt$$

$$+ Qb_r \sin rnt.\, Qa_m \cos mnt).\, dt$$

which reduces on integration to

$$\bar{P} = AQa_o + BQa_o^2 + B/2 \sum_{r=1}^{\infty} (Qa_r^2 + Qb_r^2) \qquad 2.24$$

The third term of this expression contains the coefficients of all the flow harmonics present, and must always be positive, indicating that the mean pressure drop across a non-linear stenosis of the form discussed must always be greater than that which would be predicted from the steady component of flow alone.

2.3.2 General Losses

It is surprising to those not familiar with the subject that a problem as apparently simple as steady flow through a tube with a localised constriction is not fully understood. The fact that this is so perhaps gives an insight into the difficulty of attempting to describe the behaviour of a non-homogeneous fluid with a non-Newtonian viscosity flowing in a pulsatile fashion through an ill-defined non-linear system.

One of the first sensible discussions of steady flow through a stenosis is that of May, DeWeese and Rob (1963b). Although their paper is basically experimental they suggest in an Appendix that the pressure drop across a stenosis is composed of three components, and may be written

$$\Delta P = \Delta P_s + \Delta P_c + \Delta P_e \qquad 2.25$$

where ΔP_s in the pressure drop through the stenosis predicted by Poiseuille's law, ΔP_c is a result of energy

lost due to the contraction of the stream, and ΔP_e a result of the post-stenotic expansion. May et al derive expressions for each of these terms, but as pointed out by Berguer and Hwang (1973) the derivation of these terms is hardly acceptable. Berguer and Hwang expand the theory a little further but their paper contains errors. In their discussion of contraction losses they introduce a formula which is independant of geometry, and then go on to suggest that it is only valid for mild constrictions. Clearly, any expression for losses such as this must be dependant on geometry, and indeed it seems that they have chosen a constant that would normally be relevant to a very tight stenosis (Daugherty and Franzini 1965). They also omit a bracket at the end of their section on expansion losses and once it is inserted it becomes apparent their equation is incorrect. Their analysis may however be brought to a successful conclusion if an additional term is introduced which represents energy lost as heat other than by the Poiseuille mechanism.

Evans, Quin and Bell (1978) have extended the same model slightly, whilst discussing blood pressure measurement in patients with peripheral vascular disease, and have suggested that in general the pressure drop across a stenosis with steady flow through it may be written

$$P = AQ + BQ^2 \qquad 2.26$$

where Q is the volumetric flow through the stenosis and A and B are constants. This formula will now be considered in more detail.

The major sources of loss in a stenosis are as

detailed by May et al, those due to frictional effects and those due to the incomplete transition of flow energy into lateral pressure energy and visa versa, as the cross section of the vessel changes.

2.3.3 Frictional Losses

It is clear that whenever a fluid flows through a pipe there must be a certain frictional loss, however as this loss is strongly dependant on the radius of the pipe, an unusually rapid pressure drop will occur across any narrowed section. The well known formula for such a loss is

$$\Delta P_s = fL\bar{v}^2\rho/2D \qquad 2.27$$

where f is the friction factor, L the length of the pipe, D is its diameter, $\bar{v}$ the mean velocity of flow and ρ the density of the fluid. (Daugherty and Franzini 1965)

For laminar flow it can be shown that

$$f = 64\nu/\bar{v}\,D \qquad 2.28$$

where ν is the kinematic viscosity, and thus equation 2.27 may be rewritten

$$\Delta P_s \text{ (Laminar)} = 128\,\nu LQ\,\rho/\Pi D^4 \qquad 2.29$$

This is the famed Hagen-Pouseuille equation, first analytically derived by Wiedemann in 1856, and which is unfortunately all too often used indiscriminately to predict pressure losses.

For turbulent flow the friction factor is a function both of Reynolds number ($\bar{v}D/\nu$), and the relative roughness of the pipe. Colebrook (1938) found the approximate relationship

$$f^{-\frac{1}{2}} = -2 \log_{10} (\varepsilon/3.7D + 2.51/Re.f^{\frac{1}{2}}) \qquad 2.30$$

where ε/D is relative roughness.

There is no analytical solution to this equation, but for flows with a large Reynolds number through a pipe with a rough lining the right-hand term within the bracket becomes insignificant and equation 2.30 reduces to von Karman's relationship

$$f^{-\frac{1}{2}} \simeq -2 \log_{10} (\varepsilon/3.7D) \qquad 2.31$$

For most practical purposes this approximation should be adequate for the analysis of arterial stenosis. Using this approximation the pressure drop may be rewritten

$$\Delta P_s \text{ (turbulent)} = \frac{8LQ^2\rho}{\pi^2 D^5} \left\{ -2 \log_{10} \left(\frac{\varepsilon/D}{3.7}\right)\right\}^{-2} \qquad 2.32$$

2.3.4 Expansion Losses

Although the analysis of expansion losses by Berguer and Hwang is incorrect, both they and Fry (1968) produce experimental evidence to suggest that the lateral pressure energy in a post-stenotic segment is very similar to that within the stenosis itself. This is due to the incomplete transition of kinetic energy that has been gained as a result of the higher velocity in the stenosed segment, back into lateral pressure energy. The total pressure drop across the stenosis due to the expansion losses can thus be approximately equated to the reduction in pressure between the pre-stenotic and the stenotic segment. i.e:

$$\alpha_1 \rho \bar{v}_1^2/2 + P_1 = \alpha_2 \rho \bar{v}_2^2/2 + P_2 \qquad 2.33$$

where P is the lateral pressure in the segment, and the suffices 1 and 2 refer to the pre-stenotic and stenotic segments respectively. α is a constant that has a value of 2 if the flow is turbulent, and of approximately 1 if the flow is laminar.

The volumetric flow in both segments must be identical and thus

$$\bar{v}_2^{\,2} = \bar{v}_1^{\,2} \, (r_1/r_2)^4$$

where r_1 and r_2 are the radii of the pre-stenotic and stenotic vessel. Thus equation 2.33 may be rewritten

$$P_1 - P_2 = \frac{\rho \alpha_2 \bar{v}_1^{\,2}}{2} \left(\frac{r_1}{r_2}\right)^4 - \frac{\rho \alpha_1 \bar{v}_1^{\,2}}{2} \qquad 2.34$$

Assuming the form of the flow is the same in both segments i.e: $\alpha_1 = \alpha_2 = \alpha$ this equation may be rewritten

$$\Delta P_e = Q^2 \left(\frac{1}{\Pi r_1^{\,2}}\right)^2 \frac{\rho \alpha}{2} \left\{\left(\frac{r_1}{r_2}\right)^4 - 1\right\} \qquad 2.35$$

2.3.5 Contraction Losses

As pointed out by Berguer and Hwang, the energy loss resulting from a sudden contraction is normally much smaller than that resulting from a corresponding expansion. The pressure drop due to a contraction may be written (Daugherty and Franzini 1965)

$$\Delta P_c = kQ^2\rho \, / 2 \, \Pi^2 r_2^{\,4} \qquad 2.36$$

when k is a constant in any particular geometrical configuration, but which in general varies with r_1/r_2.

Typical values of k are 0.50, 0.45, 0.42 and 0.39 for r_2/r_1 equal to 0, 0.1, 0.2 and 0.3 respectively.

2.3.6 Total Losses

Each of the losses discussed has had the form

$$\Delta P = KQ^t$$

where K is a constant related to the source of the loss, the geometry of the stenosis and the fluid flowing through it, and t is a constant which takes the value 1 or 2 depending on the source of the loss. It follows that in general the pressure drop across a stenosis may be written

$$\Delta P = AQ + BQ^2$$

where A and B are constants derived by combining the constants in equations 2.29, 2.32, 2.35 and 2.36 in a suitable manner.

2.4 Pulsatile Flow Through Narrowings in the Arterial System

The analysis of pulsatile flow through arterial stenoses is obviously more difficult than the analysis of steady flow, which is itself formidable. Probably the most useful contribution to the literature is that of Young and Tsai (1973b), although their paper is basically experimental. They derive an equation which consists of three terms and which may be written

$$\Delta P = \frac{AQ}{\Pi r_1^2} + \frac{B}{\Pi^2 r_1^4} Q|Q| + \frac{C}{\Pi r_1^2} dQ/dt \qquad 2.38$$

The first two terms of this equation are analogous to the two terms of equation 2.37 derived for steady flow. The third term is arrived at by means of a linear momentum analysis. That the system is non-linear Young and Tsai freely admit, but it is useful in the absence of any better theory.

The constants A, B, and C are related to viscous effects, convective acceleration, and inertial effects. Young and Tsai have made no attempt to relate A to the geometry of the stenosis, but B may be approximated by

$$B \simeq (r_1^2/r_2^2 - 1)^2 b \qquad 2.39$$

where b is a constant which is independant of geometry. Provided r_1 is large compared with r_2, a realistic assumption for arterial stenosis, then this equation has the same form as 2.35 the equation for expansion losses under steady flow conditions.

The linear momentum analysis suggests that C may be written in the form

$$C \simeq L_t.c \qquad 2.40$$

where L_t is the distance between pressure taps and c is a constant which is independant of geometry.

2.5 Fourier Analysis and Non-Linear Equations

The non-linearity of equations 2.37 and 2.38 makes the analysis of the relationship between blood flow through a stenosis, and the pressure drop across it more difficult to handle.

It is not possible, as it would be with a linear system, to relate the p^{th} harmonic of flow to the p^{th} harmonic of pressure difference as the flow harmonics will interact with each other. It can be shown however (see Appendix Two) that if the relationship takes the form described by equation 2.38 with the exception of replacing $Q/Q/$ by Q^2, that the p^{th} harmonic pressure difference is given by

$$\begin{aligned}\Delta Pp(t) = \Big[& AQa_p + B/2 \sum_{n=0}^{\infty} \sum_{m=o}^{\infty} \{(Qa_n\, Qa_m - Qb_n Qb_m).\delta(p,m+n) \\ & +(Qa_n Qa_m + Qb_n Qb_m).\delta(p,m-n) + (Qa_n Qa_m + Qb_n Qb_m).\delta(p,n-m)\} \\ & + C\ p.\ w.\ Qb_p \Big] \cos pwt \\ & + \Big[AQb_p + B/2 \sum_{n=o}^{\infty} \sum_{m=o}^{\infty} \{ (Qa_n Qb_m + Qb_n Qa_m).\ \delta(p,m+n) \\ & +(Qa_n Qb_m - Qb_n Qa_m).\ \delta(p,m-n) + (Qb_n Qa_m - Qa_n Qb_m).\ \delta(p,n-m) \} \\ & - C\ p\ w\ Qa_p \Big] \sin p\ wt \end{aligned} \qquad 2.41$$

where $Q(t)$ has been written as in equation 2.23, and $\delta(u,v)$ is Kronecker's delta given by

$$\delta(u,v) = 1 \quad u=v; \qquad \delta(u,v) = 0 \quad u \neq v.$$

Unfortunately, the mathematics become intractable if $Q/Q/$ is not replaced by Q^2, but equation 2.41 will be correct provided that there is no reverse component to the flow.

The equation is of interest because it demonstrates the way in which the harmonics of flow interact. It may also be of use if it is necessary to perform a Fourier analysis on the pressure and flow waveform either to smooth the data or to correct for deficiencies in the measurement system. The analysis of flow through stenoses will be dealt with further in Chapter Six on experimental measurements in dogs.

2.6 Conclusion

In conclusion it may be stated that the methods of analysis of the diseased circulation are far from perfect. There are many models, most of which are intended to explain or illuminate one particular aspect of arterial flow. For example, the model of Young and Tsai (1973) attempts to quantify the pressure drop across a stenosis, the models of Davids and Cheng (1972) and of Morgan and Young (1974) examine velocity profiles and wall shearing stresses in diseased arteries in detail, whilst the theory of Lou (1975) is particularly concerned with the radial oscillation of the artery, and the progagation speeds of pressure waves in healthy arteries.

CHAPTER THREE

EXPERIMENTAL MODELS OF THE DISEASED ARTERIAL SYSTEM

The first important contribution to the literature on the effect of stenoses within blood vessels was that of Mann et al (1938) whose interest originally lay in the effect a blood-flowmeter, which slightly constricted the blood vessel, had on the flow through the vessel. They found that a slight degree of constriction was not significant and so went on to ask the question 'how much can one constrict a blood vessel without decreasing the flow of blood?' They carried out three sets of experiments, the first set being in-vitro and the second two in-vivo, when they placed constricting units inside and outside the carotid arteries of anaesthetized dogs. They measured the percentage reduction in mean blood flow with their thermostromuhr flowmeter and found that a reduction in blood vessel area of about 80% was required to decrease significantly the flow through it.

A few years later Shipley and Gregg (1944) carried out a more comprehensive set of experiments. They used external constriction around the carotid arteries of anaesthetized dogs and measured flow with a rotameter, and mean systemic blood pressure with a directly coupled mercury manometer. In addition to making measurements under 'resting' conditions, they manipulated peripheral resistance by either injecting nitroglycerine into the vessel, or by occluding the vessel for two to three minutes prior to a measurement. They showed that the percentage decrease in flow due to a stenosis was a function of the initial peripheral resistance and the systemic blood pressure, and also noted that the peripheral

vascular bed tended to compensate for the effects of the stenosis.

Although these studies were of great interest, it was not until the sixties when reconstructive vascular surgery became a widely available treatment for vascular disease that an understanding of the relationship between the degree of constriction of a vessel, the blood flow through it, and the pressure drop across it became of paramount importance. Since this time there has been a flood of papers on the subject.

In an interesting study in 1962 Crawford et al examined the effect on blood flow and pressure of constricting varying lengths of the carotid arteries of dogs, and showed that a significant blood pressure change (appearance of gradient across the constriction) occured simultaneously with a significant reduction in blood flow, but only after considerable reduction in the lumenal area; and that the degree of arterial constriction required to produce significant changes varies with the length of the obstruction. They then measured the pressure drop and flow through the stenosed internal carotid arteries of 65 patients, both before and after endarterectomy, and were able to show that significant changes in blood flow usually occurred only after the removal of a lesion associated with a gradient. The results of carotid artery, and peripheral artery surgery are not strictly comparable, however, in that the peripheral arteries may be required to carry five or six times the resting blood flow during exercise, whereas the flow through the carotid arteries is fairly constant over a wide range of conditions. Furthermore the collateral circulation to the

brain is very much better developed than that to the limbs.

May et al (1963b) studied the effect of changing the degree and length of stenoses, and of body position on blood flow and pressure gradients in the canine iliac artery and then went on (May et al 1963c) to measure the effects of sympathectomy and exercise on these parameters. Their findings were that the critical value of stenosis (defined by them as the percentage reduction in area to produce a 20% reduction in flow) was 82% at rest, 75% following sympathectomy (which caused an increase of 176% on resting flow) and 60% during exercise induced by galvanic stimulation (which augmented the blood flow in the unconstricted artery by an average of 240%) and thus showed the importance of flow on critical arterial stenosis. All these figures were derived using stenoses with a length of 3mm.

Fiddian et al (1964), as a result of a rather curious set of experiments in which they used a dog as a blood pump, but which were effectively in-vitro, suggested that actual stenosis diameter rather than the percentage reduction in diameter is the important factor influencing blood flow, a surprising hypothesis which presumably reflected the inadequacies of their model. In the same year Vonruden et al (1964) published work on the effect of multiple arterial stenoses on blood flow in the carotid arteries of dogs, and showed that the degree of stenosis is far more important than length as far as the effect on blood flow is concerned, and that when two unequal stenoses are present, the one with the smaller lumen is almost solely responsible for determining the total flow rate, whichever stenosis is the more proximal of the two.

Keitzer et al (1965) were one of the first groups to be concerned with instantaneous values of pressure and flow in their paper on pulse changes seen in occlusive vascular disease. They demonstrated very elegantly the reduction in pulse pressure distal to a stenosis resulting from increased flow, and the return to normal of a reduced pulse distal to a stenosis upon distal occlusion of the artery, hence explaining the phenomena of 'disappearing pulses' (De Weese 1960) and paradoxical variation of pulses (Blaisdell and Gander 1961).

Various papers since this time have highlighted one or more aspects of the problem. For example Kindt and Youmans (1969) concerned themselves with the effect of stricture length on critical arterial stenosis, Youmans and Kindt (1968) and Flanigan et al (1977) reported the effects of multiple arterial stenosis, Eklof and Schwartz (1970) reported the effects of collateral flow on critical stenosis of the carotid artery, and a large number of authors including Kreuzer and Schenk (1971, 1973), Gould et al (1974a, 1974b) and Weissenhofer and Schenk (1974) have discussed the effect of vasodilatation on critical arterial stenosis, and the effect of the stenosis on 'flow reserve'.

Perhaps the most valuable experimental papers on arterial stenosis are those which attempt to reconcile the results obtained with mathematical models. Of these the earliest of note are those of May et al (1963b, 1963c) already mentioned both in Section 2.3.2. and earlier in this Chapter. Berguer and Hwang (1973) also mentioned in Section 2.3.2. followed their theoretical work with a number of dog experiments, and compared the predicted and actual losses of

kinetic energy of blood flowing through stenoses and found them to be in fairly good agreement.

Finally an excellent series of papers by D.F. Young and his associates have shed light on the mechanism by which pressure gradients form across arterial stenoses. In their first two pertinent papers (Young and Tsai, 1973a 1973b) they examined in detail the flow characteristics of models of arterial stenoses under conditions of steady and unsteady flow respectively and found that the pressure drop across a stenosis could be written in the form

$$\Delta P = \frac{K_v \mu}{2r_1} U + \frac{K_t}{2}\left[\frac{r_1^2}{r_2^2} - 1\right]^2 \rho |U| U + K_u \rho L_t \frac{du}{dt} \qquad 3.1$$

where μ is viscosity, $U = Q/\pi r_1^2$ the instantaneous cross-sectional mean velocity in the unobstructed tube, r_1 and r_2 the radii of the unobstructed tube and the stenosis respectively, ρ the density of blood, and L_t the distance between pressure taps. K_v, K_t and K_u are constants related to viscous, turbulent and inertial losses, but in general vary from stenosis to stenosis. This formula has already been discussed briefly in Section 2.4, where for the sake of clarity it was written as formula 2.38.

In a further in-vitro paper (Seeley and Young 1976) they investigated the effect of percent stenosis, length, eccentricity and multiple stenoses on pressure loss under steady flow conditions, and in particular the effect of these factors on the constants K_v and K_t in Equation 3.1. They showed that eccentricity (the amount by which the stenosed segment is off axis) made little difference, at least to stenoses of around 94%; that K_t is almost independant of geometry and has a value of approximately 1.52; and that K_v

can be written

$$K_v = 16 \frac{L_a}{r_1} \left(\frac{r_1}{r_2}\right)^4 \qquad 3.2$$

where

$$L_a = 0.83\ L + 3.28 r_2 \qquad 3.3$$

They also showed that for multiple stenoses the pressure drop cannot be predicted by summing the pressure drops which would be produced by each stenosis individually since they 'interfere' with each other unless the spacings between them exceeds some critical distance which depends on Reynolds number. In general the value of pressure drop due to two stenoses of length L in series, lies between the value of pressure drop due to a single stenosis of length 2L, and twice that due to a single stenosis of length L. All these results were of course obtained on the bench under highly artificial conditions and require in-vivo confirmation. Young et al (1975, 1977) have shown however that it is possible to predict both mean and peak pressure drops in stenosed carotid and femoral arteries in dogs using Equation 3.1. In their experiments they evaluated K_v, K_t and K_u in vitro prior to each experiment and found K_v to be close to the value predicted by Equations 3.2 and 3.3, K_t to have a value of between 1.57 and 2.31, and K_u a value of approximately 1.2. On the basis of their in-vivo experiments it appears that K_v and K_t as found from in-vitro experiments are slightly too low.

In summary, it may be said that the relationship between the pressure gradient across a stenosis and the blood flowing

through it is better understood than the influence of arterial narrowings on blood flow in arteries. This is because the stenosis is only one component of a complex system, the other important components being the resistance of the peripheral vascular bed, and the collateral circulation.

Most of the work on the flow-pressure drop relationship to date has been either theoretical or in vitro, and one of the purposes of this thesis will be to test the conclusion of this work in vivo. In particular the accuracy of Equation 3.1 and the dependency of the constants K_v, K_t and K_u on geometry will be examined. In addition the effect of various stenoses on flow and pressure within the limb will be scrutinized.

S E C T I O N B

'If you take a group of animals, all of the same strain, and all bred to have identical characteristics, and you perform on them an experiment under carefully controlled conditions, each animal will do exactly what it feels like at the time.'

The Harvard Rule
(Dewhurst 1978)

CHAPTER FOUR

EXPERIMENTAL APPARATUS

Three basic measurement techniques were used during the animal experiments. Electromagnetic Flowmetry, Doppler Velocimetry and Intra-Arterial Pressure Manometry. Each of these techniques will be discussed in this Chapter and practical details of the actual systems used given.

4.1 Electromagnetic Flowmetry

Electromagnetic Flowmetry was used throughout the animal experiments, it being the only method of measuring volumetric blood flow in a single vessel with acceptable accuracy. It has the great disadvantage in clinical practice that it requires the blood vessel first to be exposed, but this presented no problem in the animal experiments, indeed the vessel had already to be exposed for other purposes.

4.1.1 The Development of the Electromagnetic Flowmeter

The Electromagnetic blood-flowmeter is an application of Michael Faraday's well known law of electromagnetic induction, which states that when a conductor moves in a magnetic field, an e.m.f. is generated in a direction which is mutually perpendicular to both the magnetic field and the direction of motion. If $\underline{V}$ is the velocity of the conductor moving through a magnetic field of strength $\underline{B}$, then the e.m.f. $\underline{E}$ produced along a conductor of length $d\underline{l}$ is given by

$$\underline{E} = \int_{-d/2}^{d/2} \underline{V} \times \underline{B} \; dl \qquad 4.1$$

This law holds for fluids just as it does for solids, and is utilised to measure the flow of blood (the conductor) in the unopened blood vessel.

Faraday himself realised that it should be possible to investigate fluid flow in this way, and in 1832 attempted to demonstrate the effect (Faraday 1832).

"I made experiments therefore (by favour) at Waterloo Bridge, extending a copper wire nine hundred and sixty feet in length upon the parapet of the bridge, and dropping from its extremities other wires with extensive plates of metal attached to them to complete contact with the water. The wire therefore and the water made one conducting circuit; and as the water ebbed and flowed with the tide, I hoped to obtain current analogous to those of the brass ball".

The magnetic field was in this case the earths magnetic field. Unfortunately this attempt was unfruitful and Faraday obtained only irregular deflections of his galvanometer, and it was not until 1918 that potentials produced by tidal movement were recorded by Young, Gerrard and Jerome (Young et al 1920).

It was Williams (1930) that first applied the electro-magnetic flowmeter principle to a non-oceanographic problem when he measured the flow of copper sulphate solution through a non-conducting pipe in a uniform transverse magnetic field. Two years later Fabre (1932) suggested that it should be possible to measure the flow of blood through an unopened blood vessel in a similar way, however he apparently made no attempt so to do, and it was left to Kolin (1936) to publish

the first description of a practical electromagnetic blood flowmeter. Shortly afterwards Wetterer (1937), having worked independantly of Kolin, published the details of his nearly identical apparatus.

These early flowmeters employed exceedingly bulky magnets, were very inconvenient to use and gave none too reliable results. In contrast todays models are small and allow accurate recordings of instantaneous and mean flow in all but the smallest vessels to be made. Jochim (1962) has reviewed the development of the electromagnetic blood flowmeter up to 1961 in some detail.

4.1.2 Modern Electromagnetic Flowmeter

There are two basic types of electromagnetic blood flow probes, cannulating probes and probes which encircle the intact vessel (Fig 4.1). The cannulating probes are the simpler, consisting of a short length of non-conducting tube fitted with a pair of diametrically opposed electrodes. A magnetic field is applied across the tube at right angles both to the axis of the tube, and the electrodes, and the induced E.M.F. is picked off at the electrodes. The non-cannulating probes employ the vessel itself as the conduit through which the blood flows and because of the partially conducting nature of the blood vessel, have a different sensitivity to those of the cannulating type. One of the remarkable properties of the E.M. flowmeter is that its sensitivity does not change as the flow profile changes, provided that the flow is axisymmetric, and as a consequence of this if the conductivity of the vessel wall is the same as that of the blood, the vessel wall is indistinguishable, as far as the flowmeter is concerned, from a stationary layer of blood.

Indeed this arrangement has some advantage in that the flow meter is most affected by asymmetries farthest from the centre of the vessel. Edgerton (1968) has discussed the effect of differing wall thicknesses and conductivities on the sensitivity of the flowmeter, and Shercliff (1962) in his comprehensive monograph on the properties of E.M. flowmeters in general, derives a weighting function which enables the effect of rotational asymmetry to be determined. A concentration of flow near the electrodes causes an increase in sensitivity, whilst flow concentrated near the wall at right angles to the electrodes reduces sensitivity. The effect of the encircling media of the blood vessel (Wyatt 1968) and of the haematocrit of the blood (Dennis 1969) on sensitivity have also been thoroughly investigated. These factors all change sensitivity to a greater or lesser degree, however with the exception of asymmetry they do not change during any particular experiment and are therefore not of great importance. It is changes of flow which are usually required to be measured fairly accurately, and an absolute sensitivity factor may be found at the end of animal experiments by severing the artery downstream of the flow probe and allowing the blood to collect for a short time in a measuring cylinder. This may then compare with the integral of the flow as measured electromagnetically over the same time period.

Unfortunately the axial symmetry of blood flow in a given geometrical configuration can change. This is particularly so near side branches in the artery where percentage changes in flow in the side branches may not be the same as in the parent vessel. In practice this error is minimised by attaching the flow probe to a vessel as far

from side branches as is practically possible. In diseased arteries there is the additional possibility of atheromatous plaques causing flow asymmetry, and Meisner and Messmer (1970) have, in model experiments, reduced the sensitivity of a flowmeter by approximately 10% by means of a 70% stenosis, and by 25% by means of a 90% stenosis.

The E.M. flowmeter employed throughout all the experiments described was a Statham SP2201 blood flowmeter. This model was chosen for a number of reasons. It employs pulse-wave excitation, it has a non-occlusive zero balance control, the probes are calibrated, and the cuff probes are hinged.

Pulse-wave excitation flowmeters first introduced by Westersten (1967), are highly immune to induced artifactual signals that cause baseline instability. Baseline errors are discussed in detail by Wyatt (1966), and the advantage of the pulsed-field E.M. flowmeter in rejecting these artifacts is discussed by Gasking (1972). There was historically a seemingly natural progression from steady field magnets to sinusoidally excited electromagnets, to rectangular wave excitation, to the present pulsed field devices, each successive technique having an apparent advantage over each of the previous techniques.

The ability to zero an E.M. flowmeter without occluding the vessel is a major advantage, particularly if the flow through partially blocked vessels is being monitored. Occluding an artery, even for a short period of time causes an oxygen deficit in the vascular territory of that artery, and as soon as flow is re-established it augments above its resting value to overcome this deficit. This phenomena,

usually termed reactive hyperaemia, is particularly profound in diseased vessels and the return to normal resting value of blood flow may take several minutes. Even with the non-occlusive zero facility it is usual to check the zero occlusivity at the end of each run. The flowmeter must then be allowed to return to its resting value before any further measurements are taken.

The Statham blood flow probes have calibration resistors built into them which in theory take into account normal shunting effects, typical vessel wall and blood conductivity differences, and an average haematocrit of 47%, but it is of course necessary to check this calibration in any given geometrical configuration where an accurate absolute blood flow is required.

Hinged probes are highly desirable when measurements are to be made on diseased vessels in order to prevent the dislocation of an atheromatous plaque from the artery wall, a potentially disasterous event, and one which could easily occur if the vessel has to be squeezed into a fixed geometry probe.

4.1.3 Calibration of E.M. Flowmeter

The gross calibration of the E.M. flowmeter has already been discussed in the previous section, but it is of course necessary to know the frequency response of the device. This was measured using the technique of Calvert, Pullan and Bone (1975). As they point out, other techniques require specially constructed apparatus, and are difficult to execute, whilst the method they describe is simple and requires only off-line access to a digital computer. It is based on the principle

that the frequency response of a system can be calculated from the Fourier Transform of its impulse response, which may in turn be calculated from its step response (Champeney 1973). It is of course very difficult to cause a sharp step in flow but the same effect may be obtained by imposing a step on the magnet excitation current.

The flow probe was immersed in a trough of water, and a jet of saline directed through the probe to produce a steady flow signal on the flowmeter. The output was also displayed on a Medelec fibre optic chart recorder, and a series of records obtained of the effect of closing and opening a micro-switch connected so as to short out the magnet. The step response function so obtained was differentiated numerically using the relationship 4.2.

$$h(t) = -2H(t-2T)-H(t-T)+H(t+T)+2H(t+2T) \quad /10T \qquad 4.2$$

h(t) is the first differential of H at time t, and T is the time interval between successive data points. The impulse response h(t) was then transformed into Fourier space using the recursive technique described by Goertzel (1960), in order to arrive at the amplitude and phase response of the flowmeter. The results obtained were remarkably consistent, and the technique was checked by inserting filters between the flowmeter output and the chart recorder, and comparing the measured response of the total system with the predicted response, calculated from the individual responses. These too were in good agreement. The results obtained are summarised in figure 4.2.

4.2 Ultrasonic Doppler Velocimetry

Although electromagnetic flowmeters are of great use both in animal experiments and during surgery they clearly have little place in the assessment of peripheral arterial disease because they are invasive. Much work has therefore been directed into developing non-invasive techniques of measuring blood flow. The instrument which at present holds most promise is the ultrasonic Doppler velocimeter. As the name implies it is the velocity of the blood which is measured rather than its volumetric flow. Attempts have been made to derive quantitative flow from velocity by measuring the cross section of the vessel and the blood velocity profile, but it seems that at present as much useful information may be extracted from the velocity itself.

Modern ultrasonic Doppler velocimeters for use on blood flow operate at frequencies between about 2.5MHz and 10MHz. An oscillator excites a piezo-electric crystal to generate plane waves which are directed through the skin, and into the blood vessel of interest. Both the ultrasound which is scattered from the moving erythrocytes in the blood, and that which is reflected from the surrounding tissue are then received by a second piezo-electric crystal mounted alongside the transmitting crystal. Any motion of the blood results in a Doppler shift in the frequency of the scattered sound, and the resulting received signal will thus have a slightly broader spectrum than the transmitted signal. The well known equation for the shift in frequency, f_d, due to a scatterer moving with a velocity, V, at an angle to the ultrasound beam is given by

$$f_d = \frac{2\ V \cos\theta\ f_t}{C} \qquad 4.3$$

where f_t is the transmitted frequency and C the velocity of ultrasound in blood (Fig 4.3). As the velocity of blood flow is very much less than that of ultrasound in blood it is clear that the shift in frequency, f_d, will be very much less than the transmitted frequency, and indeed in all measurements of this kind the shift falls in the audio-range i.e: up to 15kHz. This fact is made extensive use of in processing the returning signals in all but the most advanced instruments, in that it is only necessary to multiply together the transmitted and received frequency, and pass the resulting product through a low-pass filter to be left with a Doppler shift signal in the audio range.

4.2.1. Development of the Ultrasonic Velocimetry Technique

The first attempts to measure the velocity of blood flow ultrasonically did not employ the Doppler effect, but rather compared the transit times of pulses of ultrasound moving firstly with the blood flow, and secondly against it (Baldes et al 1957, Franklin et al 1959, Farrall 1959). It may be shown that the difference in the two times is given by

$$t = d\left(\frac{1}{c-v} - \frac{1}{c+v}\right)\cos\theta \qquad 4.4$$

the nomenclature being the same as in equation 4.3, and d being the distance between the transmitting and the receiving crystal. Unfortunately this technique could only be used directly on blood vessels, required complex equipment, and was not very accurate (Wells 1969).

The Doppler effect, the phenomena that the observed frequency of a wave is dependant on the relative motion of the source of the wave and the observer has been known for well over a century (Doppler and Ballot 1845). Its application to the measurement of blood velocity is however fairly recent, the earliest work being reported in the nineteen sixties by Satomura and Kaneko (1960) and Franklin et al (1961), and the first practical transcutaneous device by Baker et al in 1964.

The equation for the Doppler shift in frequency has already been given for a single target (equation 4.3) but because of the complex velocity profile occuring in arteries the Doppler shift will actually extend over a range of frequencies. Most of the development work on the Doppler velocimeter since 1964 has been concerned with ways of displaying the Doppler shift signal in such a way as to give useful information about blood flow.

4.2.2. Display Techniques

Perhaps the most widely used method of displaying the Doppler frequency signal is to pass it through a frequency to voltage converter, or to be more specific through a zero-crossing detector and display the output of this on a chart recorder; indeed this was the method used by Franklin et al in 1961. The zero-crossing detector makes use of the fact that the number of zero crossings in a random signal is the root mean square frequency of the input signal, providing there is no constant phase relationship between the different frequency components (Rice 1944). The validity of applying the zero crossing detector to the

Doppler shift frequency has been discussed in detail by Flax et al (1970), who concluded that whilst the technique is valid, it introduces noise into the system which limits its use for examining the detailed waveforms of rapidly changing flows, but which in no way interferes with the measurement of the mean flow. M.K. Lunt (1975) has also discussed, in a very clear fashion, a series of errors which may arise from the use of this technique.

The other widely used method of display is the so called sonagram, which is an attempt to display frequency, amplitude and time all on the same record. This is achieved by representing time along the x axis, frequency along the y axis, and the amplitude of the corresponding signal as the blackness of the paper (Fig 4.4). The first practical method of achieving this was described by Koenig et al (1946), but there are now several ways of arriving at the same end, some of them working in real time. Coghlan and Taylor (1976) have discussed briefly the three most important ways of obtaining a signal for presentation in this manner, viz, using fast Fourier analysis, parallel filter analysers and time-compression analysers. The analyser used in the work presented in this thesis, the Honeywell SAI 51C, works on the time-compression principle.

4.2.3. Directional Doppler Techniques

It is very important to be able to distinguish between forward and reverse flow using the Doppler technique, not only to distinguish between the flow in adjacent vessels, but because reverse flow during part of the cardiac cycle is a normal finding in many healthy arteries.

The first reported and most widely used system for determining the direction of flow is that described by McLeod in 1967. His system makes use of two zero-crossing detectors and thus has all the disadvantages associated with these devices, and in addition will only work correctly in the presence of uni-directional flow. Lunt (1975) discusses these, and other errors.

Coghlan and Taylor (1976) discuss five different directional techniques, one based on single side band detection, one on Heterodyne detection and three (including McLeod's) based on phase quadrature detection.

The Sonicaid BV380 used throughout the experiments described here employs quadrature phase detection, followed by frequency domain processing, and a system which translates the Doppler shift to around 1.25kHz. This signal processing is further discussed in Appendix 3.

4.2.4. Theoretical Consideration

The interaction between the ultrasound beam and the complex movement of erythrocytes in the blood vessel is complicated, and has been studied by several authors. Perhaps the most important of these papers are those by Gosling et al (1969), which discusses the scattering of ultrasound in various source and receiver configurations and the processing of Doppler signals, and Flax et al (1970) which discusses several aspects of the theory in an attempt to evaluate the zero-crossing detector. More recently Arts and Roevros (1972) have discussed the relationship between the average velocity across the blood vessel and the power density spectrum of the received signal, and Atkinson (1976) the limitations of Doppler system due to the finite width

of ultrasonic beams.

Although the paper of Jorgenson et al (1973) is primarily on the subject of the pulsed Doppler ultrasonic velocimeter it is of interest in that it discusses how the size and shape of the sampled volume of blood can affect the sensitivity and accuracy of Doppler flowmeters.

4.2.5. Calibration of Doppler Velocimeter

Because of the simplicity of Doppler velocimeters their frequency calibration must remain correct, in that it is completely governed by equation 4.3. The sensitivity of the instrument at each frequency may however be subject to variation and must therefore be measured.

The calibration of the Sonicaid Blood Velocimeter was achieved by mixing the output from a function generator with the received Doppler signal (Fig.4.5). Because of the frequency involved it was possible to effect this simply by bringing a probe attached to the generator close to the Doppler device.

The function generator was set to 7.54MHz, the measured output frequency of the Doppler unit, and trimmed by means of a programmable voltage source. The hetrodyned output from the Doppler was fed to a Honeywell SAI 51C real time spectrum analyser, and the frequency response of the whole system measured by adjusting the injected frequency either side of the transmitted frequency using the voltage source and observing the output from the analyser on an oscilloscope. A typical set of results are shown in figure 4.6. The apparent scatter is thought to be due to the difficulty of holding the function generator steady at the centre of each

frequency bin of the analyser for a sufficient period of time. As each bin is only 100 Hz wide and the transmitted frequency is 7.54MHz this would require a short term stability of considerably better than one part in 10^5. Although only one set of results are shown, several determinations were carried out, and the scatter was found to be of a random nature. The reduction of sensitivity at 1.2kHz (corresponding to no Doppler shift) and the drop off of the response above about 3kHz are a result of the design of the Doppler unit.

4.2.6. Ultrasonic Beam Shape

It is of course of importance to know the approximate shape of the ultrasonic beam, in order to appreciate the volume of the artery that is being ultrasonically interrogated.

The beam shape of the Sonicaid transducer was calculated theoretically from the geometry of the crystals, and checked experimentally. The results obtained for the ultrasonic field at 5, 10, 15 and 20mm from the transducer face are shown in figure 4.7. Further details of the calculation are given in Appendix Four.

4.3 Intra-Arterial Pressure Measurement

All measurements of blood pressure made during the animal experiments were carried out by means of intra-arterial cannulation, this being the only reliable method of obtaining accurate instantaneous blood pressure.

4.3.1. Development of the Intra-Arterial Pressure Measurement Technique

The first description of the intra-arterial measurement of blood pressure is that of Stephen Hales in 1733 (republished by Fulton 1966).

"In December I caused a mare to be tied down on her back....; Having laid open the left crural artery about three inches from her belly, I inserted into it a brass pipe whose bore was one sixth of an inch in diameter; and to that, by means of another brass pipe which was fitly adapted to it, I fixed a glass tube of nearly the same diameter, which was nine feet in length; then untying the ligature on the artery, the blood rose in the tube eight feet and three inches perpendicular above the left ventricle of the heart..."

The technique of intra-arterial pressure measurement as it is understood today was initiated by the work of Otto Frank just after the turn of the century (Frank 1903, 1905). His manometers, which were used extensively by Wiggers (1928), employed rubber membranes and an optical recording system. Frank's design was much improved upon by Hamilton et al (1934) who replaced the rubber membranes by beryllium-copper ones, and increased the sensitivity of the optical recording system. Improvements in electronics during the second world war made it possible for physiological pressures to be obtained, processed and recorded electronically, and it was Lilley who in 1942 introduced the capacitance manometer to physiology and Wetterer who in 1943 first used a catheter tipped inductance manometer. Further details of these and other types of pressure transducers can be found in E.O. Frankes excellent paper on physiological pressure transducers (1966).

Almost all modern pressure transducers are of the strain-gauge variety. These devices utilise the fact that the electrical conductance of a wire changes as it is stretched, to sense the position of a pressure diaphragm. Four lengths of resistance wire are arranged in a Wheatstone Bridge as indicated in figure 4.8. A constant voltage is applied between points A and C, and the voltage difference between points B and D is measured. The four resistors are mechanically arranged so that movement of the pressure diaphragm in one direction causes an increase in the lengths of r_2 and r_4 and a decrease in the lengths of r_1 and r_3; and movement in the other direction causes changes in the opposite sense. In this way it is possible to record the postion of the diaphragm at any moment by measuring the voltage between points D and B, this being proportional to the displacement of the diaphragm. At one time because of the stability problems that were encountered with D.C. amplifiers all such devices were A.C. excited, but now both A.C. and D.C. excitation are widely used. Some modern transducers employ semi-conductor strain gauges, as the gauge factor of silicon (the proportional change in resistance for a given proportional change in length) is very much greater than that of the resistance wire used to construct conventional strain-gauge transducers.

4.3.2. The Theory of Fluid-Linked Manometers

Modern fluid-linked manometer systems comprise of several constituent parts, the transducer diaphragm with its attached strain-gauges as described in the previous section, a liquid filled flushing dome, and a liquid filled catheter or a manometer connecting line terminated with a

needle or cannula.

The theory of this type of system has been discussed by several authors (Hansen and Warburg 1950, Franke 1966 and McDonald 1974). As pointed out by these authors, the fluid motion within the system is basically confined to a single direction along the axis of the tube, and may be approximated to a system which is constrained to a single degree of freedom with lumped mass, compliance and damping. The compliance resides in the transducer diaphragm and the catheter wall, the damping is determined by the viscosity of the fluid, and the mass is the mass of the liquid in the catheter and the moving mass of the transducer combined.

The motion of a system such as this may be described by the equation 4.5

$$M \frac{d^2x}{dt^2} + R \frac{dx}{dt} + Sx = SK \cos wt \qquad 4.5$$

where x is displacement, M is the lumped mass, R the damping, S the stiffness and SK the driving force. This is a standard second order differential equation, the solution of which is made up of two parts, the complementary solution and the particular integral. The former is the transient solution and the solution of the complementary function 4.6

$$M \frac{d^2x}{dt^2} + R \frac{dx}{dt} + Sx = 0 \qquad 4.6$$

Assuming that at t=0 dx/dt=0 and x=A; and that the system is underdamped, i.e: $R^2 < 4MS$; the solution of equation 4.6 may be written

$$x = \frac{Aw_o^2}{w_o^2 - \beta_o^2} \exp(-\beta_o t)\cos\left\{(w_o^2 - \beta_o^2)^{\frac{1}{2}}t - \tan^{-1}\frac{\beta_o}{(w_o^2 - \beta_o^2)^{\frac{1}{2}}}\right\} \quad 4.7$$

Where w_o is the natural frequency of an undamped system given by $w_o = (S/M)^{\frac{1}{2}}$; and β_o is a damping factor which is defined by $\beta_o = R/2M$ (see Appendix Five).

The particular integral is the steady state solution of equation 4.5 and may be written

$$x = K\left\{(1-\gamma^2)^2 + 4\beta^2\gamma^2\right\}^{-\frac{1}{2}} \cos\left\{wt - \tan^{-1}\left(\frac{2\beta\gamma}{1-\gamma^2}\right)\right\} \quad 4.8$$

where γ is w/w_o and β is β_o/w_o (see Appendix Five).

It is convenient in hydraulic systems to write equations in terms of pressure and volume rather than force and displacement, and this may be achieved for equation 4.6 by dividing it through by area squared. This converts stiffness (force/displacement) to volume elasticity ($\Delta p/\Delta v$), and resistance (force/velocity) to hydraulic resistance (pressure/flow). Effective hydraulic mass M' is now given by mass/area^2, which means that in any practical manometer system the mass of the fluid in the flushing dome is negligible compared with that in the catheter, because of the relatively small diameter of the latter. The hydraulic resistance R' may be found approximately by rearranging Poiseuille's equation (equation 2.29)

$$R' = 8\mu L/\Pi r^4 \quad 4.9$$

but as the fluid flow within the catheter is oscillatory, R'

is more correctly given by equation 4.10 (McDonald 1974)

$$R' = (a^2 \mu L / M'_{10} \Pi r^4) \sin \varepsilon'_{10} \qquad 4.10$$

The variables M'_{10} and ε'_{10} are discussed in Appendix One. It is now possible to rewrite equation 4.6 as 4.11

$$\frac{L \rho \ddot{x}}{\Pi r^2} + \frac{8 \mu L}{\Pi r^4} \dot{x} + Ex = 0 \qquad 4.11$$

where E is volume elasticity ($\Delta p / \Delta v$).

From equation 4.8 it can be seen that the maximum response of the system occurs when $\gamma = (1-2\beta^2)^{\frac{1}{2}}$.

As previously pointed out the type of measurement system under discussion is usually underdamped, and indeed β is usually less than 0.2, in which case the frequency of maximum response w_m is within 4% of w_o. Furthermore the frequency of vibration observed on applying a transient change in pressure to the transducer system and then allowing it to vibrate freely is given by $w_s = w_o (1-\beta^2)^{\frac{1}{2}}$ and is within 2% of w_o for values of β less than 0.2.

The natural frequency of an undamped system, w_o is given simply by $w_o = (S/M)^{\frac{1}{2}}$ whilst the damping factor, β_o is given by $\beta_o = R/2M$. Comparing equation 4.6 and 4.11 w_o may now be written

$$w_o = r(\Pi E / \rho L)^{\frac{1}{2}} \qquad 4.12$$

and relative damping β may be written

$$\beta = \beta_o / w_o = \frac{4\mu}{r^3} \cdot \left(\frac{\rho L}{\Pi E}\right)^{\frac{1}{2}} \qquad 4.13$$

Thus, provided the compliance of the catheter is 'small' compared to the compliance of the transducer, the natural frequency of vibration is proportional to the radius of the catheter and inversely proportional to the square root of its length. Furthermore, the relative damping is proportional to the square root of the length of the catheter and inversely proportional to the cube of the radius.

If the catheter material is so compliant that the compliance of the transducer is negligible by comparison, then E, the volume elasticity will be inversely proportional to both the length and radius of the catheter and equation 4.12 and 4.13 can be written as 4.14 and 4.15

$$w_o = \frac{1}{L}\left(\frac{k \Pi r}{\rho}\right)^{\frac{1}{2}} \qquad 4.14$$

$$\beta = \frac{4\mu L}{r^2}\left(\frac{\rho}{\Pi k r}\right)^{\frac{1}{2}} \qquad 4.15$$

where k is a constant of proportionality. It is however open to doubt if the simple one dimensional analogue is relevant to this situation, and in order to overcome this defect several authors have attempted to describe the system in terms of transmission line theory (Hanson 1949, Fry 1960, Latimer 1968) but this has tended to obscure rather than illuminate the position (Gabe 1972).

4.3.3 Calibration of the Manometer System

There are two widely used techniques for calibrating manometer systems, the so called forced and free response methods. The former requires a sinusoidal pressure generator

to drive the manometer system, whose response can then be determined. Suitable pressure generators have been described by Vierhout and Vendrick (1961) and Shelton and Watson (1968) whilst Veirhout and Vendrick (1965) have discussed the theoretical requirements for such devices. The forced response method is the better of the two in that it is not necessary to assume the form of the response in advance, but the difficulty of building reliable generators has made the free response method more popular, except where large numbers of catheter systems have to be calibrated.

The free vibration method, the so called 'pop' technique has been described by Hansen (1949) and Yanof et al (1963) and makes use of the transient response of the manometer as described by equation 4.7. This was the method used to calibrate the manometer system used for the work described in this thesis.

For each determination the cannula or needle on the end of the manometer system was glued into a 20ml hypodermic syringe barrel. A piece of very thin plastic was fastened over the top of the barrel, and the barrel was pressurized through a second needle glued into the side of the syringe. This pressure was then rapidly removed by bursting the thin plastic top by means of a Bunsen Burner and the response of the pressure recording apparatus to this transient monitored. The responses were all of the type predicted by equation 4.7, that is exponentially decaying cosine waves, and from these it was possible to identify the natural frequency w_o and the relative damping β of each system. The damping was calculated from the log. dec., δ, which may be defined as the natural logarithm of the ratio of two successive positive displacement amplitudes. From equation 4.7

$$\delta = \beta_o T_s \qquad 4.16$$

where the time T_s between successive positive displacements is

$$T_s = 2\Pi / w_o (1 - \beta^2)^{\frac{1}{2}} \qquad 4.17$$

Combining 4.16 and 4.17 and remembering that $\beta = \beta_o / w_o$

$$\beta = \delta (4\Pi^2 + \delta^2)^{-\frac{1}{2}} \qquad 4.18$$

The damped natural frequency W_s can be measured directly from the recording, and the undamped natural frequency can be calculated from equation 4.17 if required. Figure 4.9 shows the frequency and phase responses of the manometer system used for the animal experiments.

4.3.4. Artifacts in Pressure Recordings

A number of artifacts which arise during intra-arterial pressure measurements have been described in the literature.

The so called end-pressure artifact arises if the catheter tip points either up or down stream. Should this occur the manometer records the sum (or difference if the catheter points down stream) of the lateral pressure energy, and the kinetic energy of the streamlines impacting on the catheter tip. This effect is fairly small in practice, assuming the density of blood to be unity and the velocity of blood flow to be 50 centimetres per second, the difference amounts to 0.94mm of mercury. It must be remembered of course that this effect is proportional to velocity squared. This artifact may be avoided when it is necessary to point the catheter upstream by blocking off the end hole and making a

side hole.

The catheter impact artifact is a result of the manometer system vibrating at its resonant frequency after being subjected to a transient pressure change at the beginning of the systolic phase of blood flow. This effect is more severe the closer the catheter tip is to the left ventricle. Both this and the previous artifact have been discussed in more detail by McDonald (1974).

A third artifact, described and evaluated by Kanai (1970) is that due to wave reflection from the tip of the catheter, but this is not of importance unless the catheter occupies a significant portion of the lumen.

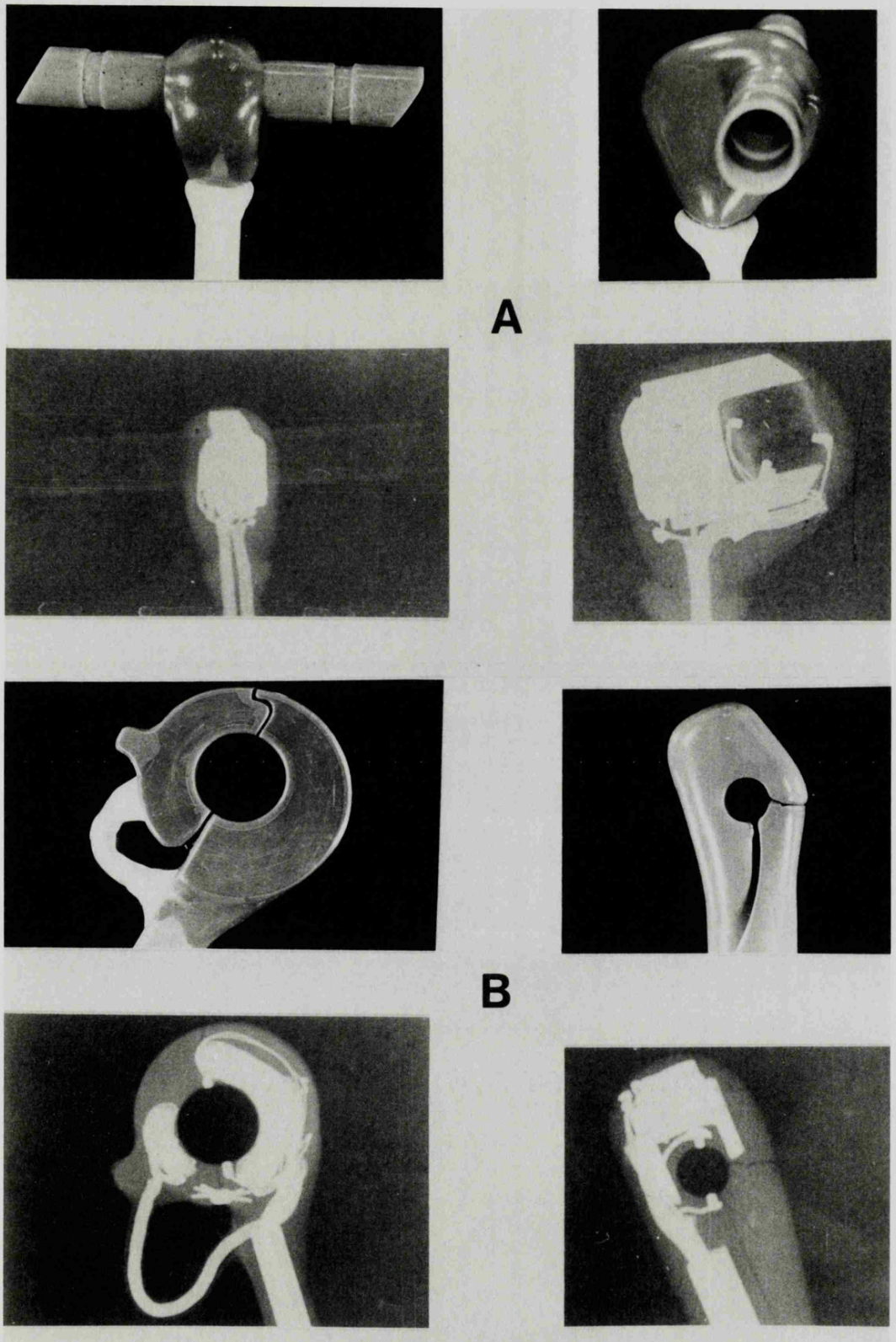


Figure 4-1. Photographs and radiographs of cannulating (A) and non-cannulating (B) electromagnetic blood-flow probes.

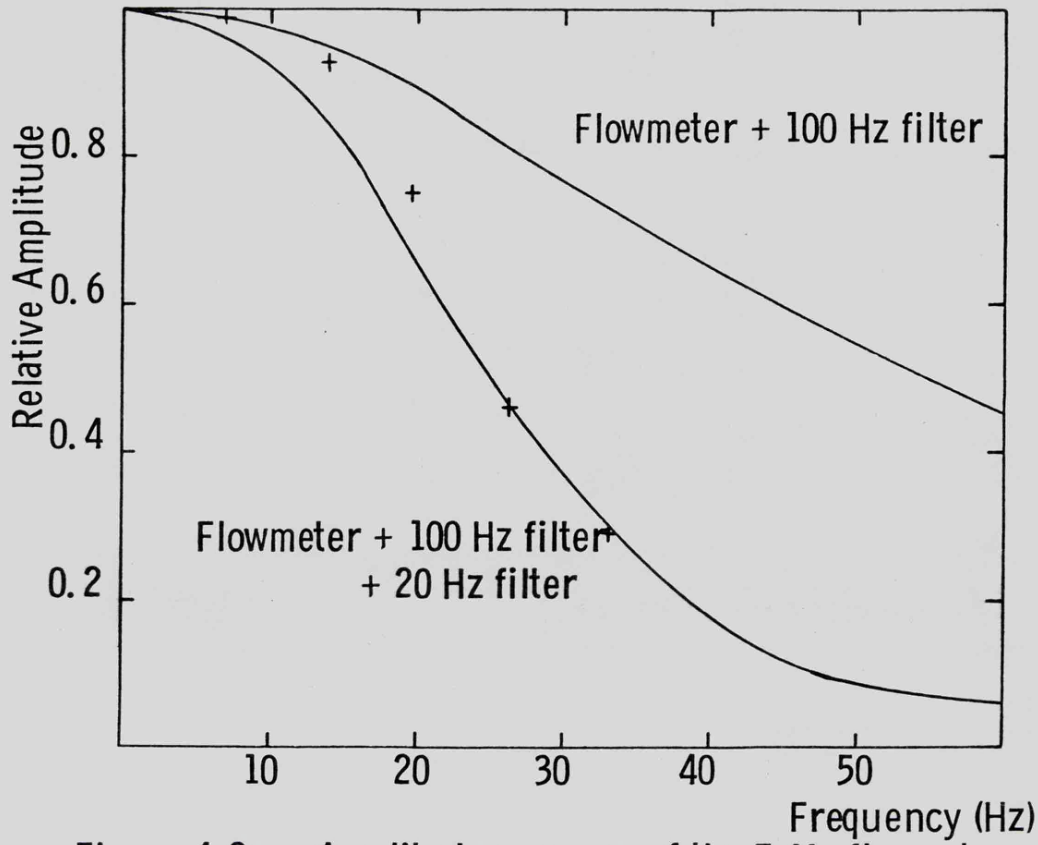


Figure 4-2a. Amplitude response of the E.M. flowmeter with different filters. The crosses have been calculated by subtracting the frequency response of the 20 Hz filter from the top curve

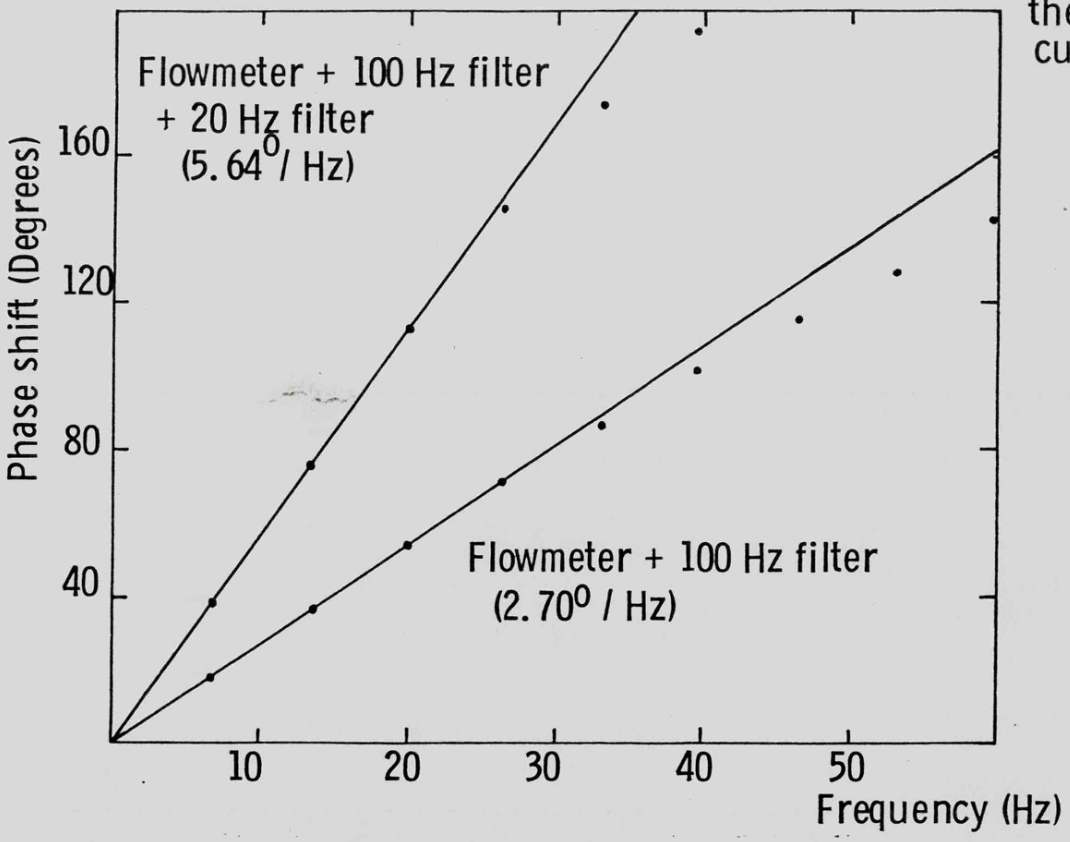
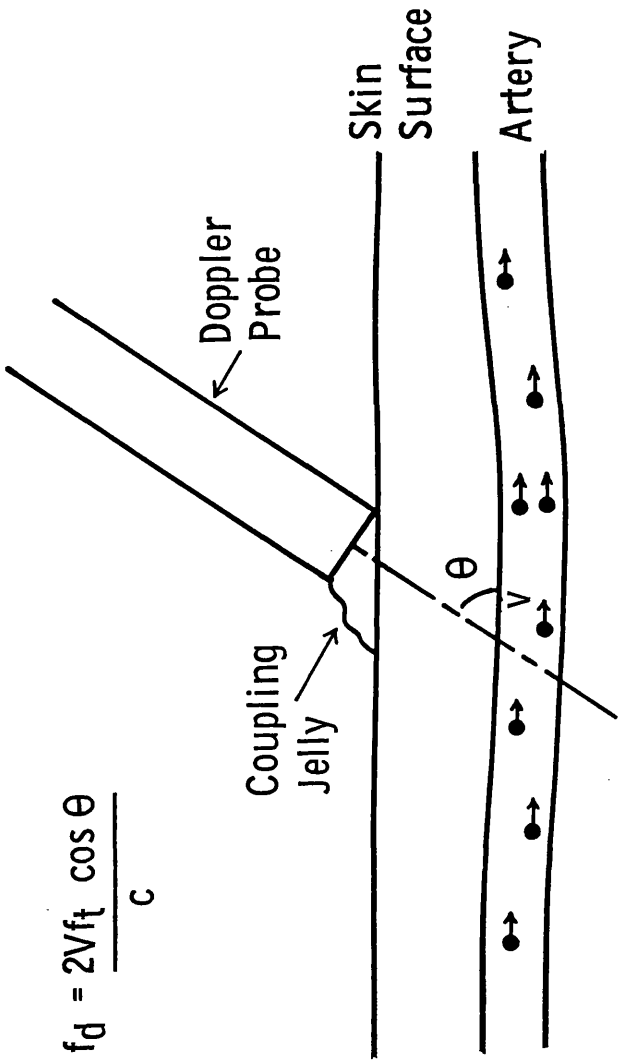


Figure 4-2b. The phase response of the E.M. flowmeter with the same filters as in fig. 4-2a. The phase shifts of 2.7°/Hz and 5.6°/Hz correspond to 7.5 ms and 15.7 ms delay respectively.



$$f_d = \frac{2Vf_t \cos\theta}{c}$$

Figure 4-3 The positioning of a Doppler ultrasonic probe during blood velocity mesurements.

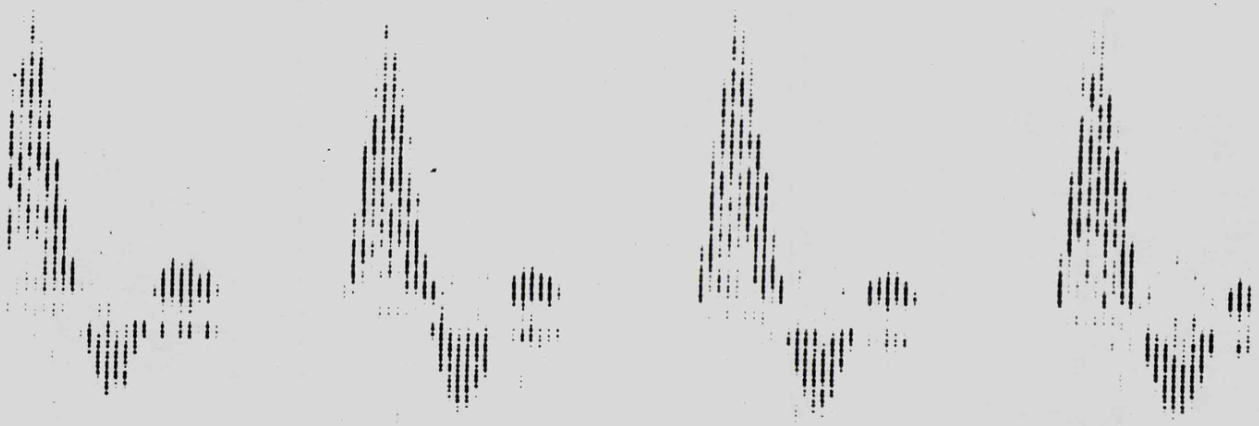


Figure 4-4. A sonagram recorded from the posterior tibial artery of a healthy volunteer.

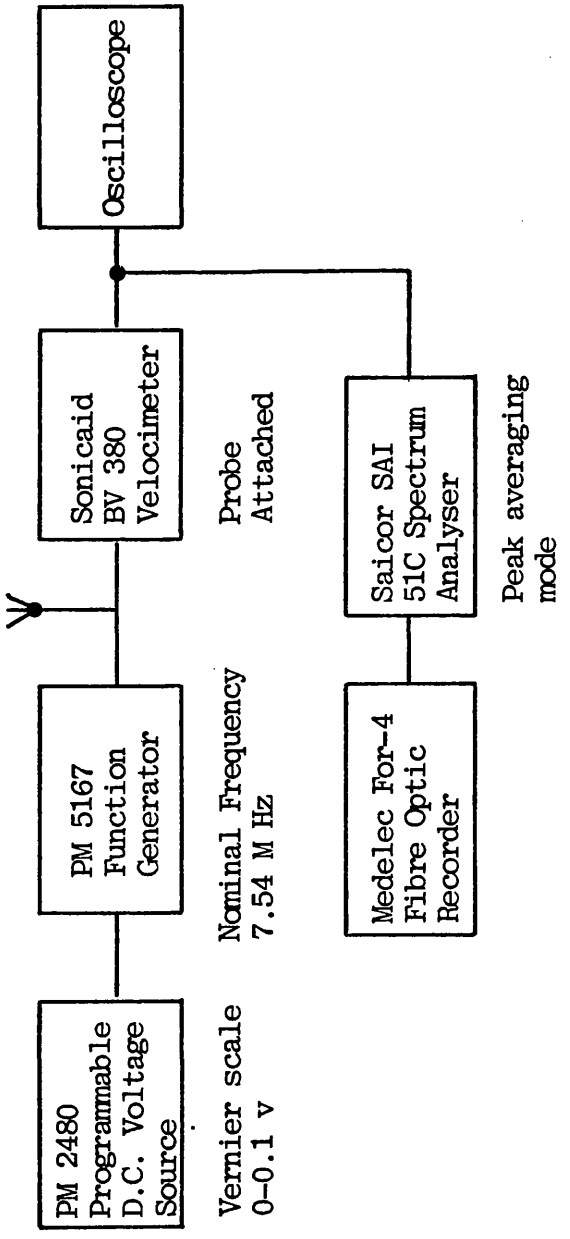


Figure 4-5 The apparatus used for the calibration of the Doppler Velocimeter

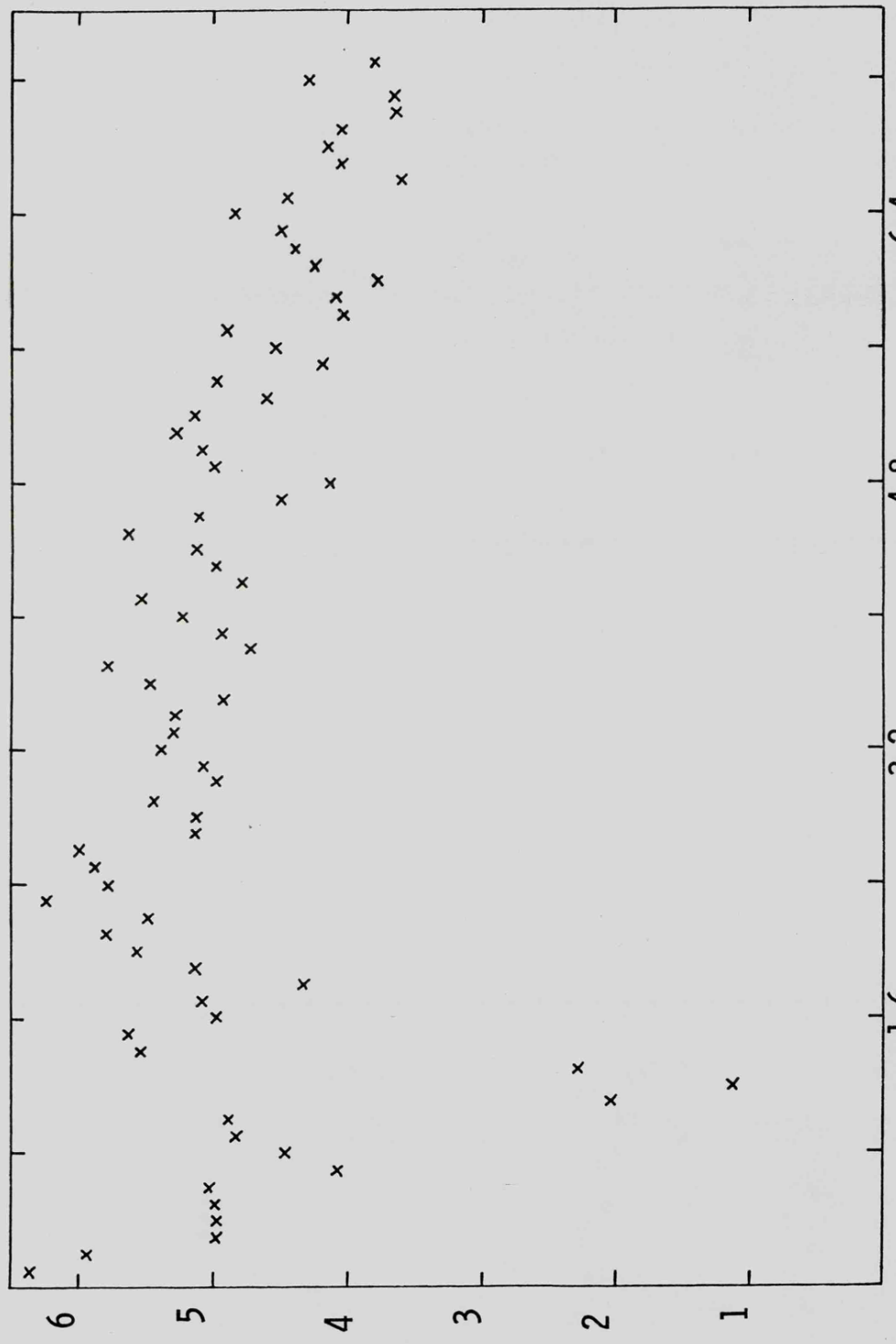


Figure 4.6. Typical set of results for the determination of the frequency response of the Doppler unit.

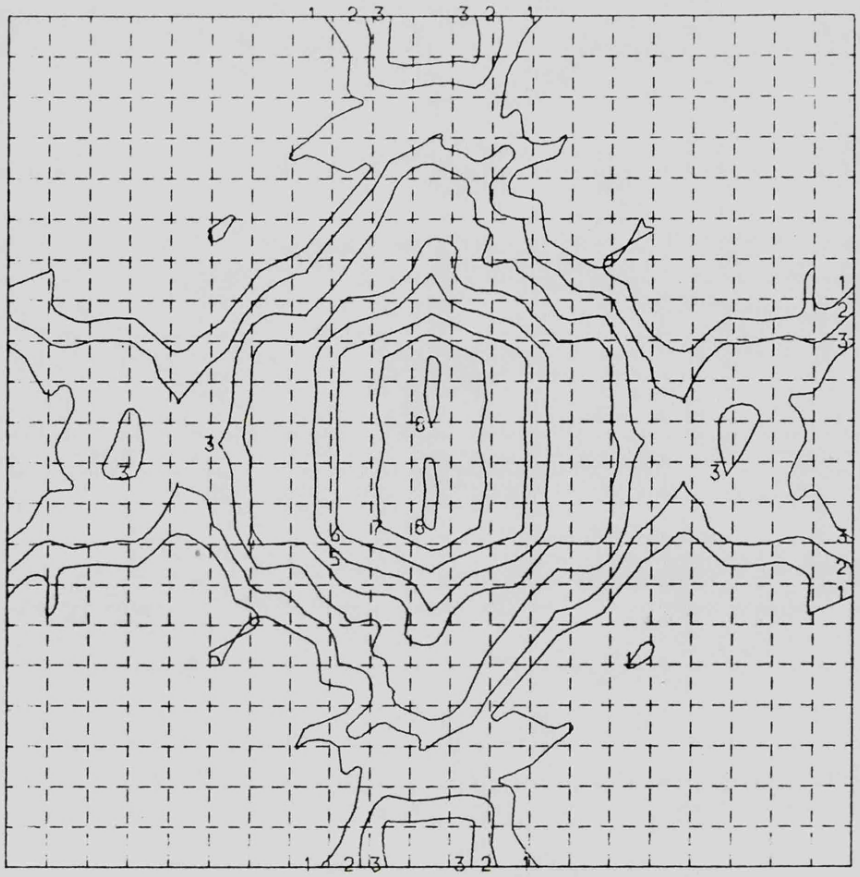


Figure
4 - 7a

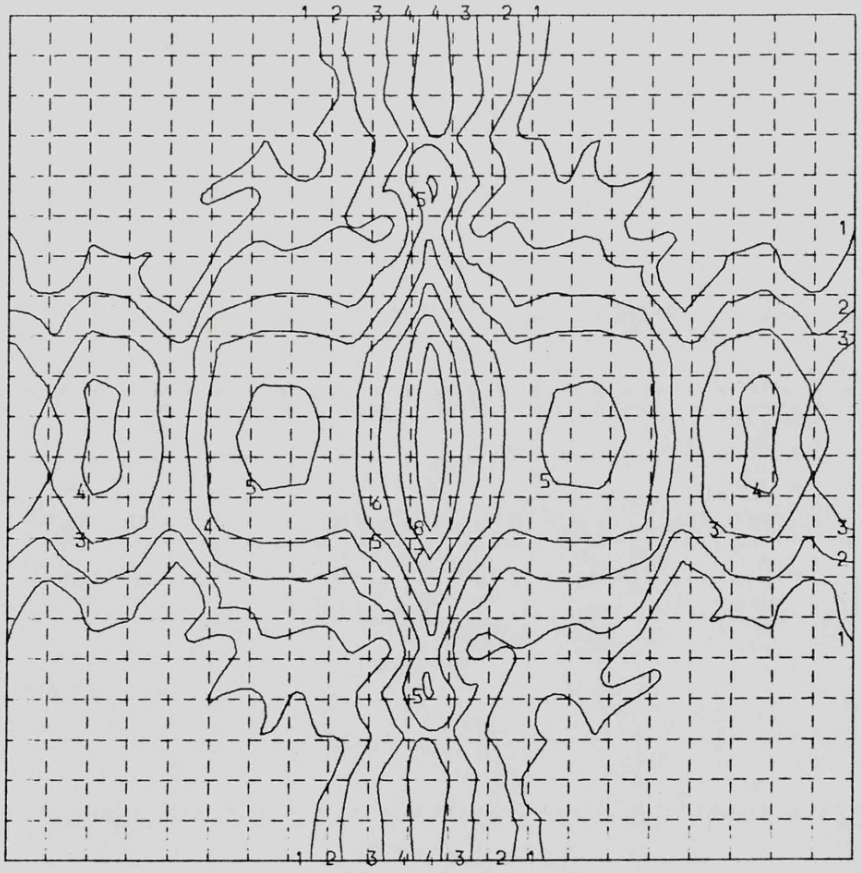


Figure
4 - 7b

Figures 4-7 a-d. Theoretical ultrasonic beam shapes at 5, 10, 15 & 20 mm from the Sonicaid transducer. Iso-echo contours are plotted at 6dB intervals, and the broken grid represents 1 mm divisions. In all experiments the probe was held in such a way that the blood vessel would lie along the x-axis of the diagram.

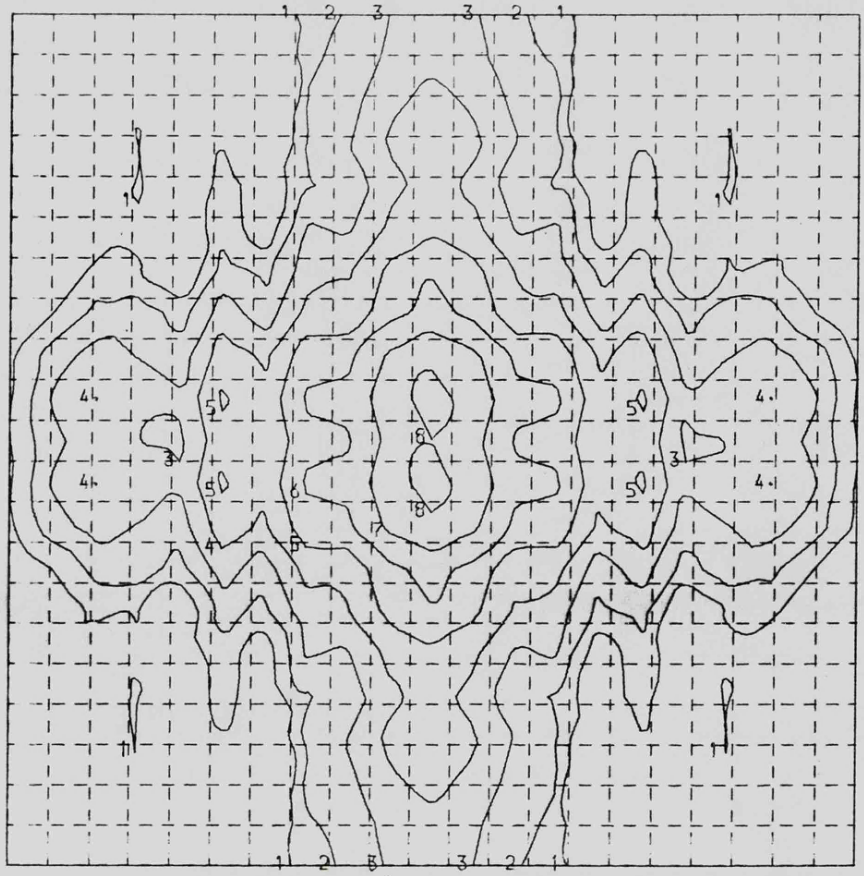


Figure 4 - 7 c

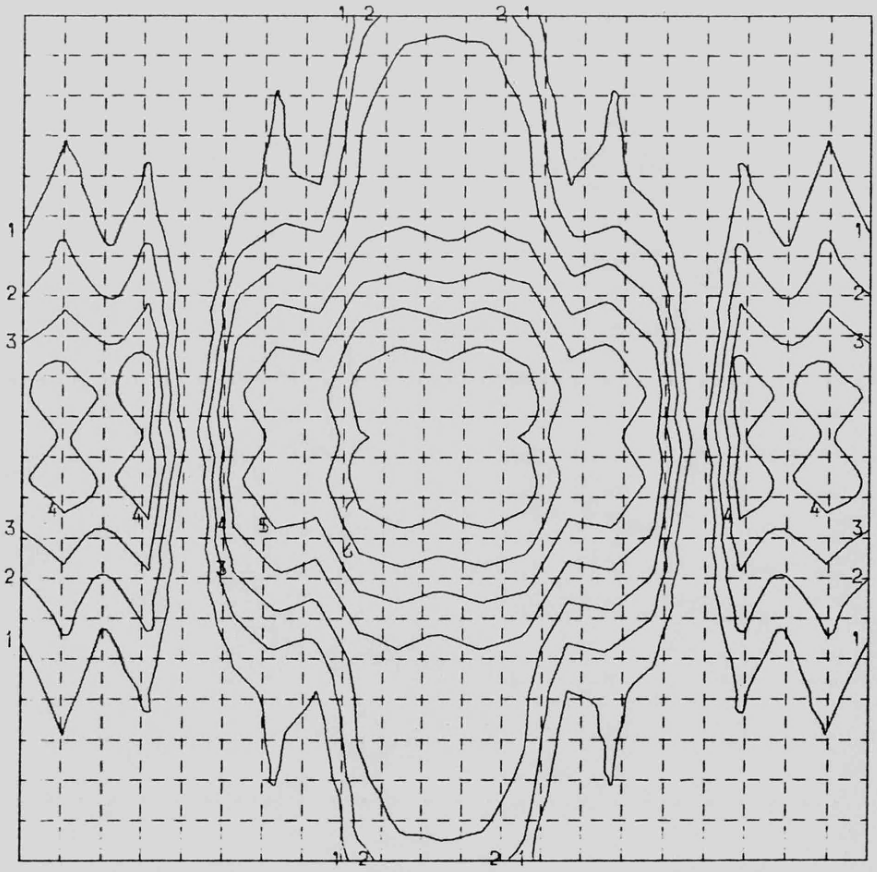


Figure 4 - 7 d.

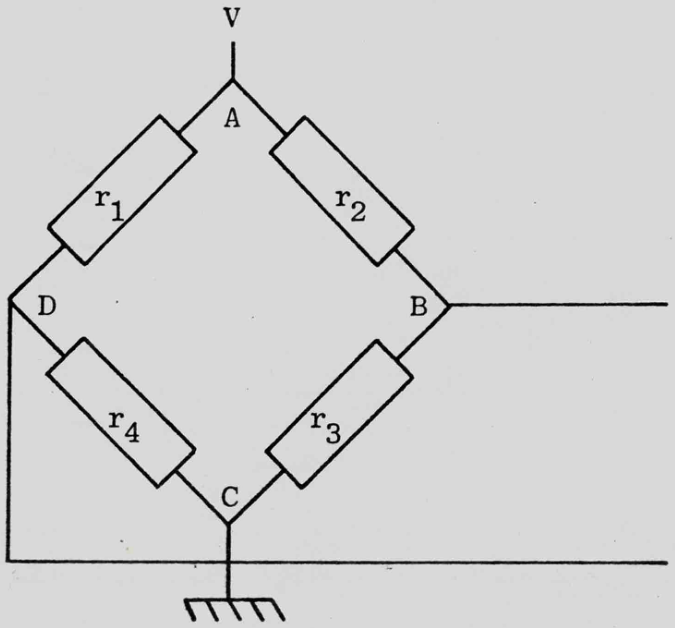


Figure 4-8 Arrangement of resistors in Wheatstone bridge

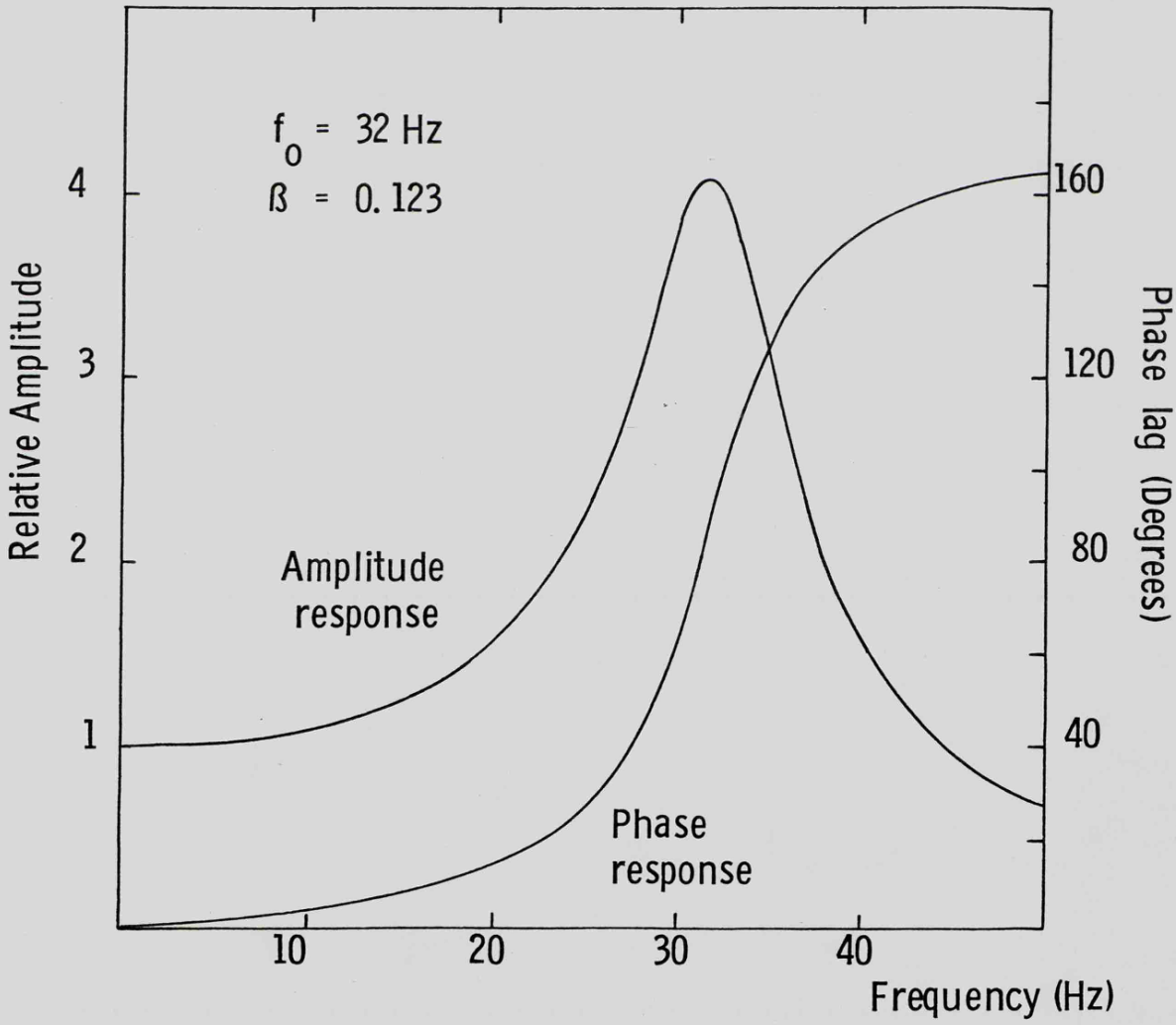


Figure 4.9. Amplitude and phase response of the manometer system.

CHAPTER FIVE

THE ANIMAL MODEL

Although the animal experiments have been divided into two groups for the purpose of reporting the results (i.e: those relating to flow and pressure, and those relating to Doppler velocity measurements), both sets of results were obtained from the same animal model.

The animal model was constantly evolving, and in total twenty experiments were carried out over a period of two years; however, only the final eleven are described here, the first nine being of a preliminary nature.

5-1 The Stenosis

The animal preparation varied from those described elsewhere in the literature in that interchangeable internal stenoses were used for all experiments. This technique combined the advantages of the external constriction technique (Mann et al 1938, Shipley and Gregg 1944, May et al 1963a) in that it was possible to examine the effects of more than one stenosis in each dog, and the implanted stenosis technique (Mann et al 1938, Young et al 1975) in that the dimensions of each stenosis were precisely known.

The stenosis assembly consisted of five parts; two "adaptors", a "stenotic insert", and two short pieces of transparent P.T.F.E. tubing (Figure 5-1).

The adaptors were designed to be inserted into the artery at the start of the experiment, and remain there whilst various inserts were fitted between them. The inserts were held in place by means of the tubing, it being

transparent to aid the correct approximation of the adaptors and inserts.

Two sizes of assembly were used, the "A" size which had a non-stenosed internal diameter of 4mm, and the "B" size which had a 'normal' internal diameter of 5mm. A large number of inserts were used during the course of the experiments, and the dimensions of these are detailed in Tables 5-1 a and b. There were four nominal lengths of stenosis, 'knife-edge', 3mm, 6mm and 9mm; and eight nominal diameters in addition to non-stenosed inserts. The inside diameter of each stenosis was chosen so that the square of its area was half that of the next larger stenosis.

5-2 The Operative Technique

All experiments were carried out on the aorto-femoral segment of greyhounds. Each dog was starved for 24 hours pre-operatively and received pre-medication of 2mg Acepromazine one hour prior to surgery. Anaesthesia was induced with Thiopentone, and maintained with oxygen and nitrous oxide with an occasional supplement of halothane, or in later experiments with pentabarbitone.

Using electro-cautery a midline abdominal incision was made and extended across the right inguinal ligament to the thigh. The abdominal aortic trifurcation was exposed and the right iliac and femoral arteries displayed. The circumference of the artery at the point at which the stenosis was to be inserted (roughly in the middle of the top third of the thigh) was then estimated by measuring the length of suture required to encircle it three times. From this figure the inside diameter was calculated by assuming the

thickness of the arterial wall to be 13% of the arterial radius. It should be noted that this could only be regarded as a very rough estimate, as the size of the artery could be seen visibly to change during the dissection procedure, particularly in response to handling. This difficulty in making an accurate measurement of the nominal arterial diameter explains why only two sizes of stenotic assembly were found to be necessary.

An eighteen gauge 'medicut' plastic cannula with a side hole was inserted through a branch of the internal iliac artery and advanced so as just to protrude into the aorta, and secured by tying a suture round branch and cannula. Two similar cannulae with end holes were inserted into the femoral artery via muscular branches, one just distal to the site earmarked for the stenosis, and one well distal to act as an injection site. (Figure 5.2) The top two cannulae were attached with saline filled manometer connecting lines to Elema-Schonander 746 pressure transducers which were in turn connected to Hewlett Packard 8805C pressure pre-amplifiers. All other branches of the iliac and femoral artery were ligated and the dog heparinised (approximately 100 units/kg).

Two transverse slits were made in the artery, approximately 3cm apart and midway between the aortic trifurcation and the first branch of the iliac artery, and the interchangeable stenosis assembly, containing a non-stenosed middle section inserted and secured. The ties encircling the two adaptors were left long and held together with arterial forceps to prevent the assembly springing apart. A Statham cannulating blood flow probe of the appropriate size was then inserted distal to the stenosis and the two pressure lines in a

similar way (Figure 5.2).

Once the preparation was complete, measurements were made of the distances between the pressure lines, the stenosis and the flow probe (Table 5-2), the wound covered, and the animal allowed to stabilise for a period of at least thirty minutes.

5-3 The Measurement Technique

Figure 5.3 is a schematic diagram of the apparatus used. The characteristics of the flow and pressure transducers, and of the Doppler velocimeter have been discussed in Chapter Four. In all, six parameters were recorded on the Brush 260 chart recorder, the pressures proximal and distal to the stenosis, the pulsatile and mean pressure differences across the stenosis, and the pulsatile and mean flow through the stenosis. The four pulsatile parameters were also recorded on a Tanberg 115 F.M. tape recorder, except when the distal pressure channel was being used to record a signal for the synchronisation of the Doppler and electro-magnetic flowmeter signals.

The pressure difference was obtained by electronically subtracting the output of the two pressure pre-amplifiers. This was found to be necessary in view of the very small differences between the top and bottom pressures when mild stenoses were present. This signal also aided in the correct balancing of the two pressure channels, when, following the usual procedure of static pressure calibration against a column of mercury, the two transducers were connected to a source of alternating pressure created by a roller pump. Each of the transducer/connecting line assemblies were flushed

until the phasic pressure difference between the two channels became minimal, thus assuring that no significant air bubbles were left in the system.

The mean pressures were obtained by filtering out the high frequency signals present in the corresponding pulsatile signals. These signals were recorded to provide real time information on the experiments and proved to be invaluable. For example, clotting in the stenosis was shown up by a contrarious movement of the mean flow and pressure difference channels, long before any change became obvious on the pulsatile channels.

The output from the Sonicaid BV380 Doppler unit was both recorded on a Uher 4400I.C. A.M. tape recorder, and analysed in real time on a modified Honeywell SAI-51C spectrum analyser whose output was displayed on a Tektronix 607 variable persistance monitor and visually recorded on a Medelec For-4 fibre optic recorder. The modification of the spectrum analyser was to allow a sweep of the first 100 frequency bins every 20ms rather than a complete sweep of all 200 frequency bins every 40ms. The second channel of the A.M. recorder was used to record synchronisation signals so that Doppler recordings could be associated with the correct electro-magnetic flow recordings.

After the half hour stabilisation period at the beginning of the experiment, recordings of the pressure above the stenotic insert (P1), the pressure below (P2), the pressure difference and of the flow wave-form were made continuously until the end of the experiment. The Doppler signal was also recorded at regular intervals, the probe being adjusted before each measurement to give the best

signal on the display monitor, before a tape recording of the raw Doppler signal was made for later analysis.

The normal insert was changed for several different stenotic inserts during the course of each experiment, and the preparation allowed to stabilise until there appeared to be no further change in pressure or flow. On some occasions, following the stabilisation period, the flow was deliberatly manipulated by means of either a vasodilating drug (papaverine hydrochloride) or a vasoconstricting drug (adrenaline). A breakdown of the measurements analysed is given in Chapter Six.

At the conclusion of each experiment the artery was severed distally, and the animal bled into a measuring cylinder to check the calibration of the flow probe.

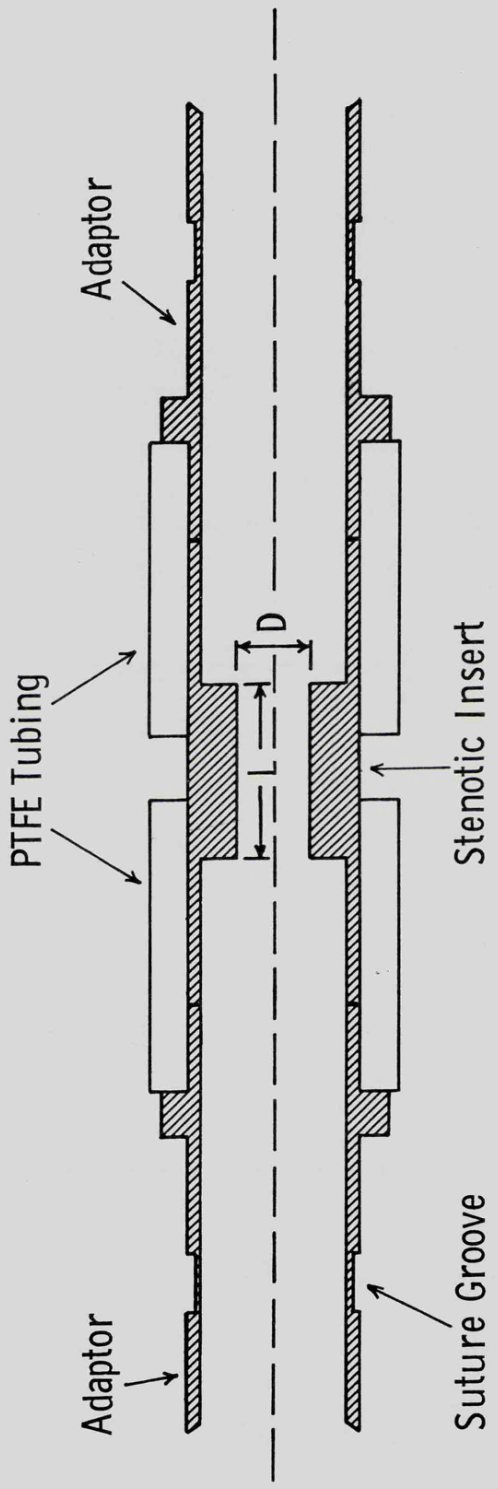


Figure 5-1 The Stenosis assembly (Approximately 4 times life size)

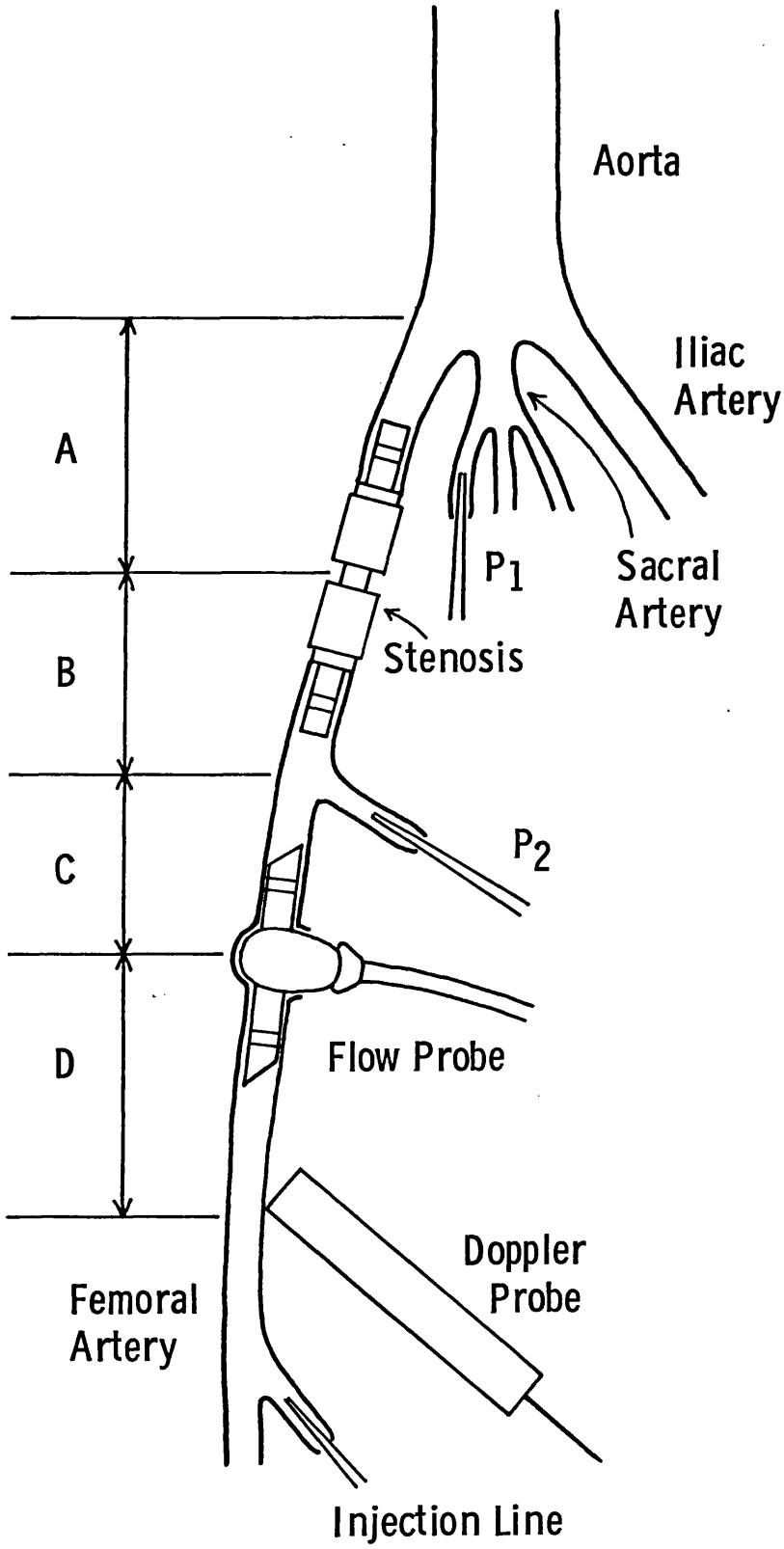


Figure 5-2 Schematic diagram of the animal model used for all experiments

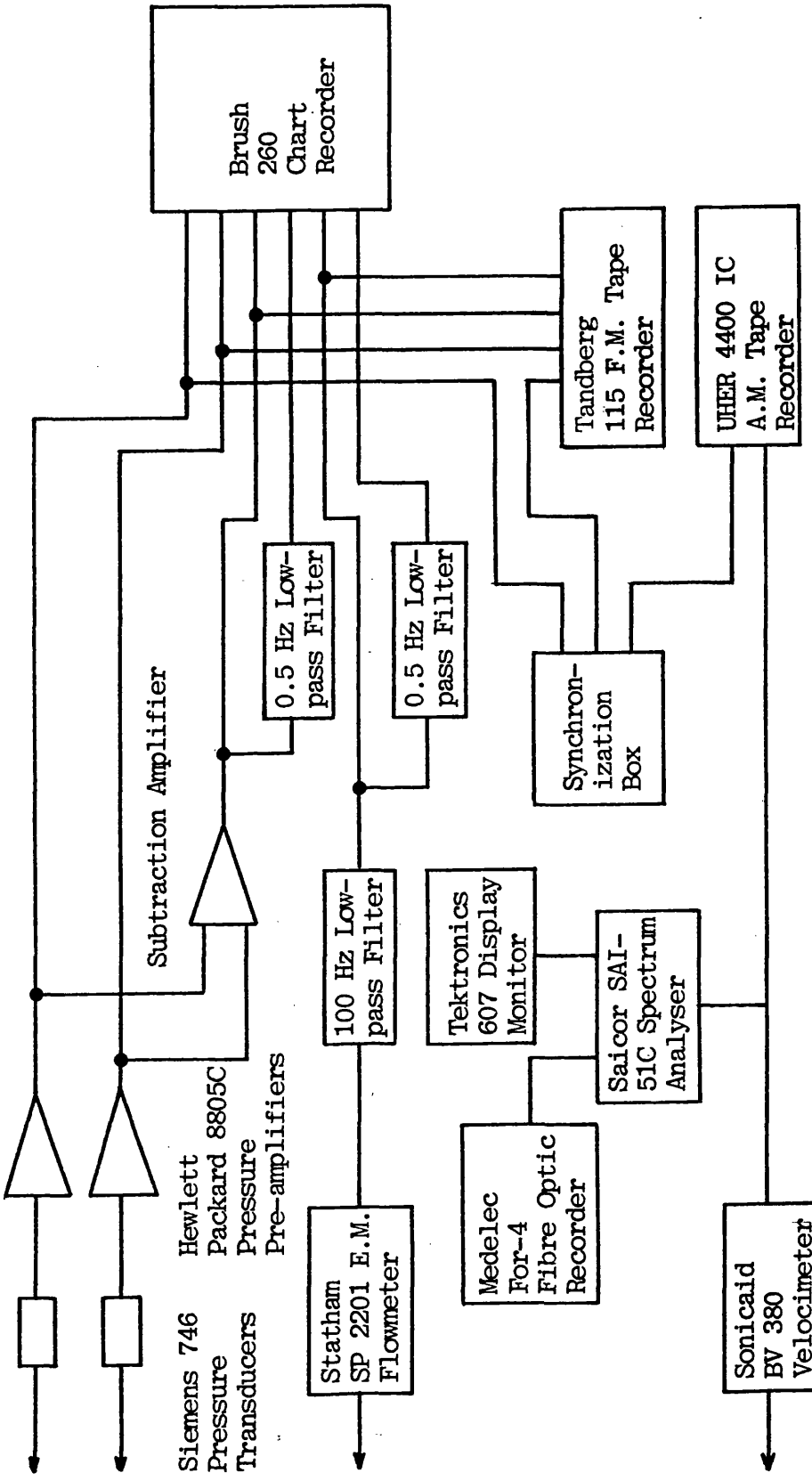


Figure 5-3 Schematic diagram of apparatus for recording flows and pressures during the animal experiments.

Table 5 - 1 a

Dimensions of 'A' series stenoses

Diameter Code	Nominal Length			
	0	3	6	9
0	4.0/00	-	-	-
2	2.69/0.94	-	-	2.69/8.53
3	2.26/0.79	-	-	-
4	1.95/0.94	-	-	1.95/8.33
5	1.60/0.86	-	-	1.60/9.02
6	1.30/0.86	-	-	1.30/9.22
7	1.10/0.84	-	-	1.10/8.97
8	0.89/1.65	-	-	-

Table 5 - 1 b

Dimensions of 'B' series stenoses

Diameter Code	Nominal Length			
	0	3	6	9
0	5.0/0	-	-	-
1	4.0/0.9	-	-	4.0/8.4
2	3.5/0.6	3.5/3.1	-	3.5/8.7
3	2.8/0.6	2.85/3.2	-	2.95/8.5
4	2.38/0.8	2.38/3.1	2.38/6.0	2.38/9.0
5	1.95/0.9	1.95/3.3	2.0/6.2	1.95/9.1
6	1.7/0.8	1.7/3.1	1.7/6.5	1.7/9.2
7	1.4/0.8	1.4/3.1	1.4/6.2	1.4/9.0
8	1.19/1.4	1.1/3.0	1.1/5.9	1.1/8.8

All dimensions are in millimetres. In each case the diameter is followed by the length.

Table 5 - 2

Data relating to the animal preparation

Dog	A*	B*	C*	D*	Arterial Circum-ference	Stenoses	Flow-Probe
10	43	44	37	135	15.5	B	4
11	40	37	33	60	15.1	B	5
12	43	45	27	50	14.3	A	4
13	48	37	35	52	20.5	B	5
14	45	50	38	45	22.1	B	5
15	55	38	45	40	20.5	B	5
16	47	43	34	60	21.3	B	5
17	42	38	42	50	23.5	B	5
18	43	40	40	60	17.8	B	4
19	38	40	37	55	17.8	B	4
20	48	38	29	40	22.1	B	4

* See figure 5 - 2. All dimensions are in millimetres.

CHAPTER SIX

EXPERIMENTAL MEASUREMENTS OF FLOW AND PRESSURE IN CANINE ARTERIES CONTAINING ARTIFICIAL STENOSES

The experiments described in this chapter were carried out to gain a better understanding of the flow-pressure relationships within diseased arteries. In addition to their intrinsic value, these measurements form a basis for the objective evaluation of the techniques of assessing peripheral vascular disease discussed in Chapters eight, nine and ten.

The diseased peripheral arterial system may be split into two components, one consisting solely of the stenosis, and the other consisting of the peripheral bed and collateral circulation. The first of these components is susceptible to mathematical analysis because of its passive nature, whilst only qualitative conclusions may be drawn about the second component. This is because the peripheral bed, and to a lesser extent, the collateral circulation are subject to neural and hormonal influences.

The results presented in this chapter have been divided into three groups, those pertaining to the stenosis, those pertaining to the distal bed, and finally those pertaining to the system as a whole.

6.1 The Raw Results

The experimental protocol was described in detail in Chapter Five. Figure 6.1 is a typical tracing obtained during the course of one of these experiments. Channel one

is a recording of the pressure proximal to the stenosis (P1), Channel two the pressure distal to it (P2), Channel three is the pressure difference across the stenosis (ΔP), whilst Channel four is the mean pressure difference ($\overline{\Delta P}$). Channels five and six are the pulsatile and mean flow through the stenosis respectively (Q and $\overline{Q}$).

The trace shows the period of reactive-hyperaemia which always followed the release of the clamps after a change of stenosis. As the flow settles down to a resting value P2 rises towards P1 and ΔP consequently drops. P1 is not affected by the hyperaemia. This period of hyperaemia provided useful information in that it was possible to analyse results from each stenosis at several different flow rates. By assuming that the distal vessels were always in the same state of vasodilation at the beginning of this period it was also possible to estimate collateral resistance (See Section 6.4).

The results were analysed on a pulse by pulse basis. It was clearly impossible to analyse the whole of what amounted to 25 hours of magnetic tape recordings, and so several typical pulses were selected from each run of each stenosis. One sample was normally taken at the peak of hyperaemia, one or two during the recovery, and two or three during the following five or ten minutes. A similar sampling regime was adopted following the occasional administration of vaso-active drugs. Table 6.1 details the order in which stenoses were inserted into each dog, and the points at which drugs were administered.

Following each experiment P2, ΔP and Q from the selected pulses were written out on a Brush 260 chart

recorder running at a speed of 125mm. s^{-1}. In total over six hundred such 'triads' were analysed. Each of these waveforms was digitised on the Leicester University digitiser, the clock rate being set such that approximately 150 pairs of co-ordinates were obtained from each waveform.

6.2 The Processing of the Results

The output from the digitiser was processed in three stages by a number of programs written for the Leicester University C.D.C. Cyber 72 computer.

6.2.1.Housekeeping the Digitiser Output

The output from the digitiser for each cardiac cycle consisted of three sets of approximately 150 pairs of co-ordinates each representing the distances in thousandths of inches from the origin of the digitiser board to a single point on each waveform. The housekeeping program turned these data into three sets of 33 y-values with appropriate dimensions (ie: millimetres of mercury or millilitres per minute). This was accomplished in two stages. Firstly the co-ordinate pairs were transformed into appropriate dimensions, and then each cycle was divided into thirty-two. The 32 values of y were found by calculating the corresponding equally spaced x-values, selecting the nearest x-values on either side of these, and calculating the required y-values by linear interpolation. A thirty-third point was also calculated which corresponded to the start of the next cycle. This was necessary to measure any drift in the mean values of each parameter during a cardiac cycle.

6.2.2. The Calculation of the Results

The second stage was to extract the required results from the housekept data. Figure 6.2 is a flow diagram of the program used for this purpose. It will be noted that some segments of the program are related to the Doppler results, and these will be discussed in Chapter Seven. The rest of the operations are detailed below :

a) The results were read and checked for consistency.

b) The results were corrected for drift. This was achieved by imposing a tilt about the 17th point of each waveform so that the 1st and 33rd points had the same y-value.

c) and d) The results were transformed into Fourier Space and corrected for the frequency response of the recording apparatus. (All the zeroth Fourier harmonics were stored for later output).

e) The resistance of the peripheral bed was calculated by dividing the zeroth harmonic of P2 by the zeroth harmonic of flow.

f) An inverse Fourier Transform was carried out on the modified harmonics of P2, ΔP and Q.

g) and h) Least squares 'best fit' values of A, B and C were calculated assuming that the relationship between P and Q is given by:

$$\Delta P = AQ + BQ|Q| + C\, dQ/dt$$

i) The corrected values of P1 were calculated from the corrected values of P2 and ΔP.

j) The maximum values of P1 and P2 were found and the pressure index distal to the stenosis found ($\hat{P2}/\hat{P1}$).

k) The maximum value of Q and the corresponding value of pressure difference were found.

l) The results were output.

Because of the large number of results obtained from each waveform and the large number of waveforms analysed, a summary of the results obtained from this last program was written to another file each time it was run. The results stored for each pulse were as follows :-

1) The Waveform Identifier (this included information about the dog, stenosis and run number).

2) Mean flow.

3) Mean Pressure difference.

4) Maximum flow.

5) Pressure difference at the time of maximum flow.

6) The apparent peripheral resistance ($\overline{P2}/\overline{Q}$).

7) Pressure Index (max P2/max P1).

8) Calculated pulsatility index.)
) see next chapter
9) Calculated modified pulsatility index)

10) A

11) B

12) C

13) $\overline{P2}/\overline{P1}$

14) Corrected peripheral resistance (see Section 6.4)

15) Pulsatility index.)
) see next chapter
16) Modified pulsatility index.)

17) K_v)
)
18) K_t) see section 6.3
)
19) K_u)

20) Mean pressure difference x nominal vessel area squared

21) Maximum pressure difference x nominal vessel area squared.

22) A code indicating whether the measurements were taken with the preparation in a stable condition.

6.2.3. Further Processing of the Results

Two additional sets of programs were written to process the results further. The first program plotted any one parameter against any other. It was written in a very general form so that any graph could be drawn simply by changing a few calls to subroutine. It was possible to draw graphs by dog, by stenosis or by both, and also to plot only results from waveforms which could be considered stable or from both stable and unstable waveforms.

The second program was based on the first, but permitted the calculation of simple statistical quantities from any desired group of results.

6.3 The Relationship between blood flow and the pressure difference across a stenosis

Figures 6.3a to 6.3f illustrate the relationship between the maximum flows through stenoses B3.9 to B8.9, and the simultaneous pressure drops. Figure 6.4 summarises the same information for all 'B' stenoses, on which four or more determinations were made, in a series of best-fit quadratic curves. The graphs have been plotted with maximum flow values because at these points the differential of flow is zero. The values obtained from the 'A' stenoses have not been included as they would fall on a different set of curves as a result of having different nominal

diameters. It can be seen that the results are remarkably well grouped.

The relationship between the flow through a stenosis and the pressure difference across it is determined solely by the stenosis, and it is thus possible to consider it without reference to the rest of the circulatory system. This relationship is discussed in this section and in particular the agreement of the results of the dog experiments with the theories of D.F. Young and his colleagues (Young D.F. et al 1973a, 1973b, 1975, 1977, Seeley B.D. and Young 1976).

The main relationship derived by Young et al has already been given in Equation 3.1

$$\Delta P = \frac{K_v \mu}{2r_1} \cdot U + \frac{K_t}{2}\left[\frac{r_1^2}{r_2^2} - 1\right]^2 \rho U|U| + K_u \rho L_t \frac{du}{dt} \qquad 6.1$$

The coefficients K_v, K_t and K_u have the virtue of being dimensionless and thus the coefficients A, B and C which were found from the dog experiments (see Section 6.2 g and h) were converted into this form. It is easily shown that

$$K_v = A. \frac{2\Pi r_1^3}{\mu} \qquad 6.2$$

$$K_t = B. \frac{2\Pi r_1^4}{\rho}\left(\frac{r_1^2}{r_2^2} - 1\right)^{-2} \qquad 6.3$$

$$K_u = C. \frac{\Pi r_1^2}{\rho L_t} \qquad 6.4$$

The values of K_v, K_t and K_u and their dependence on stenosis length and diameter are discussed below.

6.3.1 Experimental values of K_v, K_t and K_u

Coefficient K_v

The first term of Equation 6.1 represents the viscous pressure losses, and thus K_v should, under idealised steady flow conditions be given by Equation 6.5

$$K_v = \frac{16L}{r_1} \left(\frac{r_1}{r_2}\right)^4 \qquad 6.5$$

Seeley and Young (1976) found from their in-vitro steady flow studies that Equation 6.5 tended to underestimate K_v for small values of L/r_1 and to overestimate K_v for large values of the same ratio. From their experimental data they found that K_v was closer to the value given by Equations 6.6 and 6.7

$$K_v = \frac{16L_a}{r_1} \left(\frac{r_1}{r_2}\right)^4 \qquad 6.6$$

$$L_a = 0.83L + 3.28r_2 \qquad 6.7$$

The values of K_v obtained from the dog experiments described in Chapter Five are all considerably higher than those given by either Equation 6.5 or 6.6. These values are listed in Table 6.2, together with theoretical values obtained using Equations 6.6 and 6.7. It can be seen that the values obtained in-vivo are between two and five times as great as those found by Seeley and Young.

The ratio of values of K_v found by Young et al (K_{vy}) to the experimentally determined values of K_v (K_{ve}) is a function of both the length and diameter of the stenoses. An empirical equation was derived for K_v by replacing L_a

from Equation 6.6 by a new modified length L_m which was assumed to be of the form of Equation 6.8

$$L_m = C_1 L + C_2 r_2 \qquad 6.8$$

The constants C_1 and C_2 were evaluated by fitting all the experimentally determined values of K_v, and were found to be 1.95 and 17.4 respectively. The final column of Table 6.2 is a list of the 'theoretical' values of K_v obtained using Equation 6.8. It can be seen that these values agree fairly well with the values of K_{ve}.

Coefficient K_t

Coefficient K_t is an index of turbulent losses, and should theoretically under 'ideal' conditions have a value of approximately unity.

Young et al have evaluated K_t in a number of in-vitro experiments and found it to have values of 0.9 - 1.2 (Young and Tsai 1973a), 1.57 - 2.31 (Young, Cholvin and Roth 1975) and 1.35 - 1.85 (Seeley and Young 1976). The values of K_t derived from the current set of animal experiments are summarised in Table 6.3. These appear to be somewhat lower than the values found by Young et al, and the grand mean of all the B stenosis results is 0.98. The results from the A stenoses are higher but only relate to a single dog.

Coefficient K_u

The final coefficient K_u is related to the unsteady component of flow. Young et al have not discussed this quantity in detail but suggest that it may be dependant on

geometry. They state that its value is approximately unity and that a value of 1.2 gives the best overall fit to their data.

The results obtained from the dog experiments are given in Table 6.4 and it can be seen that K_u was found to be strongly dependant on the diameter of the stenosis, and possibly a function of length also. A plot of log K_u against the log of the diameter of the stenoses divided by the diameter of the arteries proved to be a virtual straight line with a gradient of -2.5. The experimental values of K_u were thus fitted to an equation of the form

$$K_u = k_1 + k_2 (r_1/r_2)^{2.5} \qquad 6.9$$

k_1 and k_2 were found to have least squares best fit values of 0.423 and 0.434 respectively. The values of K_u derived by inserting the values of r_1, r_2 and k_2 in equation 6.9 are given in Table 6.4. It can be seen that equation 6.9 seems a useful empirical expression for finding K_u.

6.3.2. Disagreement with Young's results

There is an apparent discrepancy between the results derived from the dog experiments (K_{ve}, K_{te} and K_{ue}) and those of Young et al (K_{vy}, K_{ty} and K_{uy}). The values of K_{ve} and K_{ue} are very much larger than the corresponding values derived by Young, whilst the value of K_{te} is significantly smaller the K_{ty}. The results have however been arrived at using rather different techniques.

In every case Young et al have found their values of K_{vy}, K_{ty} and K_{uy} in-vitro, and usually (with the obvious

exception of K_{uy}) under steady flow conditions. In two of their papers (Young et al 1975, 1977) they have made measurements of flow and pressure in the femoral and carotid arteries of dogs and discussed the value of Equation 6.1 for predicting pressure drops from flow, but in each case the 'K values' have first been found under highly artificial conditions. The K values derived from the present work have all been found under realistic conditions by fitting Equation 6.1 to the experimental data.

It seems rather surprising that Young's K values fit his dog experimental data so well, but a simple calculation shows that, despite the wide difference between the values of K_{vy} and K_{ve}, and between K_{ty} and K_{te}, ΔP calculated from Equation 6.1 (using a physiological range of blood velocities, and assuming $dU/dt = 0$) is very similar whichever pair of coefficients are used. Some curves of pressure difference plotted against velocity using the two pairs of coefficients are shown in Figure 6.5. The similarities are striking, but there can be no doubt that the differences between the coefficients are very real. The standard errors of the determination of K_{ve} and K_{te} are fairly small (see Tables 6.1 and 6.2) and the results consistent. For each and every stenosis investigated K_{ve} was considerably higher than K_{vy}, and for a given length there was a tendency for the differences to decrease as the stenosis became more severe. Similarly, the values of K_{te} were generally found to lie between 0.8 to 1.2 whatever the length or severity of the stenosis.

In the same way that a change in value of K_v and K_t between an idealised bench model and an animal model would

not have been apparent because of the similarity of the final answer, the discrepancy between K_{uy} and K_{ue} would not have been apparent in Young's work, as it is only in the presence of mild stenoses that the third term of Equation 6.1 becomes significant, and thus his constant low value of K_u would appear to fit his animal data well.

Young et al have summarised the data they have obtained from their animal experiments (Young et al 1977) and have listed for each of the twelve dogs between two and four pairs of measurements of maximum velocity and maximum pressure drop across the stenosis. (They only used one stenosis in each dog). From this data it is possible to calculate the values of K_v and K_t they would have obtained had they used their in-vivo data rather than trying to fit their in-vitro coefficients. A summary of these results is given in Table 6.5 along with values of K_{vy} and K_{ve} calculated from the geometry of the stenoses. It is clear that their animal experimental values are much closer to K_{ve} than K_{vy}.

It seems that there is a fundamental difference between the steady flow of a fluid with 'blood-like viscosity' in-vitro, and the flow of blood itself in-vivo. There may be several factors contributing to this difference.

In general, viscous pressure losses are higher for pulsatile flow in straight tubes than for steady flow. If the pressure loss due to the first term of Equation 6.1 is written as

$$P = k.A.U. \qquad 6.10$$

where A is independant of α (see page 2-2) and k = 1 for

steady flow, then for α = 10, k = 2 and for α = 20, k $\simeq$ 4 (Young and Tsai 1973). The values of α for the first harmonic of blood flow in the dog arteries was between 5 and 6, (giving a value of about 1.4 for k) but would be lower in the stenoses as α is proportional to radius. Because of the relatively short length of the stenosis however, it is unlikely that normal pulsatile laminar flow could be established within the stenosis, and it is possible that the 'effective α ' may be considerably higher than predicted. This point needs further investigation, but it is interesting that in long straight tubes a high value of α implies plug-like flow, the kind of flow which might be expected in a stenosis.

A further difference between the in-vitro and in-vivo experiments is the fluid. Although the glycerol-saline mixture used by Young et al in-vitro was adjusted to have a similar viscosity to blood, it is known that blood is highly non-Newtonian at shear rates of less than about 100 sec^{-1} (McDonald 1974). The graph of viscosity against shear rate presented in figure 6.7 was determined from blood samples taken at various times during the five final dog experiments. The non-Newtonian nature of blood is clearly demonstrated.

As McDonald points out, the prediction of the viscous behaviour of blood in oscillatory flow is difficult, as not only is the blood velocity profile constantly changing (and hence the shear rates at various points across the artery) but the distribution of erythrocytes within the blood vessel is non-uniform due to a cell free zone at the wall (Bayliss 1959).

Taylor (1959) has discussed the effects of the shear rate dependence of blood viscosity in pulsatile flow and concluded that in all the larger arteries the use of the asymptotic viscosity would lead to an error of less than 2% in the calculation of flow from pressure gradient. Kunz and Goulter (1967) compared the oscillatory pressure flow relationships of blood and a water/glycerol mixture in straight tubes and found the results to be in good agreement. Although both these pieces of work were concerned only with non-stenosed vessels, the effect of a stenosis is to raise shear rates, and thus presumably to assure that the blood viscosity is at its asymptotic value.

For the purposes of calculation, blood viscosity has been assumed to be 4 cP throughout this thesis.

6.3.3 Conclusions concerning bloodflow and the pressure difference across a stenosis

On the basis of the present work it seems that the pressure drop across a stenosis can be predicted to a fair degree of accuracy using Equation 6.1, but that the values of K_v, K_t and K_u derived by Young et al in-vitro require modification. Figure 6.6 is a plot of calculated values of maximum ΔP against measured values of ΔP for all the dog experiments. The former values have been calculated from Equation 6.1, with K_v calculated from Equation 6.8 and K_t taken as 0.98. The agreement is fair, but clearly not as good as it would have been with the individually fitted values of K_v and K_t. It appears that it is the constant value of K_t which is the major problem, as Equation 6.8 predicts the individual K_v values fairly well. The

experimental values of K_t were not constant although no particular trend emerged. It is possible that this might reflect the variations of entrance and exit shapes to which K_t is particularly sensitive, but which were unfortunately not completely standard.

Although the exact variation of pressure-drop with flow and stenosis geometry is of interest, only the general conclusions are of clinical value as natural arterial stenoses are always irregular.

6.4 The Variation of Peripheral Resistance with Stenosis

The peripheral resistance of a given vascular bed is simply defined as difference between arterial and venous blood pressure divided by the blood flow through the bed. Venous pressure is normally very close to zero and thus peripheral resistance may be written

$$R_p = P_a/Q_t \qquad 6.11$$

where P_a is arterial pressure and Q_t the total bed blood flow.

Applying this formula to the dog experiments, P_2 corresponds to P_a, but unfortunately Q does not correspond to Q_t, there being an additional component to the total flow, Q_c the collateral flow. The situation is depicted in terms of an electrical analogue in figure 6.8.

Under physiological conditions the contribution of Q_c is usually ignored which results in a slightly inaccurate quantity which will be termed apparent peripheral resistance R_a.

The size of the error introduced by measuring Q rather than Q_t is simply calculated. The flow through the stenosis Q, may be written

$$Q = \frac{R_c}{R_s+R_c} \cdot Q_t \qquad 6.12$$

and therefore

$$R_a = R_p (R_s + R_c) / R_c \qquad 6.13$$

If R_c is large compared with R_s then R_a and R_p are similar. Under physiological conditions R_s is the resistance of the main artery and can be ignored, however in patients with peripheral vascalar disease and in animal studies of the disease, the distinction between apparent peripheral resistance and peripheral resistance should not be disregarded.

The values of apparent peripheral resistance obtained from the dog experiments were adjusted using Equation 6.13 to obtain true peripheral resistance. In order to achieve this it was first necessary to find the collateral resistance R_c, which for the purposes of calculation was assumed not to change significantly throughout the experiment. Although this may appear an unjustified assumption the calculation becomes intractable without it. The collateral vessels between the aortic trifurcation and the lower end of the femoral artery had of course been divided during the dissection procedure. Collateral vessels do tend to enlarge in diseased limbs, but most of this change occurs over a protracted period of time.

A further necessary assumption was that the peripheral resistance always dropped to a similar value R_x in any one

dog, following the short period of arterial occlusion required to facilitate the changing of stenoses. Once again this assumption is open to criticism, but the final answers obtained were very consistent, suggesting that both this and the previous assumption were reasonable. The true value of R_x was found by averaging all the values of R_a obtained during the hyperaemia immediately following the insertion of mild stenoses. Under these circumstances collateral flow amounted to only a very small percentage of the total flow.

The value of R_c was found by making measurements of R_a with severe stenoses in-situ, and assuming R_p to be equal to R_x. Finally it was confirmed that R_c was indeed large compared to the resistance of the stenosis, assumed to be insignificant at the start of the calculation. The values of collateral resistance for each dog fell in the range of 0.27 to 0.57 mm. Hg.min.ml^{-1}, with the exception of that for dog 12, the animal with vessels which required 4mm nominal diameter stenoses due to the small calibre of its vessels.

Table 6.6 shows the results by dog. Unfortunately it was not possible to weigh the animals at the time of the experiment, but dogs which were subjectively thought to be large had the lowest collateral resistances, whilst the small dogs had relatively large collateral resistances.

The values of corrected peripheral resistance (CPR) are plotted against stenoses in figure 6.9; the letters A to K represent values from dogs 10 to 20. There is a large amount of scatter as might be expected with results from animals of varying size, and so, in order to normalise

the results, all values of CPR were divided by R_x to produce a quantity referred to as relative peripheral resistance (RPR). Unfortunately because of the tortuous way in which this quantity is derived large systematic errors could occur between the results from different dogs. Many stenoses were only tested in one or two dogs, and this could correspondingly bias the results; however, stenoses 2.9 to 7.9 were all extensively tested in dogs 13, 14, 15 and 19, and so it is the results from these dogs and stenoses which have been chosen to examine changes in peripheral resistance with stenosis. The values of RPR are graphed in Figure 6.10, the error bars represent the standard errors of the means. There is no statistical difference between the values of RPR for any of the stenoses, the overall mean value being 3.03. Reference to Figure 6.9 confirms that for any particular dog there is no obvious trend in CPR values.

There is little quantitive data in the literature concerning the effect of stenoses on peripheral resistance although a number of studies have been carried out on patients with intermittent claudication and rest pain (Weale et al 1964, Sumner and Strandness 1970, Bliss 1971).

Strandness and Sumner (1975) have stated that : 'In general, as the proximal resistance increases the resistance of the distal vascular bed decreases. The effect of this re-adjustment is to keep the total limb resistance constant at rest'. Assuming that the change in peripheral resistance is under the control of a negative feedback mechanism then this last statement would seem reasonable, and an arterial stenosis would only have

a significant effect on peripheral resistance if its magnitude was comparable to that of the peripheral bed.

Because of the non-linearity of the pressure flow relationship across an arterial stenosis, it is not possible to derive a true value for its resistance, but an approximate value may be derived by averaging the ratio of mean pressure to mean flow for each stenosis, and the results of such a calculation are shown in Table 6.7. It is also possible to find an average 'resting' peripheral resistance for each dog simply by multiplying the value of R_x by the mean value of RPR (ie: 3.03). These values are given in Table 6.6 and fall between 0.45 and 1.64 mm. Hg.min.ml^{-1}. Finally the values of collateral resistance are known to fall in the range of 0.27 to 1.35 mm.Hg.min.ml^{-1}. By taking a mean of the values of R_c, and of resting peripheral resistance, it can be shown that the peripheral resistance would drop to 90%, 81% and 74% of its resting value with stenoses '6', '7' and '8' respectively, if it were to completely compensate for the effects of the stenosis. Unfortunately no results are available for the '8' stenosis, but the relatively small percentage change in peripheral resistance necessary to compensate for the milder stenoses could almost explain the apparently constant values of relative peripheral resistance. It will be suggested in the next section that this is not so.

The changes in peripheral resistance resulting from proximal resistance changes need further experimental investigation. There are however many problems associated with measurements on the peripheral bed. Experimental techniques themselves will inevitably affect the peripheral bed, and variables such as ambient room temperature,

anaesthetic technique, hypo-volaemia and surgical damage to nervous tissue must all be considered. An attempt has been made in the present work to take into account the effect of collateral resistance and the labile nature of peripheral resistance, and the results are encouraging. One factor which makes investigation particularly difficult is that even if the peripheral bed completely compensates for the effects of a stenosis, a very severe stenosis would be necessary to change the peripheral resistance by a large percentage.

6.5 The Effect of Stenosis Severity on Blood Flow and Pressure

The changes in flow and pressure distal to an arterial stenosis are controlled by three factors, the peripheral bed, the collateral bed, and the stenosis itself. Each of these three components has already been considered individually.

Clearly resting levels of blood flow through a stenosis depend on the size of the dog, and so the results for each dog have been normalised to the resting flow with a "0" stenosis in situ. The mean values of relative flow for each dog have been plotted against stenosis in Figure 6.11. Three points are immediately apparent. There is a very wide scatter of results, the mean flows for the mild stenoses are all greater than for the "0" stenoses, and there is a decrease in flow as the severity of the stenosis increases. The scatter is a normal finding in these types of experiments and is presumed to be due to variations in peripheral resistance (Shipley and Gregg 1944, Fiddian

et al 1964). The high mean flow values through the mild stenoses are a curious finding and can only for the present be interpreted as spurious points. Clearly any further experiments along the same lines should include some mild stenoses to exclude the possibility of this being a real effect. The third point is more interesting and suggests that the peripheral resistance is not compensating for the effects of the stenoses. Using the values of mean R_c and 'resting' peripheral resistance calculated in the previous section it is easily shown that the peripheral bed could completely compensate for even an '8' stenosis, whereas the decrease in flow suggests that it has not even begun to compensate. Even from the raw animal data it is apparent that the peripheral bed could 'do better' as there is a period of marked hyperaemia following the release of the occlusive clamp, (typically the flow increases between 50 and 100%).

The evidence that stenoses can change peripheral resistance seems scant. The idea seems to have been suggested by Shipley and Gregg (1944) to explain the sudden increase in the pressure drop across a stenosis as it becomes very severe, however, as May et al (1963) pointed out it is not necessary to evoke this concept at all. Flanigan et al (1977) have suggested that auto-regulation cannot be an important factor in determining flow through a stenosis as they found almost identical results from mean flow through stenoses in-vitro and in-vivo. Many other authors mention auto-regulation but neither demonstrate its existence by experiment nor quote any references. As previously mentioned (Section 6.4) some workers have made

measurements in patients with vascular disease and shown that their peripheral resistance is slightly lower, but this may be a long term effect, and could be due either to collateral development or ischaemic damage to small vessels. In this context it is interesting to note that in some patients with severe rest pain resting foot blood-flows may be greater than normal, presumably due to some such mechanism (Schraibman and Ledingham 1969, McEwan and Ledingham 1971).

None of the results of the current experiments suggest that stenoses have any effect on the peripheral bed.

The relationship between the severity of a stenosis and the pressure drop across it is easier to investigate than the severity-flow relationship, as the top pressure (P_1) can always be considered a reference pressure. The effect of stenosis severity on pressure drop is shown in figures 6.12 and 6.13. The abscissas represent the stenoses rather than any index of stenosis severity. The ordinate of figure 6.12 is mean P_2 divided by mean P_1, and shows an orderly increase as the severity of the stenoses increases. It can also be seen that for the tighter stenoses length is important in determining the pressure drop.

Figure 6.13 shows the change in pressure index (Max P_2/Max P_1) with stenosis severity. This will be further discussed in Chapter eight, where it will be seen that, despite its apparent promise as a diagnostic test, in reality techniques of measurement reduce its value.

Two points of interest arise when figure 6.13 is

compared with figure 6.12. Although mean P_2/mean P_1 never exceeds unity, in some cases pressure index does for mild stenoses. This is a frequent finding in healthy subjects and may be explained by wave reflection. The second point is the pressure index is more sensitive to stenosis severity than mean P_2/mean P_1, an effect that would be expected because of the larger flow through the stenosis in the former case.

There is a much wider scatter of results for the tighter stenoses and this is thought to reflect the labile activity of the peripheral bed. The resistance of mild stenoses is such that even large changes in flow cause little change in absolute pressure drop, whilst any change of flow through the tight stenoses leads to a profound change in pressure drop.

6.6 Conclusions

The flow and pressure results obtained from the dog experiments have been discussed in the relevant sections of this chapter.

The evidence suggests that although equation 6.1 derived by Young et al can be used for predicting pressure losses across a stenosis the values of the constants K_v, K_t and K_u need re-examining. The results from the present study suggest that compared with Young's values K_v should be increased, K_t decreased and that K_u is highly dependant on the diameter of the stenosis.

It must be borne in mind that although the current experiments were carried out in-vivo, the model was still of a highly idealised nature,ie: non-diseased elastic

arteries with a single smooth rigid symmetrical constriction. In reality, stenoses are much less regular, and varying degrees of arterial disease may affect a large portion of the circulatory system. Although it is satisfying to be able to predict the effects of stenoses from their geometry, only the crudest of measurements can be made on the shape of real arterial narrowings. The concept of 'equivalent stenosis' will be introduced in Chapter eleven in an effort to reconcile animal and patient results.

The results of measurements on the peripheral bed suggest that in these experiments the resistance did not vary in response to a stenosis being inserted in the artery, but that it was effected by the ischaemia resulting from the complete occlusion of the main artery. The problems of measuring peripheral resistance in an experimental preparation have already been discussed, and the results are open to at least two interpretations. The first is that the peripheral bed does not, at least in the short term, compensate for increases in the resistance of the proximal bed. The second possible explanation which could apply also to other experimental studies of the same type is that most of the sympathetic tone of the arterioles was abolished by the anaesthetic and surgical techniques, and that the increase in flow following the complete occlusion of the artery was due to an active dilatation of the skeletal muscle arterioles, primarily caused by locally produced metabolites.

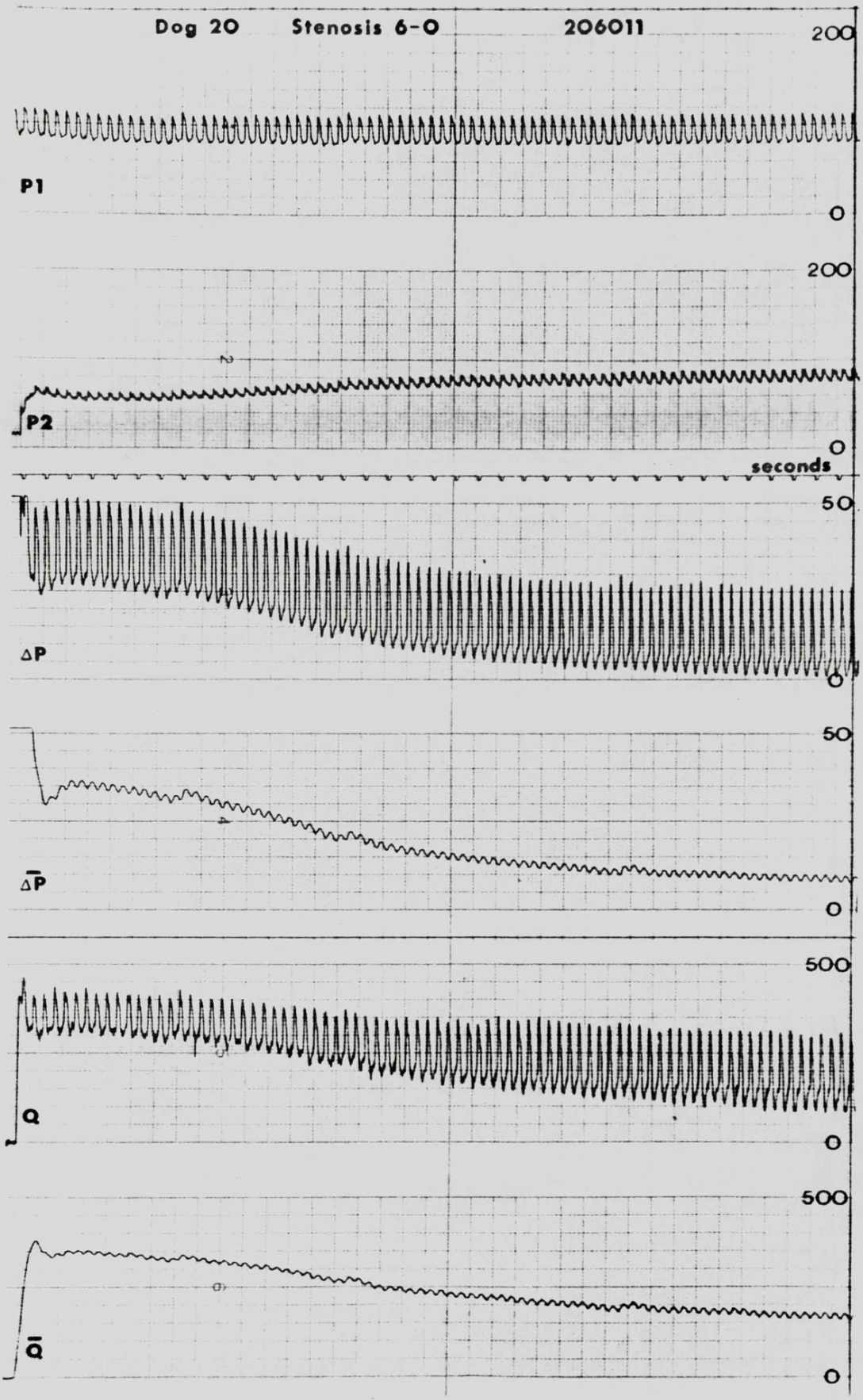


Figure 6.1. Typical recording of flows and pressures following the release of the clamps. This particular result was obtained from dog 20 with a B6-0 stenosis. All the flows are in ml/minute, all the pressures are in mm.Hg.

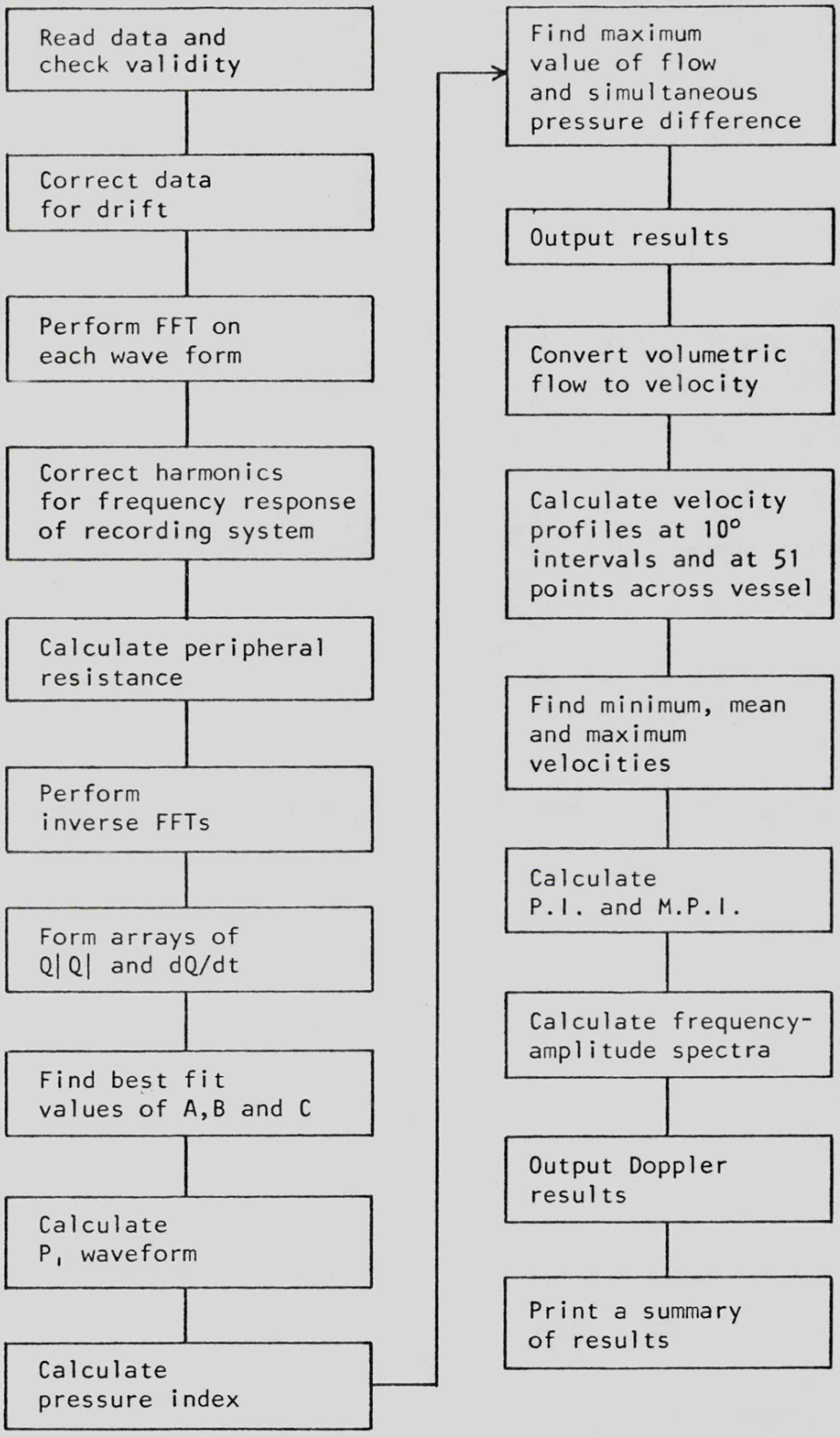


Figure 6.2 Flow diagram of program used for processing the results from the dog experiments

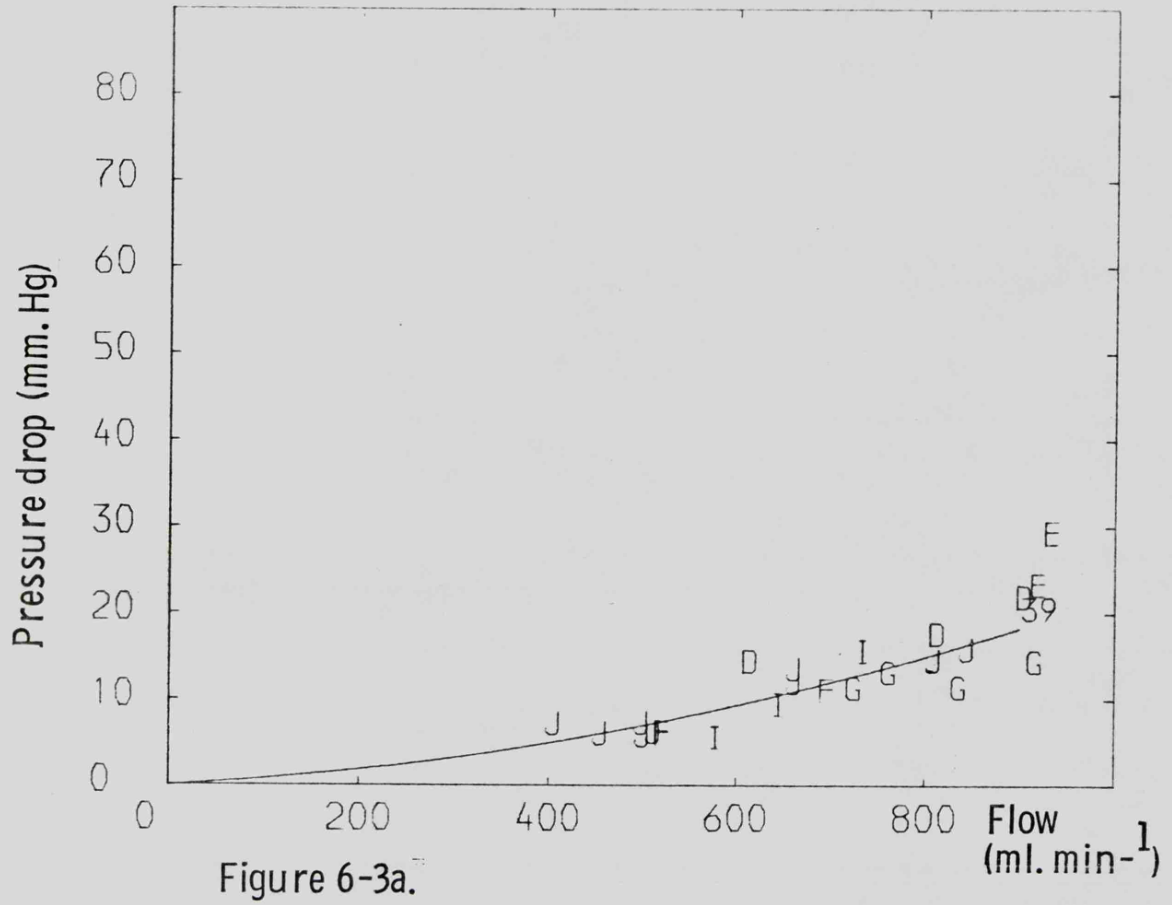


Figure 6-3a.

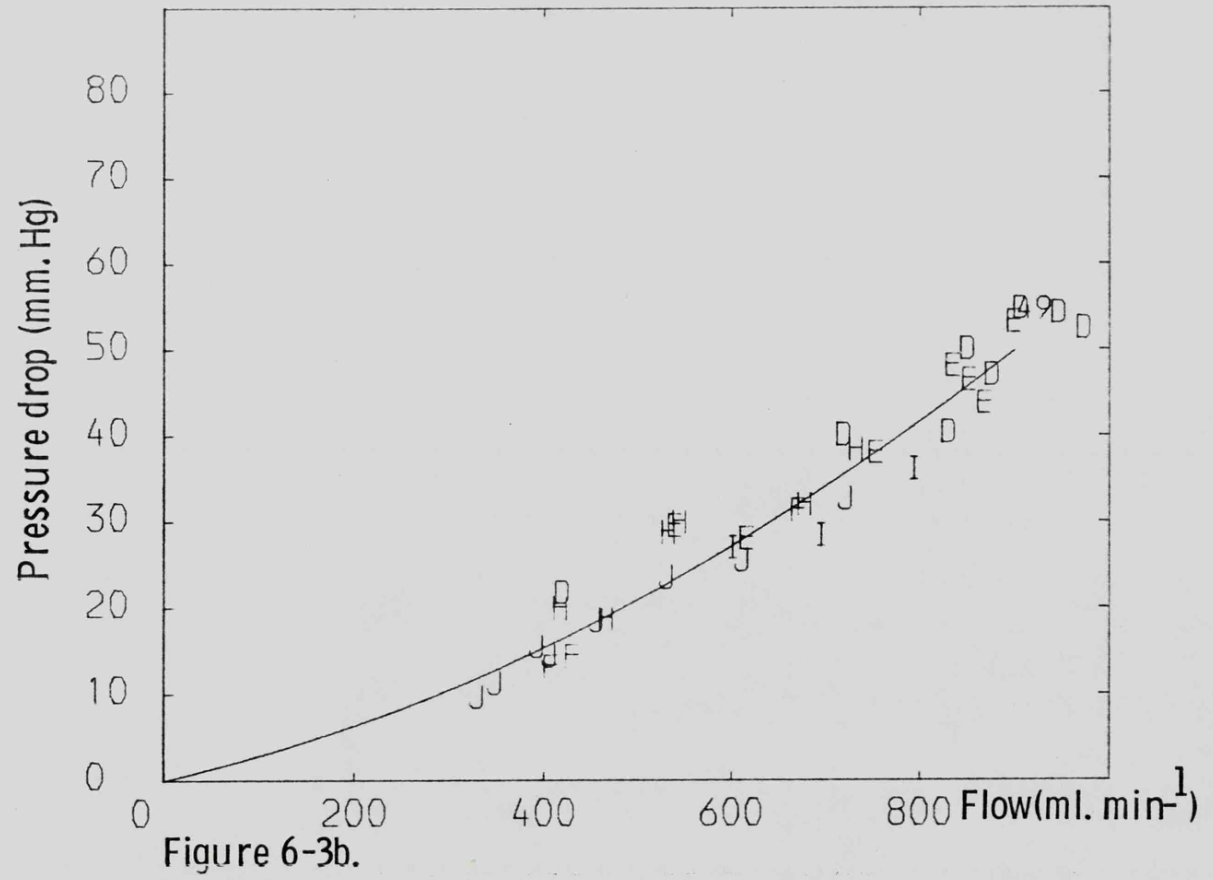


Figure 6-3b.

Figures 6-3 a-f. Pressure drops across various stenosis at the time of maximum flow, plotted against that flow. Each letter (A-K represent dogs 10-20 respectively) indicates one determination. The curves are least-squares best-fit lines.

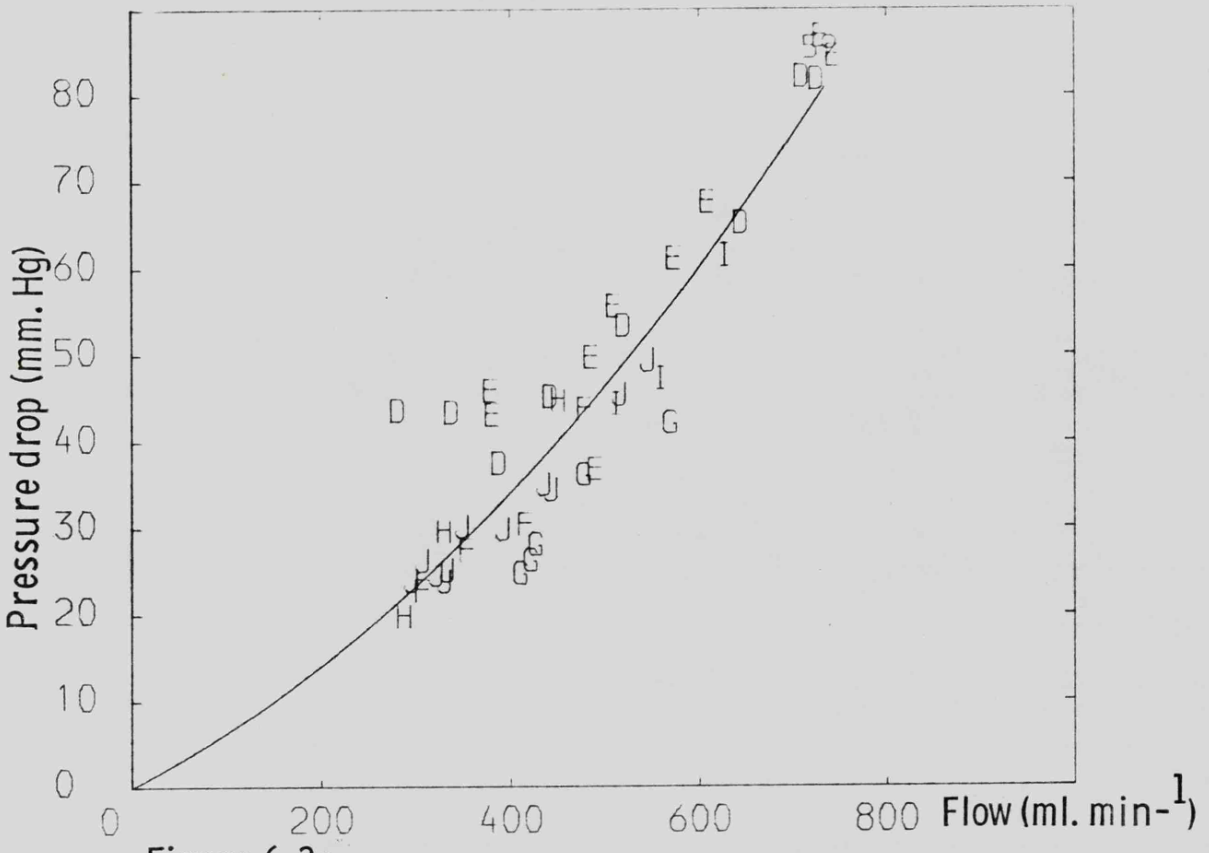


Figure 6-3c.

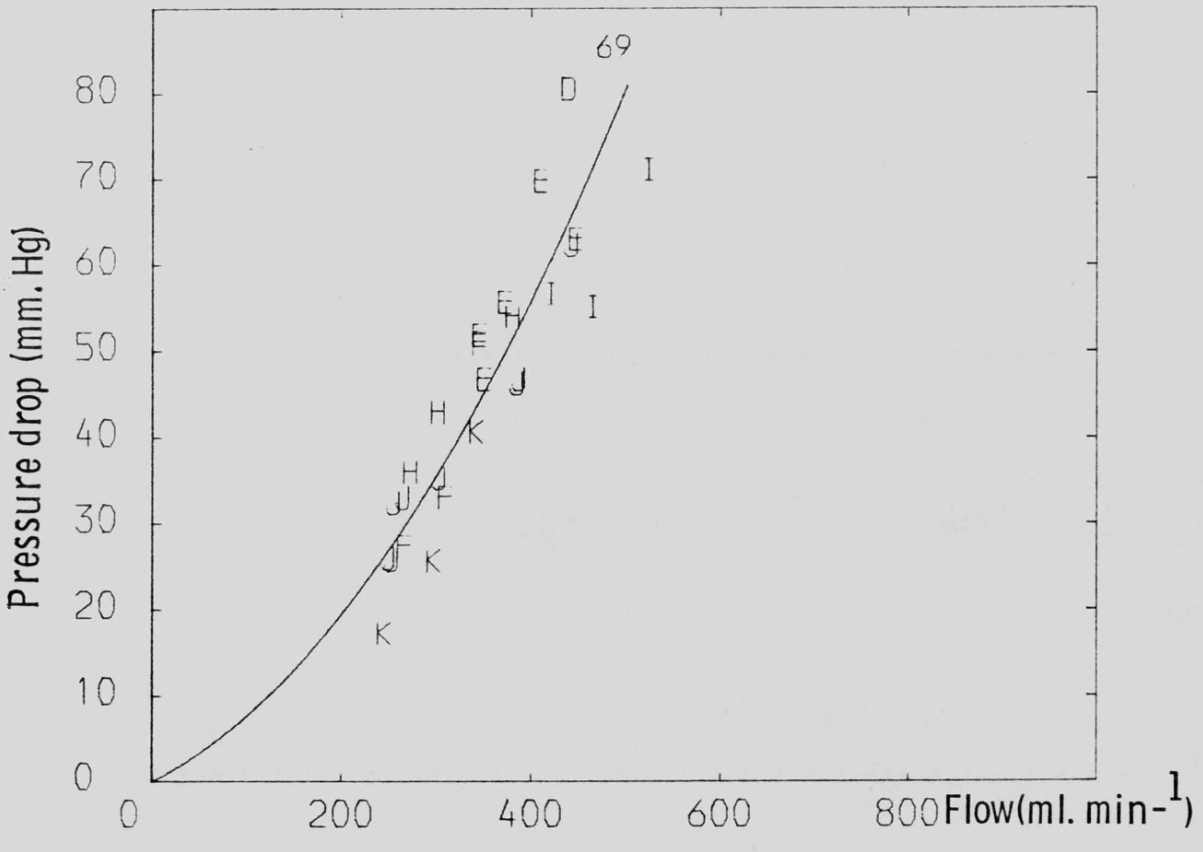


Figure 6-3d.

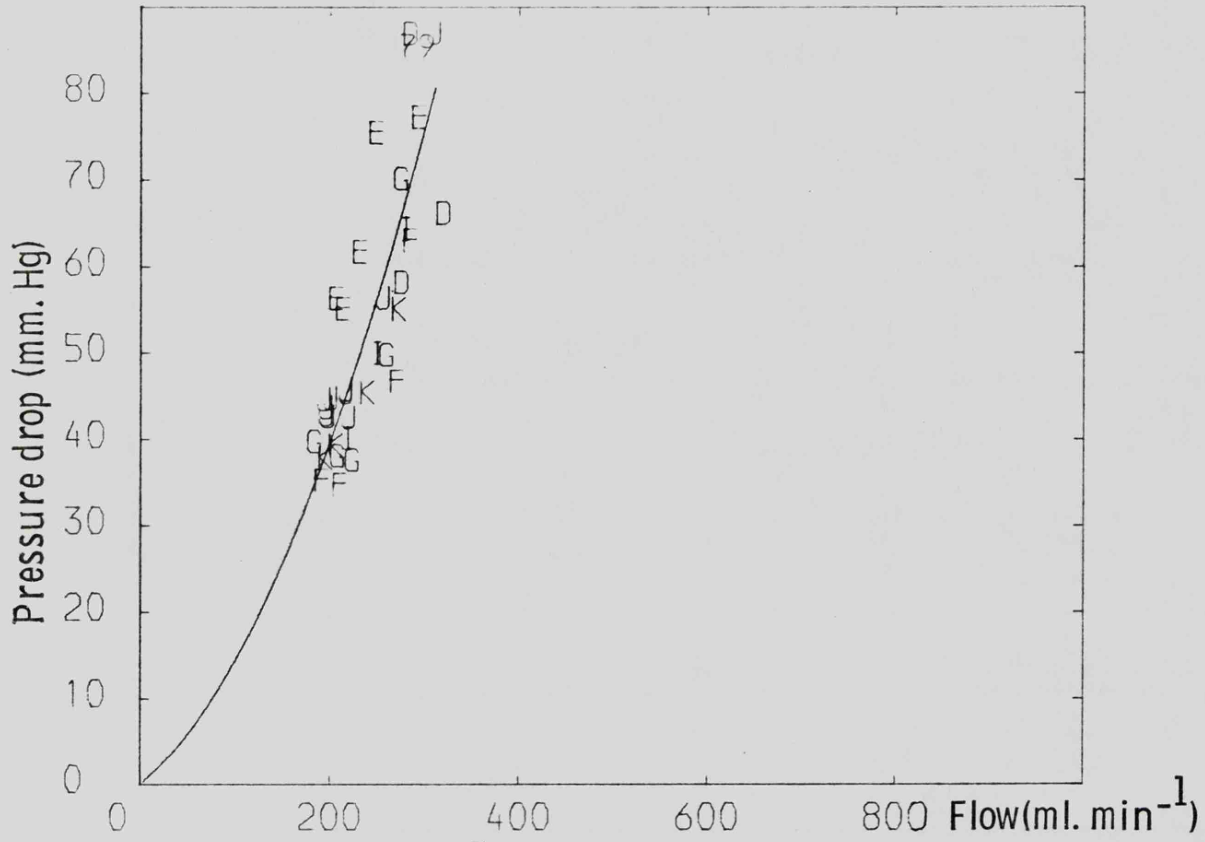


Figure 6-3e.

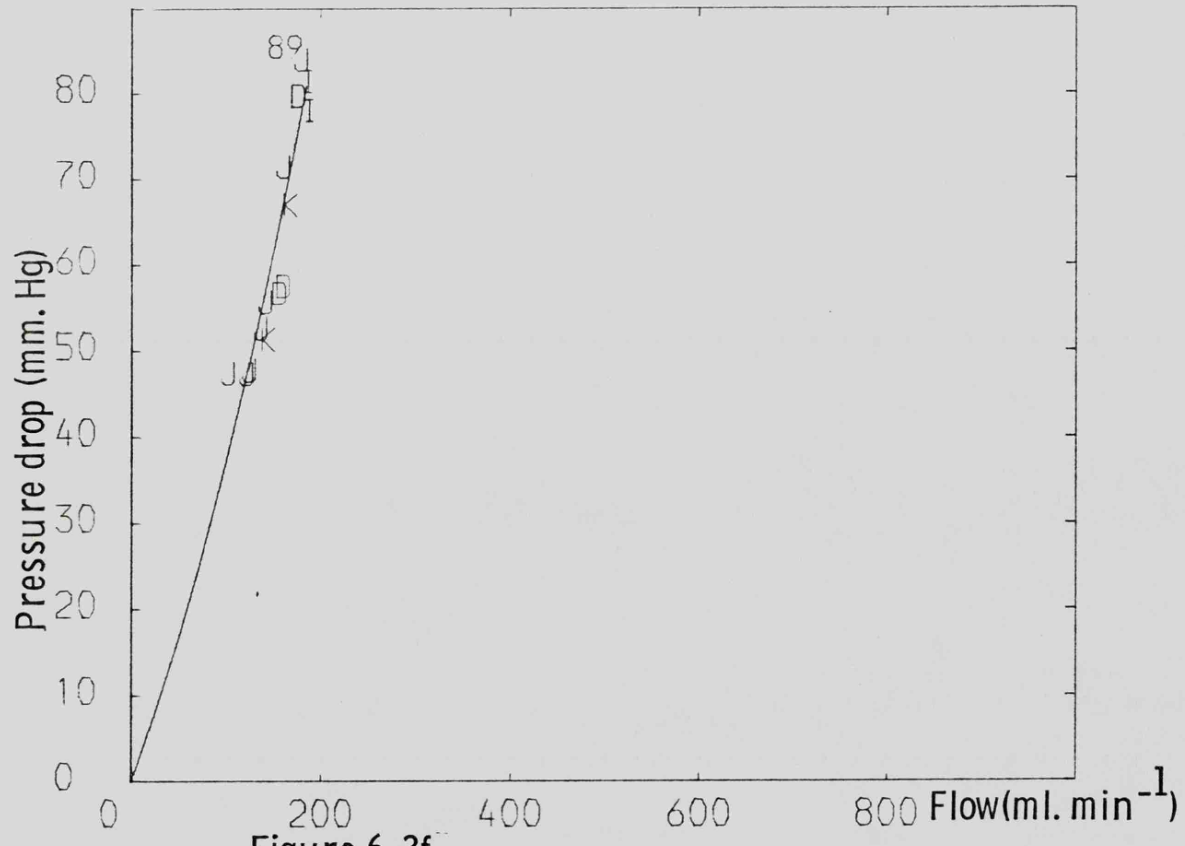


Figure 6-3f.

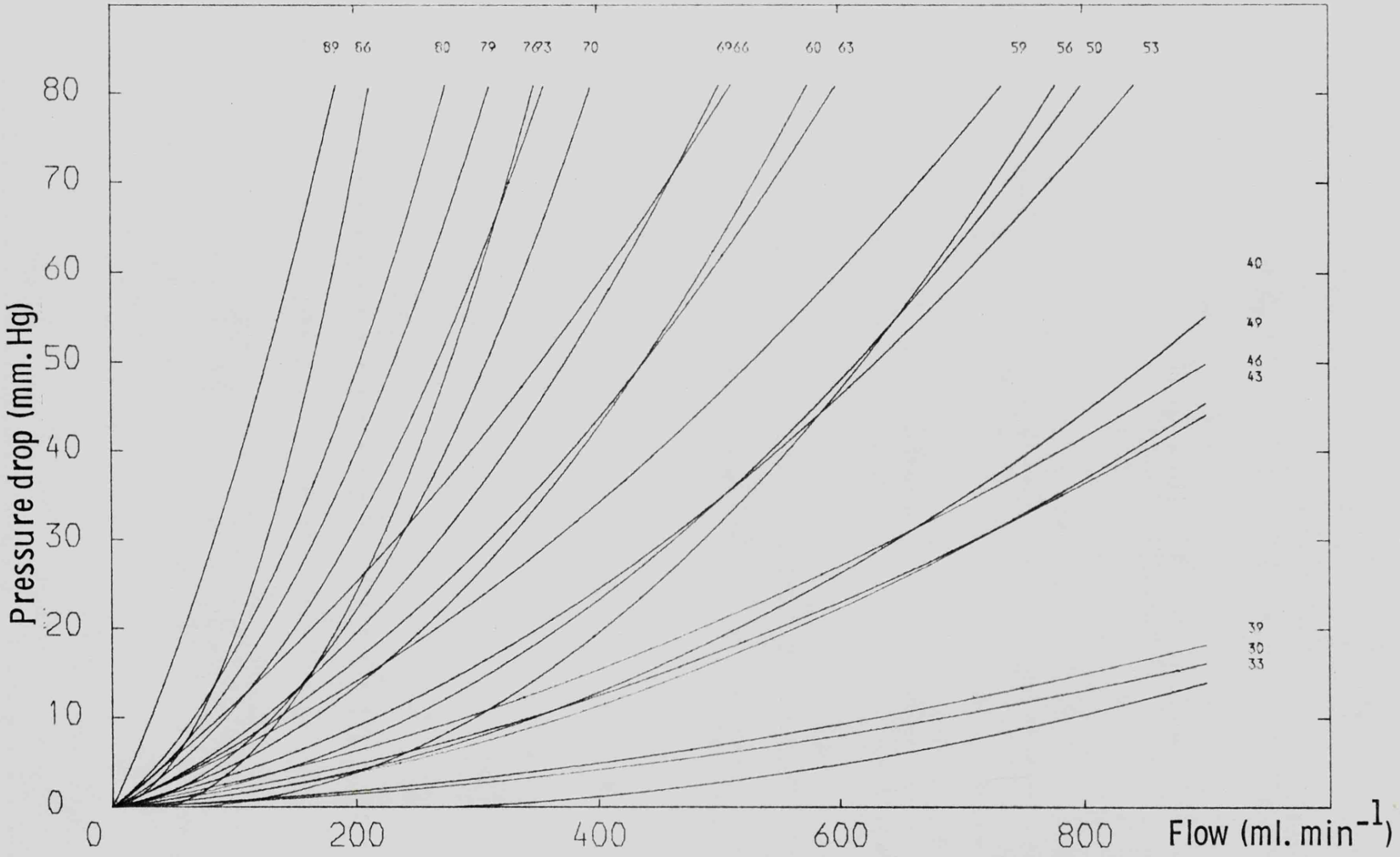


Figure 6-4. Least-squares best-fit quadratic curves showing the relationship between maximum flow and simultaneous pressure drop for the 'B' stenoses.

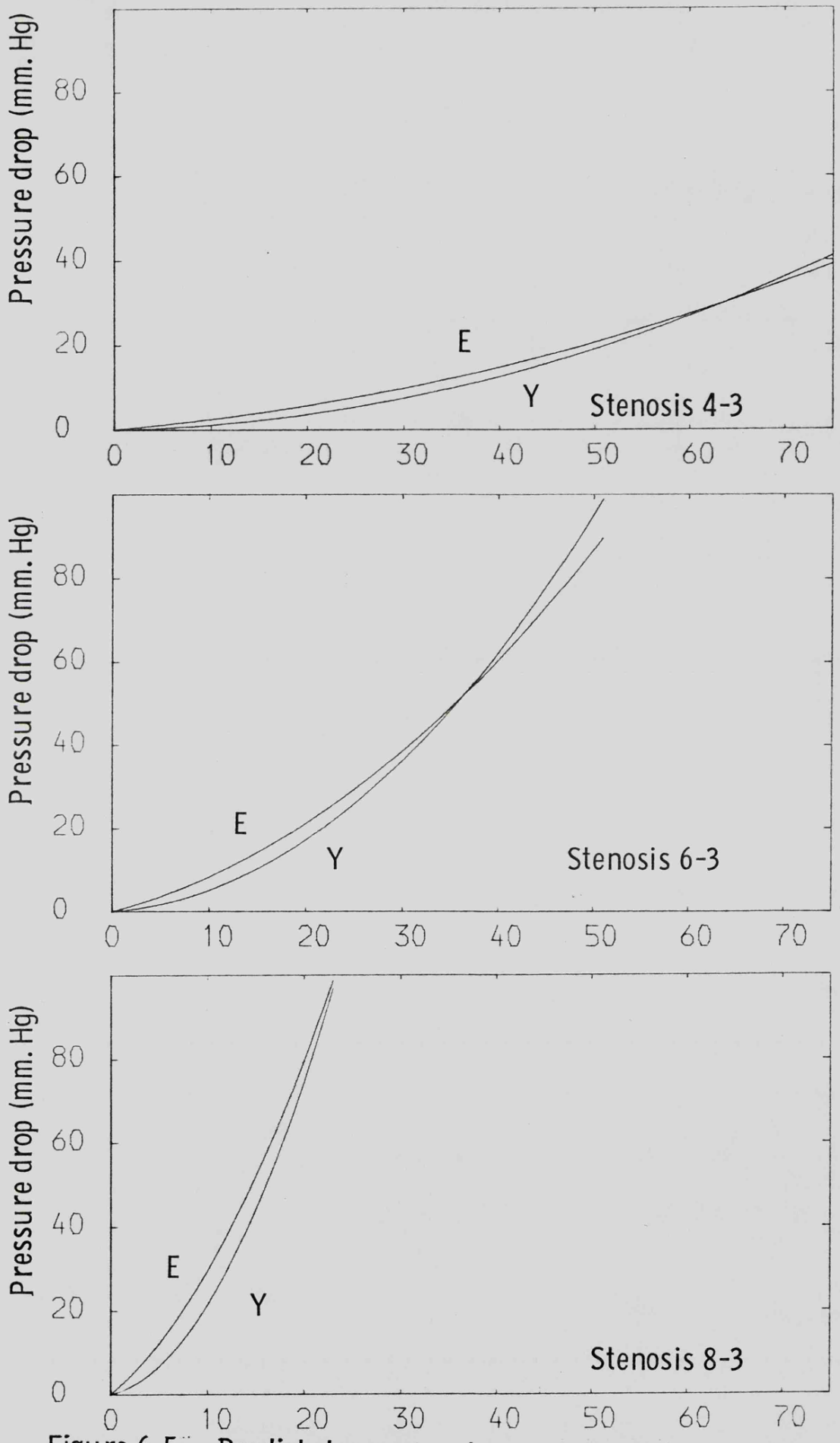
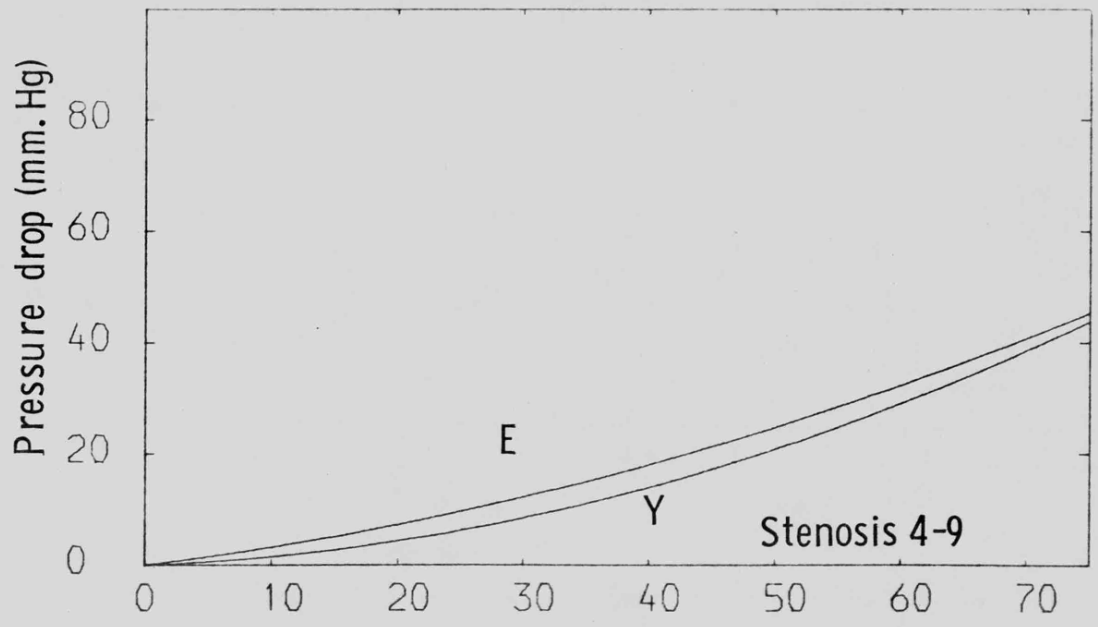
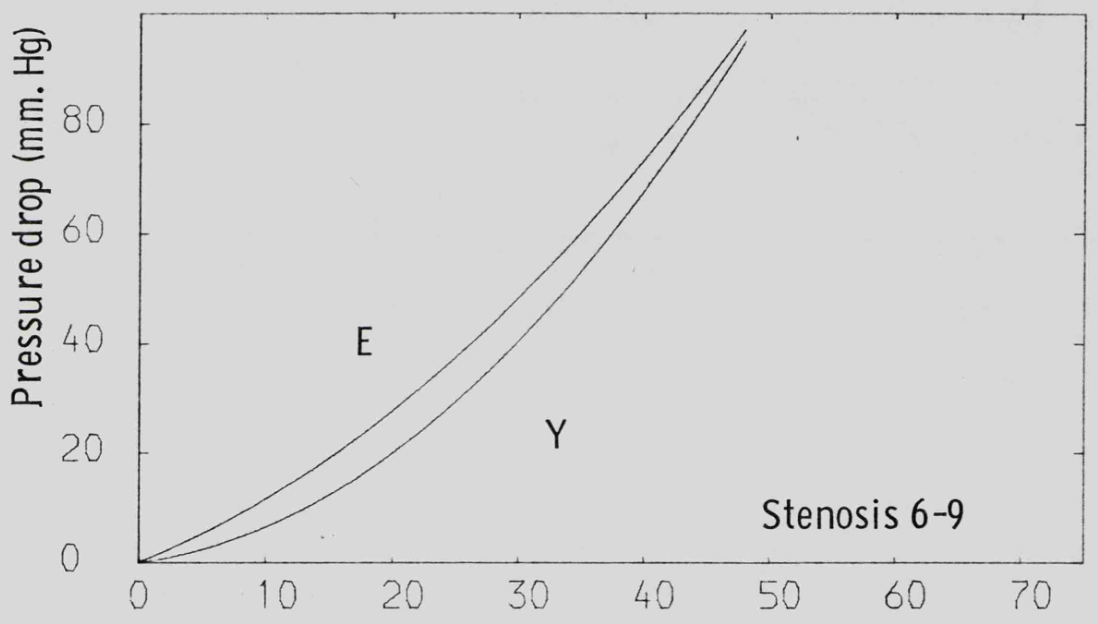


Figure 6-5. Predicted pressure drops across varjous stenoses plotted against blood velocity (cm. s^{-1}) using Young's coefficients (Y) and the coefficients found from the present work (E)





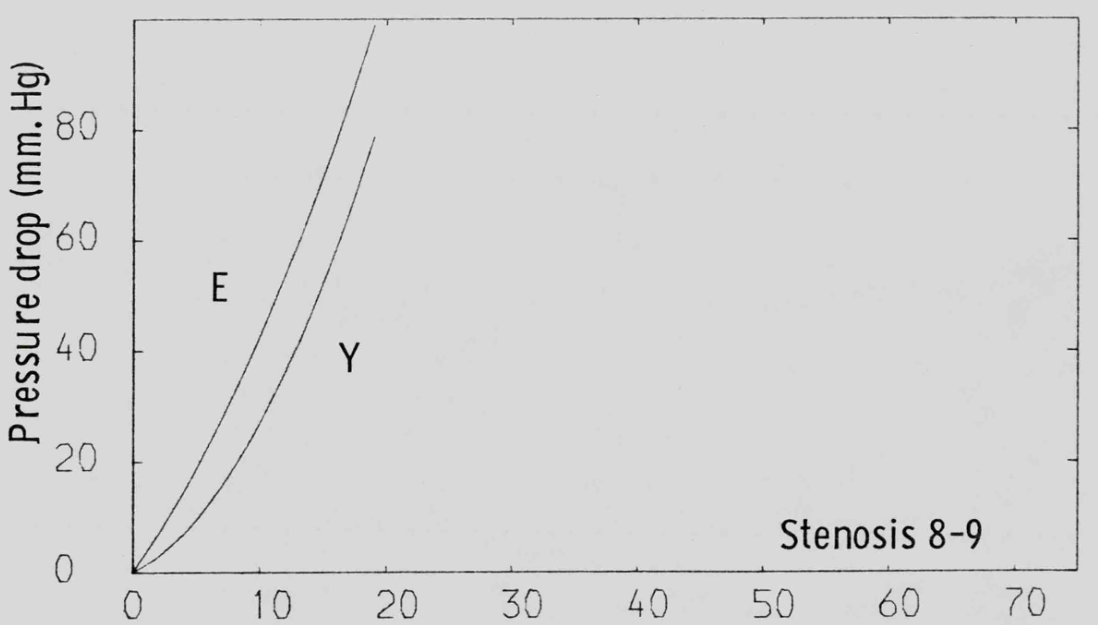


Figure 6-5. Continued.

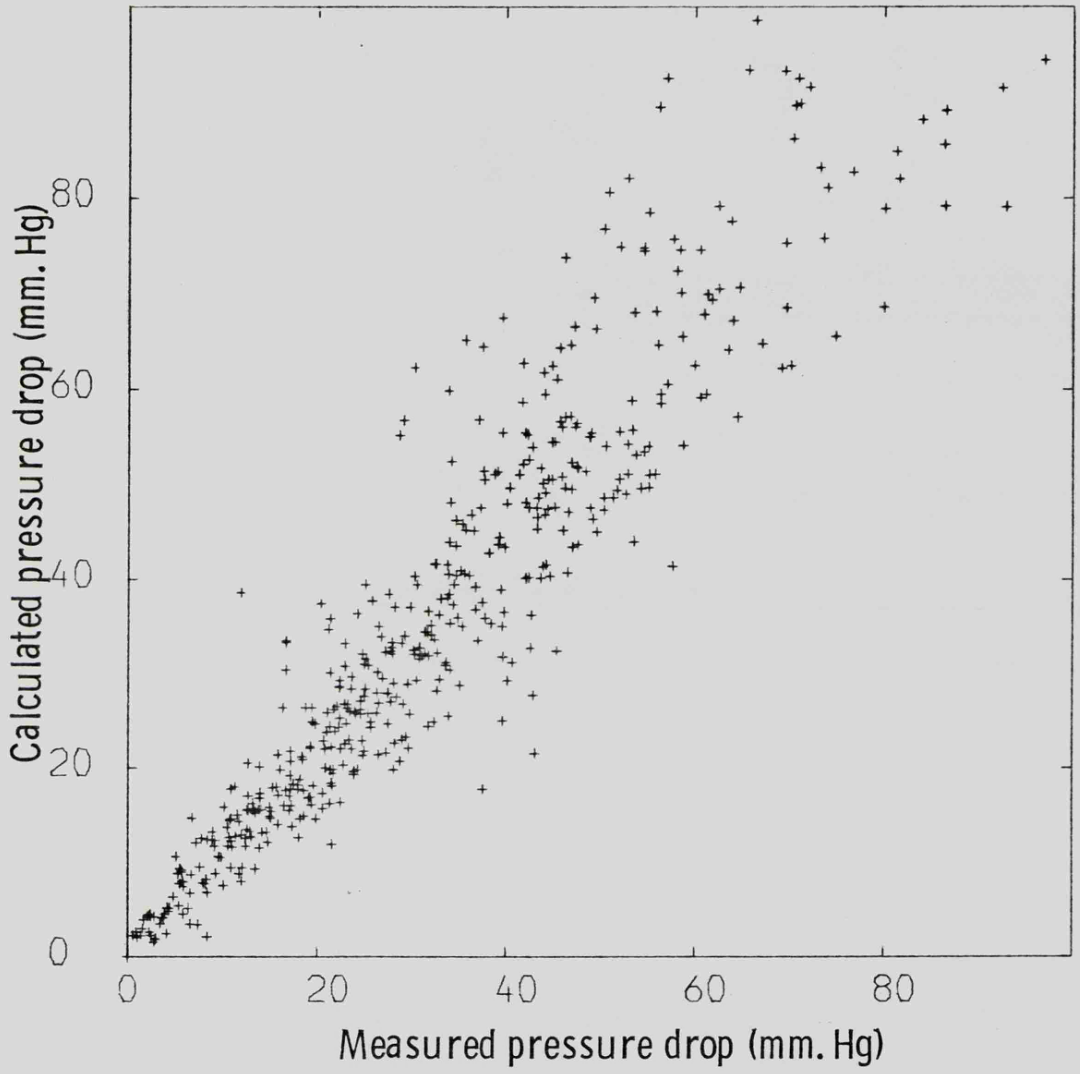


Figure 6-6. Calculated pressure drop at the time of maximum flow plotted against measured pressured drop for all the dog experiments. The former values have been calculated from equation 6.1 with K_v calculated from equation 6.8 and K_t taken as 0.98.

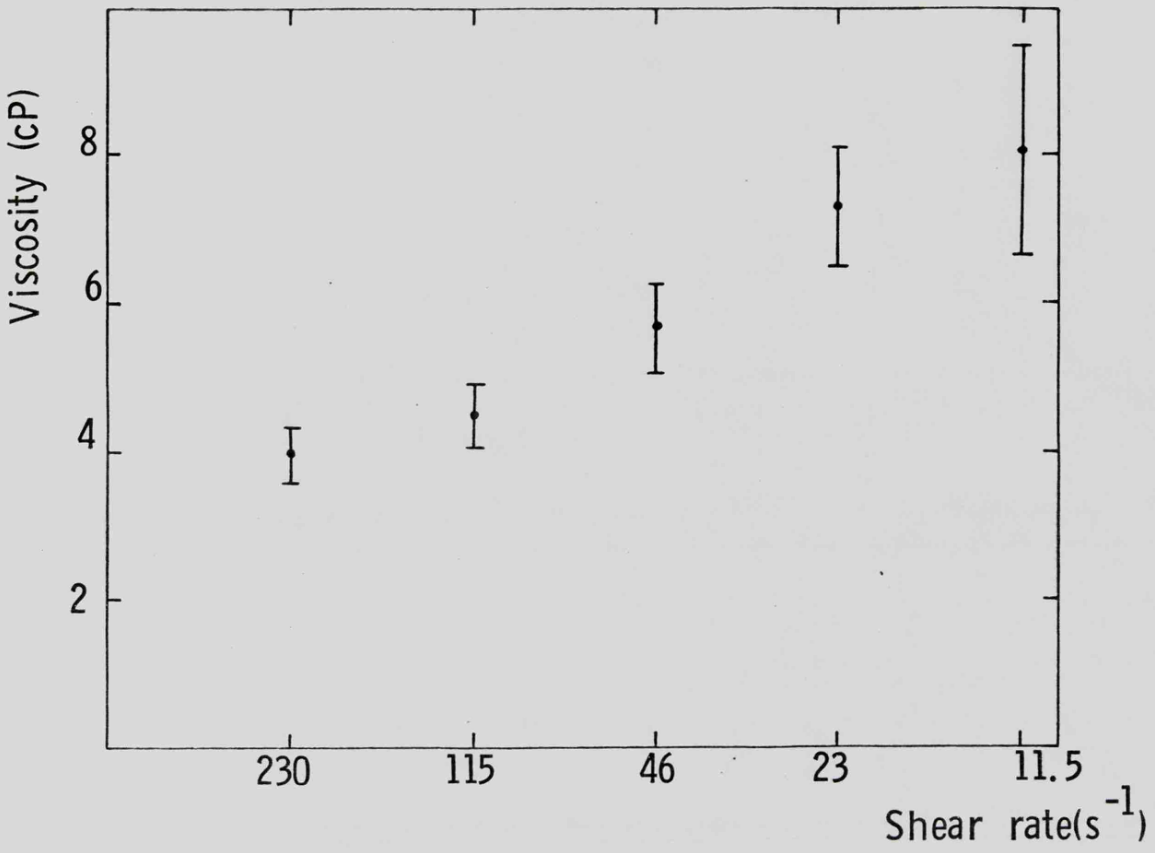


Figure 6.7. The viscosity of dog blood at various shear rates.

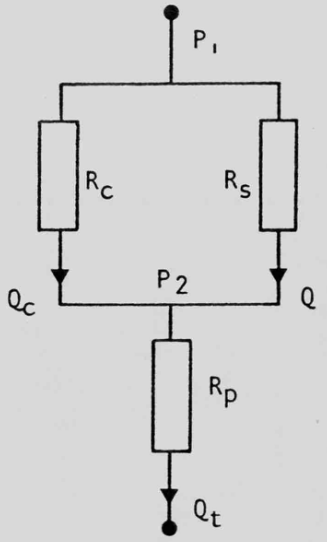


Figure 6.8 Electrical analogue of limb blood flow. R_s is the resistance of the stenosis, R_c the collateral resistance, and R_p the resistance of the peripheral bed.

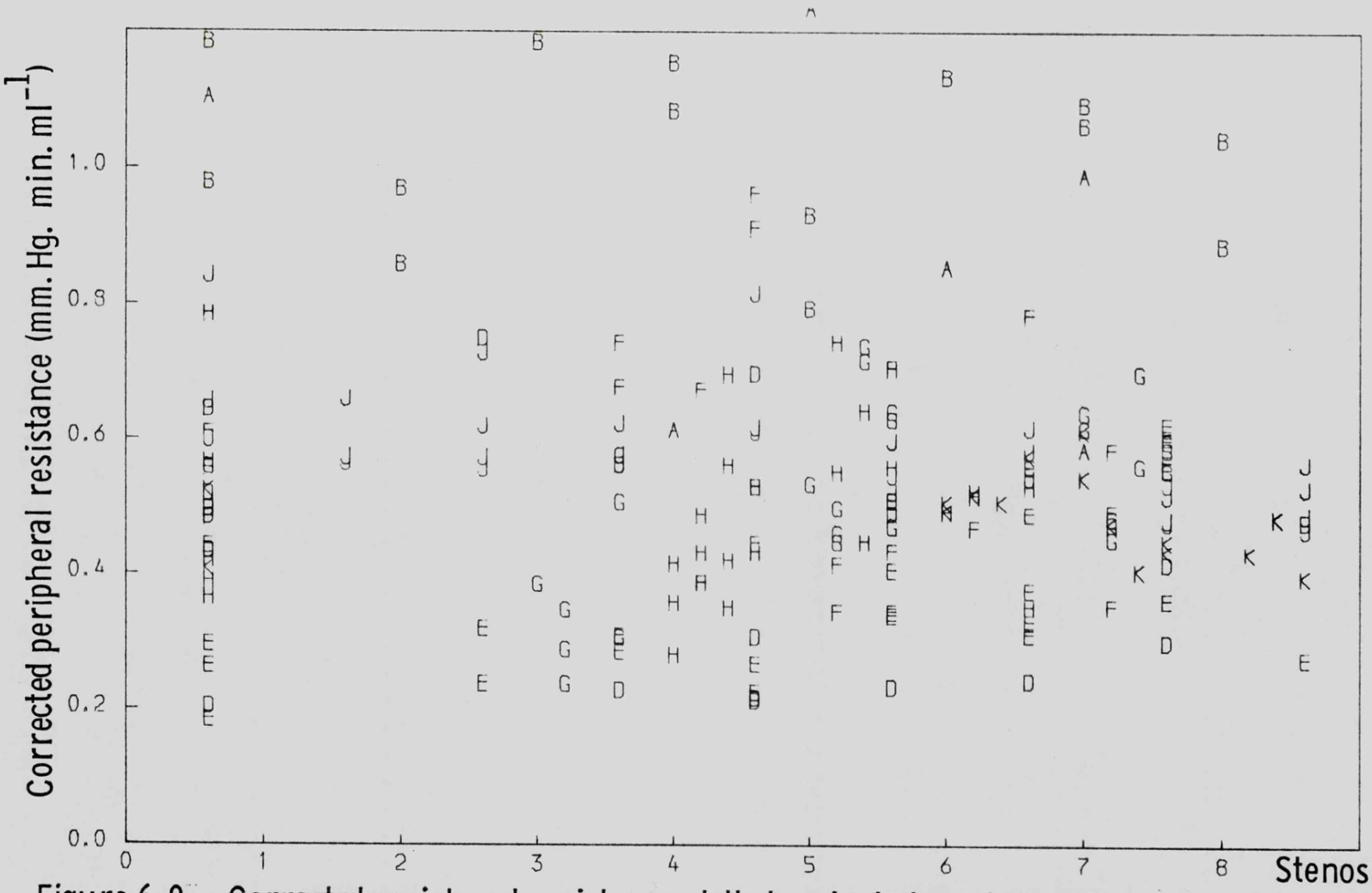


Figure 6-9. Corrected peripheral resistance plotted against stenosis for all dogs. Some of the results, particularly from dog 12, are off scale but follow the same trends. These have been ommitted to keep the scale fairly large. The results from the 'zero' stenosis have been plotted between 0 and 1, whilst the results from the other stenoses have been plotted in four columns with the knife-edge stenosis above its corresponding x-value. This convention has been adopted for all other graphs upon which 'stenosis' is used as an axis.

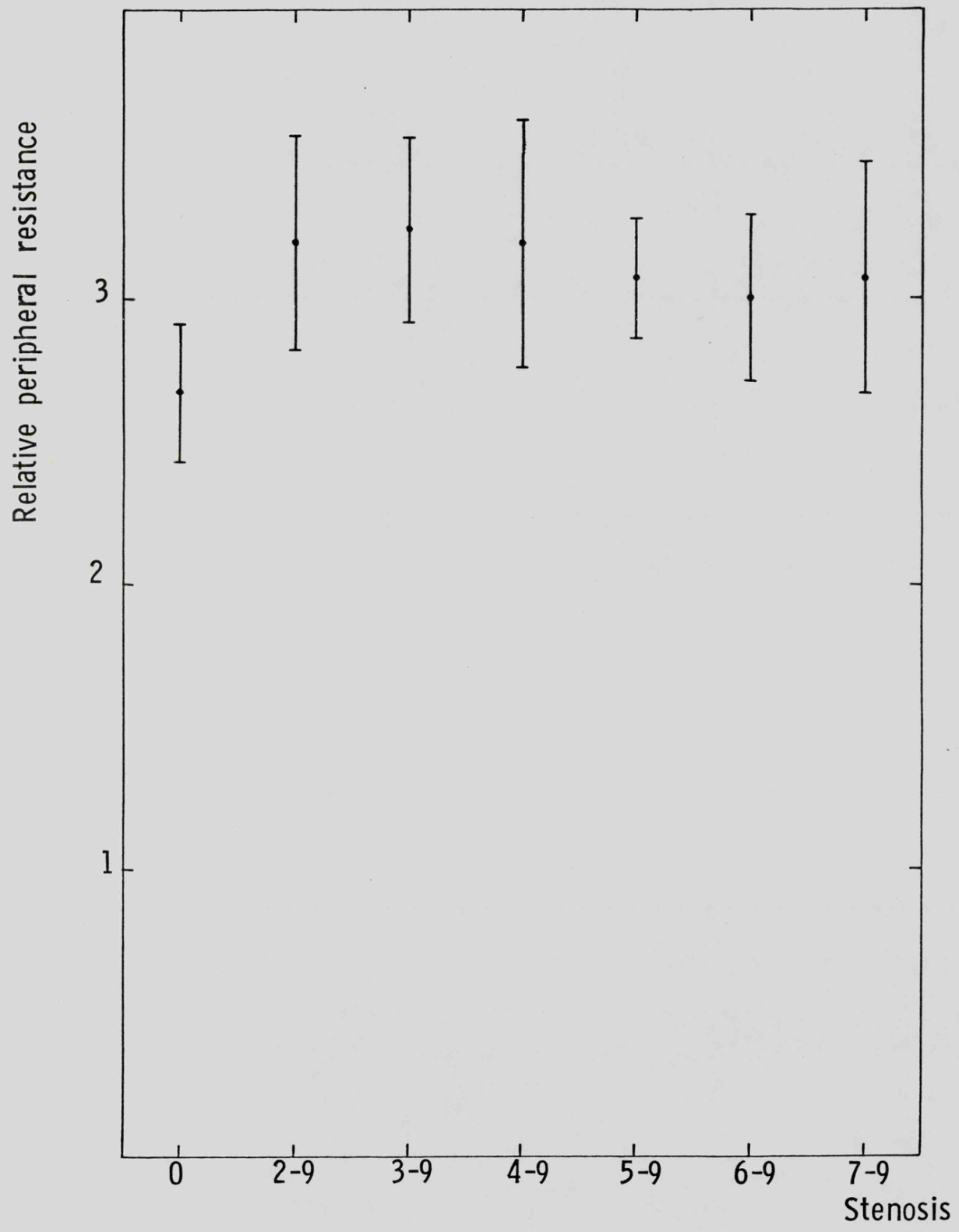


Figure 6-10. The effect of stenosis on relative peripheral resistance.

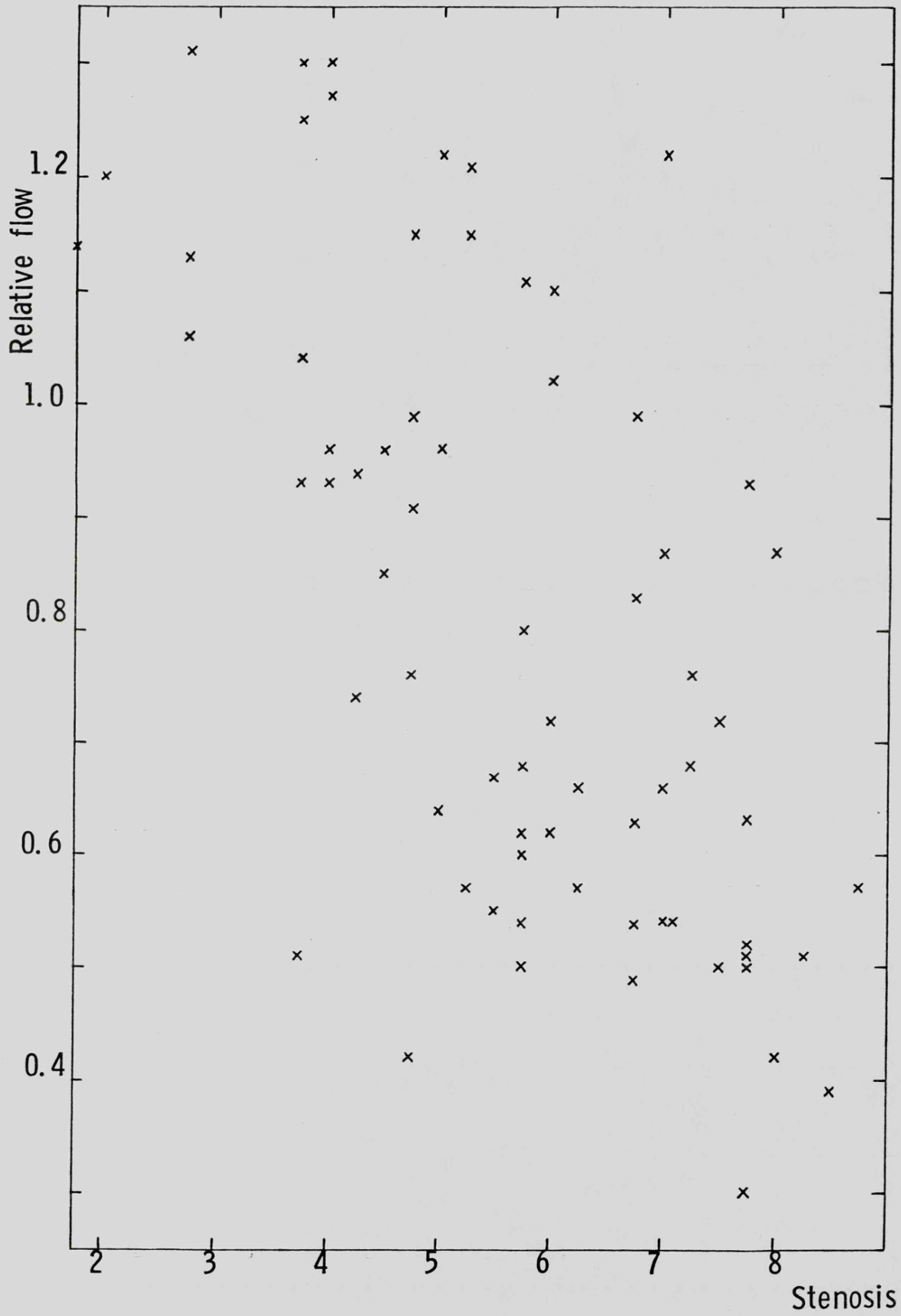


Figure 6.11. Mean values of relative flow for each dog plotted against stenosis.

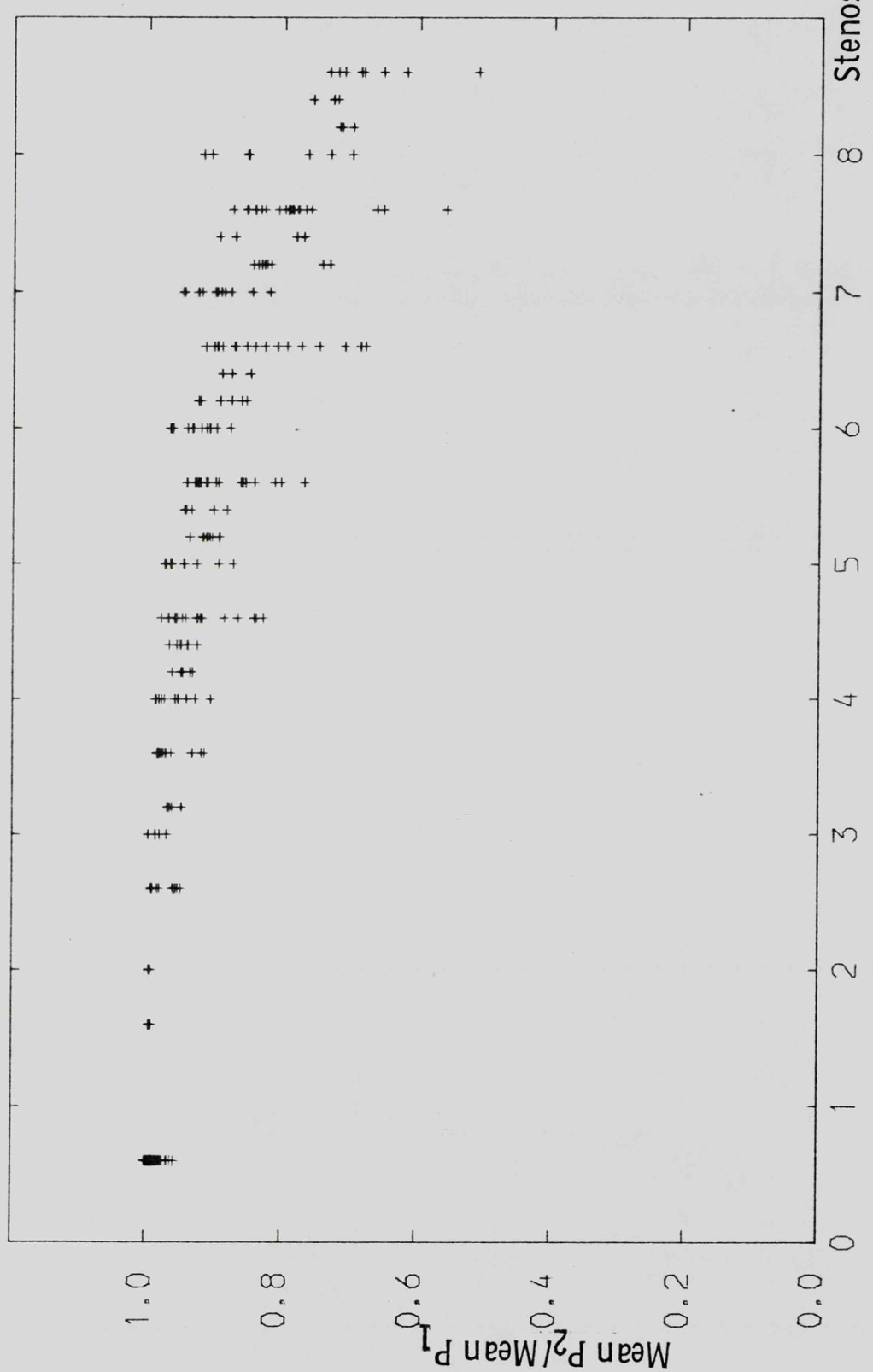


Figure 6-12. Mean P_2 divided by mean P_1 plotted against stenosis. Only stable results are included.

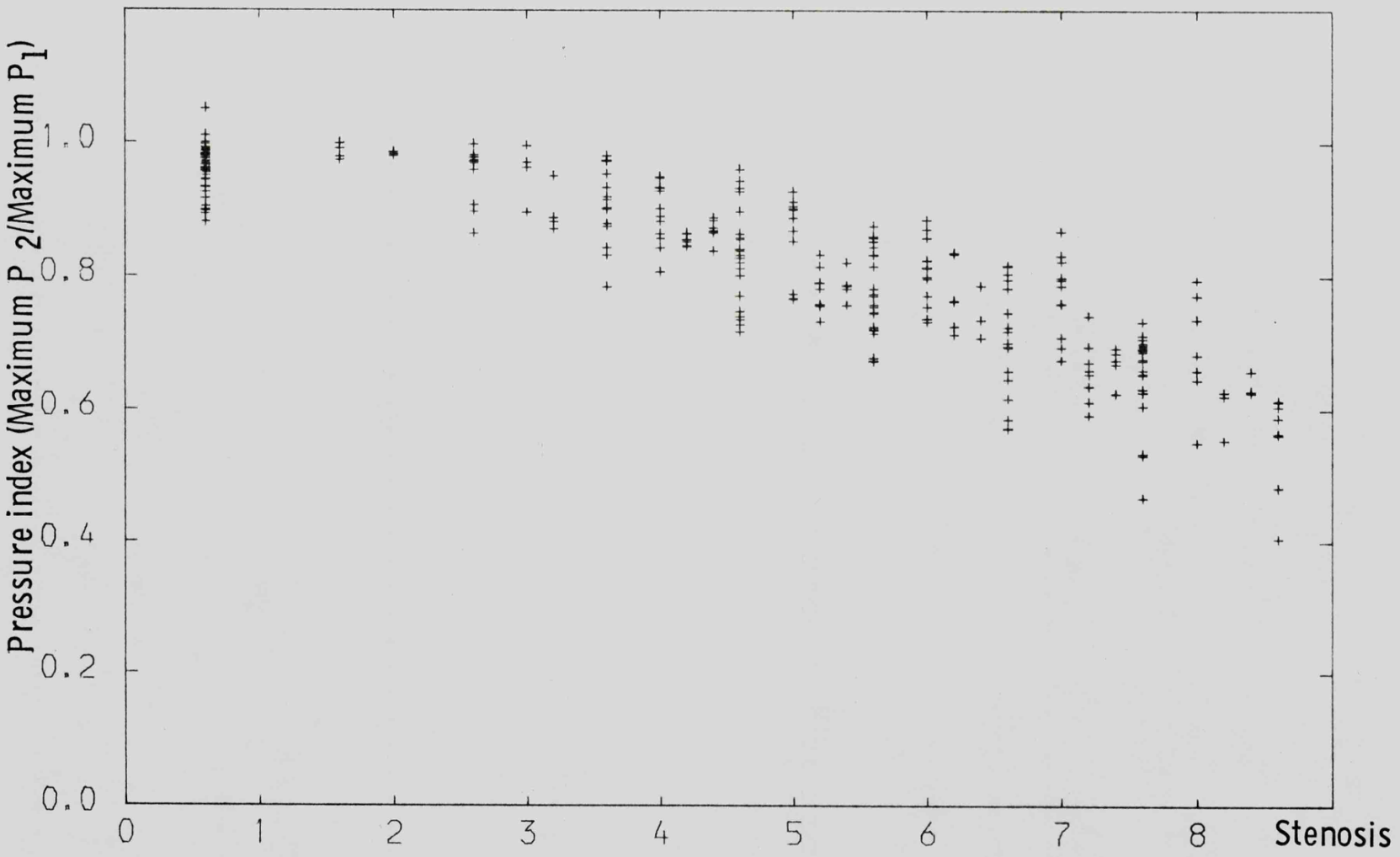


Figure 6-13. Pressure index plotted against stenosis. Only stable values are included

Table 6 - 1

Breakdown of dog Experiments

Dog 10

S	N	U	D
0	1	1	
50	2	0	
70	2	1	
60	3	1	
80	2	1	
40	2	1	
0	1	1	
60	3	1	
50	2	1	
40	1	1	
70	3	1	
0	1	1	
60	7	0	V
80	2	0	V
50	2	0	
40	3	0	
0	2	0	

Dog 11

S	N	U	D
0	1	1	
70	2	1	
80	1	1	
50	1	1	
30	1	0	
40	2	1	
0	2	1	
20	2	1	
80	1	1	
50	3	1	
30	3	1	
70	2	1	
40	3	1	
60	2	1	
20	2	1	
0	2	1	
60	6	0	V

Dog 12

S	N	U	D
0	1	1	
60	5	1	
50	4	0	
80	4	1	
40	3	1	
70	3	1	
30	3	1	
20	3	1	
0	3	1	
49	2	1	
79	4	1	
29	1	1	
69	1	1	
59	2	1	
50	3	0	
59	7	0	
0	1	1	
40	3	1	

Dog 12 (contd)

S	N	U	D
60	2	1	
50	3	1	
70	2	1	
80	3	1	
50	5	0	V

Dog 13

S	N	U	D
0	1	1	
69	1	1	
49	4	2	
79	1	0	
59	2	1	
0	2	1	
39	2	1	
89	1	0	
29	2	0	
69	1	0	

Table 6 - 1 (contd)

Dog 13 (contd)

S	N	U	D
59	1	0	
49	3	1	
79	2	1	
0	2	2	
39	3	1	
0	2	1	
59	3	1	
0	1	1	
49	1	1	
0	1	0	
59	2	1	
0	1	1	
79	2	1	
29	2	1	
89	3	1	

Dog 14

S	N	U	D
0	1	0	
49	3	1	
0	3	1	
39	3	1	
59	2	1	
69	1	1	
29	2	1	
89	2	1	
0	1	1	
49	3	1	
89	2	1	
39	3	1	
59	3	1	
79	2	1	
29	3	1	
69	2	1	
0	4	2	
59	4	3	
69	4	3	
49	3	2	
79	4	3	

Dog 15

S	N	U	D
53	1	1	
73	1	1	
43	2	1	
0	3	1	
63	2	1	
43	3	1	
73	4	2	
53	3	1	
0	2	2	
59	4	2	
39	3	2	
79	4	2	
49	4	2	
69	3	2	

Dog 16

S	N	U	D
33	5	3	
53	5	3	
73	4	3	
39	4	3	
59	5	3	
79	5	3	
0	1	1	
30	1	1	
50	3	1	
0	1	1	
70	3	2	
56	4	2	
76	4	2	
53	1	1	

Table 6 - 1 (contd)

Dog 17

S	N	U	D
0	2	1	
46	5	3	
40	5	3	
43	5	3	
49	6	3	
0	3	2	Pr
66	2	1	
60	3	1	
63	3	2	
69	3	2	
0	3	2	
56	3	2	
50	2	0	
53	3	2	
59	3	2	
0	3	2	
46	3	2	

Dog 18

S	N	U	D
46	3	0	
73	2	0	
50	3	0	
59	3	0	
56	3	0	
80	3	0	
69	3	0	
89	3	0	
49	3	0	
33	3	0	
76	2	0	
63	3	0	
53	2	0	
83	2	0	
70	3	0	
40	3	0	
0	1	0	
39	3	0	
60	3	0	
43	3	0	

Dog 18 (contd)

S	N	U	D
0	2	0	
66	3	0	
30	2	0	
79	3	0	
46	3	0	V

Dog 19

S	N	U	D
79	5	2	
59	7	2	
39	5	2	
69	4	1	
29	6	2	
19	4	2	
49	4	2	
89	3	2	
0	3	1	Pr
79	4	2	
59	4	2	
39	4	2	

Dog 19 (contd)

S	N	U	D
69	4	2	
29	3	2	
19	4	2	
49	4	2	
89	4	2	
0	2	1	
79	1	0	
59	1	0	
29	1	0	

Dog 20

S	N	U	D
0	1	0	
76	3	1	
80	3	1	
66	3	1	
0	1	1	
89	3	2	
79	4	2	
60	4	2	
83	3	2	

Table 6 - 1 (contd)

Dog 20 (contd)

S	N	U	D
73	3	1	
63	4	2	
0	1	1	
86	3	2	
69	3	1	
70	4	2	
0	3	2	
86	2	0	V

Key: S = Stenosis Number N = Number of Results
U = Number of Synchronous Ultrasound Recordings
D = Drugs, Pr = Practolol, V = Vasoactive Drugs.

Table 6 - 2

Experimental and Theoretical Values of K_v

Stenosis	Number of Determination	K_{vy}	K_{ve}	K_{ve}/K_{vy}	K_{vf}
A 4 - 0	3	573	1467 ± 215	2.56	2726
A 5 - 0	15	1017	2923 ± 329	2.87	4813
A 6 - 0	7	1942	5180 ± 1198	2.67	8878
A 7 - 0	5	3750	5422 ± 829	1.45	16474
A 8 - 0	7	7927	18387 ± 10390	2.32	30729
A 5 - 9	8	3154	7416 ± 1297	2.35	9834
A 7 - 9	4	6499	13950 ± 1994	2.15	19586
B 3 - 0	3	332	777 ± 444	2.3	1661
B 4 - 0	18	569	2610 ± 308	4.6	2776
B 5 - 0	17	1092	5630 ± 595	5.2	5179
B 6 - 0	30	1699	6730 ± 633	4.0	7830
B 7 - 0	17	3082	11100 ± 1090	3.6	14306
B 8 - 0	10	6210	13800 ± 2070	2.2	26096
B 3 - 3	7	444	1920 ± 103	4.3	1882
B 4 - 3	11	807	3890 ± 337	4.8	3335
B 5 - 3	14	1642	6810 ± 667	4.1	6473
B 6 - 3	10	2614	9720 ± 2050	3.7	9978

Table 6 - 2 (contd..)

Experimental and Theoretical Values of K_v

Stenosis	Number of Determination	K_{vy}	K_{ve}	K_{ve}/K_{vy}	K_{vf}
B 7-3	14	5071	19300 ± 2190	3.8	18976
B 8-3	3	11723	40400 ± 2500	3.4	42128
B 4-6	13	1108	4300 ± 295	3.9	4040
B 5-6	7	2110	7440 ± 661	3.5	7373
B 6-6	8	3969	11600 ± 2800	2.9	13154
B 7-6	7	7772	17900 ± 2610	2.3	25271
B 8-6	5	18310	48100 ± 2000	2.6	57578
B 1-9	2	211	911 ± 44	4.3	800
B 2-9	3	345	1880 ± 863	5.4	1264
B 3-9	19	628	1900 ± 214	3.0	2231
B 4-9	34	1419	5800 ± 335	4.1	4769
B 5-9	38	2972	10200 ± 611	3.4	9602
B 6-9	27	5041	13700 ± 1300	2.7	15675
B 7-9	30	10192	27700 ± 2600	2.7	30956
B 8-9	15	24868	59900 ± 3990	2.4	73028

K_{vy} are values found using Young's formulae, K_{ve} are experimental values (± 1 standard error), and the values of K_{vf} have been calculated from the 'best fit' coefficients derived from the current experiments.

Table 6 - 3

Experimental Values of K_t

Stenosis	Number of Determinations	K_t
A 2-0	3	3.53 ± 0.20
A 3-0	3	2.14 ± 0.25
A 4-0	6	1.53 ± 0.14
A 5-0	15	1.60 ± 0.12
A 6-0	7	1.97 ± 0.45
A 7-0	5	1.39 ± 0.06
A 8-0	6	2.04 ± 0.20
A 4-9	2	1.85 ± 0.05
A 5-9	9	2.09 ± 0.27
A 7-9	4	1.83 ± 0.28
B 3-0	3	1.15 ± 0.54
B 4-0	18	1.17 ± 0.13
B 5-0	17	0.71 ± 0.09
B 6-0	30	1.06 ± 0.06
B 7-0	17	0.81 ± 0.08
B 8-0	10	1.17 ± 0.09
B 3-3	7	0.54 ± 0.11
B 4-3	11	0.74 ± 0.12
B 5-3	14	0.75 ± 0.09
B 6-3	10	0.83 ± 0.11
B 7-3	14	0.87 ± 0.11
B 8-3	3	0.41 ± 0.17
B 4-6	13	0.79 ± 0.09
B 5-6	7	0.82 ± 0.13
B 6-6	8	1.44 ± 0.21
B 7-6	7	0.93 ± 0.14
B 8-6	5	0.24 ± 0.10
B 1-9	2	2.14 ± 1.44
B 2-9	3	4.12 ± 2.79
B 3-9	19	0.94 ± 0.12
B 4-9	34	0.78 ± 0.08
B 5-9	38	1.09 ± 0.13
B 6-9	27	1.07 ± 0.10
B 7-9	30	1.00 ± 0.12
B 8-9	15	0.74 ± 0.13

Table 6 - 4

Experimental and fitted values of K_u

Stenosis	Number of Determinations	K_u	K_{uf}
A 2-0	3	1.43 ± 0.04	1.59
A 3-0	3	1.84 ± 0.08	2.23
A 4-0	6	1.91 ± 0.12	3.04
A 5-0	15	3.44 ± 0.19	4.71
A 6-0	7	7.17 ± 0.65	7.63
A 7-0	5	10.3 ± 2.00	11.37
A 8-0	6	21.4 ± 4.48	19.01
A 4-9	2	3.14 ± 0.07	3.04
A 5-9	9	6.15 ± 0.70	4.71
A 7-9	4	17.9 ± 1.98	11.37
B 3-0	3	1.62 ± 0.15	2.27
B 4-0	18	2.60 ± 0.20	3.20
B 5-0	17	3.78 ± 0.30	4.99
B 6-0	30	5.61 ± 0.29	6.86
B 7-0	17	8.08 ± 0.69	10.88
B 8-0	10	17.3 ± 1.78	16.13
B 3-3	7	1.48 ± 0.07	2.19
B 4-3	11	2.45 ± 0.19	3.20
B 5-3	14	3.82 ± 0.20	4.99
B 6-3	10	6.08 ± 0.51	6.86
B 7-3	14	10.1 ± 0.97	10.88
B 8-3	3	16.7 ± 1.48	19.54
B 4-6	13	3.03 ± 0.18	3.20
B 5-6	7	4.48 ± 0.48	4.71
B 6-6	8	7.79 ± 0.49	6.86
B 7-6	7	11.5 ± 1.31	10.88
B 8-6	5	15.8 ± 2.56	19.54
B 1-9	2	1.17 ± 0.04	1.18
B 2-9	3	2.85 ± 1.26	1.48
B 3-9	19	1.93 ± 0.17	2.05
B 4-9	34	3.38 ± 0.11	3.20
B 5-9	38	5.58 ± 0.24	4.99
B 6-9	27	7.36 ± 0.37	6.86
B 7-9	30	11.9 ± 0.76	10.88
B 8-9	15	23.5 ± 1.56	19.54

The values of K_{uf} have been calculated from the empirical relationship $K_{uf} = 0.423 + 0.434 (r_1 / r_2)^{2.5}$

Table 6 - 5

Values of K_v extracted from Young's experimental Results

Dog No.	D_0	D_1	L	K_{vy}	K_{vf}	K_{ve}	K_{tf}
1	0.42	0.126	0.84	8502	15680	25720	0.72
2	0.36	0.110	0.72	7924	30422	24076	1.93
3	0.44	0.202	0.88	1738	6620	5687	1.56
4	0.43	0.202	0.86	1597	4632	5248	1.23
5	0.45	0.259	0.90	759	1710	2597	2.05
6	0.38	0.253	0.76	448	-	1578	-
7	0.50	0.153	1.00	7890	16300	23950	1.75
8	0.41	0.126	0.82	7764	-	23584	-
9	0.41	0.200	0.82	1390	-	4603	-
10	0.38	0.200	0.76	1052	1809	3536	1.24
11	0.37	0.221	0.74	664	1959	2287	25.2 *
12	0.44	0.285	0.88	495	-	1733	-
							1.50 ± 0.47

K_{vy} are values found using Young's formulae, K_{vf} and K_{tf} are experimental best fit values, and K_{ve} are the values calculated using the coefficients derived from the current experiments. Blanks have been left where K_{vf} or K_{tf} were found to be negative, and the apparently spurious result from dog 11 (marked with an asterisk) has been omitted from the statistics on K_{tf}

Table 6 - 6

The resistance of the collateral and distal vascular beds.

Dog No.	Collateral Resistance	Minimum Peripheral Resistance	Resting Peripheral Resistance (3.03 R_X)
10	0.36	0.33	1.00
11	0.46	0.47	1.42
12	1.35	0.54	1.64
13	0.33	0.18	0.55
14	0.57	0.15	0.45
15	0.39	0.17	0.52
16	0.27	0.16	0.48
17	0.32	0.19	0.58
18	0.49	0.22	0.67
19	0.52	0.15	0.45
20	0.56	0.15	0.45

All resistances are measured in mm.Hg. min. ml^{-1}

Table 6 - 7

'Average' values of stenosis 'resistance'

Stenosis	Resistance	Total Segmental Resistance*	Value of peripheral resistance required to compensate*
1	0.004	0.754	0.746
2	0.008	0.758	0.742
3	0.012	0.762	0.738
4	0.036	0.784	0.716
5	0.070	0.812	0.688
6	0.092	0.828	0.672
7	0.194	0.891	0.609
8	0.319	0.946	0.554

All resistances are measured in mm. Hg. min. ml^{-1}.

* These values have been calculated from the average values of collateral resistance, and resting peripheral resistance for dogs 13 - 20

i.e. $\overline{R}_c$ = 0.51 and $\overline{R}_p$ = 0.75. The results from stenoses of different length have been combined for this table as diameter is the more important factor.

CHAPTER SEVEN

EXPERIMENTAL RESULTS RELATING TO DOPPLER VELOCITY MEASUREMENTS IN THE CANINE MODEL

The Doppler results described in this chapter correspond to the flow and pressure results described in Section 6.5, that is, they relate to the whole diseased arterial segment, and are affected by both the stenosis itself and the peripheral bed.

7.1 Processing the Results

The Doppler signals from the animal experiments were recorded on an A.M. tape recorder, as described in Chapter five, for later processing. In each case a simultaneous set of electromagnetic flow and intra-arterial pressure measurements were made and analysed in the way described in Chapter six.

The tapes were played back through a Honeywell SAI-51C spectrum analyser and the output recorded in the form of a sonagram on a Medelec fibre-optic chart recorder (see Chapter four, Section 2.2). A sonagram recorded from a human artery is shown in Figure 4.4.

The spectrum analyser, which has been briefly mentioned in Chapters four and five, was of the time-compression type. The real time signal is stored in a rotating shift register which is continuously being read at a very much faster rate, thus effectively speeding up the signal. This enables the signal to be analysed, apparently in real time, at several different frequencies

by one swept filter. The SAI-51C analyser was designed to output 200 frequency bins every 40ms. This was found to be too slow to produce adequate sonagrams, and so the analyser was modifed to output only the first 100 frequency bins every 20ms.

The simultaneous electromagnetic flow and pressure recordings were initally processed in the fashion described in the previous chapter, but in addition further calculations detailed in Section 7.4 were carried out on the electromagnetic flow waveform.

7.2 Pulsatility Index and Modified Pulsatility Index

There have been many attempts to classify sonagrams in an objective fashion, but the most wide-spread method is that introduced by Gosling and co-workers in 1971, that of measuring pulsatility index (PI). It is the variation of this, and of modified pulsatility index (MPI) a slightly revised quantity, with stenosis which will be discussed in this chapter.

PI was originally defined in terms of the Fourier coefficients of the sonagraphic waveform, but is now defined as the maximum vertical excursion of the waveform divided by its mean height (Gosling 1976). It has been found that this quantity is closely related to the Fourier PI, but the former is now generally used because of its relative simplicity.

The way in which PI is defined means that when there is reverse flow present the vertical excursion is taken to be the maximum velocity minus the minimum velocity, whilst in the absence of reverse flow it is taken as the maximum

velocity minus the minimum value the maximum velocity reaches during the cycle (see Figure 7.1).

The change of definition of PI is important in that the absence or otherwise of reverse flow is a major contributory factor in its calculation. This may be advantageous in that reverse flow is normally present in healthy arteries, but it is incidental rather than intentional. One recurring problem with calculation of PI is that it is sometimes difficult to determine whether reverse flow is present. Indeed in borderline cases the reverse flow component may come and go from pulse to pulse.

Because of these difficulties a 'modified pulsatility index' has been introduced in this work, in which the vertical excursion of the Doppler waveform is taken to be the maximum velocity irrespective of the presence or absence of reverse flow. This means if there is no reverse flow present, the minimum velocity is taken to be zero. The mean is of course unaffected.

It must be stressed that values of pulsatility index obtained from animal experiments are not directly comparable with those which might be obtained from human patients, but that the response of PI to changes of stenoses and peripheral resistance is likely to be similar in both cases.

7.3 Changes of PI with Stenosis Severity

Figures 7.2 and 7.3 are graphs of PI and MPI plotted against stenosis. Only stable results have been included. The figures on the graphs represent the number of occurrences of a particular result. The graphs are presented in this way as PI and MPI could only be measured to an accuracy of one decimal place.

It is immediately apparent that the PIs distal to a very tight stenosis are low, but that the PIs distal to more moderate stenoses take on a wide range of values. It appears there is a factor other than the severity of the stenosis, presumable peripheral resistance, important in determining PI. The modified pulsatility indices follow the same trend except that the lower values are compressed together.

In order to test the hypothesis that peripheral resistance is an important factor in determining PI the stenoses were divided into two groups on the basis of their severity, (Group I - stenoses 0 to 4.9; Group 2 - 6.0 to 8.9), and a graph of PI against corrected peripheral resistance (PR) plotted for each of these groups. The results are shown in Figures 7.4 and 7.5. Recalling the limitations of corrected peripheral resistance, discussed in Chapter six, it is evident that PI is indeed a function of both stenosis severity and peripheral resistance. The values of PI distal to severe stenoses are more tightly grouped not because, as might be thought, peripheral resistance tends to remain low distal to a severe stenosis, but rather because PR seems to have little effect on PI where tight stenoses are involved. The PI distal to mild stenoses appears to be highly dependant on PR.

The clinical implication of these findings are not absolutely clear. There is no doubt that the PR of patients undergoing Doppler tests will vary widely depending on a variety of factors such as how recently they have walked, and the ambient temperature, but perhaps more important is the fact that their PR may be modified by the

disease process. PI may well be dependant on disease distal to the site of measurement as well as on proximal disease. Further animal work on the effect of two or more stenoses on PI would help to clarify this issue. The clinical value of PI is further discussed in Chapter ten.

7.4 The Relationship Between Electromagnetic Flowmeter and Doppler Velocimeter Waveforms

Volumetric flow and blood velocity are normally investigated entirely separately although it is clear they must bear a very close relationship to each other. If this relationship were known then findings from one measurement could be applied to the other. For example, the effect of stenosis on PI might be deduced from changes in the E.M. flowmeter waveform. Furthermore the agreement between derived and measured waveforms could form a test of the adequacy of the theory used to obtain the former.

The relationship between the velocity waveform and the volumetric flow waveform is fairly simple. Provided the ultrasound beam insonates the blood vessel uniformly, the mean frequency shift may be obtained by summing the frequency components of the Doppler signal according to equation 7.1

$$\bar{f} = \sum_{n=o}^{fmax} f_n . A_n^{\,2} \; / \sum_{n=o}^{fmax} A_n^{\,2} \qquad 7.1$$

$\bar{f}$ is the mean Doppler shift, f_n the frequency and A_n the amplitude of the n^{th} frequency bin. Mean velocity may be found from the mean Doppler shift using equation 4.3, and mean volumetric flow by multiplying mean velocity by the vessel cross-sectional area.

The conversion of instantaneous volumetric flow into velocity distribution and hence to Doppler spectra is considerably more difficult and depends on the type of flow occurring in the vessel. An attempt has been made to develop Womersley's laminar flow theories to this end, and to predict PIs and MPIs from electromagnetic flowmeter waveforms and finally to compare these predictions with simultaneously measured PIs.

It is possible to show that if the volumetric flow waveform is expressed as a Fourier series

$$Q = Q_o + \sum_{n=1}^{\infty} Q_n \cos(\omega_n t - \phi_n) \qquad 7.2$$

then the instantaneous velocity of a single lamina at a distance y = r/R from the axis of the vessel (where R is the radius of the vessel) is given by

$$w = \frac{1}{\pi R^2} \left\{ 2Q_o (1-y^2) + \sum_{n=1}^{\infty} Q_n |\Psi|_n \cos(\omega_n t - \phi_n + \varepsilon_{\psi n}) \right\} \qquad 7.3$$

(see Appendix six). The functions Ψ and ε_ψ are plotted against y for various values of α in figures A6 and A7.

Using equation 7.3 the velocity distributions across the vessels were calculated at 15 degree intervals throughout the cardiac cycle from each electromagnetic flow waveform of interest. Figure 7.6 shows six such distributions from one cycle. For the purposes of calculating PI and MPI it was only necessary to identify the maximum and minimum velocity in each distribution and to calculate the indices directly from these, however it is a simple matter to assign a weighting appropriate to the cross-sectional area of blood moving at any given

velocity, and from this predict corresponding frequency-amplitude graphs. The weighting factor is dependant on the ratio of the ultrasonic beam size to the vessel size, but if the beam is larger than the vessel it is proportional to the radial co-ordinate y. The six theoretical spectra calculated from the velocity distribution in figure 7.6 are presented in figure 7.7 alongside the corresponding six experimental spectra derived from the synchronous Doppler signals. For the purposes of this calculation it was assumed that the ultrasonic beam was larger than the vessel diameter. Reference to figure 4.7 shows this to be a fair approximation. The correspondence between the two sets of spectra is encouraging in view of the approximations made concerning the beam shape, the angle between the vessel and the probe (taken as 45^{o}), and the highly idealised laminar flow model employed. The various stages necessary to calculate the spectra from the electromagnetic flow waveform are shown in figure 6.2.

Pulsatility indices and modified pulsatility indices were calculated from each electromagnetic flowmeter waveform having a synchronous Doppler measurement and compared with the experimental values. The results are shown in figures 7.8 and 7.9. Once again the results are encouraging.

7.5 Discussion

There has, to the knowledge of the author, been no prior attempt to evaluate PI in an animal model. This approach has proved to be productive as it enables the different factors influencing PI to be evaluated. It is apparent that peripheral resistance influences PI significantly, although this has not previously been

regarded as important. This effect requires further investigation to establish whether disease distal to the site of Doppler measurements can influence PI significantly.

There appears to be little difference between PI and MPI, except that by definition MPI cannot have a value of less than unity, and thus there is not the same dispersion of values measured from diseased waveforms as with PI. The significance of reverse flow has not been evaluated. It is known that reverse flow only occurs in fairly healthy arteries (although the distal bed influences this also) and thus the weight implicitly attached to reverse flow in the calculation of PI may be of value. The use of MPI however avoids the problems which occur in border-line cases when reverse flow occurs only during some cardiac cycles.

The agreement between the theoretically calculated values of PI and MPI, and the experimental determinations is good. This is of interest as it is much easier to monitor E.M. flowmeter waveforms continuously during animal experiments than Doppler waveforms. It is also of interest as it appears that Womersley's laminar flow theory is adequate to predict PI even distal to severe stenoses.

The clinical value of PI is discussed in Chapter ten.

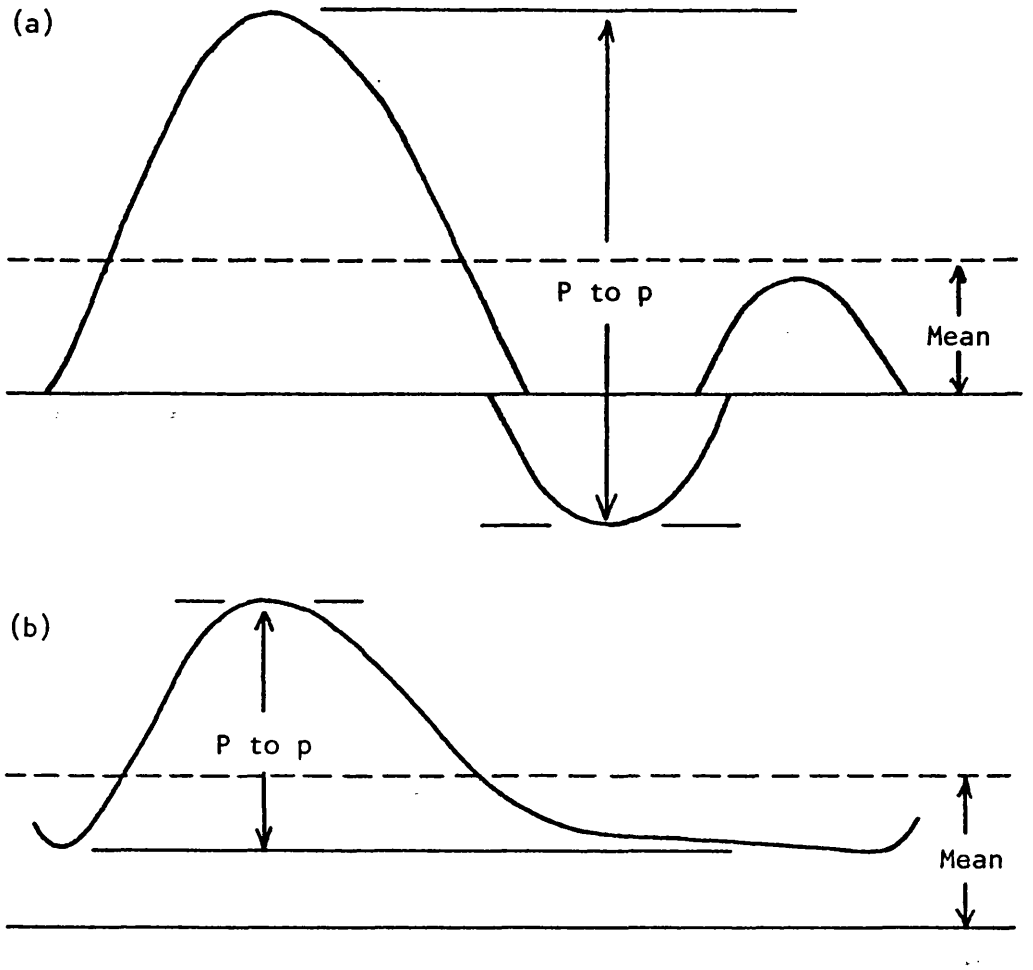


Figure 7.1 The definition of Pulsatility index in the presence (a) and absence (b) of reverse flow.

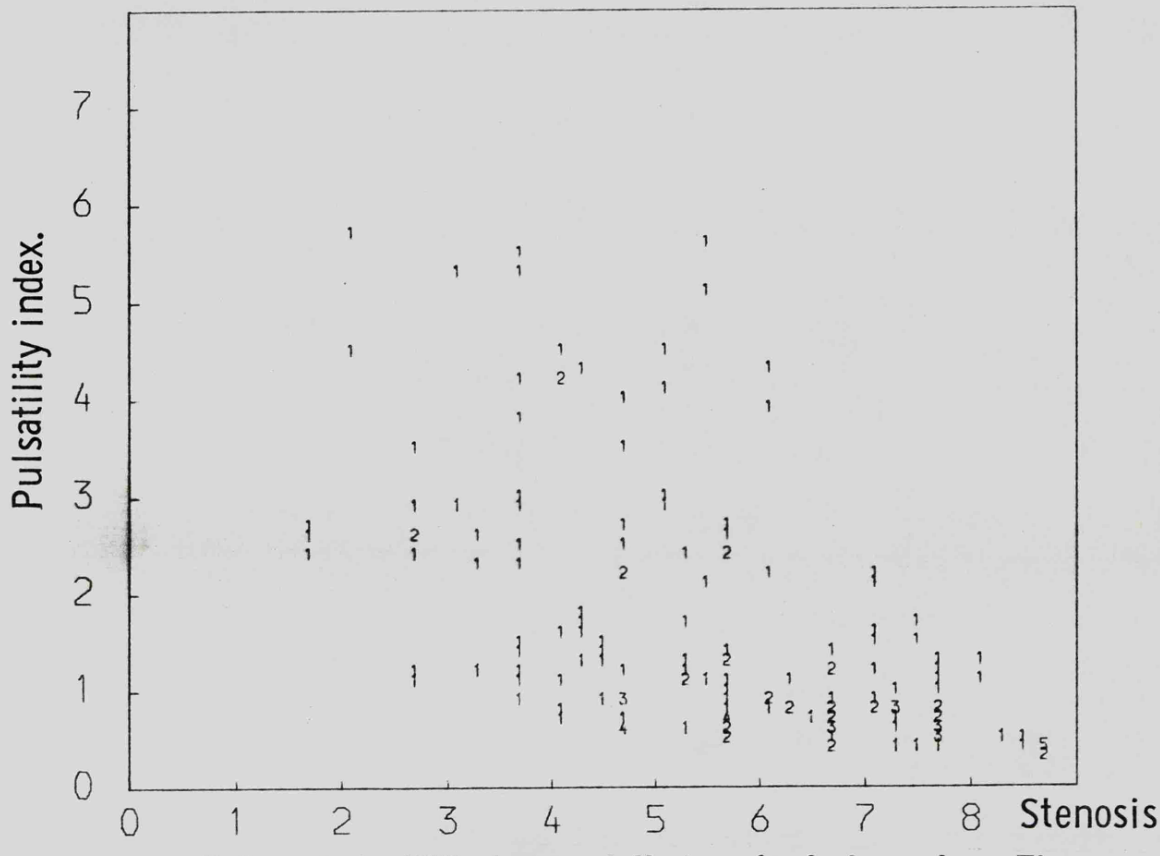


Figure 7-2. Pulsatility index plotted against stenosis. The numbers indicate the number of occurances of a result at that point.

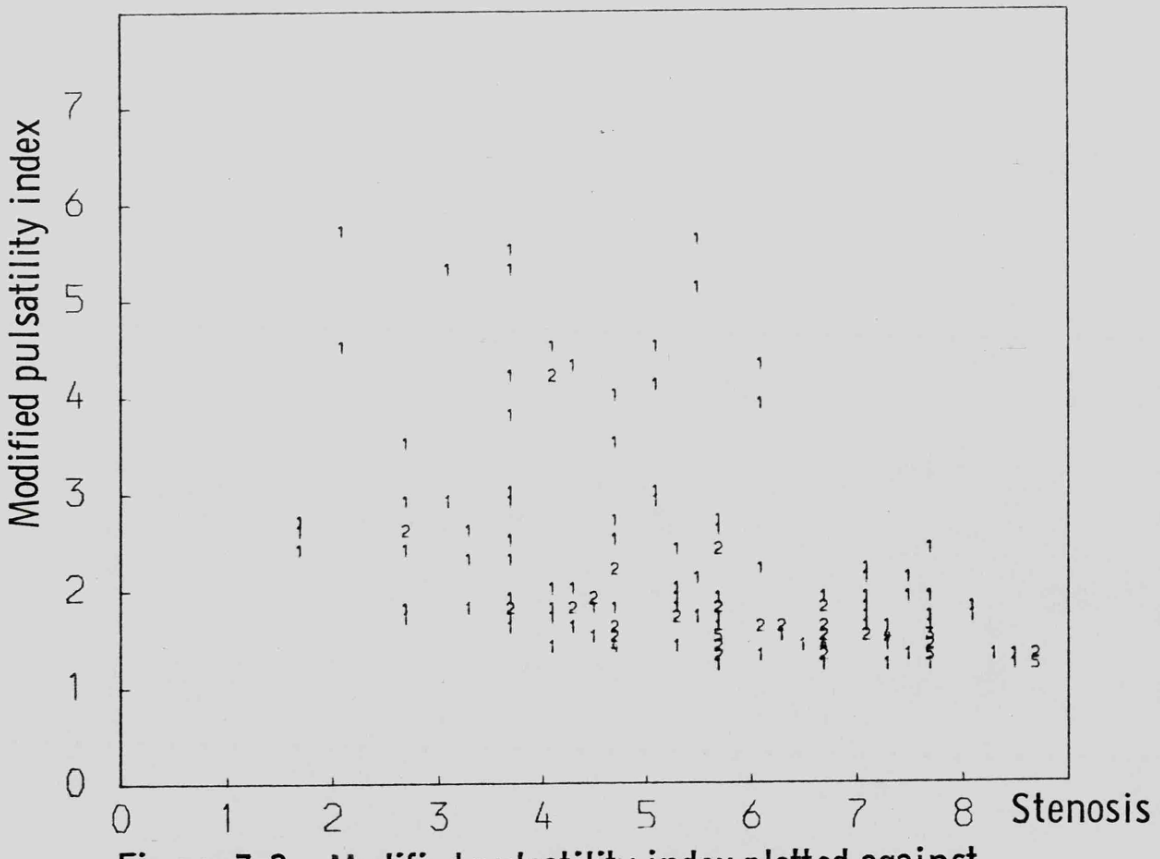


Figure 7-3. Modified pulsatility index plotted against stenosis.

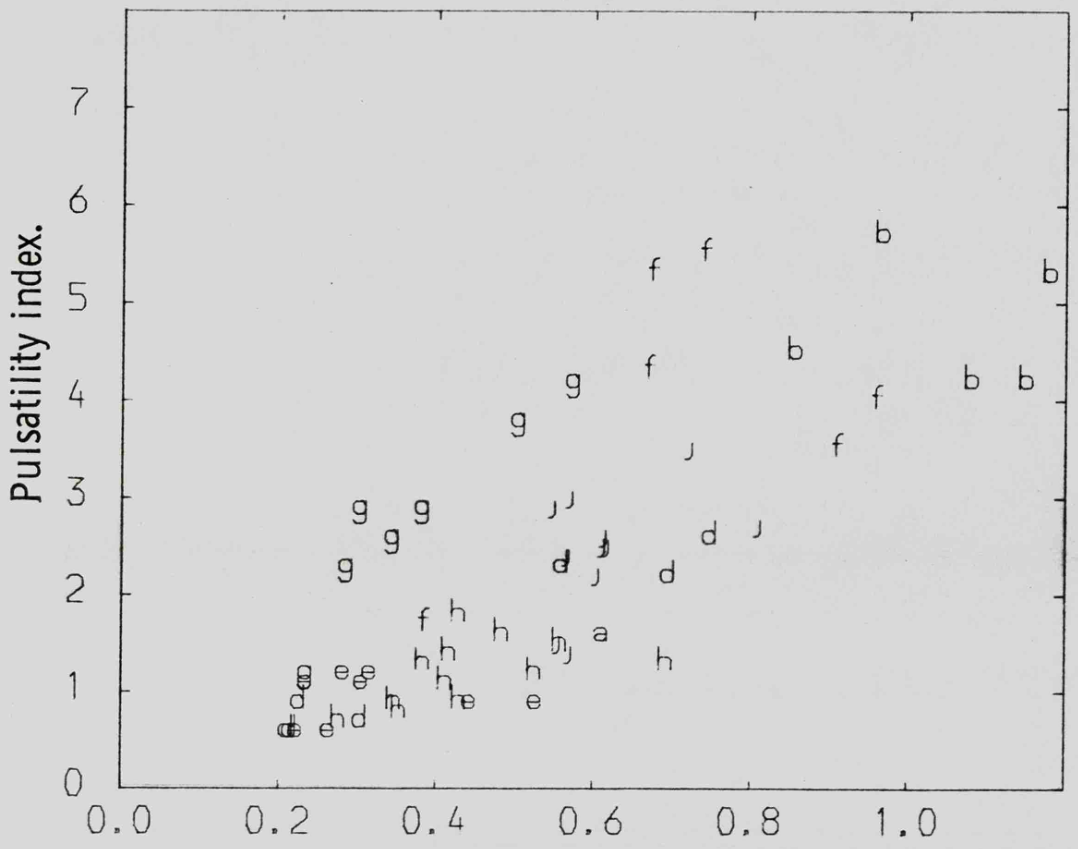


Figure 7-4.

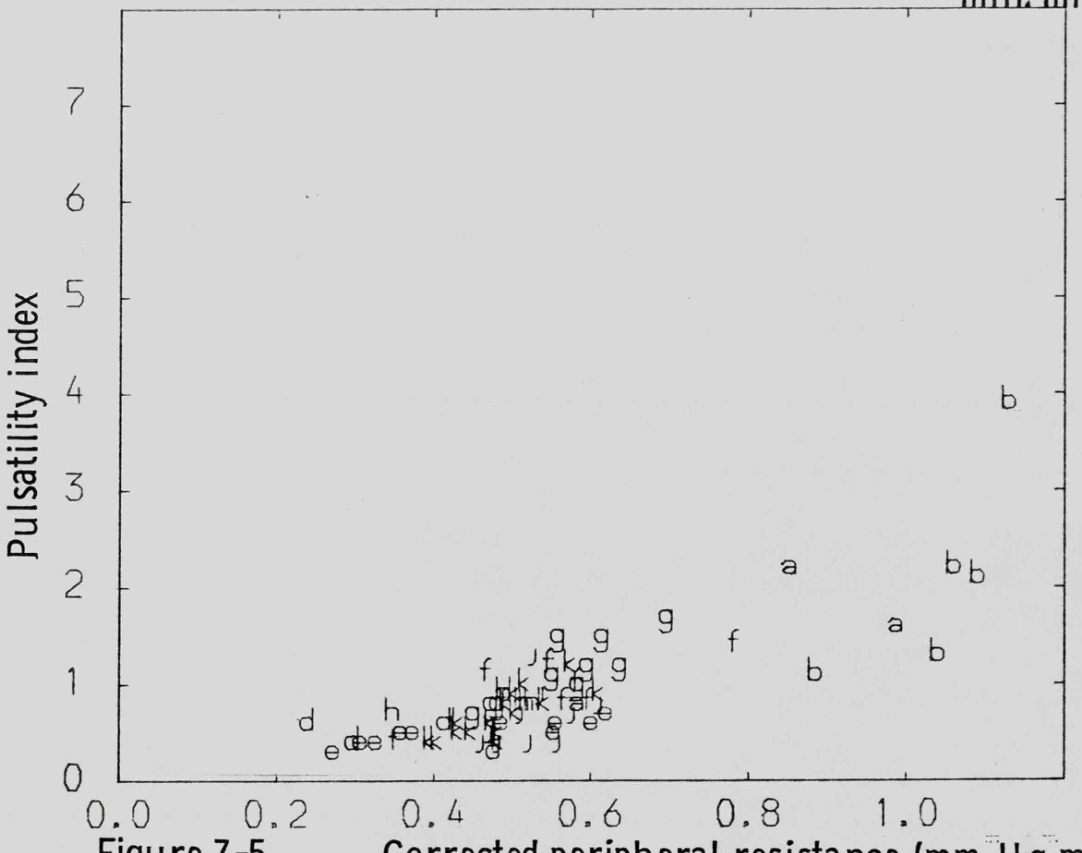


Figure 7-5

Pulsatility index plotted against peripheral resistance for stenoses 2.0 to 4.9 (figure 7-4) and for stenoses 6.0 to 8.9 (figure 7.5)

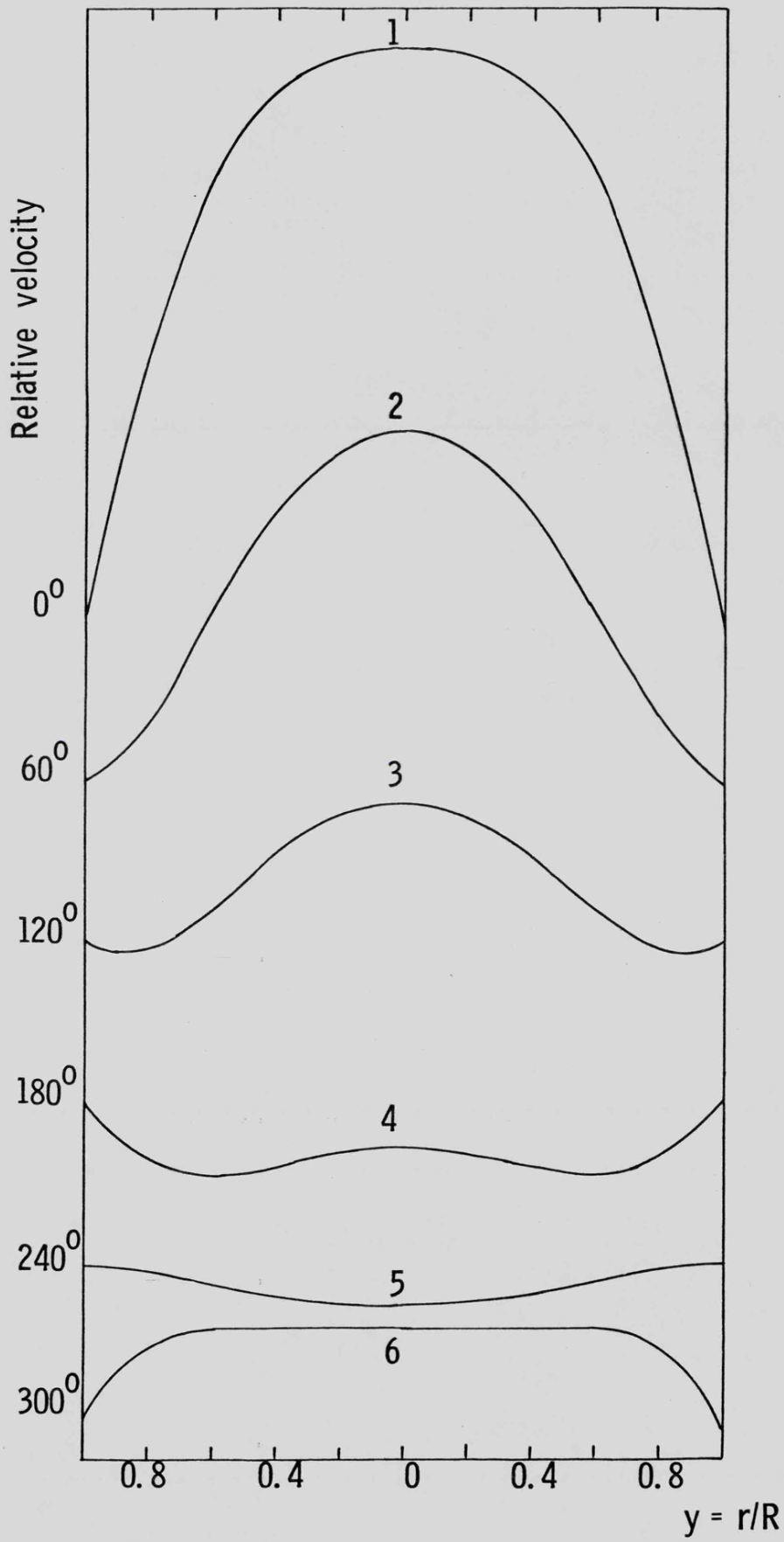


Figure 7.6. The theoretical velocity distributions across a vessel at 60° intervals

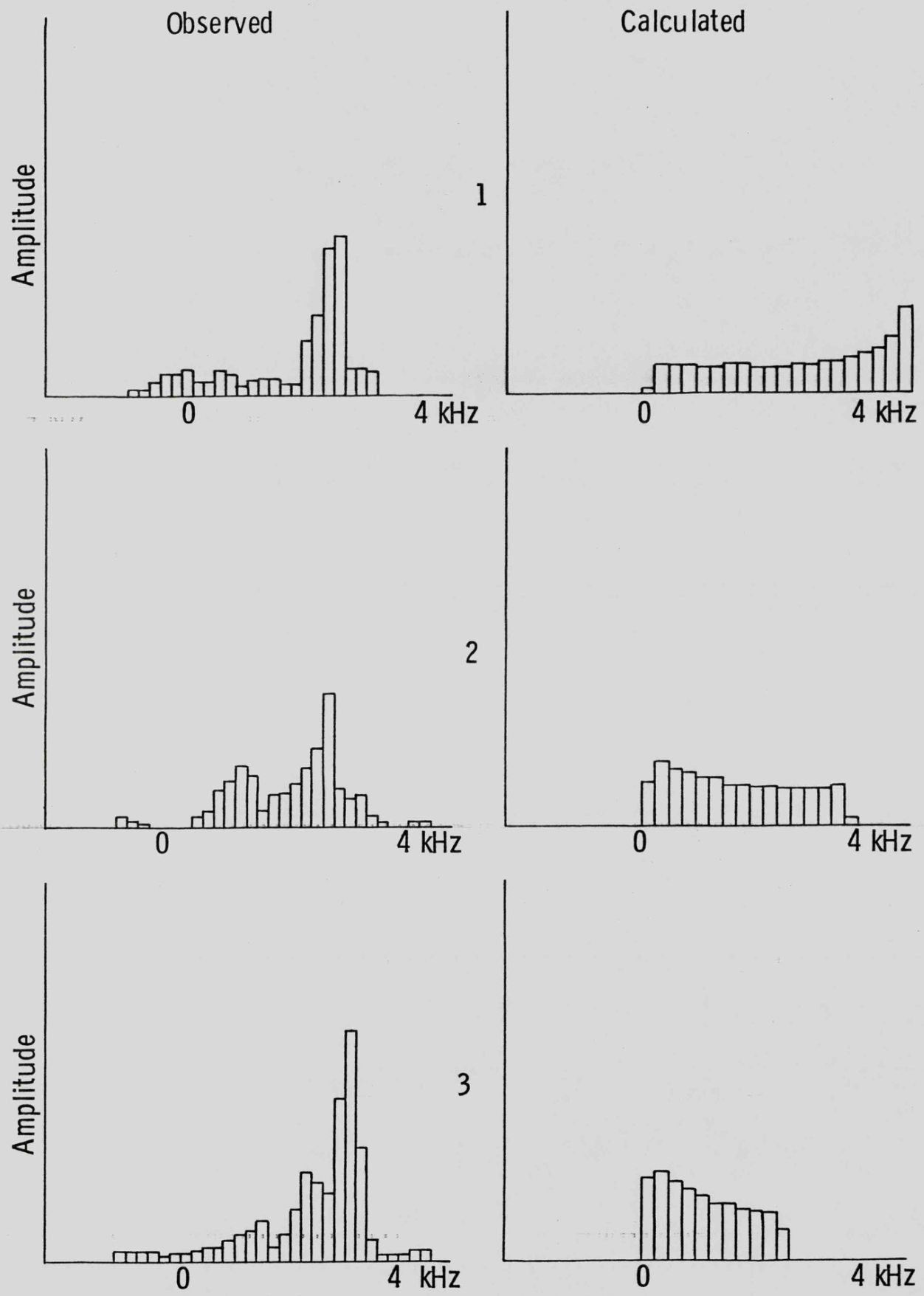


Figure 7.7. Observed and calculated Doppler spectra at 60^{o} intervals distal to a 4-3 stenosis.

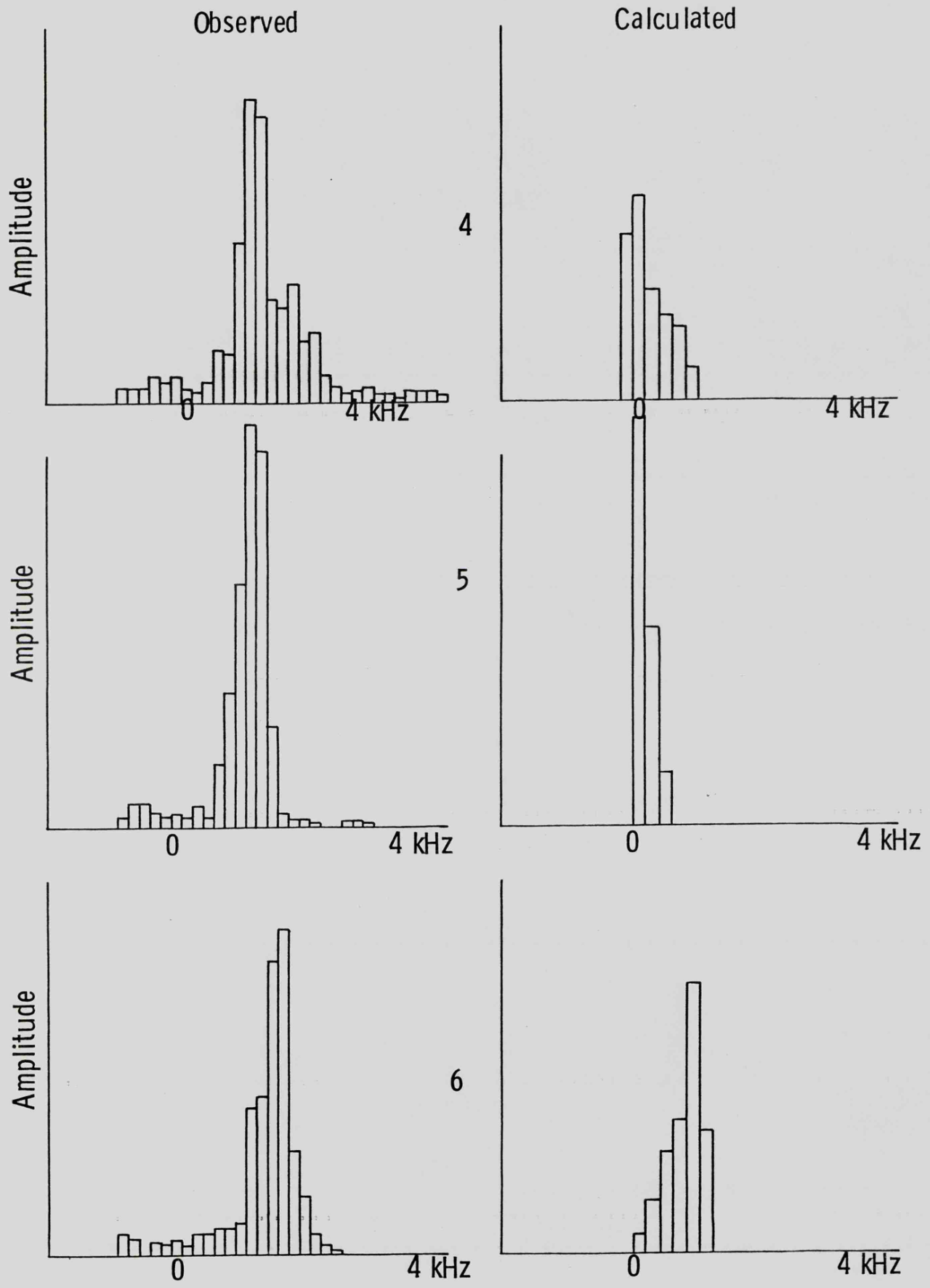


Figure 7.7 continued.

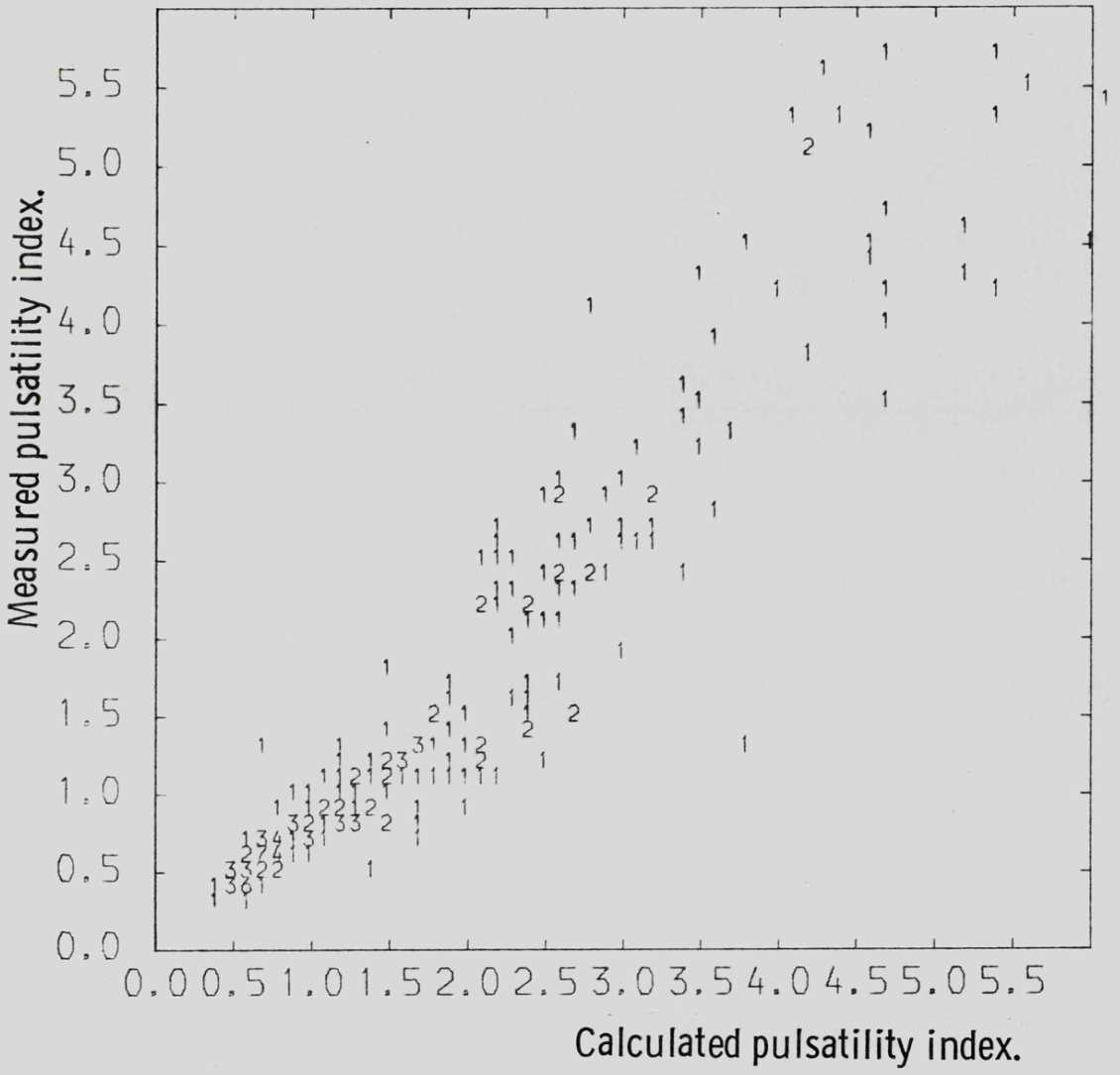


Figure 7-8. Measured pulsatility index plotted against calculated pulsatility index. The numbers represent the number of occurences of a particular result.

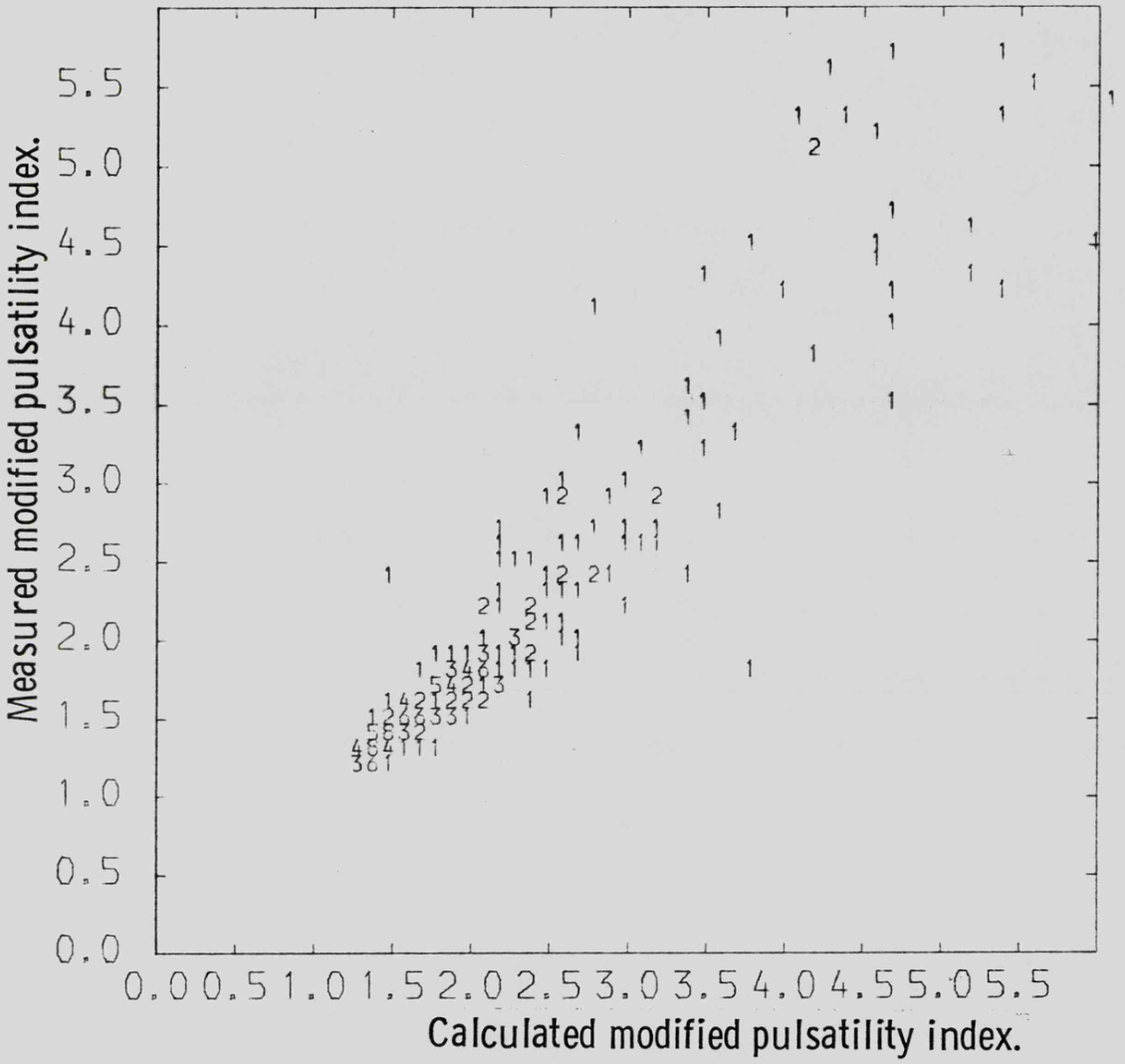


Figure 7-9. Measured modified pulsatility index plotted against calculated modified pulsatility index. The numbers represent the number of occurances of a particular result.

S E C T I O N C

'The truth is rarely pure, and never simple'

Oscar Wilde (1895)
The Importance of Being Earnest

CHAPTER EIGHT

INDIRECT PRESSURE MEASUREMENTS

One of the more popular methods of assessing the site and severity of peripheral arterial disease is that of indirect blood pressure measurement.

8.1 Methodology

In general the method consists of placing a pneumatic cuff around a patient's limb at a site where the blood pressure is to be determined, placing a flow detector (usually an ultrasonic Doppler velocimeter) over an artery distal to the cuff, inflating the cuff until the flow can no longer be detected, and then allowing the cuff to deflate slowly until flow is again observed. The pressure within the cuff at the onset of flow is then regarded as being the systolic pressure within the artery at the point at which the cuff has been applied. This assumption alone seems unjustified in the light of evidence that will be presented in this Chapter. Moreover the technique requires the further supposition that if there is a 'significant' narrowing in the artery proximal to the point of measurement, then the systolic pressure at this point will be observably reduced. This will in many cases not be so. The remarkable aspect of this technique is not that its results are poor, but that it works at all.

The measurement of blood pressure in an attempt to define the site of arterial disease was introduced by Winsor

in 1950. With the demonstration by Satomura and Kaneko (1960) that the Doppler shift of a beam of ultrasound backscattered from moving erythrocytes could be utilized for blood velocity measurements, the detection of flow in badly diseased arteries became easy, and in consequence the measurement of systolic arterial blood pressure also (Strandness 1966, Yao 1968).

It is now usual for the results of pressure determinations on the lower limbs to be normalized to brachial pressure in order to reduce both intra and inter-patient variations resulting from changes in systemic pressure (Strandness 1969, Yao 1970, Siggard Anderson 1971, Eastcott 1973). This quantity, referred to as pressure index, is defined as lower limb systolic pressure divided by brachial systolic pressure.

Since its introduction this method of localising peripheral arterial disease has gained wide acceptance and popularity, probably due to its simplicity and inexpensiveness. Pressure index has been shown to correlate with both radiographic findings, and with the severity of symptoms for different groups of patients (Yao 1970, Cutajar et al 1973, Kawai et al 1975, Chamberlain et al 1975). Unfortunately the overlap between the groups is such that the technique is of limited value for the assessment of individual patients.

It has in addition been proposed as a useful technique for selecting patients for arteriography (Carter 1969), assessing the response of patients to medical therapy (Postlewaite 1975), and for following up patients after various surgical procedures (Lewis 1974).

8.2 Patient Experiments

The experiments to investigate pressure index may be divided into three groups, those to assess the reproducibility of the technique in one patient, those to compare pressure index with symptoms and radiographic findings, and those to examine the effect of inflating a pneumatic cuff on the pressure in diseased arteries. In all the experiments pressure index was determined in a standard fashion. Arm and calf pressures were measured using cuffs of 22x13cm as recommended by the American Heart Association (Kirkendall et al 1967) placed either at the maximum convexity of the biceps or the gastrocnemius, and thigh pressures with a cuff measuring 50x18cm placed at mid-thigh level. The cuffs were inflated to 20mm Hg above the pressure required for flow to disappear, and then deflated at approximately 4mm.Hg.sec^{-1}. The pressure was read to the nearest 2mm Hg at the onset of flow, as detected by a Parks 802 Doppler velocimeter. Thigh pressure index was defined as thigh systolic pressure divided by brachial systolic pressure, and calf pressure index as calf systolic pressure divided by brachial systolic pressure, using for brachial pressure whichever arm had the higher pressure, and for calf pressure whichever pedal artery had the higher pressure.

8.2.1. Reproducibility

The reproducibility of the technique was assessed with the cuffs remaining in place between measurements, and with the cuffs reapplied between readings.

Initially, fifty seven sets of ten readings of thigh, calf and brachial pressure were made on nineteen patients

with peripheral vascular disease, and the coefficient of variation of each of these sets calculated. Subsequently ten pairs of readings of brachial and calf pressure were made on twelve patients, the same cuff being used alternatively on the two sites. The coefficients of variation of both the calf pressures and of the pressure indices were calculated for each of these sets of readings.

The results of all these tests are shown in figure 8.1. In each case the coefficients of variation ranged up to 10%. The first column of results are the coefficients of variation from the arm, thigh and cuff results. The median value is 4%. When the results from the three sites were examined individually they had the same median values and spreads, indicating that each site is subject to roughly the same variation. Columns two and three were the results obtained when the cuff was reapplied between each measurement, the former being the coefficients of variation of the calf pressure measurements, the latter those of the calf pressure indices. These two groups of results are very similar to the first group.

The major contribution to the variation is probably the spontaneous fluctuation of the patient's systemic blood pressure, both cyclicly with respiration and irregularly as a result of stress and other variables. Figure 8.2 is a recording of the common femoral artery pressure of a recumbent patient sedated with Valium 10mg I.M. and showing no obvious stress. The needle puncture through the anaesthestised groin skin was uneventful. The fluctuation in this example are larger than those normally encountered, but demonstrate well both the cyclic and irregular components of blood pressure variation.

8.2.2 The correlation between pressure index, radiographic findings and symptoms

The uniplanar translumbar or femoral-aorto arteriograms of 83 limbs were examined and graded on a four point scale according to the most severe lesion in the aorto-iliac, and the femoro-popliteal segments. All the gradings were carried out without knowledge of the clinical situation or of the pressure indices of the patient and arteriograms were only entered into the series if all the vessels of interest were clearly visualised. The grading system used was as follows :-

0 = Normally Patent

1 = Irregular atheroma (less than 20% encroachment on vessel lumen)

2 = Stenosed (more than 20% encroachment)

3 = Occluded

The thigh and calf pressure indices of each patient were measured in the usual way, and the results compared with the radiographic findings.

Thigh pressure index is shown plotted against the radiological findings for the aorto-iliac segment in figure 8.3, whilst 8.4 shows calf pressure indices plotted against the grade of the worst lesion in the total aorto-popliteal segment. Although there is a tendency for patients with radiographically demonstrable disease to have a lower pressure index, there is a large overlap between the groups. It is known that arteriograms can be misleading, but this is normally as to the degree, rather than to the presence or absence of disease. Arteriograms which show occlusions or a complete absence of disease appear to be fairly reliable, which makes

the overlaps of pressure indices of patients with x-ray grades of 0 and 3 difficult to explain if pressure index is a reliable predictor of arterial narrowings.

The absence of any definitive test with which to compare radiographs, pressure indices, or indeed any other test for peripheral arterial disease has been mentioned briefly in the introduction to this thesis, and will be further discussed in Chapter Eleven.

Fifty seven patients were also classified by their presenting symptoms into those with intermittent claudication and those with rest pain. The calf pressure indices of these two groups have been plotted separately on figure 8.5. Although the means of the two groups are clearly different ($p < 0.005$) there is a considerable overlap. This overlap could, in part, be due to the inability of the calf cuff to detect distal disease.

8.2.3 The effect of inflating a pneumatic cuff on local blood pressure

Intra-arterial pressure was measured continuously in the common femoral artery of 25 patients, either pre-operatively under local anaesthesia or per-operatively under general anaesthesia, whilst a thigh cuff was inflated to above systemic systolic pressure. Tests were also carried out during femoro-popliteal vein grafting procedures when the popliteal artery was punctured, and a calf cuff inflated to above systolic pressure. Figure 8.6 demonstrates the kind of results obtained. Although the cuff has not affected common femoral pressure, there is a marked rise in popliteal artery pressure. Figure 8.7 shows the percentage rise in common femoral systolic pressure in response to the inflation

of a thigh cuff in 16 patients with minimal radiographically demonstrable aorto-iliac disease, and in 9 patients with severe disease. The mechanism of this pressure rise is discussed in Section 8.3

8.3 Discussion

The measurement of systolic blood pressure in healthy vessels by the occlusive cuff technique has been well investigated (Korotkoff 1905, Geddes 1966, Kirkendall 1967) and indeed is now the standard technique for measuring blood pressure in all but the most ill patients. It has been compared extensively with pressures measured directly by arterial puncture (Ragan 1941, Steele 1941, Kotte 1944, Roman 1965) and has been found to be accurate to within ± 10mm Hg in the majority of patients. In order to achieve this accuracy however, there has been a certain amount of 'optimisation' of cuff dimensions.

It has been shown by several investigators (Ragan 1941, Pickering 1955, Karovonen 1964, Simpson 1965) that the pressure measured by the occlusive cuff technique is dependant on the size of the patient's limb, and in order to measure the pressure correctly, the correct size of cuff must be employed (Figure 8.8 is redrawn from Pickering 1955 and shows the magnitude of the correction required). Cuff sizes have been chosen empirically to give the best agreement with direct pressure measurements, and this may well mask systematic errors in the technique.

It is a basic principle of all measurement techniques that the measurement should disturb the system of interest by as small amount as possible, otherwise the values obtained will

be in error. It seems probable that even in the case of a healthy artery the occlusion of the artery by a cuff will change the pressure distribution within the artery by at least a small amount, a perturbation which may have been hidden as a result of the aforementioned optimisation. A simple calculation based on transmission line theory (see Appendix 7) suggests that this error could be of the order of 10%.

The situation that is met with in diseased arteries is much worse. The basis of the method of detecting arterial narrowing depends on the presence of a pressure drop across the narrowing. If a pressure drop is present, then it must be a result of flow through the stenosis. Any technique of pressure measurement that alters the flow as an integral part of the method must therefore be suspect. The first point to consider however is whether or not there will, under normal circumstances, be a significant pressure drop across a diseased section of artery. The answer to this of course revolves around the definition of significant. Any narrowing in the arterial tree will cause additional energy to be dissipated, but unless the resulting pressure drop is greater than 10mm Hg it will be impossible to detect using an occlusive cuff technique with all its inherent inaccuracies. Reference to Figure 6.4 will show that a stenosis of somewhat greater than 70% would normally be required to produce such a drop.

Clearly the situation is somewhat different under augmented flow conditions such as those experienced by patients during exercise, when much smaller encroachments into the arterial lumen may become haemodynamically significant and

thus limit their ability to walk. The larger pressure drop caused by augmentation in flow has been exploited by some authors in an attempt to increase the sensitivity of the test. Yao et al (1970) exercised their patients on a treadmill before measuring pressure index, whilst Chamberlain et al (1975) use a stepping stool for the same purpose. These tests are open to the objection that the measurement itself alters the pressure just as the tests following rest.

The degree to which the changes in flow produced by the occlusion cuff affect the results depends on the geometrical relationship between the stenosis and cuff. At the instant the pressure is read from the sphygmomanometer the flow through the vessels lying beneath the cuff must be very low. The effect this has on the flow through the stenosis depends on its proximity to the cuff. If for example the cuff is placed just distal to the stenosis, then the flow through it will be low and consequently the pressure drop also. If there are many branches between the cuff and the site of the stenosis then it is possible that the flow through the stenosis may be virtually unaffected (Figure 8.9b). Any reduction in flow as a consequence of the inflation of the cuff reduces the pressure drop recorded by the technique, and as the change in flow is an unknown quantity, normal findings must be treated with caution.

It is also possible that a reduced pressure index may return to normal due to the progression of the disease. If, for example, a branch between the cuff and the stenosis that was originally patent became occluded, then the inflation of the cuff would have a greater effect on the blood flow through the stenosis (this situation is depicted in Figure 8.9c). This means that the cuff technique may be misleading

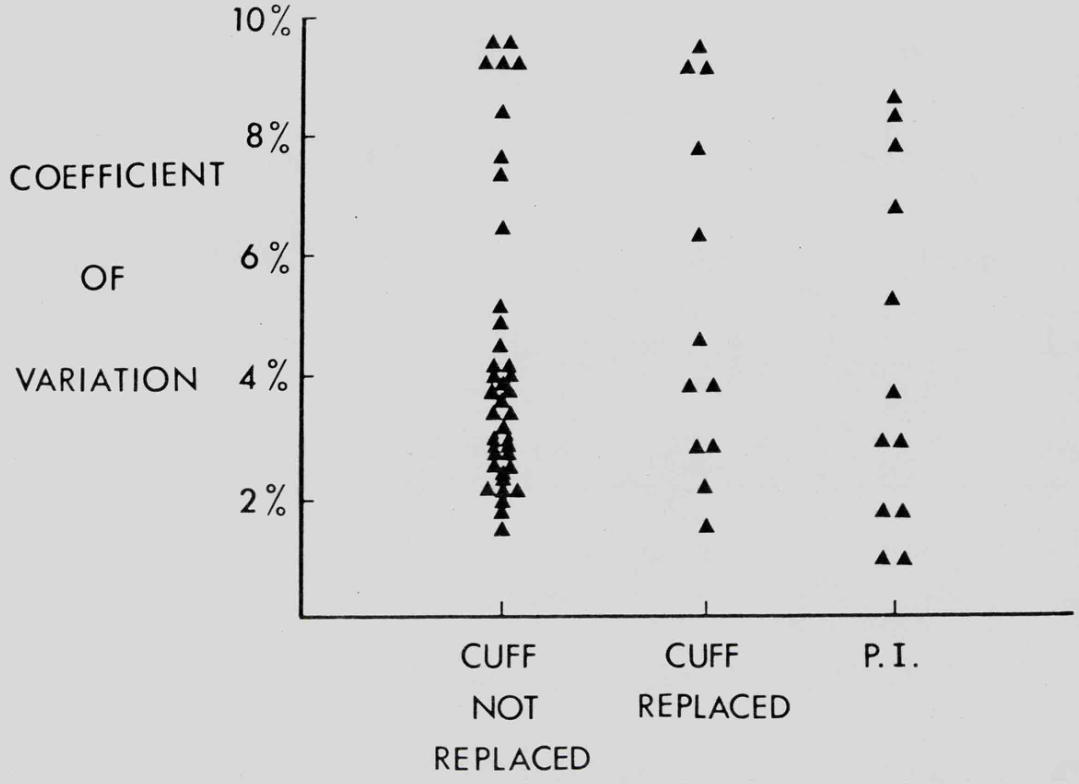
when used for assessing drug therapy, as an increase in pulsatility index could be interpreted either as an improvement or a deterioration in the disease.

8.4 Conclusion

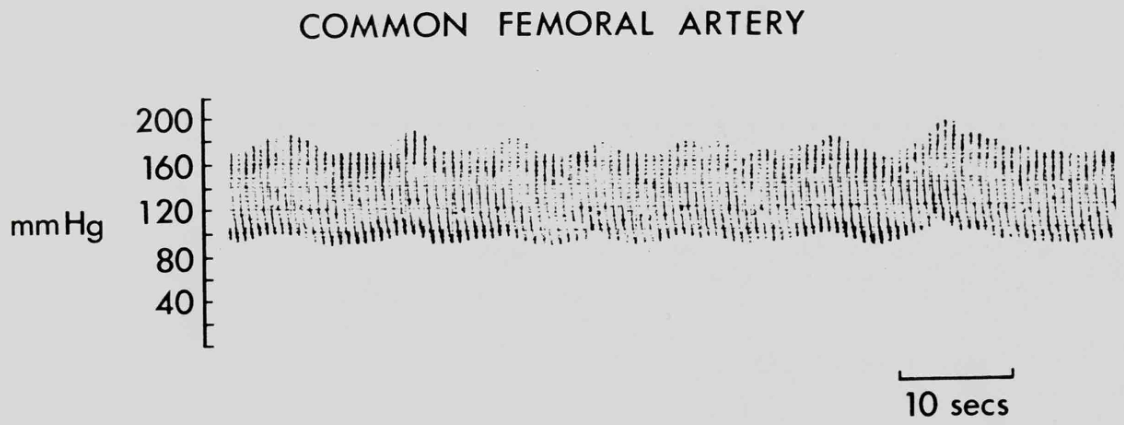
Despite its wide acceptance, the use of indirect pressure measurement as a diagnostic test for arterial stenoses is of limited value.

Because of the inaccuracies of the inflatable cuff technique for measuring arterial pressure, only pressure drops of greater than 10 or 15mm Hg can be reliably detected, which in turn means that only severe arterial narrowings may be diagnosed. In addition, the interference with blood flow, caused by the inflation of the cuff, further reduces the value of the technique in certain situations. In view of these factors it is not surprising that there is little correlation between thigh and calf pressure indices and radiographic findings for individual patients.

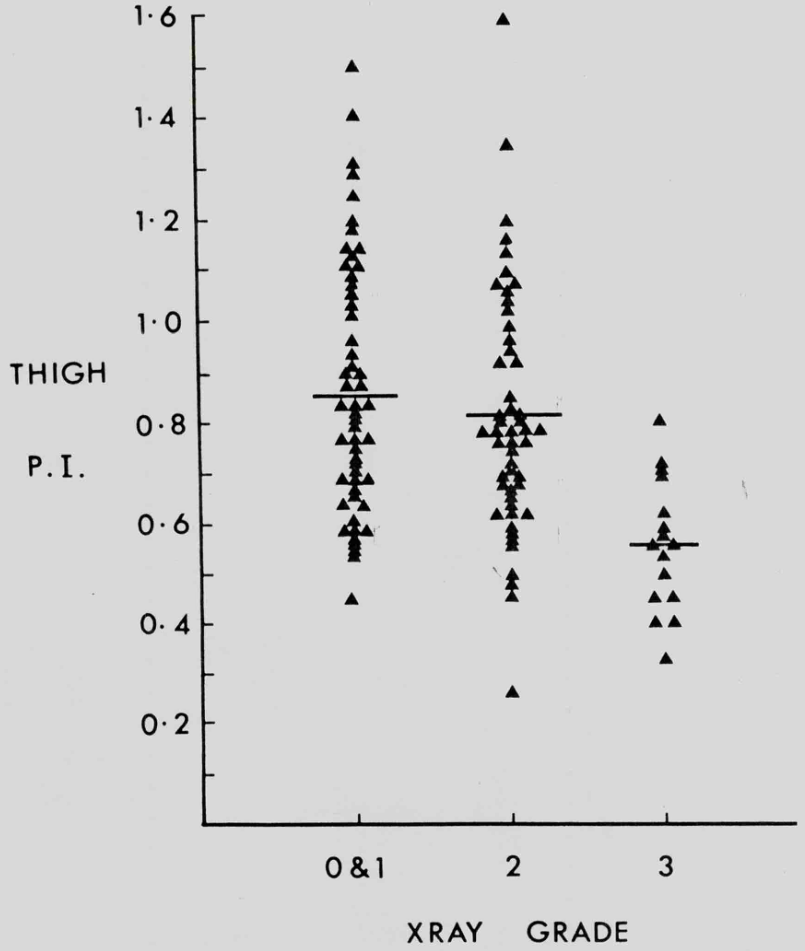
The ability to detect severe arterial disease at some distance means that the method may be used as a screening technique. If ankle pressure index is reduced following exercise then it is possible to infer the presence of vascular disease, however any attempt to localise or grade the disease could be misleading. A normal pressure index does not imply the absence of disease.



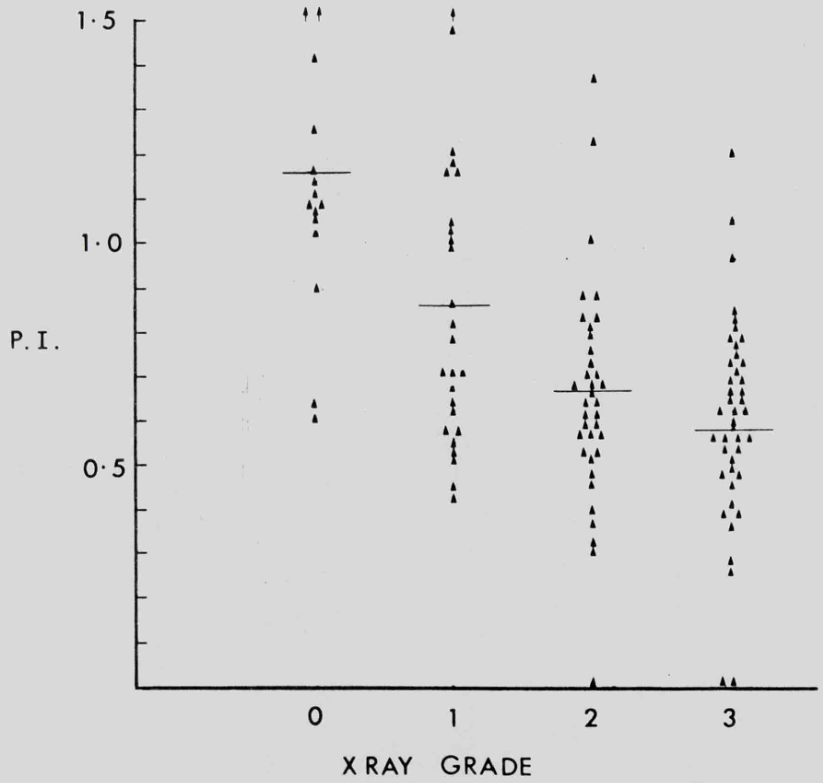
Reproducibility of indirect pressure measurement in patients with arterial disease (Figure 8.1)



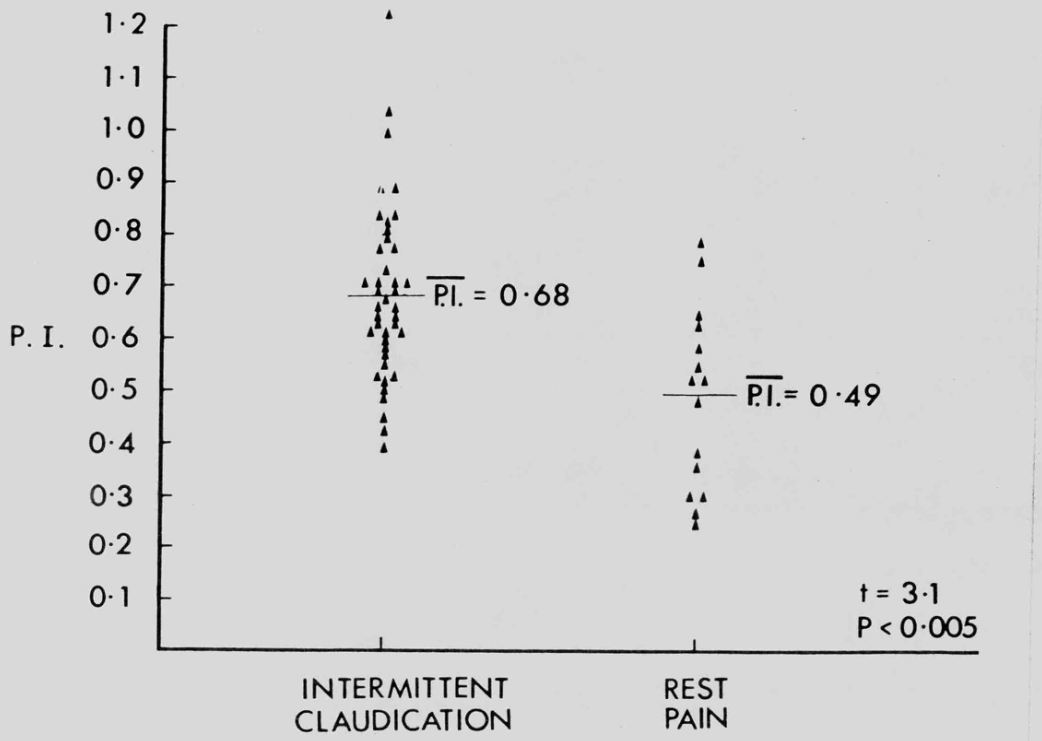
Spontaneous fluctuations in the common femoral pressure of a recumbent patient (Figure 8.2)



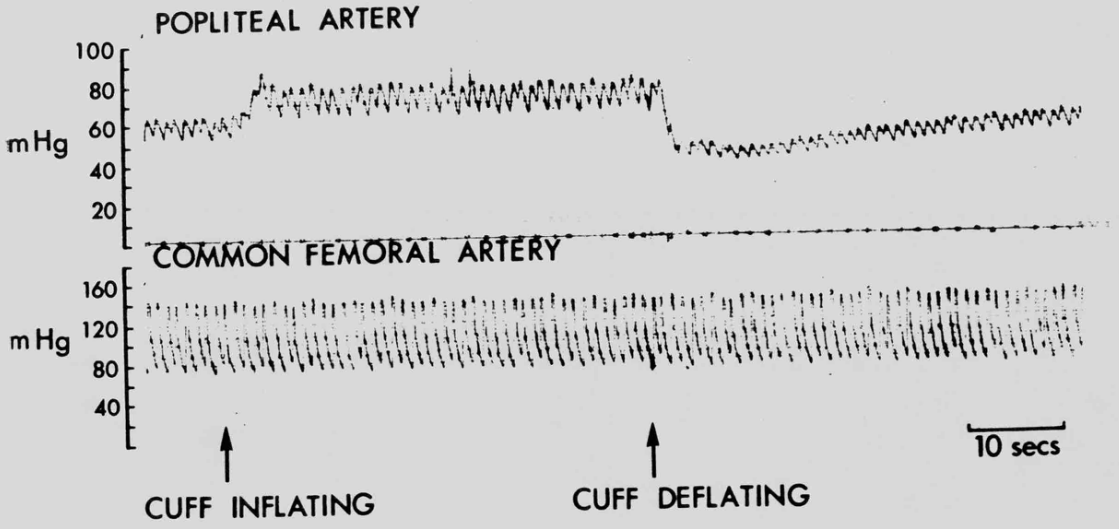
Thigh pressure indices from patients with varying degrees of aorto-iliac disease (Figure 8.3)



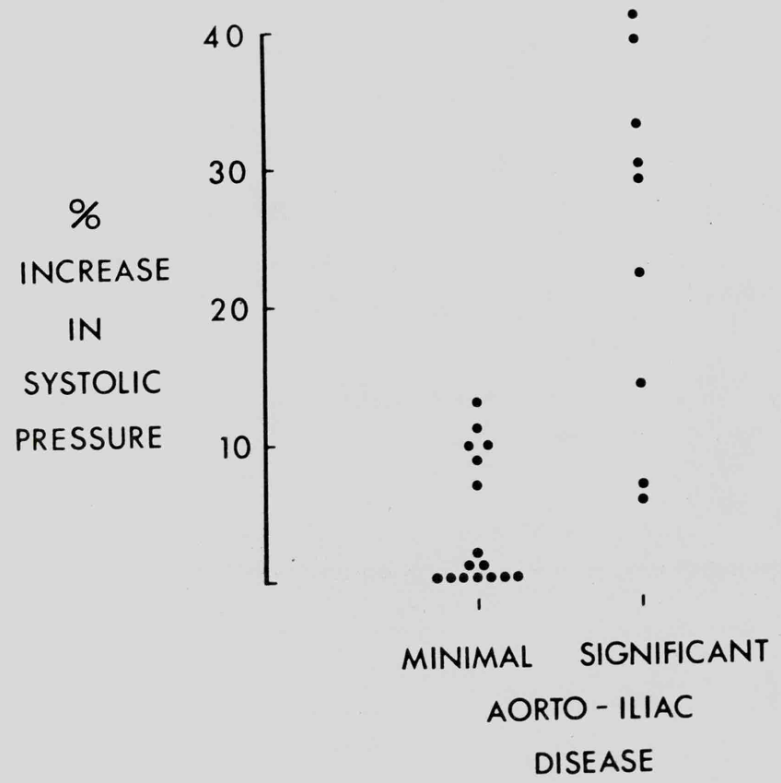
Calf pressure indices from patients with varying degrees of aorto-femoral disease (Figure 8.4)



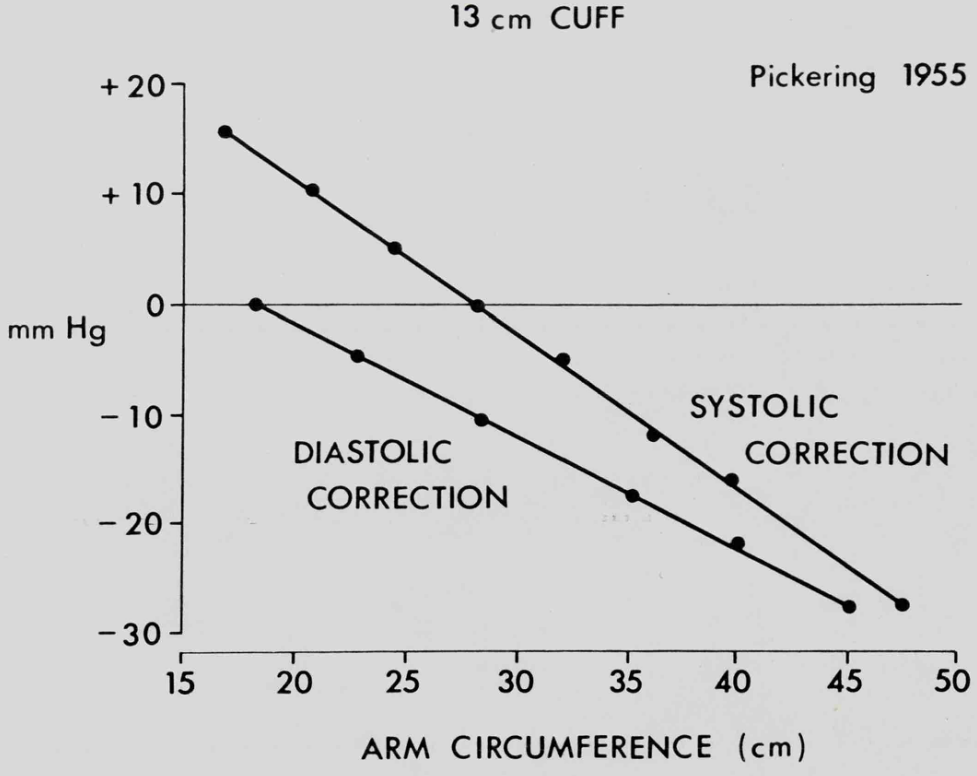
(Figure 8.5) Calf PI's of patients with intermittent claudication and with rest pain.



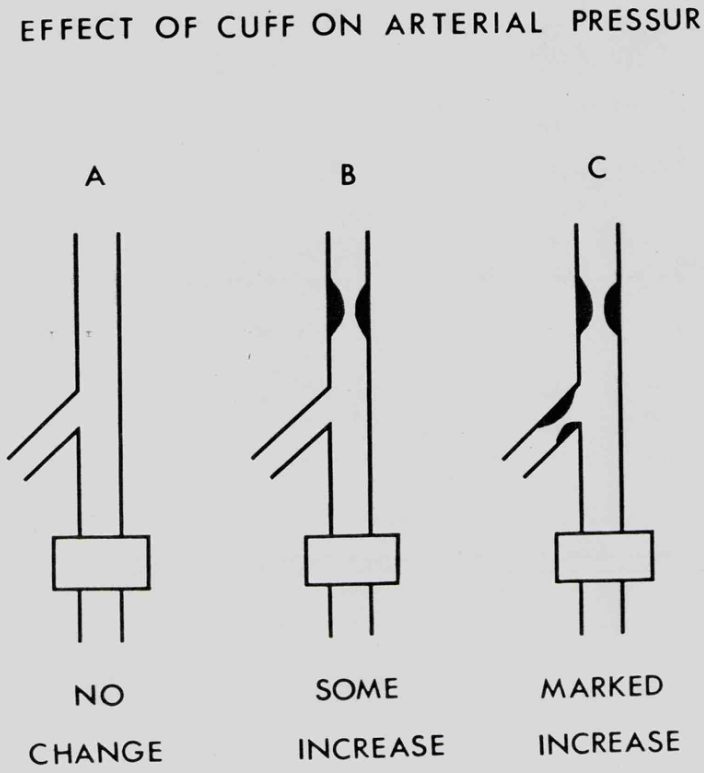
(Figure 8.6) The effect on popliteal artery pressure of inflating a calf cuff on a patient with femoral artery disease.



(Figure 8.7) The effect of a thigh cuff on the common femoral artery pressure in patients with and without aorto-iliac disease.



(Figure 8.8) Corrections necessary to compensate for different arm sizes when making indirect pressure measurements.



(Figure 8.9) The configurations of occlusive cuffs and atheroma discussed in the text.
In A, with no proximal atheroma, inflation of the cuff produces little change in pressure. In B, with proximal atheroma but a large collateral branch, inflation of the thigh cuff will partly reduce flow through the proximal atheromatous section, and there will be a small increase in pressure. In C, inflation of the cuff will substantially reduce the flow through the proximal segment, and there will be a marked increase in the pressure.

CHAPTER NINE

DIRECT PRESSURE MEASUREMENT

Direct pressure measurement is not a commonly used technique for assessing peripheral arterial disease in the same way as indirect pressure measurement, but has been suggested by the author and two surgical colleagues as a test of the aorto-iliac segment (Quin, Evans and Bell 1975). The rationale of the test, its effectiveness, its shortcomings and possible improvements are discussed in this chapter.

9.1 Methodology

Although direct pressure measurement is not open to the same objections of inaccuracy as the cuff technique, the intra-arterial pressure throughout the vascular tree varies due to viscous and turbulent energy losses, gravity, and reflected waves, and thus small additional pressure losses are difficult to detect and quantify. This means that despite the precise nature of intra-arterial pressure measurement only severe stenoses can be reliably detected under resting conditions.

Quin et al have sought to overcome this limitation by manipulating the flow through the artery of interest by means of vaso-dilating drugs. Reference to figure 6.4 will show that even large flow changes through a mild stenosis affect the pressure drop little, whilst changes in flow through a severe stenosis have a profound effect on pressure drop. It is not necessary to be able to quantify the original pressure drop in order to observe

this effect.

The standard test of the aorto-iliac segment as described by Quin et al consists of numbing the groin skin with lignocaine, and inserting a nineteen gauge needle, attached via a manometer connecting line to a pressure transducer, into the common femoral artery. The pressure is then allowed to stabilise before the injection of 20mg of papaverine. The response of the pressure within the artery is observed, and the presence or absence of significant aorto-iliac disease inferred from the severity of the induced drop in pressure. This standard test will be called the "papaverine test".

9.2 The Dose Response of Papaverine

The papaverine test is clearly dependant upon the drug inducing consistent changes in blood flow. The use of papaverine during surgery on patients with vascular disease is not new (Golding and Cannon 1966, Bernhard et al 1968, 1971, Bliss 1973) but it has been used in doses of between 5mg and 40mg, and there appears to be no documentation of its dose-response curve. In order to investigate the dose-response curve a number of experiments were performed during surgery when it was possible to place an electro-magnetic flow probe around the common femoral artery, and measure accurately changes in flow produced by the drug. Fifteen experiments were performed, all on patients undergoing reconstructive vascular surgery, nine of whom had intermittent claudication, and six of whom had rest-pain or gangrene.

Three doses of papaverine, 10, 20 and 30mg were injected into the common femoral artery of each patient in a random order, and the maximum flow induced in each case measured using an electromagnetic flowmeter. A typical result obtained following a dose of 20mg is shown in figure 9.1. The papaverine has increased the flow in the common femoral from 160ml min^{-1} to 590ml min^{-1}, whilst the common femoral pressure has fallen from 144/94 to 88/64. There is very little change in the aortic pressure.

The dose response curves of the two groups of patients are shown in figures 9.2 and 9.3. The response of flow to the drug appears to increase little above 20mg, and as in one patient a 30mg dose appeared to produce a transient second degree heart block, a 20mg dose was used for all subsequent tests.

The results from the patients with intermittent claudication are all fairly similar, whilst there is a large spread of results for the patients with rest pain. Possible explanations for this spread are that some patients with rest pain already have widely dilated distal vessels as a result of ischaemia, or that they have such severe disease that large increases in flow are impossible because of the consequent haemodynamically 'impossible' pressure drop.

Although the flow was allowed to fully recover between each dose of papaverine in each patient, it was thought possible that the doses might interact in some way, and so in a further ten patients with mixed symptoms two doses of papaverine, 20mg, were injected intra-arterially, the second dose being administered as soon as the flow had returned to

normal following the first. The results of this are shown in figure 9.4, there is apparently little or no interaction.

9.3 Clinical Trials

Having established that the effects of papaverine on blood flow were reasonably predictable on a small group of patients with intermittent claudication, a trial was carried out to find the effect of 20mg papaverine on the common femoral pressures of conscious patients, who had either unquestionably diseased or unquestionably normal aorto-iliac segments.

Patients were considered to have normal aorto-iliac segments if they had a normal femoral pulse and there was no sign of a stenotic lesion on their arteriogram, and to have significant disease if they had x-ray evidence of a stenosis of 20% or more, and also a reduced femoral pulse. Twenty per cent was chosen arbitrarily, and may seem a little mild, however, this was a reduction in the lateral diameter of the vessel which is usually less affected by atheroma than the anterior-posterior diameter. Borderline cases, and cases which did not fulfil both the criteria necessary for admission to one or other group were omitted from the trial.

The standard papaverine test, as described in section 9.1 was carried out on a total of 95 claudicating limbs, and the percentage drop in systolic pressure recorded in each case. In 32 of these cases the dose was also repeated to test the reproducibility of the pressure drop. Figure 9.5 summarises the results obtained, and this shows that the papaverine test separates out the two groups well. Figure 9.6 shows the reproducibility of the pressure drop.

9.4 Inaccuracies in the Papaverine Test

Two possible sources of error in the papaverine test are unexpected drops in central arterial pressure, and unexpectedly large or small increases in flow following the administration of the drug.

The former source of error has been investigated in twenty four patients undergoing aorto-iliac reconstructive surgery, during which it was possible to insert a pressure line directly into the aorta. Each patient received a dose of 20mg of papaverine into the common femoral artery, and the decrease in the aortic systolic pressure was recorded. The percentage drop in pressure for each patient is shown in figure 9.7. The changes range up to 10%. There are two possible explanations for this rather high figure, one is disease proximal to the aortic needle, the other a true drop in central pressure. These measurements were made at operation, when some of the patients may have been hypovolaemic. It was certainly noted in other experiments that papaverine has a profound effect on the central pressure of patients who are grossly hypovolaemic. It is difficult to measure the effect of papaverine on the central pressure of conscious patients, but it is unlikely that the effects are greater. It is useful to monitor the contra-lateral common femoral pressure during the papaverine test, if it remains constant then the central pressure must also have done so, however if it should fall this could be as a result of aortic disease or of a fall in central pressure, and the results of the test must be treated with caution.

The second possible source of error in the papaverine

test is that the flow may not change by the expected factor. Reference to figure 9.2 shows that flow increases resulting from papaverine injections in patients with intermittent claudication, are fairly but not completely reliable. Any spurious result will obviously reduce the accuracy of the test. One way of reducing this possible error might be to monitor the increase in flow with a Doppler velocimeter. The results of papaverine on the blood flow in patients with rest-pain are too variable to be relied upon, and the papaverine test is not recommended for this group of patients.

9.5 Discussion

The measurement of intra-arterial pressure in patients with peripheral vascular disease is not new (Cappelen and Hall 1960, Weismann and Upson 1963), however, it has never become popular in the same way as indirect pressure measurement. This is presumably because of its invasive nature, because under resting flow conditions it has little more to offer than non-invasive measurements, and because of the limited sites at which such measurements may be made. Despite the apparent dangers of placing a needle in a badly diseased artery, no complications have been observed by the author in two hundred or so femoral punctures carried out by his clinical colleagues, and indeed this would be expected from the low complication rate of this technique in aortography, in which a much larger needle is used (Kottke et al 1964, Boujoutsos and Morris 1973). Per-cutaneous intra-arterial pressure measurements can only be made at a limited number of sites, and the papaverine test has only been applied to the common femoral artery to date. However,

it might be possible to extend the technique to other sites, perhaps the dorsalis pedis artery, using a micro-needle technique, such as that described by Barras (1973). Drug injection could not in this case be made at the same site, but might be through a second needle placed in the common femoral artery. The common femoral site is however an important one, as information is obtained about the aorto-iliac segment, information that is essential to the surgeon contemplating a femoro-popliteal graft.

Reduction in pressure distal to a stenosis during increased flow has been noted by several authors in the form of disappearing pedal pulses following exercise in patients with intermittent claudication, (De Weese 1960, Keitzer et al 1965). Indeed, Moore and Hall (1971) devised a test to detect unrecognised aorto-iliac disease utilising this fall in pressure. Their test involved exercising their patients to claudication with a pedal ergometer, whilst monitoring the common femoral pressure. They showed there was a fall in pressure distal to a stenosis, but unfortunately their results were complicated by rises in systemic pressure due to the exercise, which tend to mask moderate falls due to disease.

The papaverine test is very similar to the test of Moore and Hall, except that the blood flow increase is induced by a vaso-dilating drug rather than exercise. The drug does not have the same effect on systemic pressure but produces roughly the same flow increase as that produced by exercise in patients with arterial disease (Pentecost 1964, Folse 1965).

The clinical trials described in section 9.3 were

carried out on patients who clearly had either little disease or severe disease, and the results were apparently satisfactory. Unfortunately, it is for the patients with disease lying between these two extremes that such tests are most needed. Once again the problem of there being no absolute test occurs. If the papaverine test is carried out on patients with borderline aorto-iliac disease, then the results cannot be tested for their accuracy. Hopefully, one of the results of the work described in this thesis will be a standard, and the reader is once again referred to Chapter eleven for a discussion of the problem.

Comparison of the papaverine test with Doppler results (of the type described in the next chapter) and radiographic evidence produces some anomalous results,* but at present it is not possible to adjudicate between the techniques.

9.6 Conclusions

Intra-arterial pressure measurement at rest has little to offer over and above indirect pressure measurement.

The papaverine test appears to be a useful test for arterial disease, although confirmation of its efficacy must await the introduction of a standard test to which it can be compared. Unfortunately, the papaverine test cannot be directly evaluated using a dog model, as the drug affects the animal's central pressure before producing a flow increase comparable with that which it produces in humans. The flow-pressure drop relationship investigated in Chapter six and referred to in this chapter is of course independent of any such effects.

It is possible that the accuracy of the papaverine

* See page 11-3.

test might be improved by monitoring the blood flow changes induced by the drug, with an ultrasonic Doppler velocimeter. One disadvantage of the test as it stands, is that it is only applicable to the common femoral artery, but it may be possible to extend the technique to other sites using a micro-needle technique. A fall in pressure in the common femoral of 20% or more, in the absence of a pressure drop in the contralateral common femoral is indicative of significant disease, but a smaller drop should not be regarded as precluding aorto-iliac disease.

The papaverine test is not suitable for investigating patients with rest-pain, but in the event of severe aorto-iliac disease contributing greatly to this symptom, the resting common femoral pressure would normally be reduced sufficiently to be detected without a flow increase being necessary.

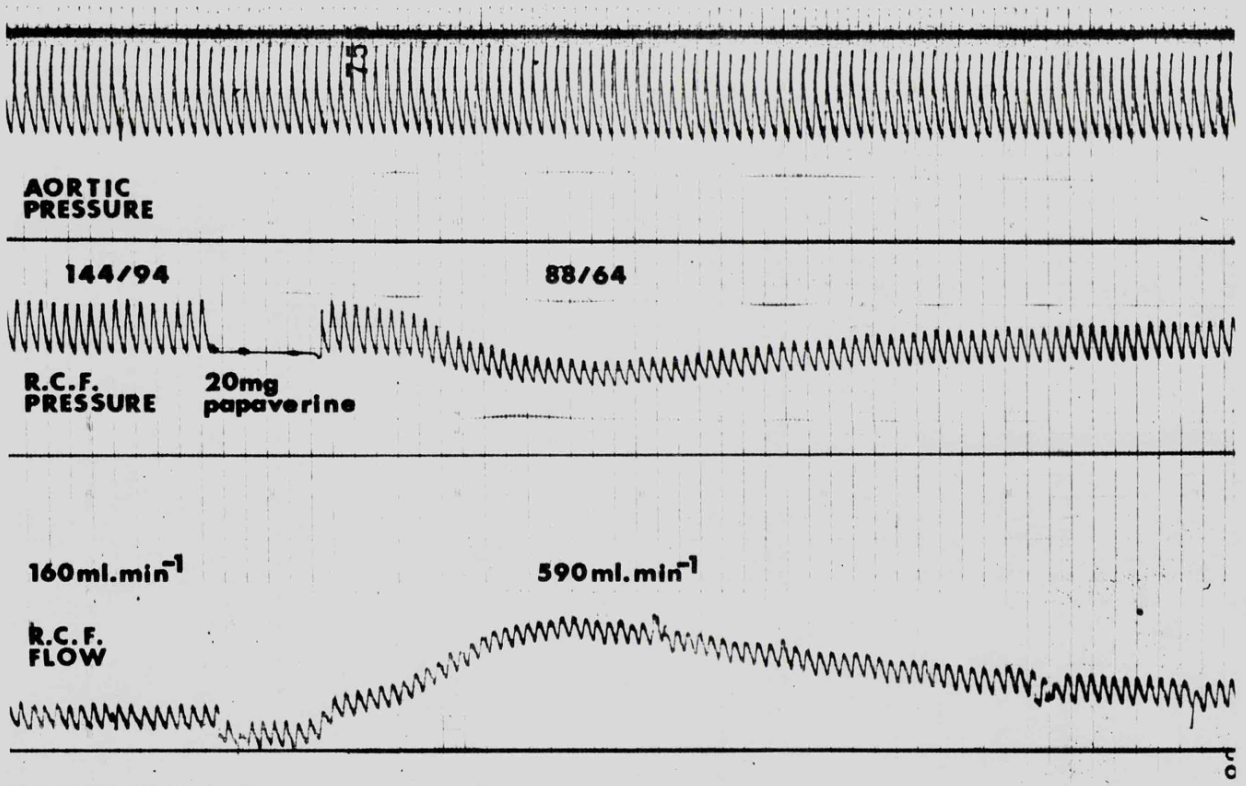


Figure 9-1. The effect of 20 mg. of papaverine in a patient with right iliac artery disease.

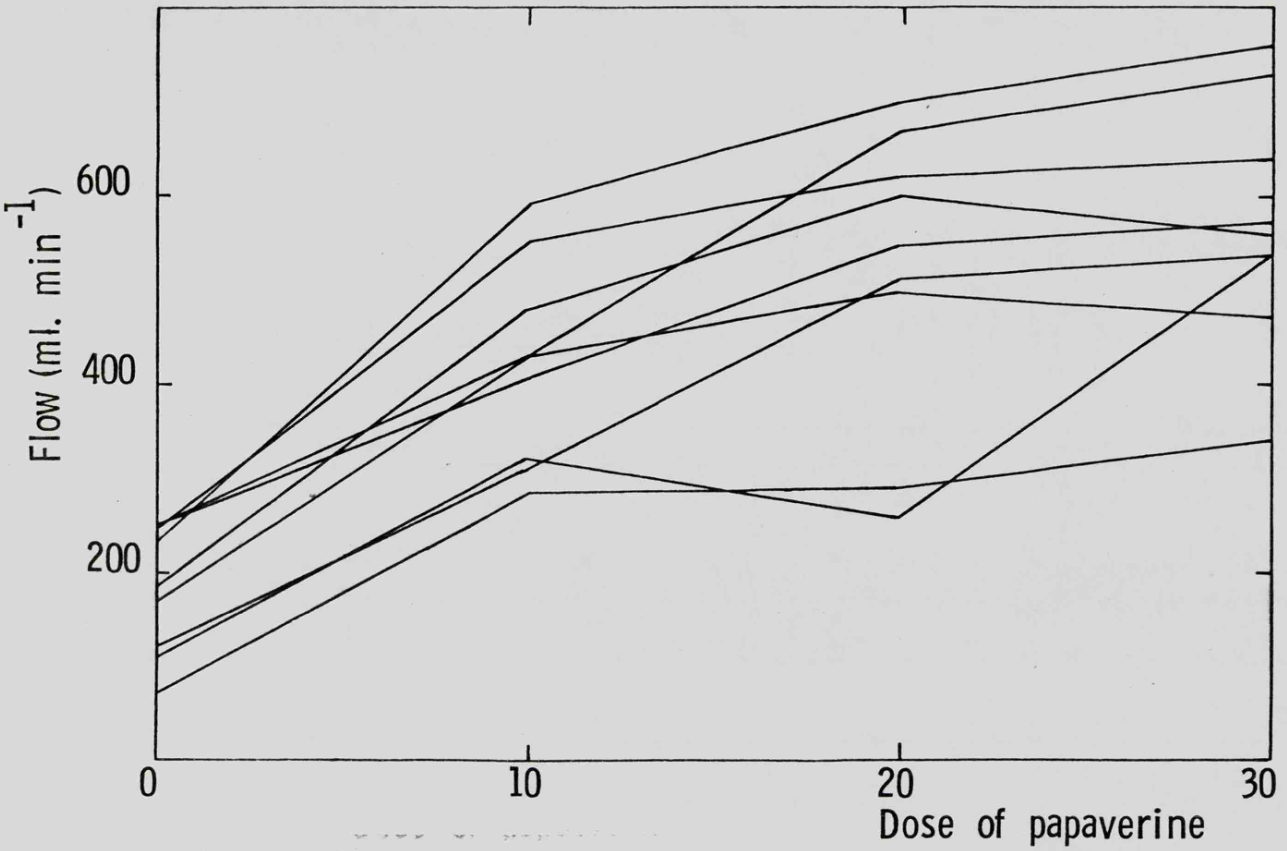


Figure 9.2. Dose response curve of papaverine in patients with intermittent claudication.

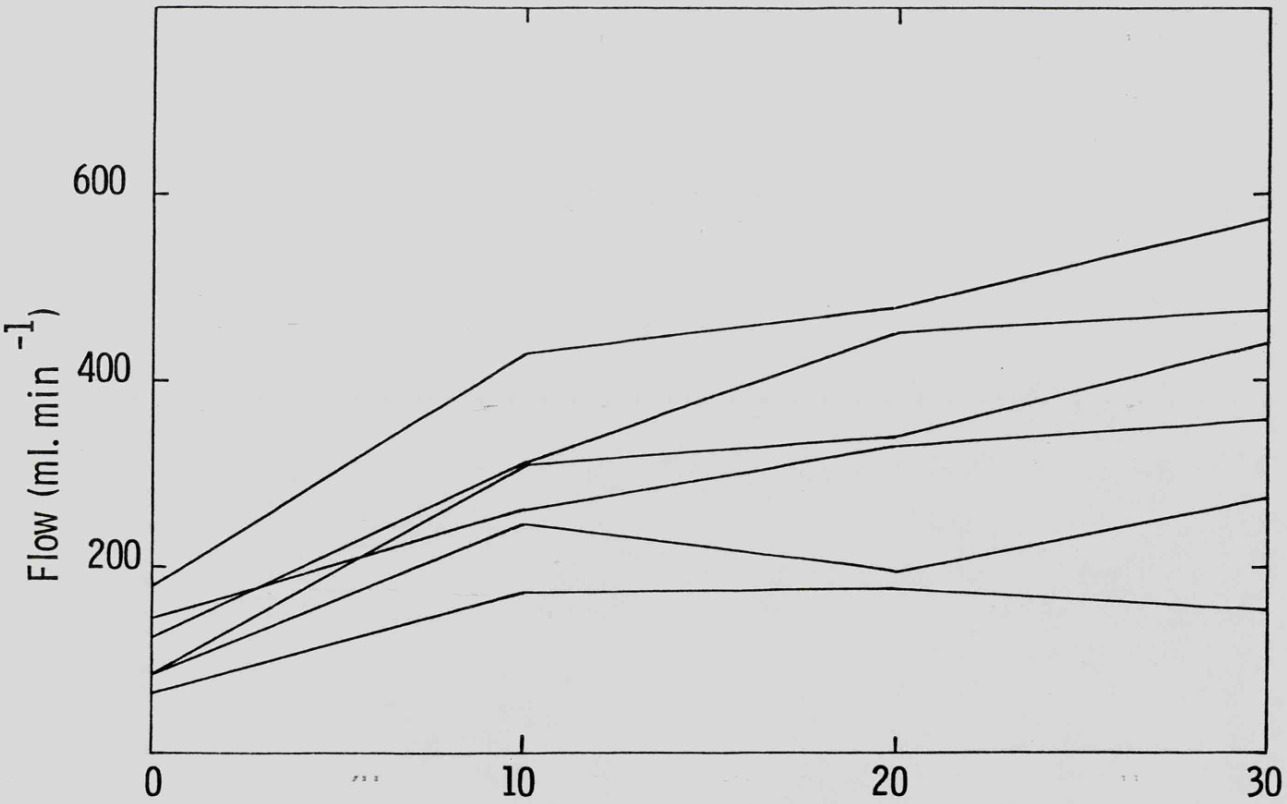


Figure 9.3. Dose response curve of papaverine in patients with rest pain.

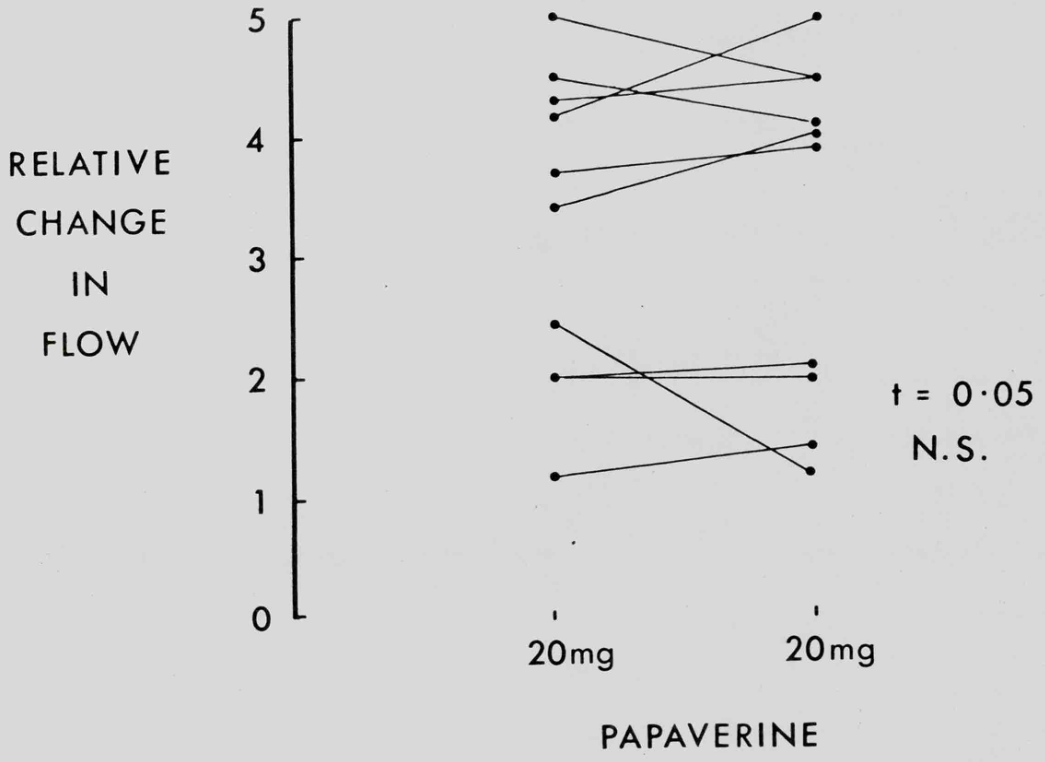


Figure 9-4. Reproducibility of the flow increase caused by 20 mg. of papaverine.

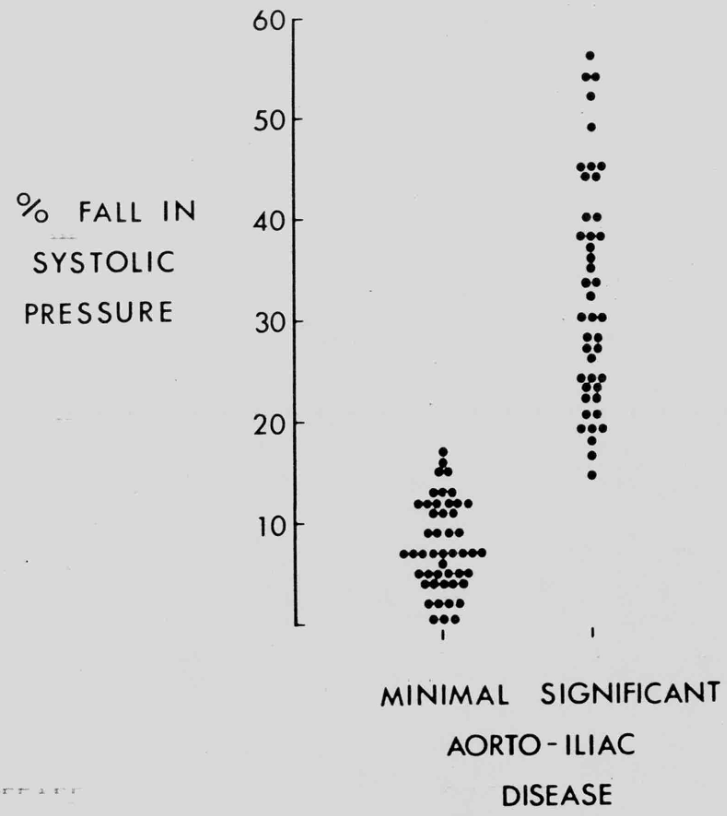


Figure 9-5. The percentage fall is systolic pressure resulting from the administration of 20 mg of papaverine in patients with and without aorto-iliac disease.

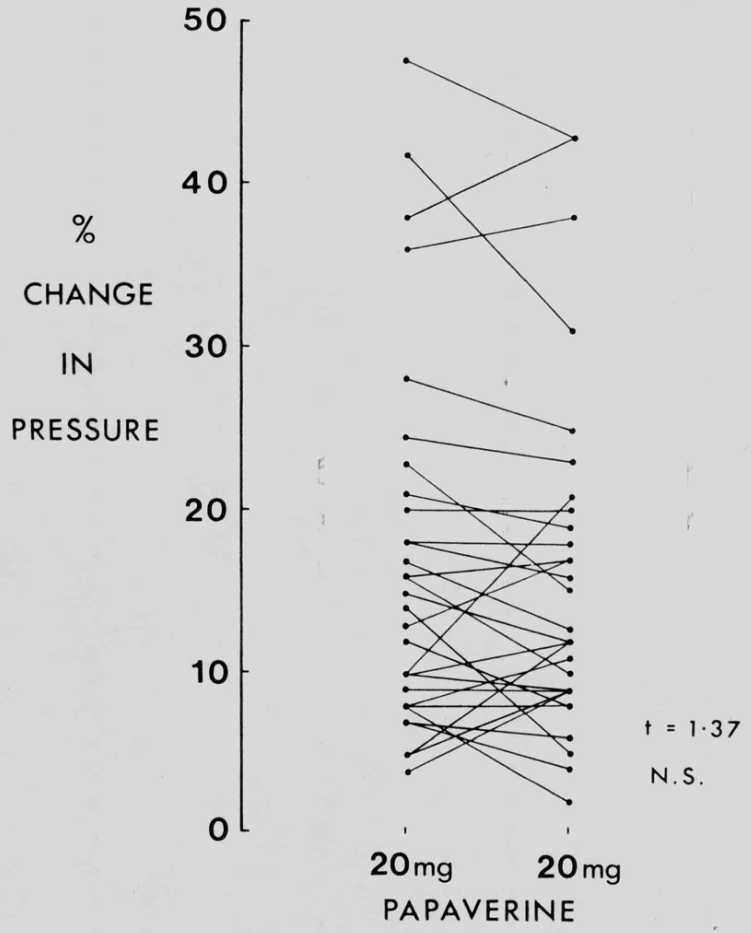


Figure 9.6. Reproducibility of the drop in common femoral pressure induced by 20 mg of papaverine.

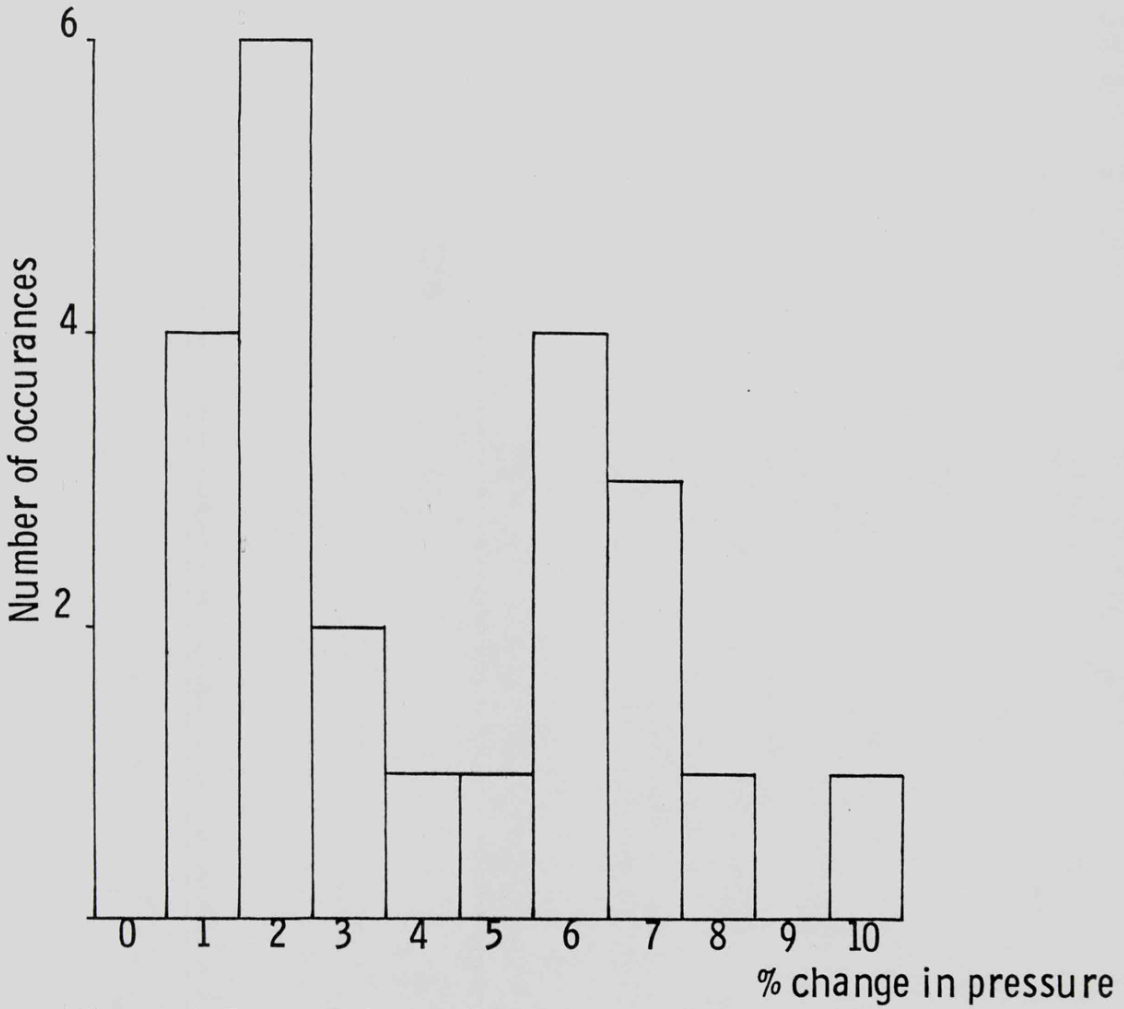


Figure 9.7. Fall in aortic pressure following the administration of 20 mg of papaverine into one common femoral artery.

CHAPTER TEN

CLINICAL ULTRASONIC VELOCITY MEASUREMENTS

Ultrasonic Doppler shift measurements have already been introduced in Chapters four and seven. In this chapter, patient measurements will be discussed in conjunction with results from Chapter seven.

10.1 The Interpretation of Ultrasonic Doppler Signals

Two basic methods of displaying ultrasonic Doppler signals, one using zero-crossing detection, the other using spectral analysis, have been discussed in Chapter four. Various authors have attempted to classify the traces obtained using these techniques, but the method which is at present most popular is the pulsatility index method discussed in Chapter seven.

Although Strandness et al (1967) reported on the damping of sonagraphic traces obtained distal to diseased vessels, it was not until 1971, when Gosling et al introduced Fourier Pulsatility Index (see section 7.2), that an attempt was made to quantify the differences between the waveforms measured from diseased and non-diseased vessels. In that paper Gosling et al showed that in normal subjects PI increases as the distance from the heart increases, this is not so in patients with arterial disease, and that the pulse wave 'transit-time' is also increased in patients with diseased limbs. This last parameter was measured by recording sonagrams simultaneously at two sites in the arterial tree and measuring the difference between

the two onset times. In a further paper by the same group of workers (Fitzgerald et al 1971), it was suggested that the dynamic capability of the collateral circulation of a segment of artery could be assessed by measuring the damping factor and transit time across that segment, (damping factor being defined as distal PI divided by proximal PI), there was however little evidence that this classification was of clinical value.

Since this time there has been a spate of publications in which PI is of central importance. Woodcock et al (1972) compared the changes in waveform pulsatility and transit time with limb perfusion as measured with a thigh occlusion cuff and strain-gauge plethysmograph placed at mid-calf level. Although a broad inverse correlation was shown to exist, the scatter of results was very wide, moreover the value of total limb perfusion as an index of disease severity is questionable. Gosling and King (1974) compared the results of arteriography with those of 'ultrasonic angiology' in 85 segments of 33 patients and found agreement in 89% of cases, a rather surprising finding as they defined their normal range in terms of the mean $\pm$ one standard deviation. Charlesworth et al (1975) found that there was a highly significant difference between the success rates of femoro-popliteal bypass grafts in two groups of patients, one group having femoral PIs of less than 4, and the other PIs of greater than 4. Johnston and Taraschuk (1976) compared PI with graded arteriograms and ankle systolic pressure measurements and found fairly good agreement between the ankle results, but there was a large overlap between femoral artery PIs from patients with different

degrees of arteriographically apparent disease.

A similar, but more rigorous, attempt to quantify the effect of disease on Doppler waveforms has been adopted by Morris and co-workers (Morris et al 1975, Woodcock et al 1975) who calculated the impulse response of a segment of vessel from the input and output velocity-time waveforms. This approach seems promising, but as yet has only been applied to the femoro-popliteal segment and has not been extensively evaluated clinically.

Other workers have tried to derive indices from zero-crossing traces but in view of the limitations of this technique (see Section 4.2.2.) and the difficulties with the vastly superior traces obtained by true spectral analysis, these seem doomed to failure. Nicolaides et al (1976) suggest an equation derived by multi-variate analysis to predict the probability of an artery being diseased; the variables they measured for this purpose were the height of the zero-crossing trace, the acceleration time, the initial deceleration time, and the so called waveform index (a quantity analogous to PI). Finally, Waters et al (1977) devised a quantity they called 'proximal damping quotient' from a zero-crossing trace and the R-wave of an E.C.G. This introduces another highly variable quantity, the contractility of the heart.

10.2 Patient Experiments

The measurement of PI was evaluated as a diagnostic test of the aorto-iliac segment in the same way as was previously used for the papaverine test. The femoral PIs of a series of 31 patients suffering from intermittent claudication were measured using the same equipment as

described in Section 7.1. Each patient was allowed to rest for at least twenty minutes before measurements were made. An ultrasonic Doppler probe was placed on each femoral artery successively and adjusted until the best trace was obtained on the monitor. This trace was then recorded on a Medelec fibre-optic recorder and later analysed with the help of a planimeter. The 62 limbs on which measurements were made, were divided into three groups depending on the clinical and arteriographic findings in each case. Group I consisted of patients with both normal femoral pulses and little or no evidence of disease on their arteriograms (< 20% diameter reduction), Group III of patients with reduced femoral pulses and arteriographically demonstrable disease, and Group II of the remaining patients in whom the arteriographic and pulse findings seemed at variance with each other. The results are presented in figure 10.1. Although the means of the three groups are clearly different (7.12, 3.50 and 3.16 for Groups I, II and III respectively), there is a large overlap between the groups which suggests the technique is of limited value for assessing the individual patient.

10.3 Discussion

The results from the patient experiments are disappointing because although Group II presents a clinical problem, Groups I and III are clinically distinct and a large overlap would not be expected. Once again the lack of a decisive test is a problem.

The reason for the overlap of Groups may well be connected with the effect of the peripheral bed on PI discussed in Chapter seven, and more specifically with

disease distal to the site of measurement. Distal disease can only increase PI, and it is interesting that if a PI of 4 is taken as being the limit of normality for the aorto-iliac segment (Charlesworth et al 1975), then 32 of the 33 results in Group I would be assessed correctly, whilst 4 of the 10 results in Group III would be assessed incorrectly on account of the PI being too high - a possible consequence of a raised PR due to distal disease. Further examination of the arteriograms in Group III showed that only two of the four limbs with high femoral PIs had severe femoro-popliteal disease, and no apparent reason why the other two values should be high. Further work on the factors influencing PI is clearly needed.

The results of the experiments described both in this chapter and in Chapter seven suggest that a low value of PI is indicative of significant disease, whilst a high value must be treated with caution.

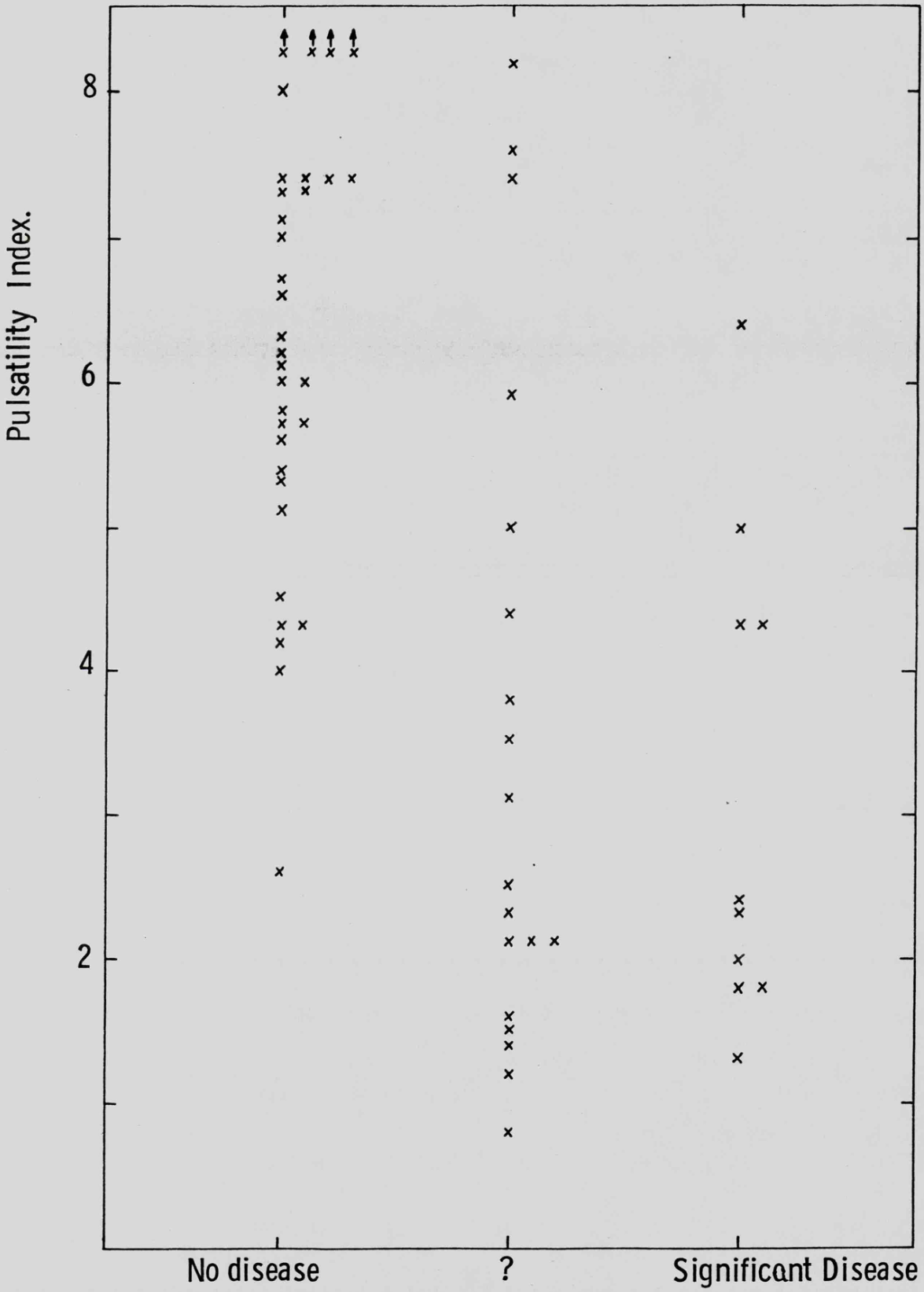


Figure 10. 1. The pulsatility indices for three groups of patients divided according to the clinical findings.

S E C T I O N D

'This is not the end. It is not even the beginning of the end.'

Sir Winston Churchill (1942)

CHAPTER ELEVEN

THE ASSESSMENT OF OCCLUSIVE PERIPHERAL ARTERIAL DISEASE

There are several reasons why arterial grafts fail (see section 1.6), but the two which may be avoided by assessing a patient accurately are inadequate 'run-in' and poor 'run-off'. The work in this thesis has been primarily concerned with the detection of disease proximal to the site of measurement, particularly in the aorto-iliac segment.

The difficulties of assessing the arterial bed are many, but two are particuarly severe. A number of tests have been proposed for the assessment of arterial disease, but it is difficult to determine their relative merits as there is no standard against which they can be compared. Also, the effect of disease on graft survival is known only in qualitative terms, so even were it possible to quantify disease precisely, considerably more work would have to be carried out before haemodynamic measurements could be relied upon always to indicate the best operation in any circumstances.

11.1 The Value of Tests currently used to assess Peripheral Vascular Disease

The accuracy of tests currently used in the assessment of peripheral vascular disease have been discussed in Chapters seven to ten, where it has been stressed that although general conclusions may be drawn about their accuracy, further work is necessary. Indirect pressure

measurement is of little use, particularly for assessing the aorto-iliac segment, but direct pressure measurement and ultrasonic Doppler measurements both show some promise. There are however discrepancies between the two tests and occasional results that are so contrary to the clinical findings that they are difficult to accept. In a study just completed by the author and W.W. Barrie, 65 limbs were classified according to clinical results as definitely normal (35), definitely abnormal (14) and possibly abnormal (16). For each group the results of direct arterial pressure and Doppler measurements were compared with the clinical results. In group I (definitely normal), 84% of the pressure tests and 94% of the Doppler tests agreed with the clinical findings, whilst the figures for group II (definitely abnormal), were 85% and 67% respectively. More interesting were the results from group III, in which the clinical assessment failed to give a satisfactory answer. In eight of these patients the two tests agreed, but in the other eight they were at variance with each other. Both tests could not be correct.

Clearly an objective test, with which clinical tests can be compared is required.

11.2 Equivalent Stenosis

The difficulty of quantifying the 'severity' of a stenosis from geometrical factors has been mentioned in Chapter six. It is however much easier to quantify severity in haemodynamic terms. One quantity which could be used for this purpose is stenosis resistance (ie pressure drop/flow) but this is dependent on vessel size and flow itself. Peripheral resistance units (resistance/volume of tissue

perfused) make some allowance for vessel size, but are not very practical and are also a function of flow. A possible solution to the problem is to make use of the relationship expressed in equation 6.1 to find an 'equivalent stenosis'

By measuring the maximum pressure drop across a stenosis at a number of different maximum flows and fitting a curve to these values, it is possible to find the linear coefficient K_v, which for any stenosis configuration ($L:r_1:r_2$ constant) is constant. Stenoses of roughly the same 'severity' will have similar K_v values. However, it must be recognised that a single value cannot completely characterise a quantity which is a function of more than one variable. It is proposed that the term 'equivalent stenosis' should be used to indicate stenoses that are equivalent in the sense that their K_v values are the same, and that this should be used as an objective measure, albeit approximate, of stenosis severity.

Clearly 'equivalent stenosis' is of no use for assessing patients directly, as it can only be measured at operation, but it could form a valuable standard against which other less objective, but more convenient tests can be compared. The equivalent stenosis concept could also be used to investigate the effect of disease on graft survival if appropriate measurements were made at each vascular operation.

The measurement of 'equivalent stenosis' should be carried out across an unbranched segment of artery, otherwise the volumetric flow will not be the same throughout the segment. This can be achieved by occluding any major branches between the two pressure measurement sites, but

this requires access to the arterial segment under investigation. Thus, unfortunately, it would not normally be possible to measure the K_v value of the iliac segment during a femoro-popliteal operation, unless the internal iliac artery happened to be occluded. This restricts the use of the technique, but it should be possible to make useful measurements at most vascular operations. More information will be obtained on segments that are thought clinically to be diseased than on those that are thought to be normal.

The measurement of r_1 could present a slight problem because of the branching and tapering of the arterial tree, but it would be possible to avoid this by always referring the measurements on a particular segment to a fixed point on that segment. The value of a standard such as 'equivalent stenosis' needs investigating.

11.3 Concluding Remarks

The haemodynamic effects of arterial stenoses, and the accuracy of a number of diagnostic tests have been examined in this thesis. This work has posed more questions than it has answered, the most important of which are enumerated below:-

1) Why do the in-vivo 'K' values differ from their in-vitro counterparts?
2) Does the peripheral bed compensate for the increase in limb resistance resulting from an arterial stenosis?
3) Is pulsatility index greatly influenced by disease distal to the site of measurement?

4) Why do the Papaverine test and the ultrasonic pulsatility index disagree so completely on some occasions?

All these questions are important and require further investigation.

The aim of any treatment for peripheral arterial disease is to enable the patient to walk further and thus be more self-sufficient, or in more severe cases to abolish rest-pain and prolong life. The assessment of peripheral vascular disease is difficult, and it is perhaps because of this that these objectives are apparently sometimes lost in the search for parameters that can be measured objectively. There are two important questions that any complete assessment of the patient must answer. Which, if any, operation will benefit the patient, and which, if any, operation will be successful in the long term.

There are a number of factors which make these questions difficult to answer. Peripheral vascular disease is a dynamic disease and a decision regarding the suitability of an operation which was correct at the time it was made, may well later become incorrect as a result of advancing disease, and a graft that was viable may consequently fail. Another factor is the lack of detailed knowledge concerning the reason for graft failure, and even the mechanism of claudication.

A more satisfactory approach to the treatment of patients with peripheral vascular disease would be to tackle the disease process itself, rather than merely

bypassing diseased arteries. At present this is impossible, the disease can at best be retarded, but hopefully P.V.D. will one day become a medical, rather than a surgical problem.

'The cure for this ill is not to sit still,
Or frowst with a book by the fire;
But to take a large hoe and a shovel also,
And dig till you gently perspire'.

Rudyard Kipling
Just-So Stories

Special Functions Arising From Womersley's Theory

M_o' and ε_o'

The solution to equation 2.1 has been written in terms of M_o' and ε_o' which are both complex functions of α and y as defined in equations A1.1 and A1.2

$$M_o'(\alpha,y) = (1+h_o^2 - 2h_o \cos\delta_o)^{\frac{1}{2}} \qquad \text{A1.1}$$

$$\varepsilon_o'(\alpha,y) = \tan^{-1}\left(\frac{h_o \sin\delta_o}{1-h_o\cos\delta_o}\right) \qquad \text{A1.2}$$

where $$h_o = \left(\frac{Ber^2(\alpha y) + Bei^2(\alpha y)}{Ber^2(\alpha) + Bei^2(\alpha)}\right)^{\frac{1}{2}} \qquad \text{A1.3}$$

and $$\delta_o = \tan^{-1}\left(\frac{Bei(\alpha)}{Ber(\alpha)}\right) - \tan^{-1}\left(\frac{Bei(\alpha y)}{Ber(\alpha y)}\right) \qquad \text{A1.4}$$

The Kelvin functions Ber and Bei are the real and imaginary parts of a complex Bessel function of order zero, and can be calculated from the following summations (Sneddon 1966).

$$Ber(x) = \sum_{s=o}^{\infty} \frac{(-1)^s(\tfrac{1}{4}x^2)^{2s}}{(2s!)^2} \qquad \text{A1.5}$$

$$Bei(x) = \sum_{s=o}^{\infty} \frac{(-1)^s(\tfrac{1}{4}x^2)^{2s+1}}{(2s+1)!^2} \qquad \text{A1.6}$$

The functions M_o' and ε_o' have been plotted against y for various values of α in figures A-1 and A-2.

M'_{10} and ε'_{10}

M'_{10} and ε'_{10} which first appear in equation 2.3, which describes volumetric flow through a rigid pipe, are necessarily functions of a alone. M'_{10} and ε'_{10} are defined in equation A1.7 to A1.10

$$M'_{10}(a) = (1+h_{10}^2-2h_{10}\cos\delta_{10})^{1/2} \qquad \text{A1.7}$$

$$\varepsilon'_{10}(a) = \tan^{-1}\left(\frac{h_{10}\sin\delta_{10}}{1-h_{10}\cos\delta_{10}}\right) \qquad \text{A1.8}$$

$$h_{10} = \frac{2}{a}\left(\frac{Ber\ 1^2(a) + Bei\ 1^2(a)}{Ber^2(a) + Bei^2(a)}\right)^{1/2} \qquad \text{A1.9}$$

$$\delta_{10} = \frac{3\Pi}{4} - \tan^{-1}\left(\frac{Bei\ 1\ (a)}{Ber\ 1\ (a)}\right) + \tan^{-1}\left(\frac{Bei(a)}{Ber(a)}\right) \qquad \text{A1.10}$$

Ber 1 and Bei 1 are the real and imaginary parts of a complex Bessel function of order one, and may be calculated from equation A1.11 and A1.12 (Abromowitz and Stegum)

$$Ber\ 1(x) = \frac{x}{2}\sum^{\infty}\frac{\cos(\frac{3}{2}+s)\ \Pi/2}{s!\ \ (s+1)!}\left(\frac{x^2}{4}\right) \qquad \text{A1.11}$$

$$Bei\ 1(x) = \frac{x}{2}\sum^{\infty}\frac{\sin(\frac{3}{2}+s)\ \Pi/2}{s!\ (s+1)!}\left(\frac{x^2}{4}\right)^s \qquad \text{A1.12}$$

M'_{10} and ε'_{10} are plotted against a in figures A-3 and A-4.

M''_{10} and ε''_{10}

The functions M''_{10} and ε''_{10} which first appear in equation 2.4 are functions of a, Poisson's ratio σ, and k. The definition of k is dependant upon the model. It is the ratio of the wall thickness to the radius of the vessel in the free elastic model, and a constant related to the additional mass, elastic constraint, and internal viscous damping of the wall (as defined in equation 2.15) in the constrained elastic tube model.

$$M''_{10} = \left| 1 + \eta F_{10}(a) \right| \qquad \text{A1.13}$$

$$\varepsilon''_{10} = \text{phase}\ (1 + \eta F_{10}(a)) \qquad \text{A1.14}$$

where F_{10} and η are defined in equations A1.15 to A1.19

$$F_{10}(a) = \frac{2J_1(ai^{3/2})}{ai^{3/2}\, J_o(ai^{3/2})} \qquad \text{A1.15}$$

$$\eta(a,\sigma,k) = \frac{2}{x(F_{10}-2\sigma)} - \frac{(1-2\sigma)}{F_{10} - 2\sigma} \qquad \text{A1.16}$$

$$x(a,\sigma,k) = \frac{G \pm (G^2 - (1-\sigma^2)\, H)^{1/2}}{1 - \sigma^2} \qquad \text{A1.17}$$

$$G(a,\sigma,k) = \frac{1.25 - \sigma}{1 - F_{10}} + (k/2 + \sigma - 0.25) \qquad \text{A1.18}$$

$$H(a,k) = \left(\frac{1+2k}{1-F_{10}}\right) - 1 \qquad \text{A1.19}$$

The arterial wall has been shown to expand and contract isovolumetrically (Lawton 1954, Carew et al 1968) and thus has

a Poisson's ratio of 0.5. The value of k for the free elastic model appears to fall between 0.10 and 0.16 (Bergel 1960, Peterson 1960, Gow and Taylor 1968) and has been taken as 0.13 in all free elastic tube calculations. M''_{10} and ε''_{10} have been plotted on figures A-3 and A-4 with σ = 0.5 and k= 0.13. If the constrained elastic tube theory is used then k tends to minus infinity as the constraint is increased, and M''_{10} and ε''_{10} tend to M'_{10} and ε'_{10} respectively. The relatively minor difference this makes is clearly seen from figures A-3 and A-4.

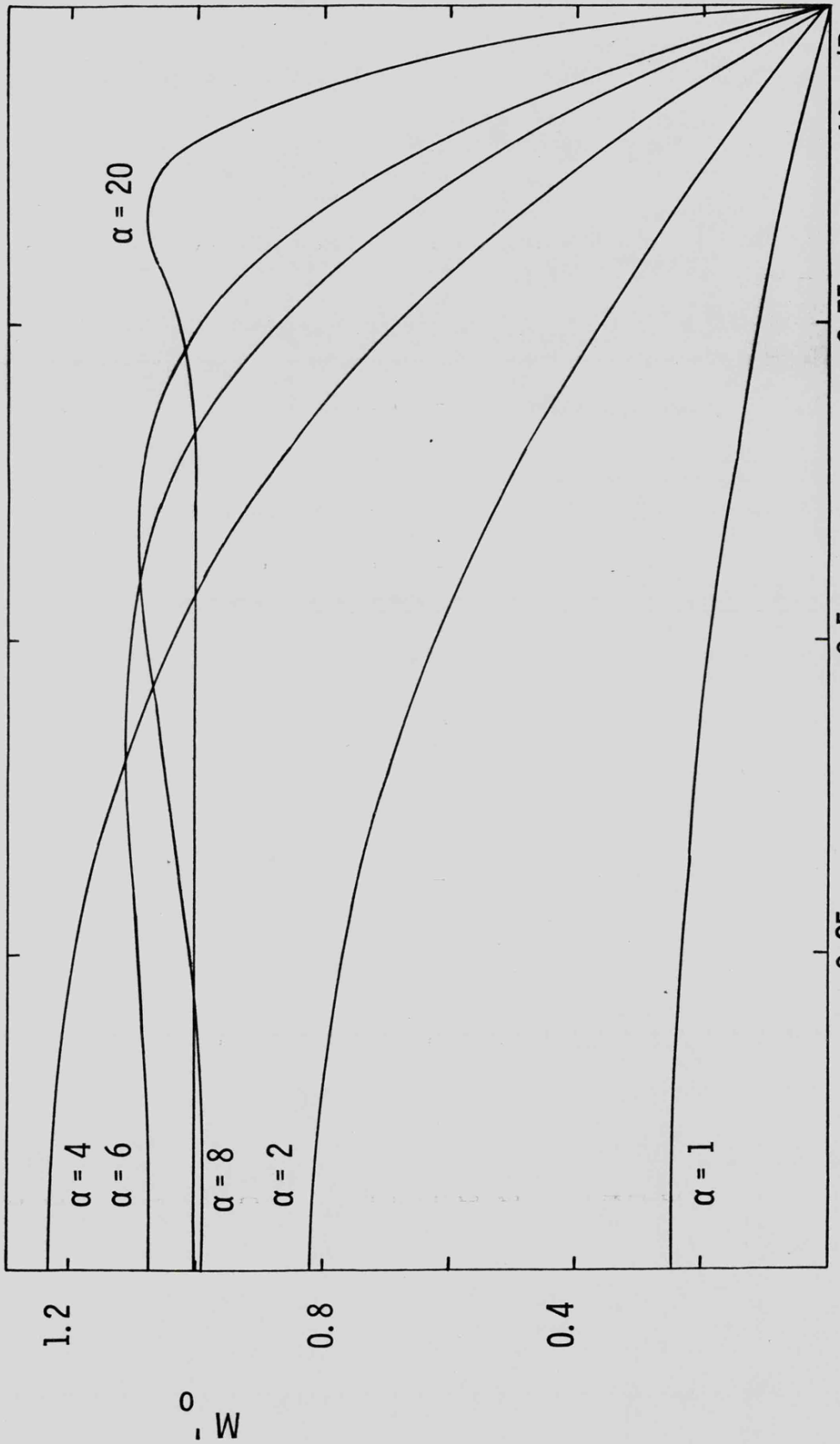


Figure A.1. The function M'_0 plotted against the radial co-ordinate y for various values of α

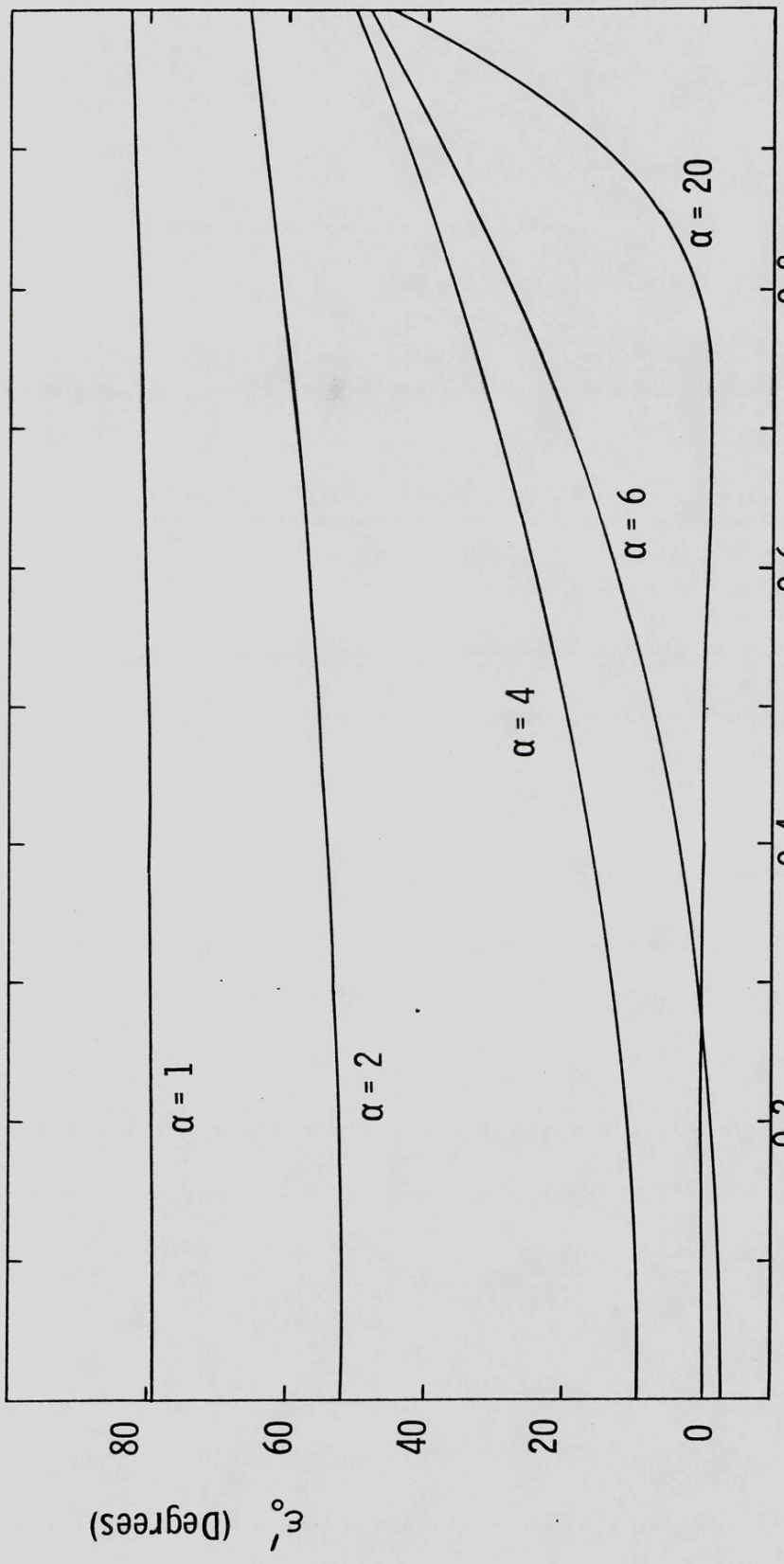


Figure A.2. The function ε_o' plotted against the radial co-ordinate y for various values of α.

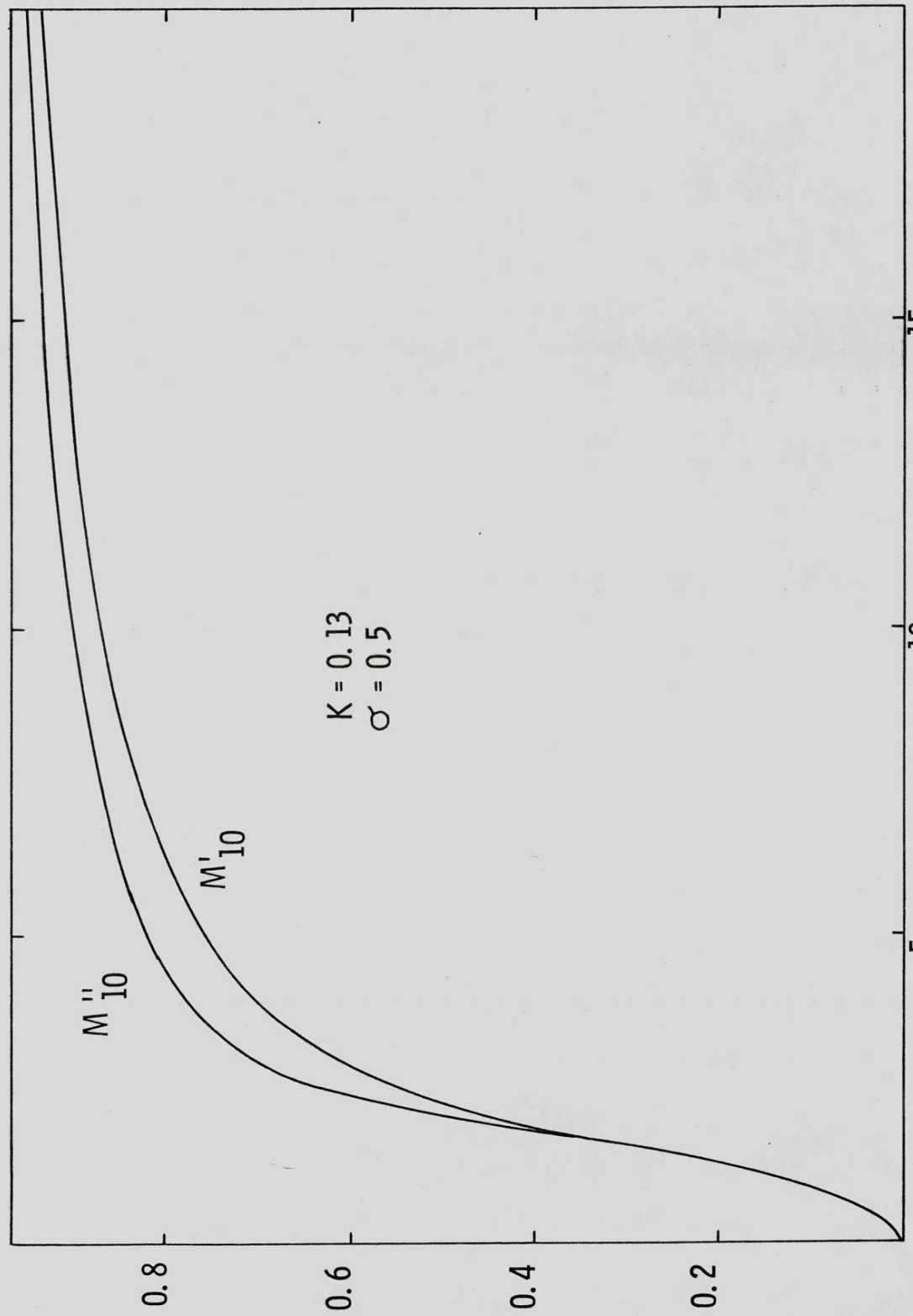


Figure A 3. The variation of M'_{10} and M''_{10} with α

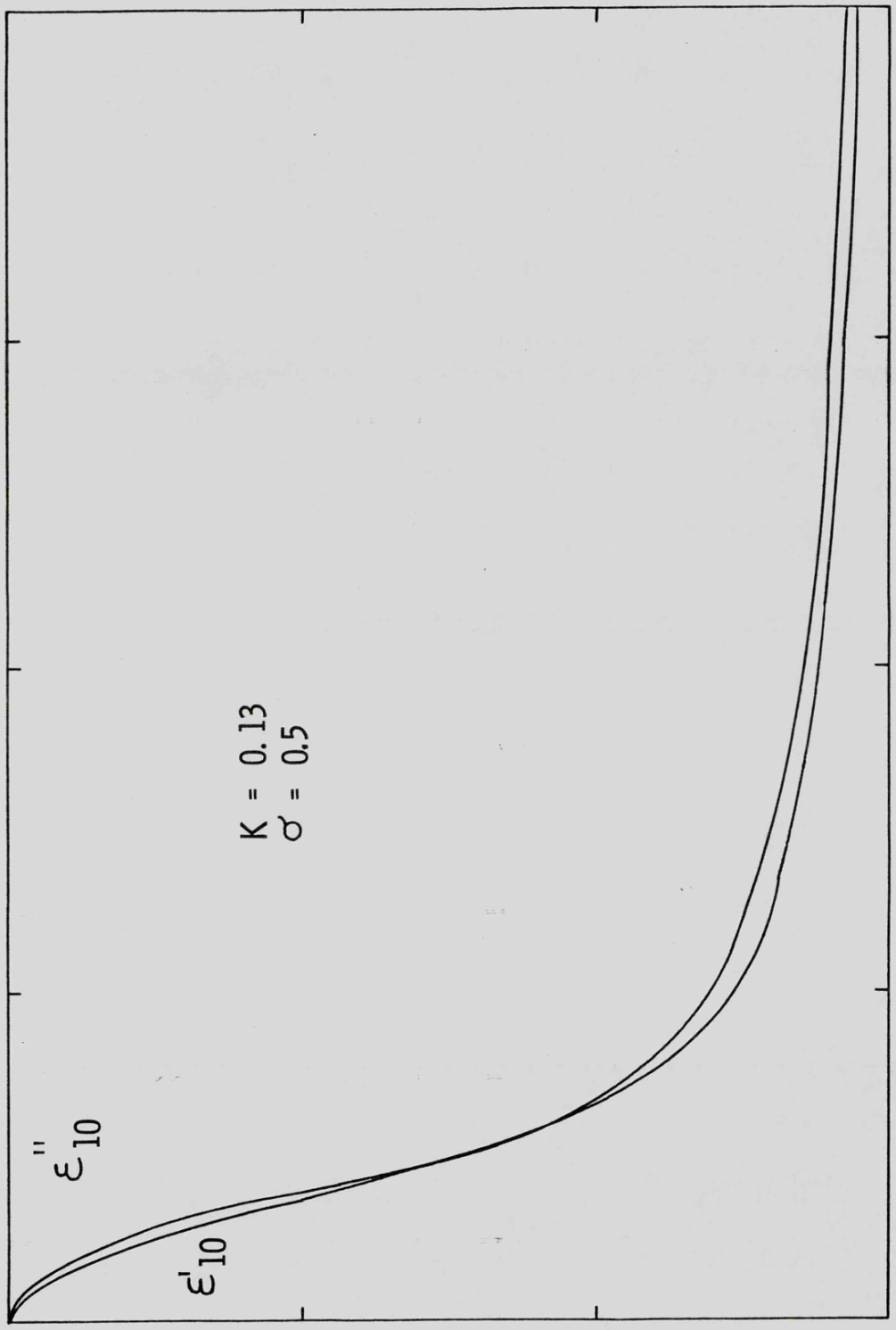


Figure A.4. The variations of ε'_{10} and ε''_{10} with α

The Relationship Between Pressure Difference and Flow Harmonics in a Non-linear System

Equation 2.38 forms a useful description of the relationship between pressure difference across, and flow through an arterial stenosis. Unfortunately the presence of the modulus of flow makes it impossible to relate the harmonics of pressure difference and flow to each other, however, if $Q|Q|$ is replaced by Q^2 then the problem becomes considerably more straightforward. Assuming there is no reverse flow equation 2.38 may be rewritten

$$\Delta P = AQ + BQ^2 + C\frac{dQ}{dt} \qquad A2.1$$

Also, provided that the flow is periodic, Q(t) may be expressed as a Fourier series:-

$$Q(t) = \sum_{n=o}^{\infty} Qa_n \cos nwt + Qb_n \sin nwt \qquad A2.2$$

and Qa_p and Qb_p can be found from equation A2.3 and A2.4 ($P > 0$, for $P=0$ equation A2.3 must be divided by two.)

$$Qa_p = \frac{2}{T}\int_o^T Q(t) \cos pt \ .dt \qquad A2.3$$

$$Qb_p = \frac{2}{T}\int_o^T Q(t) \sin pt. \ dt \qquad A2.4$$

Substituting A2.2 into A2.1 the p^{th} harmonic ($p > 0$) of the pressure difference will be given by

$$P_p = \Big\{ AQa_p + \frac{2B}{T}\int_o^T \sum_{n=o}^{\infty}\sum_{m=o}^{\infty} (Qa_n Qa_m\ Z_1 + Qb_n Qb_m\ Z_2$$

$$+ Qa_n Qb_m\ Z_3 + Qb_n Qa_m\ Z_4)dt + pw\ CQb_p \Big\} \cos pwt$$

$$+ \Big\{ AQb_p + \frac{2B}{T}\int_o^T \sum_{n=o}^{\infty}\sum_{m=o}^{\infty} (Qa_n Qa_m\ Z_5 + Qb_n Qb_m\ Z_6$$

$$+ Qa_n Qb_m\ Z_7 + Qb_n Qa_m\ Z_8)dt - pw\ CQa_p \Big\} \sin pwt \qquad \text{A2.5}$$

where Z_1 to Z_8 are defined below

Z_1 = cos nwt. cos mwt. cos pwt.

Z_2 = sin nwt. sin mwt. cos pwt.

Z_3 = cos nwt. sin mwt. cos pwt.

Z_4 = sin nwt. cos mwt. cos pwt.

Z_5 = cos nwt. cos mwt. sin pwt.

Z_6 = sin nwt. sin mwt. sin pwt.

Z_7 = cos nwt. sin mwt. sin pwt.

Z_8 = sin nwt. cos mwt. sin pwt.

The intergrals of Z_1 to Z_8 can be evaluated as follows:-

$$\frac{2}{T}\int_o^T Z_1.dt = \frac{1}{T}\int_o^T \cos(m+n)wt.\cos pwt.dt + \frac{1}{T}\int_o^T \cos(m-n)wt.\cos pwt.dt$$

$= 0 \quad p \neq m+n$ $\qquad$ $= \frac{1}{2} \quad p = m-n$

$= \frac{1}{2} \quad p = m+n$ $\qquad$ $= \frac{1}{2} \quad p = n-m$

$= 0$ otherwise

$$\frac{2}{T}\int_o^T Z_2.dt=\frac{1}{T}\int_o^T \cos(m-n)\ wt\ \cos\ pwt.dt-\frac{1}{T}\int_o^T \cos\ (m+n)wt.\ \cos\ pwt.dt$$

$= \frac{1}{2}$ p=m-n $\qquad$ $= -\frac{1}{2}$ p=m+n

$= \frac{1}{2}$ p=n-m $\qquad$ $= 0$ $p \neq m+n$

$= 0$ otherwise

$$\frac{2}{T}\int_o^T Z_3.dt = 0 \qquad \frac{2}{T}\int_o^T Z_4.dt = 0$$

$$\frac{2}{T}\int_o^T Z_5.dt = 0 \qquad \frac{2}{T}\int_o^T Z_6.dt = 0$$

$$\frac{2}{T}\int_o^T Z_7.dt = \frac{1}{T}\int_o^T \sin(m+n)wt\ \sin\ pwt.dt+\frac{1}{T}\int_o^T \sin(m-n)wt.\ \sin\ pwt.dt$$

$= 0$ $p \neq m+n$ $\qquad$ $= \frac{1}{2}$ p=m-n

$= \frac{1}{2}$ p=m+n $\qquad$ $=-\frac{1}{2}$ p=n-m

$= 0$ $p \neq m-n$ or n-m

$$\frac{2}{T}\int_o^T Z_8.dt=\frac{1}{T}\int_o^T \sin(m+n)wt\ \sin\ pwt\ dt+\frac{1}{T}\int_o^T \sin(n-m)wt\ \sin\ pwt\ dt$$

$= 0$ $p \neq m+n$ $\qquad$ $= \frac{1}{2}$ p=n-m

$= \frac{1}{2}$ p=m+n $\qquad$ $=-\frac{1}{2}$ p+m-n

$= 0$ $p \neq m-n$ or n-m

Equation A2.5 may thus be rewritten

$$\Delta Pp(t) = \Big[AQa_p+B/2 \sum_{n=o}^{\infty} \sum_{m=o}^{\infty} \Big\{ (Qa_n Qa_m - Qb_n Qb_m).\delta(p,m+n)$$

$$+ \quad (Qa_n Qa_m + Qb_n Qb_m) \cdot \delta(p,m-n) + (Qa_n Qa_m + Qb_n Qb_m) \cdot \delta(p,n-m) \Big\}$$

$$+ \quad C\, pw\, Qb_p \Big] \cos pwt$$

$$+ \quad \Big[AQb_p + B/2 \sum_{n=o}^{\infty} \sum_{m=o}^{\infty} \Big\{ Qa_n Qb_m + Qb_n Qa_m) \cdot \delta(p,m+n)$$

$$+ \quad (Qa_n Qb_m - Qb_n Qa_m) \cdot \delta(p,m-n) + (Qb_n Qa_m - Qa_n Qb_m) \cdot \delta(p,n-m) \Big\}$$

$$- \quad CpwQa_p \Big] \sin pwt$$

where $\delta(u,v)$ is Kronecker's delta given by

$$\delta(u,v)=1 \quad u=v \quad ; \quad \delta(u,v) = 0 \qquad u \neq v$$

APPENDIX THREE

Separation of Forward and Reverse Doppler Signals

Figure A-5 shows diagramatically the way in which a returning Doppler signal is processed in order to obtain forward and reverse components offset about a pilot frequency.

The received signal V_{in}, is composed of three terms in this particular example, a signal at the transmitted frequency, $A_s \cos w_c t$; a signal due to movement towards the probe, $A_f \cos(w_c+w_f)t$; and a signal due to movement away from the probe, $A_r \cos(w_c-w_r)t$. This total signal is mixed with two quadrature signals, $\sin w_c t$, and $\cos w_c t$, to obtain the signals V_1 and V_2 which are then low-pass filtered to give V_a and V_b. V_a and V_b may be calculated as follows

$$V_1 = A_s \cos w_c t . \sin w_c t + A_f \cos(w_c+w_f)t . \sin w_c t$$

$$+ A_r \cos(w_c-w_r)t . \sin w_c t$$

which may be written

$$V_1 = \frac{A_s}{2} \sin(2w_c)t + \frac{A_f}{2} \left\{ \sin(2w_c+w_f)t + \sin(-w_f)t \right\}$$

$$+ \frac{Ar}{2} \left\{ \sin(2w_c-w_r)t + \sin(w_r) \right\}$$

which after filtering out all components of the order w_c leaves

$$V_a = -\frac{A_f}{2} \sin w_f t + \frac{A_r}{2} \sin w_r t$$

Similarly, V_2 may be expanded to give

$$V_2=\frac{A_s}{2}(1+\cos 2w_c t) + \frac{A_f}{2}\left\{\cos w_f t+\cos (2w_c+w_f)t\right\} + \frac{A_r}{2}\left\{\cos -w_r t + \cos (2w_c -w_r)t\right\}$$

which after low pass filtering leaves

$$V_b = \frac{A_f}{2}\cos w_f t + \frac{A_r}{2}\cos w_r t + \frac{A_s}{2}$$

The A.C. components of V_a and V_b are then mixed with $\sin w_p t$ and $\cos w_p t$ respectively, and the two resultants summed to leave the forward and reverse components of the Doppler signal offset about the pilot frequency w_p.

$$V_{out} = \frac{A_f}{2}\sin w_f t.\sin w_p t + \frac{A_r}{2}\sin w_r t.\sin w_p t + \frac{A_f}{2}\cos w_f t.\cos w_p t + \frac{A_r}{2}\cos w_r t.\cos w_p t$$

which may be expanded to give

$$V_{out} =-\frac{A_f}{4}\left\{\cos(w_f-w_p)t-\cos(w_f+w_p)t\right\} + \frac{A_r}{4}\left\{\cos(w_r-w_p)t-\cos(w_r+w_p)t\right\} + \frac{A_f}{4}\left\{\cos(w_f-w_p)t+\cos(w_f+w_p)t\right\} + \frac{A_r}{4}\left\{\cos(w_r-w_p)t+\cos(w_r+w_p)t\right\}$$

or $$V_{out} = \frac{A_f}{2}\cos(w_f+w_p)t + \frac{A_r}{2}\cos (w_r-w_p)t$$

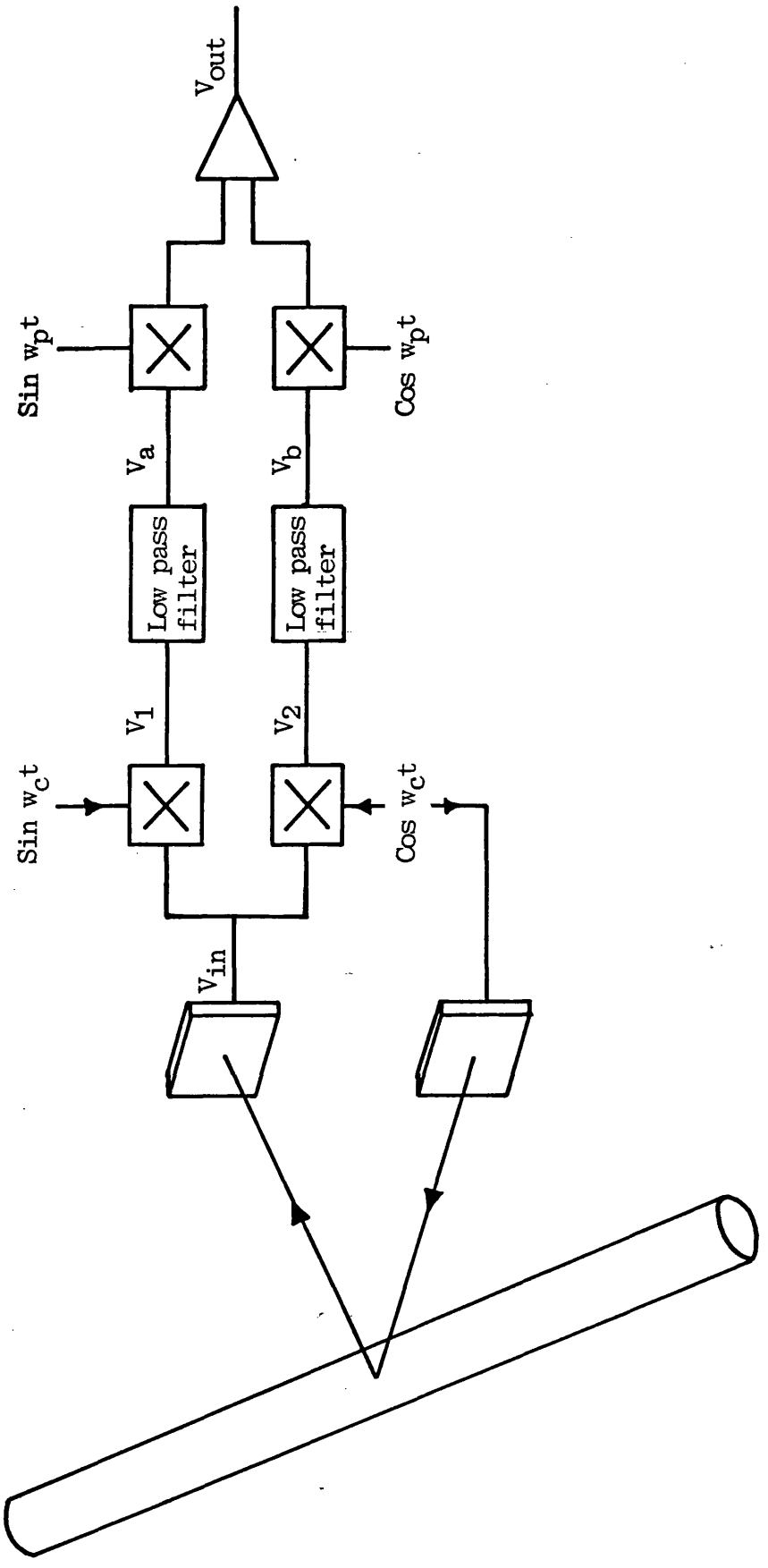


Figure A-5 Schematic diagram of the seperation of the forward and reverse components of the Doppler signal.

APPENDIX FOUR

The Calculation of the Ultrasonic Beam Shape

The theoretical beam shape of the Sonicaid Ultrasonic Doppler velocimeter was calculated on the Leicester University C.D.C. Cyber 72 computer. Each crystal of the transducer was assumed to move sinusoidally in a piston-like fashion, and the characteristics of transmitting and receiving crystal were assumed to be identical. Each crystal was divided into a large number of small elements and the total intensity of ultrasound at each point in the field was calculated by summing the contributions from each element.

The first stage of the "calculation" was to measure the dimensions, separation and orientation of the crystals. The first two parameters were found using a travelling microscope, whilst the orientation was measured ultrasonically. This was achieved by mounting the transducer in a test rig, exciting each crystal with short pulses of ultrasound, and finding the point in the plane at several distances from the transducer at which a target gave the largest echoes at the same crystal. The target used was a small ball-bearing which acted as a point reflector. Previous computation had shown that the maximum intensity of the ultrasonic field due to a single rectangular crystal, always occurs at its centre, and thus it was possible to calculate the orientation of each crystal from these intensity measurements. Each crystal was found to measure 2mm x 5mm and to be inclined at 7.5^{o} to the centre line of the transducer. The centres of the two crystals were found to be 2.75mm apart.

For the purpose of calculating the ultrasonic beam shape each crystal was divided into 4000 equally sized elements, and the ultrasonic intensity at each point in the field obtained by summing the contributions due to each of these elements. The total effect of the transmitting and receiving crystals was calculated at 100 points on a 10mm by 10mm matrix at distances of 5, 10, 15 and 20mm from the crystal. This matrix was calculated so that one of its corners corresponded to the centre of the beam. It was then possible to form a 20mm x 20mm matrix by reflecting the values obtained about the x and y axes thus taking advantage of the two-fold symmetry of the field. Figures 4.7 a-d were plotted on the Leicester University graph plotter using the 'Culham Ghost' routine 'contra'.

Finally, experimental measurements were made on the Sonicaid transducer employing the same test rig as was used for determining the orientation of the beam, the only difference being that both crystals were used at the same time, one in a transmitting mode, and one in a receiving mode. Once again pulsed ultrasound was used to ensure that the returning echo originated from the target. Each pulse had a duration of about ten cycles to ensure a field distribution similar to a steady state distribution. Measurements of intensity were made along the two axes of symmetry at 5, 10, 15 and 20mm from the transducer face. The general shapes of the results were the same as the theoretical results although they differed in detail. These differences were presumed to be due to the inadequacies of the idealised theoretical model used. It would have been impossible to predict the results found by experiment exactly

as they were not even symmetrical where expected.

The results shown in Figure 4.7 a-d are a useful guide to the ultrasonic beam shape generated by the Sonicaid Doppler Velocimeter.

APPENDIX FIVE

Mathematical Analysis of Fluid-linked Manometer Systems

The motion of a fluid linked manometer system may be described by the linear second order differential equation A5.1 (see section 4.3.2)

$$M\frac{d^2x}{dt^2} + R\frac{dx}{dt} + Sx = SK\cos wt \qquad A5.1$$

where M is the lumped mass, R the damping and S the stiffness of the system, the solution of this equation is composed of two parts, the complementary function and particular solution.

The complementary function is found by solving the equation

$$M\frac{d^2x}{dt^2} + R\frac{dx}{dt} + Sx = 0 \qquad A5.2$$

Assuming the solution to be of the form $x_c=\exp(\alpha t)$, then

$$x_c=C_1\exp\left\{-\beta_o+(\beta_o^2-w_o^2)^{\frac{1}{2}}\right\}t + C_2\exp\left\{-\beta_o-(\beta_o^2-w_o^2)^{\frac{1}{2}}\right\}t \qquad A5.3$$

where $\beta_o = R/2M$ and $w_o^2 = S/M$

If when t = 0 the system is at the limit of its travel, then dx/dt = 0 and x = A. Thus

$$x_{(t=o)} = C_1 + C_2 = A \qquad A5.4$$

and $$\frac{dx}{dt}_{(t=o)} = C_1\left\{-\beta_o+(\beta_o^2-w_o^2)^{\frac{1}{2}}\right\} + C_2\left\{-\beta_o-(\beta_o^2-w_o^2)^{\frac{1}{2}}\right\} = 0 \qquad A5.5$$

thus

$$C_1=\frac{A}{2}\left\{1+\frac{\beta_o}{(\beta_o^2-w_o^2)^{\frac{1}{2}}}\right\} \quad C_2=\frac{A}{2}\left\{1-\frac{\beta_o}{(\beta_o^2-w_o^2)^{\frac{1}{2}}}\right\}$$

Most practical manometer systems are underdamped and thus

$$\beta_o < w_o$$

Therefore $(\beta_o^2-w_o^2)^{\frac{1}{2}}=i(w_o^2-\beta_o^2)^{\frac{1}{2}}$ where the quantity in the brackets is real, and equation A5.3 may be written

$$x_c=\frac{A}{2}\exp(-\beta_o t)\left\{2\cos(w_o^2-\beta_o^2)^{\frac{1}{2}}t+2i\frac{\beta_o}{(w_o^2-\beta_o^2)^{\frac{1}{2}}}\sin(w_o^2-\beta_o^2)^{\frac{1}{2}}t\right\} \quad \text{A5.5}$$

or

$$x_c=\frac{Aw_o^2}{w_o^2-\beta_o^2}\exp(-\beta_o t)\cos\left\{(w_o^2-\beta_o^2)t-\tan^{-1}\frac{\beta_o}{(w_o^2-\beta_o^2)^{\frac{1}{2}}}\right\} \quad \text{A5.6}$$

It will be noted that if R=0, i.e. there is no damping then $\beta_o=0$ and $x=A\cos w_o t$, and thus w_o is the natural frequency of an undamped system.

The particular solution to equation A5.1 $x_p(t)$ can be found by assuming the solution takes the form of a periodic function. Assuming then

$$x_p = A\sin wt + B\cos wt \quad \text{A5.7}$$

we have

$$-M(w^2A \sin wt + w^2B \cos wt) + RwA \cos wt - Rw\,B \sin wt$$

$$+ SA \sin wt + SB \cos wt = SK \cos wt \qquad \text{A5.8}$$

Equating the sine and cosine terms

$$A = \frac{SKRw}{(Rw)^2+(S-Mw^2)^2} \qquad B = \frac{SK(S-Mw^2)}{(Rw)^2+(S-Mw^2)^2}$$

Now combining the sine and cosine contributions

$$x_p = \frac{SK}{\{(Rw)^2+(S-Mw^2)^2\}^{\frac{1}{2}}} \cos\left\{wt - \tan^{-1}\left(\frac{Rw}{S-mw^2}\right)\right\} \qquad \text{A5.9}$$

Recalling that $w_o^2 = S/M$ and $\beta_o = R/2M$ it is possible to eliminate R, S and M.

Thus

$$x_p = K\left\{(1-\gamma^2)^2 + 4\beta^2\gamma^2\right\}^{-\frac{1}{2}} \cos\left\{wt-\tan^{-1}\left(\frac{2\beta\gamma}{1-\gamma^2}\right)\right\} \qquad \text{A5.10}$$

where $\gamma = w/w_o$ and $\beta = \beta_o/w_o$

APPENDIX SIX

CALCULATION OF VELOCITY PROFILES FROM INSTANTANEOUS VOLUMETRIC FLOWS

It will be recalled from Chapter two that the equation of motion of flow of a viscous liquid in a long straight circular tube under the influence of a periodic pressure gradient may be written

$$\frac{\partial w}{\partial t} = \frac{-1}{\rho}\frac{\partial p}{\partial z} + \nu\left(\frac{\partial^2 w}{\partial r^2} + \frac{1}{r}\frac{\partial w}{\partial r}\right) \qquad \text{A6.1}$$

If the periodic pressure gradient is written in terms of an exponential, $dp/dz = A^* e^{i\omega t}$, then the solution for the velocity, w, of a lamina at a distance $y = r/R$ from the axis is given by

$$w = \frac{A^*}{i\omega\rho}\left\{1 - \frac{J_o(\alpha y i^{3/2})}{J_o(\alpha i^{3/2})}\right\} e^{i\omega t} \qquad \text{A6.2}$$

(Womersley 1957a). The instantaneous volumetric flow may be obtained from equation A6.2, by integrating over the area of the tube to give equation A6.3

$$Q = \frac{\pi R^2 A^*}{i\omega\rho}\left[1 - \frac{2J_1(\alpha i^{3/2})}{\alpha i^{3/2} J_o(\alpha i^{3/2})}\right] e^{i\omega t} \qquad \text{A6.3}$$

Given Q, the instantaneous volumetric flow, it is thus possible to calculate w as a function of α and y.

$$w = \frac{Q}{\pi R^2}\cdot\left(\frac{\tau J_o(\tau) - \tau J_o(y\tau)}{\tau J_o(\tau) - 2J_1(\tau)}\right) \qquad \text{A6.4}$$

where $\tau = \alpha i^{3/2}$. If Q is now expressed as a Fourier series.

i.e: $$Q = Q_o + \sum_{n=1}^{\infty} Q_n \cos(n\omega_n t - \phi_n) \qquad \text{A6.5}$$

and the term in the large bracket of equation A6.4 is written Ψ, having a phase ε_ψ and modulus $|\psi|$, the velocity of a single lamina may be written

$$w = \frac{1}{\Pi R^2}\left\{ 2Q_o(1-y^2) + \sum_n Q_n |\Psi|_n \cos(\omega_n t - \phi_n + \varepsilon_{\psi n}) \right\} \quad \text{A6.}$$

$|\Psi|$ and ε_ψ are plotted against y for various values of α in Figures A6 and A7.

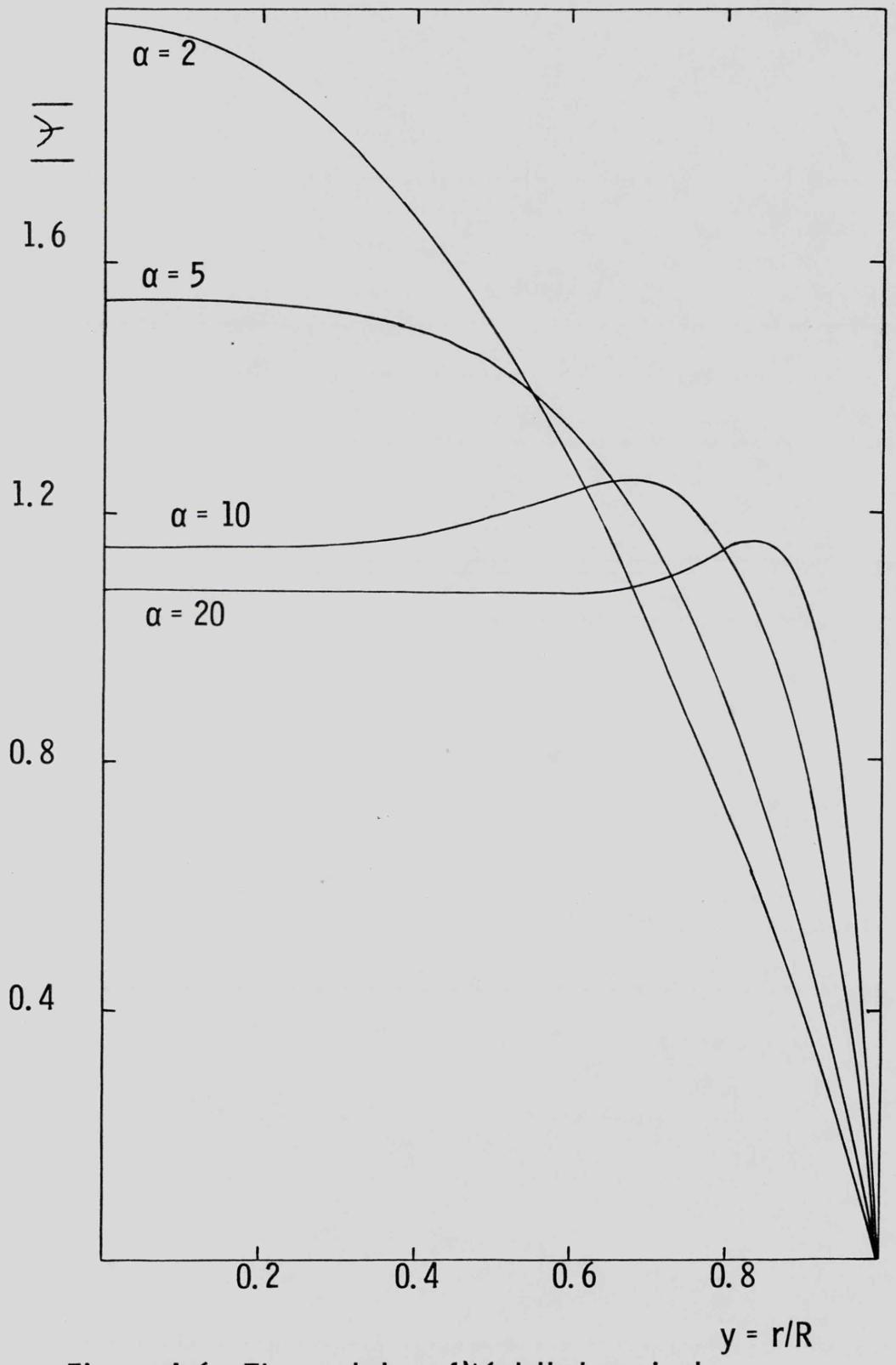


Figure A 6. The modulus of Ψ plotted against the radial co-ordinate y for various values of α. See appendix six.

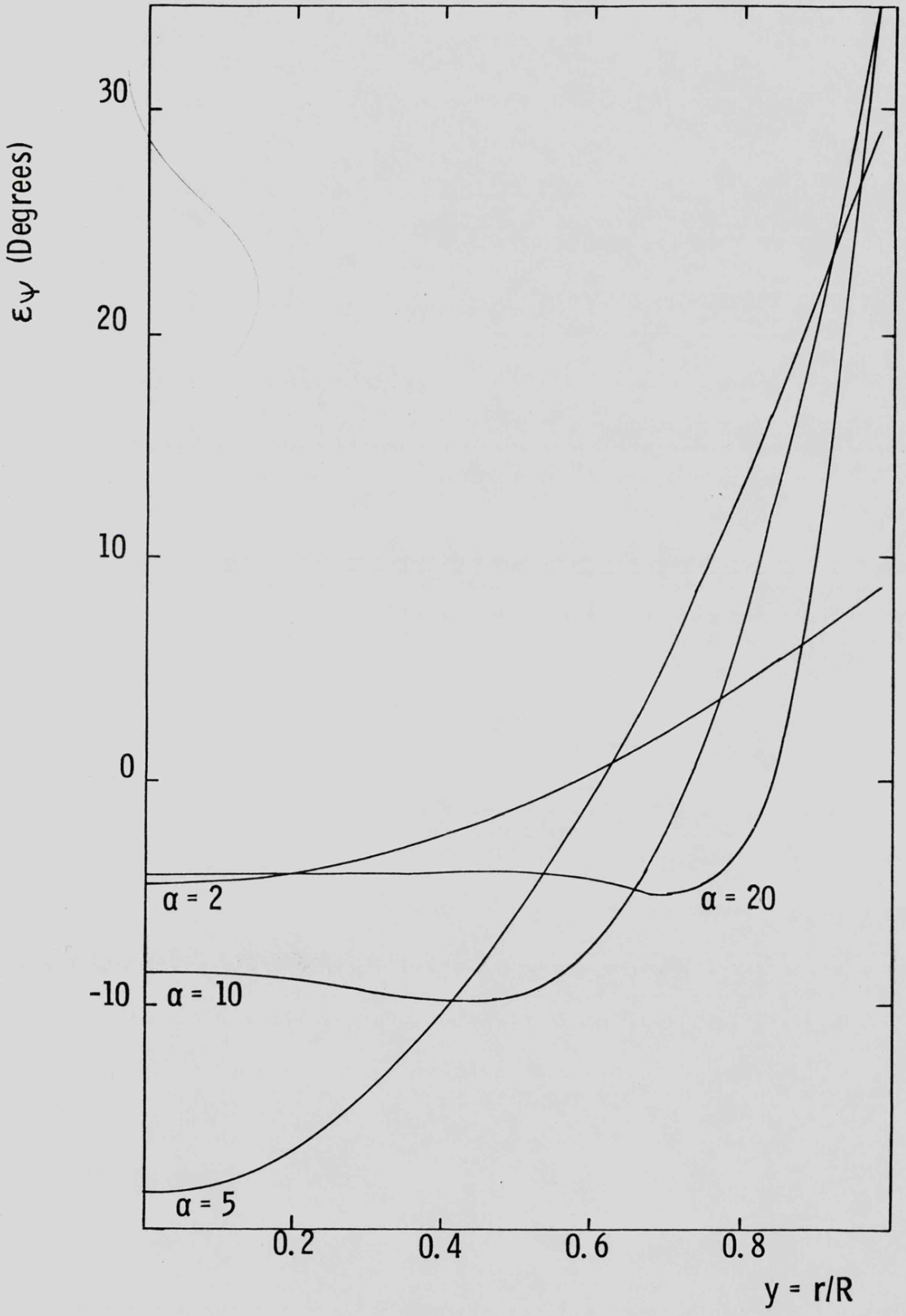


Figure A7. The phase of Ψ plotted against the radial co-ordinate y for various values of α.

APPENDIX SEVEN

A THEORETICAL SOLUTION FOR THE EFFECT OF INFLATING A PNEUMATIC CUFF ON A HEALTHY ARTERY

It seems likely that the inflation of a pneumatic cuff around a limb will change the pressure distribution within the arteries of that limb by modifying the reflected waves. A simple calculation based on transmission line theory suggests that this change could be of the order of 10%.

The general solutions for the voltage and current distributions along infinite electrical transmission lines are well known (Connor F.R. 1972), and may be written as equations A7.1 and A7.2 if pressure (P) is substituted for voltage, and flow (Q) for current

$$P(x) = P_s \cosh \gamma x - Q_s Z_o \sinh \gamma x \qquad \text{A7.1}$$

$$Q(x) = Q_s \cosh \gamma x - \frac{P_s}{Z_o} \sinh \gamma x \qquad \text{A7.2}$$

Z_o is the characteristic impedence of the line, γ the propagation coefficient, and the subscript 's' denotes 'source' or 'sending'.

These equations may be modified and combined to give equation A7.3 for the pressure distribution along a finite artery occluded with a pneumatic cuff. l is the total length of the artery

$$P(x) = P_s(\cosh \gamma x - \tanh \gamma l \sinh \gamma x) \qquad \text{A7.3}$$

Expressing the hyperbolic functions in exponential form it can be shown

$$P(x) = P_s \frac{\exp(\gamma(x-\ell)) + \exp(\gamma(\ell-x))}{\exp(\gamma\ell) + \exp(-\gamma\ell)} \qquad \text{A7.4}$$

Now writing $y = 1-x$, and the propagation coefficient $\gamma = a+j\beta$, where a is an attenuation coefficient and β a phase change coefficient

$$P(x) = P_s \left\{ \frac{\cosh(ay+j\beta y)}{\cosh(a\ell+j\beta\ell)} \right\} \qquad \text{A7.5}$$

The amplitude and phase of P(x) may be found from equations A7.6 and A7.7 respectively.

$$\left| P(x) \right| = P_s \left\{ \frac{\cosh 2ay+\cos 2\beta y}{\cosh 2a\ell+\cos 2\beta\ell} \right\}^{\frac{1}{2}} \qquad \text{A7.6}$$

$$\text{Phase}\left\{P(x)\right\} = \tan^{-1}(\tanh ay \tan \beta y) - \tan^{-1}(\tanh a\ell \tan \beta\ell) \qquad \text{A7.7}$$

The values of a and β depend upon the assumptions that are made about the artery and blood. For the purposes of this calculation Womersley's visco-elastic model was used, in which the blood is assumed to be a viscous fluid flowing through a visco-elastic tube. Womersley defined a complex wave velocity c such that

$$\frac{c_o}{c} = X-jY = \left(\frac{1-\sigma^2}{M'_{10}}\right)^{\frac{1}{2}} \exp(-j\varepsilon'_{10}/2)\ \{1-jnT\} \qquad \text{A7.8}$$

where c_o is the Moens-Korteweg velocity and

$T = \Delta E/2 + \Delta\sigma/3$. (see equations 2.9 and 2.11 to 2.20).

M'_{10} and ε'_{10} are the functions described in Appendix one, σ Poisson's ratio, n the angular frequency, and E Young's modulus.

The phase velocity c_1 is given by c_o/X, and thus

$$\beta = \frac{nX}{c_o} = \frac{n}{c_o}\left(\frac{1-\sigma^2}{M'_{10}}\right)^{\frac{1}{2}}\left\{\cos\left(\frac{\varepsilon'_o}{2}\right) - nT\sin\left(\frac{\varepsilon'_o}{2}\right)\right\} \qquad \text{A7.9}$$

The attenuation coefficient a is given by

$$a = \frac{nY}{c_o} = \frac{n}{c_o}\left(\frac{1-\sigma^2}{M'_{10}}\right)^{\frac{1}{2}}\left\{\sin\left(\frac{\varepsilon'_o}{2}\right) + nT\cos\left(\frac{\varepsilon'_o}{2}\right)\right\} \qquad \text{A7.10}$$

The values of a and β are dependent on frequency and so in order to calculate the shape of a wave at various points along the artery it is necessary to find the Fourier components of the waveform at a known point along the line, modify each according to equations A7.6, A7.9 and A7.10, and then perform an inverse transform. This procedure was carried out on a typical pressure waveform recorded from the femoral artery of a patient. The way in which its shape at the termination varied with the total length of the line was computed, as were the theoretical systolic pressure levels. These values were found to vary widely depending on the length of the artery as shown in figure A.8.

This calculation can only be regarded as being very rough as the tapering and branching of the artery was ignored, and the source waveform was taken from the femoral artery of a patient with disease. The variation of the systolic pressure is however quite large and it might be concluded that inflatable cuffs do indeed change the pressure distribution within arteries significantly.

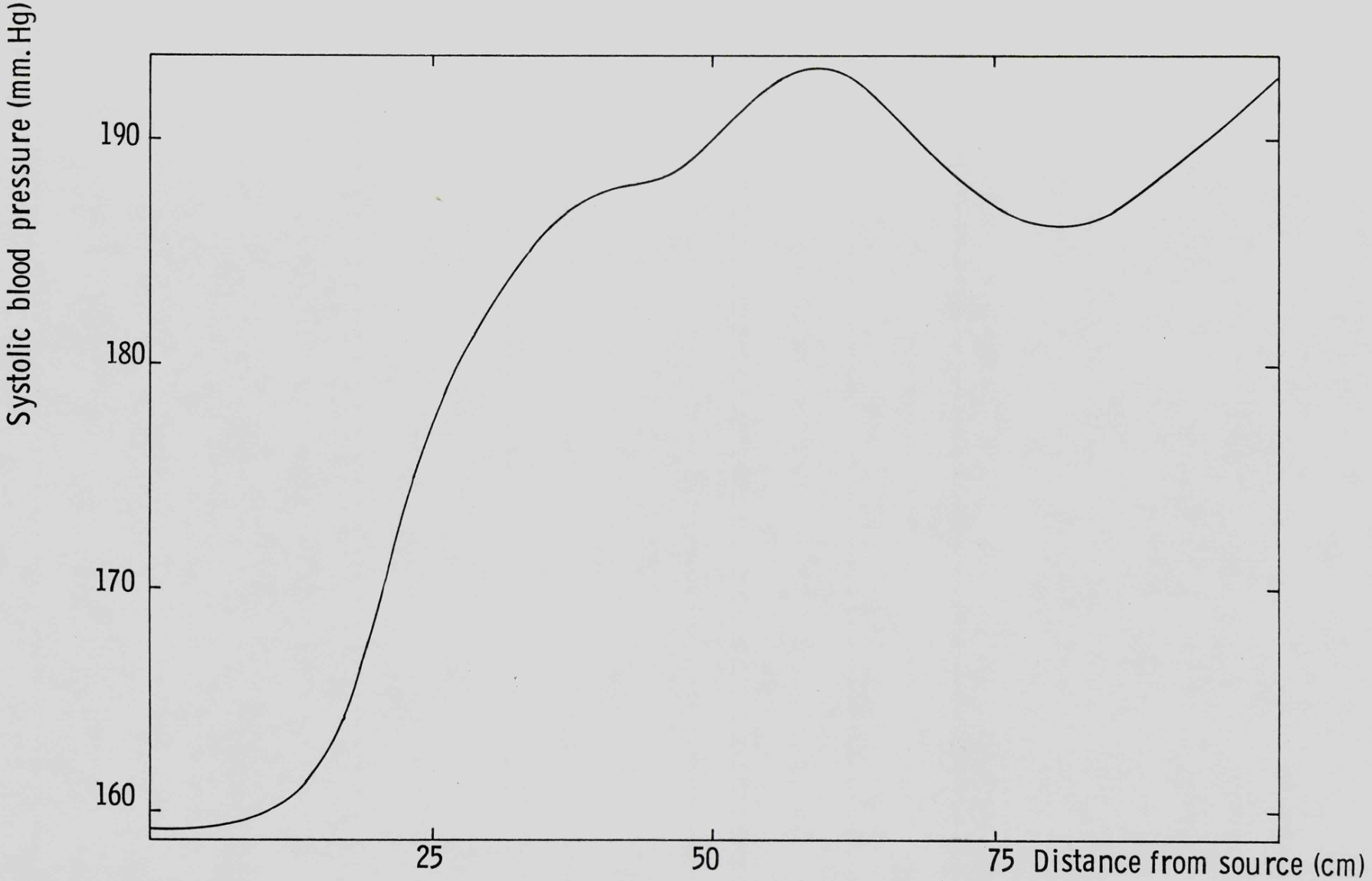


Figure A.8. The effect of measuring occlusive cuff pressure at various distances from the source.

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