VENOUS ULCERATION: A CLINICAL AND LABORATORY INVESTIGATION

By

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BSc MB ChB FRCS

A thesis submitted for the degree of

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From

The Department of Surgery, The University of Leicester.

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The work on which this thesis is based is my own independent work except where acknowledged

J. M. Scriven

March 1999
Dedicated to Sharon and Lucy.
A Thesis Submitted for the Degree of Doctor of Medicine.

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Abstract

Venous ulceration is currently managed in a variety of clinical settings using various methods achieving variable results. No agreement exists advising on management strategies for venous ulceration. The aim of this thesis was to address this deficiency by examining the operative and non-operative treatment of venous leg ulcers.

Colour duplex scanning, ambulatory venous pressure measurements and photoplethysmography were used to define the venous abnormalities described and document the effects on venous haemodynamics of surgical interventions. The non-operative management of ulceration was addressed within a prospective randomised trial comparing four layer and short stretch compression bandages. The effects of saphenous vein surgery on ulcer healing and venous haemodynamics were assessed in limbs with superficial reflux alone or in combination with deep venous reflux. Similarly, perforating vein surgery was studied in limbs with co-existing full length deep reflux. A minimally invasive technique for the correction of popliteal vein reflux was developed.

Colour duplex scanning is recommended to define the underlying venous abnormality and individual ulcer management should be based on these findings. Thus: in the presence of full length deep venous reflux neither saphenous nor perforating vein surgery has a beneficial role; these limbs require compression bandaging. Where compression bandaging is required short stretch or four layer are of equal efficacy but four layer are probably safer in very oedematous or very thin limbs. An alternative multi-layer bandage is described. In limbs with saphenous reflux alone, disconnection of the saphenous system results in rapid ulcer healing without associated compression therapy and an ongoing haemodynamic improvement. Limbs requiring popliteal venous valve reconstruction may benefit from the endovenous technique described.
SYNOPSIS

The work described in this thesis was intended to explore a number of controversies pertaining to the clinical management of patients with venous ulceration. Chapter 1 provides an introduction to the thesis and Chapter 2 describes chronic venous insufficiency and explores the aetiological theories of venous ulceration, methods of clinical investigation and describes the treatment of venous ulceration using operative and non-operative approaches. Six investigative chapters follow. Chapter 3 describes the patterns of venous reflux encountered in patients with ulceration by examining the work of a dedicated venous ulcer clinic during a 12 month period. Chapter 4 reports the results of a prospective randomised trial comparing the efficacy of four layer and short stretch compression bandages. In addition the sub-bandage pressure profiles of four layer and short stretch bandages are described with respect to individual component layers and overall performance. Finally in this chapter the development of a fully FP10 prescribable multi-layer bandage is described.

The operative treatment of venous ulceration is examined in the remaining chapters. Chapter 5 examines the role of saphenous vein surgery and the value of pneumatic cuffs to predict the outcome of saphenous vein surgery. The controversial role of perforating vein surgery is examined in Chapter 6, and Chapter 7 describes the improved efficacy obtained by basing the treatment of venous ulceration be this surgical or non surgical on the specific pattern of venous reflux on an individual patient basis.

Chapter 8 reports a laboratory model to devise an endovenous device for the correction of popliteal vein reflux and the subsequent use of this device in a patient.

Finally, the results are reviewed and areas for future research are discussed.
ACKNOWLEDGEMENTS

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The Talley Two Oxford Pressure Monitor was provided courtesy of Vernon Carus Limited, and Johnson & Johnson Interventional System Limited provided the stents, balloons and moneys for ongoing clinical work with regards to deep venous stenting to them I am grateful.
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<tr>
<td>ABPI</td>
<td>ankle brachial pressure index</td>
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<tr>
<td>ANOVA</td>
<td>analysis of variance</td>
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<td>APG</td>
<td>airplethysmography</td>
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<td>AVP</td>
<td>ambulatory venous pressure</td>
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<td>CFV</td>
<td>common femoral vein</td>
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<td>CVI</td>
<td>chronic venous insufficiency</td>
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<td>df</td>
<td>degrees of freedom</td>
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<td>dL</td>
<td>decilitre</td>
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<td>DVT</td>
<td>deep venous thrombosis</td>
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<td>EF</td>
<td>ejection fraction</td>
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<td>EV</td>
<td>ejection volume</td>
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<td>FLB</td>
<td>four layer bandage</td>
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<td>FP10</td>
<td>family practitioner 10</td>
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<td>g</td>
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<td>Hb</td>
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<td>LDS</td>
<td>lipodermatosclerosis</td>
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<td>LRR</td>
<td>light reflection rheography</td>
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<td>LSB</td>
<td>long stretch bandage</td>
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<td>LSV</td>
<td>long saphenous vein</td>
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<td>mmHg</td>
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<td>mmol</td>
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<td>µmol</td>
<td>micromoles</td>
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<td>NHS</td>
<td>National Health Service</td>
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CHAPTER ONE

GENERAL INTRODUCTION

Chronic venous disease and venous ulceration have been recognised by physicians for over 2000 years when 'superficial venous thrombosis' and 'compression therapies' were described as treatments respectively. Unfortunately, advances in the management of venous ulceration have lagged far behind those in other areas of medicine and in particular vascular surgery. The mainstay of treatment for venous ulceration is still compression therapy, using a wide range of products and methods with variable success. The role of venous surgery in the treatment of venous ulceration is often dismissed without serious consideration.

A significant volume of research has been performed into the microvascular pathophysiology responsible for ulceration but fewer data exist on which to base the day to day clinical management of this large population of patients. It would seem logical to examine the role of the underlying venous abnormality as a cause of venous hypertension in an attempt to prevent ulceration and re-ulceration in addition to directing researchers to the end result of such venous hypertension – the 'microangiopathy'. One significant obstacle to venous research is the lack of a suitable means of venous imaging, however, the advent of colour duplex scanning has revolutionised this aspect of venous investigation. It is now possible to examine the venous system of the leg repeatedly and non-invasively with great anatomical accuracy.

The purpose of the studies described in this thesis was to define the venous abnormalities present in a population of patients referred to a dedicated venous
ulceration clinic and to subsequently examine the role of operative and non-operative therapies in terms of clinical efficacy and venous haemodynamics.

Chapter Two reviews the clinical and economic aspects of venous ulceration and describes the current aetiological theories of ulceration. The most commonly used methods of investigating and imaging the venous system in terms of its structure and function are described as well as an appraisal of the various methods of treatment of venous ulceration both conservative and operative.

Chapter Three used colour duplex scanning to characterise the venous abnormalities present in a consecutive series of 88 patients (104 limbs) referred over a 12 month period. This identified superficial venous reflux as the sole venous abnormality in over half the limbs with venous reflux and that this occurred often in the absence of visible varicose veins. In addition, identifiable post-thrombotic venous changes were not as common as previously described and perforating vein reflux was also uncommon, affecting only 42% and 11% of limbs respectively.

A large range of products are available for the non-operative treatment of venous ulcers. One form of compression bandaging in particular, four layer (Charing Cross), is being popularised, and at the time the work in this thesis was underway, the components used in the Charing Cross bandage were not available via the NHS by way of an FP10 prescription. However, alternative components are available and Chapter Four investigates the merits of four layer bandages compared to a popular alternative, the short stretch bandage and concludes that they are of equal efficacy although the four layer system may have an advantage if used in limbs at the extremes of the range of dimension seen in practice. Following on from this study I have described the development of a fully FP10 prescribable alternative with comparable physical properties to the Charing Cross system.
Turning to the operative management of venous ulceration, Chapter Five examines the role of saphenous vein surgery in limbs with saphenous vein reflux alone and those with saphenous and deep venous reflux combined. Colour duplex scanning was used to identify the pattern of reflux in the 25 limbs examined and venous function was assessed pre- and postoperatively using the gold standard test of ambulatory venous pressure measurement. I found that in the absence of deep venous reflux, saphenous vein ligation alone was curative without recourse to adjunctive postoperative compression therapy and resulted in an immediate and ongoing improvement in venous haemodynamics. Whereas, in those limbs with saphenous and deep venous reflux combined saphenous vein ligation was of no value in terms of efficacy or venous haemodynamics. Many rely on the use of tourniquets or pneumatic cuffs to separate those limbs with deep and/ or superficial reflux and on the basis of these cuff tests plan venous surgery. This can only be of value if the tests are accurately predicting the outcome of such surgery; this is examined in Section 5.3. The ability of a 2.5 cm wide cuff to occlude the saphenous system is assessed using colour duplex scanning and photoplethysmography and found to be ineffective at compressing the saphenous system reliably. When compared to saphenous vein disconnection (the ultimate vein 'occluder') I concluded that cuffs were of no useful predictive value in deciding on which limbs to offer saphenous venous surgery. The role of perforating vein surgery is under scrutiny in the U.K. and North America. Chapter Six failed to identify any local venous abnormality using photoplethysmography in the region of calf perforating veins in limbs with associated full length deep venous reflux suggesting that in this group of patients perforating vein surgery is not indicated. I did not examine the role of perforating vein surgery in limbs with normal deep veins because the literature indicates that perforating vein surgery in this situation is not required to achieve ulcer healing and freedom of recurrence in the short-term.
The above research would be of little value if its application conferred no patient benefit. Chapter Seven applies the findings of Chapters 3, 4, 5, and 6 to tailor the prescribed treatment for an ulcer based on the underlying pattern of venous reflux. Patients in whom ulcerated limbs possessed superficial reflux only were offered saphenous vein surgery without perforating vein surgery and those limbs with full length deep venous reflux or who declined superficial venous surgery were offered four layer compression bandaging. When these guidelines were applied over a 12 month period ulcer healing rates rose from 55% at one year to 70% for those limbs treated with four layer bandaging. Those limbs offered surgery achieved an 80% healing rate at one year.

The final experimental chapter (Eight) describes the laboratory work involved in the development of an endovenous device for the correction of popliteal venous reflux. The feasibility of such a device was established using a human cadaveric vein model and the ability of the deployed device to withstand a hydrostatic pressure of 100 mmHg was achievable. Finally, the successful deployment of this device in a patient is described.

The final chapter in this thesis summarises the findings of the experimental chapters and outlines areas for future investigation.
CHAPTER TWO

CHRONIC VENOUS INSUFFICIENCY:- AETIOLOGY, INVESTIGATION AND MANAGEMENT

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2.6 PHARMACOLOGICAL THERAPY OF VENOUS ULCERATION
2.1 CHRONIC VENOUS INSUFFICIENCY WITH REFERENCE TO VENOUS ULCERATION

2.1a. Definition and Economic Impact

Porter and Moneta (1995), on behalf of the Ad Hoc Committee on Reporting Standards of the Joint Council of the Society for Vascular Surgery and the North American Chapter of the International Society for Cardiovascular Surgery define Chronic Venous Disease as follows:

' an abnormally functioning venous system caused by valvular incompetence with or without associated venous outflow obstruction, which may affect the superficial venous system, the deep venous system, or both. '

The clinical condition resulting from Chronic Venous Insufficiency (CVI) encompasses a spectrum of skin disease ranging from normal, mild eczema through to lipodermatosclerosis and eventually ulceration, the most serious and costly complication of CVI. Venous leg ulcers are defined as an area of epidermal discontinuity persisting for four or more weeks occurring as a result of venous hypertension and calf muscle pump insufficiency (Douglas et al., 1995).

A clinical diagnosis of venous ulcer includes the following criteria (Douglas et al., 1995):

(i) The centre of the ulcer must originate within the gaiter region of the leg;

(ii) The presence of skin pigmentation (a feature of lipodermatosclerosis);

(iii) The exclusion of arterial disease by an Ankle Brachial Pressure Index (ABPI) >0.8.

Ulcers out-with the gaiter area are unlikely to be venous (but not exclusively so) and ulcers of mixed venous and arterial aetiology are not uncommon (Salaman et al., 1995).
Venous ulceration presents a significant health problem in the U.K. both in terms of local and national health economics and the general wellbeing of those patients with ulcerated limbs. In the U.K. as a whole venous ulceration effects 100,000 people at any one time (Callam et al., 1985) and in Leicester a recent audit identified 1600 patients with active ulceration. As a comparison only 20,000 people are treated for lower limb critical ischaemia each year (Coleridge-Smith, 1994). Venous ulcers are a chronic and recurring condition with 50% of ulcers persisting for over 1 year (Cornwall et al., 1986; Nelzen et al., 1994) and 59% of ulcers being recurrent (Nelzen et al., 1994). This incurs a significant expense as the treatment for each ulcer costs £2,000 - £4,000 per annum (Bosanquet, 1992) largely for care in the community. The cost to the National Health Service has been estimated at £150- £600 million per annum (Wilson, 1989) with British industry losing 500,000 working days per annum through absenteeism because of ulceration.

2.1b. Classification, Incidence and Prevalence

The spectrum of venous disease is so wide that careful classification is a prerequisite for any epidemiological study; classification apart, difficulty can arise when extrapolating from the study cohort to the general population in terms of the age and sex of study cohort and whether this group were recruited from a working environment, hospital or community clinic.

As part of the Basle Study II, Widmer (Widmer et al., 1977) described three degrees of CVI as follows:
Class I  varicose veins only, without skin changes.

Class II  hyper- or depigmentation of the skin with subcutaneous induration (Lipodermatosclerosis).

Class III  ulceration.

This clinically based classification, however, takes no account of the pathophysiology involved. To encompass the advances in knowledge and investigative techniques a more recent and extensive classification system has been devised – C. E. A. P. (or Hawaii) Classification (Straub Foundation, 1995). This allows classification of the affected limb in four areas:

CLINICAL CLASSIFICATION (Co-*) based on defined objective clinical signs suffixed as A for asymptomatic limbs or S if symptoms exist.

A(E)TIOLOGICAL CLASSIFICATION (Ec, Ep, or Es) as either congenital, primary (undetermined cause) or secondary (with known cause).

ANATOMICAL CLASSIFICATION (As, d, p) allowing any combination of refluxing systems to be defined. A more detailed anatomical description is catered for defining the individual segment of vein affected.

PATHOPHYSIOLOGICAL CLASSIFICATION (Pr,o) delineating the presence of venous reflux or obstruction or both with the allowance to indicate which venous segments are affected.

Although CVI represents a spectrum of disease it has been estimated that 6 % of the general population in Western industrialised countries suffer from some degree of CVI with skin changes (Widmer Classes II and III, or C 4-6) of whom 0.5 - 1.0 % have open ulcers (class III, or C 5) (Laing, 1992; Dale et al., 1983). Not only does the incidence of CVI vary between countries, but also between differing areas of the same country depending on the local population characteristics and referral patterns. Two
British studies have reported an overall ulcer prevalence of 0.18% (Cornwall et al., 1986) (London) and 0.148% (Callam et al., 1985) (Scotland) with a female predominance of 1.6 - 2.8:1 (Callam et al., 1985; Nelzen et al., 1994); the annual incidence in Newcastle has been calculated as 0.35% (Lees et al., 1992). Although venous ulceration can effect young patients (Callam et al., 1985; Nelzen et al., 1994), up to 70% of venous ulcers occur in those aged over 70 years (Cornwall et al., 1986) and the point prevalence increases with advancing age from 0.3% for those aged 61 - 70 years to 2.1% in those over 80 years (Cornwall et al., 1986). In 1981, estimates for the percentage of the population aged over 60 years in various regions was 16.3% in Harrow, 13.9% in North West Thames Region and 14.9% in the Outer London Boroughs (Cornwall et al., 1986); this gives an indication of the size of the problem which will be reflected nationwide. The size of the problem is compounded when the ulcer recurrence rate is considered; in Cornwall’s study (Cornwall et al., 1986), 50% of ulcerated limbs in patients aged over 40 years had had an active ulcer for over 12 months.

2.2 AETIOLOGY OF VENOUS ULCERATION

2.2a Vascular Abnormalities

Venous ulceration results from prolonged venous hypertension (Burnand, 1990; Cheatle et al., 1991a), the incidence of ulceration being proportional to the degree of venous hypertension (Nicolaides et al., 1993; Nicolaides, 1986; Payne et al., 1996). Venous hypertension is the consequence of calf muscle pump failure which can result from primary musculoskeletal pathologies such as paraplegia (Negus, 1992c), poliomyelitis (Burnand, 1990) or severe lower limb arthritis (Burnand, 1990; Back et al.,
1995) or more usually from an abnormality of the veins themselves. The venous abnormalities resulting in calf pump failure may rarely be congenital such as primary valve aplasia (Lodin et al., 1958; Plate et al., 1983), congenital arteriovenous fistulae or defective fibrinolysis (Sarin et al., 1996) and thus repeated thrombotic episodes. However, calf muscle pump failure is almost always acquired secondary to venous reflux, obstruction or a combination of the two involving the deep, superficial and perforating veins in various combinations.

Venous hypertension has been considered to result almost exclusively from post-thrombotic deep venous damage either in the form of reflux or obstruction with any co-existing superficial venous abnormality occurring as a secondary phenomenon. This has been found to be the case in up to 50% of ulcerated limbs presenting to St. Thomas’ Hospital (Stacey et al., 1988b). Doubt has been cast on this hypothesis by Humans in 1938, (cited by Scott 1992) who differentiated between ‘varicose ulcers’ associated with superficial varicose veins and often cured by removal of the same, and ‘venous ulcers’ that were intractable and not influence by varicose vein surgery. In addition, Kistner (1980) described primary valve failure of the deep venous system suggesting that not all cases of deep venous reflux were of a post-thrombotic origin. In 1988 Raju and Fredericks (Raju et al., 1988) demonstrated that over 70% of ulcerated limbs had deep venous reflux either alone or in combination with superficial reflux which they considered to be a secondary phenomenon. Using light reflection rheography and tourniquets McEnroe et al. (1988) found that 72% of ulcerated limbs had deep venous reflux alone with only 13% having isolated superficial venous reflux. Despite this, however, the role of primary varicose veins in contributing to venous hypertension is well recognised (Hoare et al., 1982; Labropoulos et al., 1994). More recently, colour duplex scanning has allowed very accurate anatomical and functional assessment of the
venous system, and in doing so has demonstrated the relative proportions of limbs having deep and/or superficial venous reflux. This represents a significant advance as the proportion of limbs with isolated superficial venous (and hence surgically correctable) reflux has been found to range from 38% to 72%; isolated deep reflux 5% to 15%; and a combination of deep and superficial venous reflux in 28% to 48% (Myers et al., 1995; Grabs et al., 1996; Shami et al., 1993; van Rij et al., 1994). Now that the anatomical distribution of reflux can be clearly identified specific therapeutic measures can be employed in each patient on an individual basis.

Not only is the distribution of reflux in terms of the number and nature of venous systems involved important (Christopoulos et al., 1988) but so is the degree of reflux in terms of its distal extent. This is particularly relevant in the case of the popliteal valve(s) (Bradbury et al., 1996) which have been described as the ‘Gatekeeper’ of the calf muscle pump. Even in the presence of post-thrombotic deep vein obstruction neither venous hypertension nor ulceration occur if the popliteal valves are competent (Schull et al., 1979) or if post-thrombotic changes are confined to the calf and do not extend across the knee into the femoral veins (Stacey et al., 1991).

Van Rij (1994) has demonstrated that calf pump failure may result from volume overload caused by venous reflux from any system of veins and that high volume reflux that exceeds the calf pump ejection volume is associated with ulceration.

The contribution of the perforating veins to venous hypertension is frequently debated but remains unclear (Ruckley et al., 1996; Coleridge-Smith, 1996b). John Gay (cited in Negus, 1992c) described calf and ankle perforating veins in 1867 and Cockett coined the term ankle blow-out syndrome (Cockett et al., 1953) describing what was considered to be the most important factor in venous ulceration - direct calf perforating vein incompetence. This hypothesis was re-enforced by the idea that direct calf
perforating veins may transmit high intra-muscular exercise pressure directly to the
subcutaneous venous networks around the medial and lateral maleoli (Negus, 1992c;
Bjordal, 1984). Unfortunately, the various procedures for interrupting these perforating
veins was met with disillusionment rather than a cure for ulceration suggesting that
perforating vein reflux per se is not the cause of ulceration. Several studies have
examined the direction of blood in the perforating veins in normal limbs and those with
varying degrees of venous reflux (McMullin et al., 1991c; Sarin et al., 1992a; Bjordal,
1970; Bjordal, 1972) and found that many perforators exhibit bi-directional flow
depending on the local conditions. Even when outward (deep to superficial) flow is
present the haemodynamic effects are variable and not necessarily significant (Zukowski
et al., 1991). Despite numerous studies of the veins and their valves it appears that
venous reflux is not the only determinant of the ambulatory venous pressure (normal or
otherwise) and that various mechanisms exist such as vein wall collapse to interrupt the
hydrostatic column acting on the ankle (Raju et al., 1993).

2.2b Microvascular Abnormalities

It is apparent that venous hypertension can result from a number of sources, but
why does it result in the clinical changes seen in the skin namely lipodermatosclerosis
and eventually ulceration? A number of theories have been postulated including stasis
hypoxia (Homans, 1917) and arteriovenous shunts (Piulachs et al., 1953) both having
been subsequently rejected (Blalock, 1929; Lindemayr et al., 1972). Changes in the
cutaneous microcirculation observed in CVI may be responsible for macroscopic skin
damage.
2.2bi  The Fibrin Cuff Theory

Histological studies performed by Browse and Burnand in 1982 (Browse and Burnand, 1982) proposed the fibrin cuff theory of venous ulceration. They had demonstrated, in a dog model, that experimentally induced venous (and hence capillary) hypertension resulted in enhanced leakage of fibrinogen from the capillary lumen into the pericapillary space (Burnand et al., 1982a) where it polymerised to the 'fibrin cuff' (Burnand et al., 1982b; Falanga et al., 1987). The fibrin thus formed was not degraded because of the reduced fibrinolytic activity present in these patients (Browse et al., 1977a); it thus remained forming a proposed oxygen and nutrient diffusion barrier giving rise to ulceration. Transcutaneous oxygen tensions have been found to be either reduced (Gardner et al., 1993; Stacey et al., 1987) or elevated (Dodd et al., 1985) in the gaiter region of limbs with CVI compared to normal limbs, however, the validity of these studies is questionable in view of the physiological manipulation of the microcirculation required to obtain a measurement (Dodd et al., 1985; Hanna et al., 1995). Direct needle electrode measurements are reported to show reduced intracutaneous oxygen tensions but of an insufficient degree to result in frank ulceration (Roszinski et al., 1995). Xenon diffusion experiments (Cheatle et al., 1990), lightguide spectrophotometry (Hanna et al., 1995) and theoretical calculations (Michel, 1990) have failed to demonstrate the existence of an oxygen diffusion barrier despite the undoubted presence of pericapillary fibrin cuffs. Faced with this evidence it seems unlikely that the skin of limbs with CVI is significantly hypoxic. Therefore some other phenomenon must be responsible for the tissue damage seen in venous skin changes and ulceration.
2.2bii The White Cell Trapping Hypothesis

White cells, in particular Polymorphonuclear Leukocytes (PMNL), play an integral role in microcirculatory dynamics. Leukocyte margination and activation play an important role in the tissue damage resulting from ischaemia, when adherent to endothelium PMNLs become activated releasing proteolytic enzymes and permitting the release of free radicals resulting in a cycle of tissue damage leading to further PMNL activation.

Leukocytes are ‘lost’ from the normal lower limb circulation on dependency. After a period of lower limb dependency up to 30% of the circulating white cells are lost from saphenous vein blood (Moyses et al., 1987; Thomas et al., 1988). Capillaroscopic examination of the microcirculation demonstrated fewer cutaneous capillaries in limbs with CVI compared to normals (Scott et al., 1989) suggesting that the capillaries in limbs with venous hypertension are in some way damaged, possibly by these ‘trapped’ white cells.

The capillaries in CVI are grossly abnormal (Fagrell, 1979; Fagrell, 1982). This venous microangiopathy (Bollinger et al., 1990) varies in severity in proportion to the degree of venous hypertension and encompasses the morphological changes of capillary tortuosity (glomerular like), microthrombosis (Haselbach et al., 1986) and pericapillary halo (micro oedema) formation (Haselbach et al., 1986; Franzeck et al., 1993). Histological studies have confirmed the microvascular thrombosis by visualising capillaries packed with erythrocytes especially marked in areas of skin with atrophie blanche (Belcaro et al., 1988). The abnormal flow through these capillaries encourages the margination and activation of white cells (Coleridge-Smith et al., 1988b) and hence tissue damage via the release of free radicals, proteolytic enzymes and chemotactic factors (Shami et al., 1992). Further evidence for Coleridge-Smith’s White Cell
Trapping Hypothesis is provided by the work of the Middlesex Hospital (Coleridge-Smith, 1998). Neutrophil degranulation is observed during experimental venous hypertension by a rise in plasma levels of elastase (a primary neutrophil granule enzyme) and lactoferrin (a secondary neutrophil granule enzyme) (Saharay et al., 1997a; Shields et al., 1994a). The cell surface marker CD11b expression is elevated by neutrophil degranulation suggesting an upregulation of neutrophils during experimental venous hypertension. Experiments in subjects with venous disease confirm increased neutrophil adhesion (Saharay et al., 1997b) and degranulation (Shields et al., 1994b) when compared with controls lacking venous disease.

Not only is there a microvascular abnormality but cutaneous lymphatic capillaries are also abnormal forming a network of obliterated lymphatic vessels contributing to the peripheral oedema and tissue damage (Bollinger et al., 1982; Bollinger et al., 1990; Franzeck, 1995).

Thus the morphological results of venous, thence capillary hypertension result in PMNL adhesion and activation with the subsequent release of proteolytic enzymes and free radicals. This results in tissue damage and further PMNL response, the end result being lipodermatosclerosis and ulceration.

Finally, all the above microscopic findings and the clinical characteristics of venous ulceration can be explained by an aetiological theory based on the pattern of skin strain in the lower leg (Chant, 1999).

2.3 INVESTIGATION OF VENOUS DISEASE

As with all disease states investigation commences with a full clinical history encompassing an assessment of the patient's general health, followed by a complete
physical examination to elicit any co-existing conditions that may influence the course of the disease and/or its treatment modalities. Despite this it is occasionally still not clear what the aetiology of a leg ulcer may be. The use a hand held Doppler and sphygmomanometer to measure the ankle : brachial pressure index (ABPI) is a mandatory initial test of the vascular tree. This will identify any limbs with arterial insufficiency (ABPI < 0.8) whose ulcer may be of pure arterial or a mixed arterial/venous aetiology. Section 2.3 describes methods of investigating the venous system assuming a normal arterial system.

The various methods of venous investigation were designed to provide information about the anatomical distribution of venous reflux/obstruction, its extent and pathophysiology and also information about the aetiology of the observed venous dysfunction. The number of methods available and their application has formed the basis of a number of publications and higher degree theses (McMullin,1993). This section provides an outline of the more frequently cited methods appearing in the venous literature.

The methods employed can be classified in two ways: 1) whether they provide morphological or haemodynamic data or 2) are the tests invasive or non-invasive.

1) Invasive Venography, (Morphology).
   Venous Pressure Monitoring, (Haemodynamic).

   These methods involve the cannulation of a vein with/without exposure to ionising radiation and radiological contrast media.

2) Non-invasive Plethysmography (Photo, Air, Straingauge) (Haemodynamic).
   Light Reflection Rheography (Haemodynamic).
   Foot Volumetry (Haemodynamic).
2.3a Invasive Techniques

2.3ai Venography

Two methods are available; Ascending and Descending.

Ascending Contrast Venography

This method involves the cannulation of a dorsal foot vein to allow the injection of contrast medium. The ascent of the intravenous contrast is observed by X-Ray screening and hard/ digital copies are obtained of the venous system. Contrast is encouraged to pass into the deep veins by the application of an ankle tourniquet occluding the superficial veins at this level. This procedure is considered to be the 'gold standard' investigation for the detection of acute calf vein thrombosis (van Bemmelin et al., 1994b) and also the standard by which new investigative techniques are compared (Nicolaiides, 1998). In patients with a chronic venous disorder it is used to examine primarily for incompetent perforating veins (van Bemmelin et al., 1994b) although this has been shown to carry a 13% false positive rate when compared with operative findings (O'Donnell et al., 1977). The reported side effects of skin necrosis, venous thrombosis and contrast allergy are less common with the use of modern non-ionic, iso-osmolar contrast media (Lea-Thomas, 1992).

In the rare condition of congenitally absent venous valves in which patients typically develop ulceration at a young age, the ascending venogram has a typical appearance of smooth walled and valveless veins (Plate et al., 1983).
Dynamic venography recorded onto 'cine film' gives useful information in particular with regards to perforating and calf vein function (Gardner & Fox, 1993).

**Descending Contrast Venography**

This investigation examines the deep veins for valvular incompetence (Taheri et al., 1983; Herman et al., 1980). It involves injecting a bolus of radio-opaque contrast medium directly into the common femoral vein, with the patient tilted to a semi erect position (commonly 60° head up) and performing a Valsalva manoeuvre to close the venous valves. This forces blood in a caudal direction along the deep veins, the flow of which is normally halted by the closure of the venous valves. In cases of valvular incompetence the contrast can be observed with X-Ray screening passing through the incompetent valves down the limb until a functioning valve is reached. At that level the valve sinus is seen and no contrast passes beyond that level. Although essentially a qualitative method, an estimate of the degree of reflux can be gained from the degree of contrast leakage through each valve and the extent of flow of contrast down the leg. Kistner (Kistner et al., 1986) described four grades of reflux as follows:

**Grade 1)** A wisp of contrast passes through the valve cusps and extends into the proximal superficial femoral vein (SFV)

**Grade 2)** Significant reflux of contrast with filling of the distal SFV, but not into the popliteal vein

**Grade 3)** Reflux passing through the popliteal vein into the proximal calf veins

**Grade 4)** Cascading reflux from the common femoral vein to the ankle.

Grades one and two reflux are found in some clinically normal limbs and are, therefore, not necessarily considered pathological.
As well as giving an indication of the degree of reflux, descending venography can also give information about the aetiology of the valvular incompetence as shortened, scarred valves may be apparent in the post-thrombotic state. This technique is limited in the situation of competent proximal valves with reflux beyond. These proximal functioning valves mask distal reflux by preventing contrast medium reaching the area of interest.

2.3aii Ambulatory Venous Pressure Measurement

Ambulatory venous pressure (AVP) measurements have been considered the 'gold standard' test of venous haemodynamic function for many years, being useful prognostically and diagnostically in patients with chronic venous insufficiency (Belcaro et al., 1992; Nicolaides, 1998; Payne et al., 1993). Importantly it is the only method available that allows direct measurement of intravenous pressure and the effect of ambulation on this. The procedure involves cannulating a superficial vein on the dorsum of the foot and via a fluid filled tube the cannula is connected to a pressure transducer and recording device. During the recording of the AVP the subject stands erect weight bearing on the contralateral leg to that being examined. The limb in question is held dependent with the foot resting on the ground. At rest the pressure in the foot vein is proportional to the height of the subject. Once a steady state has been reached, the subject is asked to perform a standardised exercise e.g. walking on a treadmill, repeated ankle dorsiflexions or more usually heal raises (Sarin et al., 1996) (10 at one second intervals for example). At the end of the exercise the pressure in the foot vein will drop to approximately 20% of the resting pressure in normal limbs. This value is termed the ambulatory venous pressure. Immediately on cessation of the exercise the pressure in the vein begins to increase towards the resting pressure (determined by arterial inflow and
venous reflux), the time taken from cessation of exercise to reach the pre-exercise resting pressure is known as the venous refill time. Normal subjects demonstrate a refill time of more than 20 seconds (Randhawa et al., 1984). For accuracy the time to reach 90% of the pre-exercise level is taken as the end point of the refill time (RT90) (Figure 2.1).

In cases of valvular incompetence the pressure drop on exercise is less than in the normal leg and the RT90 is of a shorter duration. In 1988 the sub-committee on reporting standards in venous disease correlated venous refill time with the severity of venous reflux. Normal venous filling time is greater than 20 s; severe CVI has a refill time of less than 5 s; moderate disease 5 to 15 s and mild 15-20 s. With an obstructed venous outflow system, the pressure in the foot vein may increase on exercise. Although an abnormal AVP and RT90 are associated with venous ulceration (Schull et al., 1979; Nicolaides, 1986) these measurements give no indication of the degree of valvular incompetence. As a measure of overall venous function the Pressure Relief Index (PRI) can be calculated as follows:

$$PRI = RT90 \times (RP - AVP)$$

where PRI = Pressure Relief Index

$$RT90 = 90\% \text{ Refill Time (seconds)}$$

$$RP = \text{Resting Venous Pressure (mmHg)}$$

$$AVP = \text{Ambulatory Venous Pressure (mmHg)}$$

The use of a narrow (2.5 cm) pneumatic cuff to occlude the superficial veins has been used to help differentiate between deep and superficial reflux. By occluding the
superficial veins the pressure recorded at the foot will represent that in the deep system as the two systems communicate in the foot (Nicolaides, 1986).

![Diagram](image)

Figure 2.1 Diagrammatic representation of a typical normal AVP recording adapted from Nicolaides, 1986. Venous pressure (mmHg) along the y axis, time (seconds) x axis, (Po) the resting pressure before exercise, (P) the ambulatory pressure after exercise, 90% RT the 90% Refill Time.

2.3b Non-Invasive Techniques

Many methods of inferring blood flow from limb volume changes have been described and are detailed below.

2.3bi Photoplethysmography (PPG)

Photoplethysmography was developed to provide a non-invasive method of determining RT90. The technique involves the measurement of infra-red light absorption by haemoglobin in the skin capillaries (Coleridge-Smith, 1996). The probe (a light source and light sensitive diode) is applied to the skin with clear double sided tape proximal to the medial maleolus (Rashid et al., 1996), the subject then exercises as with
AVP assessment causing a reduction in dermal blood flow which increases with cessation of exercise (Sarin et al., 1996). The result is a tracing similar to that obtained by direct venous pressure measurement, the post exercise refilling times correlating with direct venous pressure measurements (Abramowitcz et al., 1979). PPG refill times do not quantitate the degree of venous reflux (Nicolaides et al., 1987) although by calibrating the PPG claims have been made that absolute venous pressure can be calculated (Norris et al., 1983). However, attempts to relate PPG RT90 with sites of underlying venous malfunction have failed to demonstrate significant correlation with pressure measurements (Fischer et al., 1985) and Van Bemmelin (van Bemmelin et al., 1994c; van Bemmelin et al., 1992) and Rosfors (Rosfors, 1990) conclude that PPG ought to be limited to the study of local skin capillary plexuses and not the lower limb venous system as a whole.

2.3bii Light Reflection Rheography (LRR)

As with PPG this is a test of dermal capillary plexus blood flow; it differs from PPG in that the probe used to make the measurements has three infra-red light sources (Arora et al., 1993; Williams et al., 1994) to obtain data from a larger and hence more representative area of skin, the aim being to accommodate local variations in capillary blood flow. Measurements are made in the same way as PPG. Although it forms a useful screening tool in cases of suspected deep vein thrombosis (Thomas et al., 1991) the same limitations apply to its use in venous reflux as with PPG.

2.3biii Airplethysmography (APG)

Early studies described by (van Bemmelin et al., 1994a) demonstrated that venous volume is related to the hydrostatic column and this changes in the lower limb
with various changes in posture and on walking. In addition, the rate of change of the volume increase on standing erect varied in patients with varicose veins and post-thrombotic limbs. Airplethysmography is a technique allowing the measurement of these volume changes in the lower limb (Belcaro et al., 1992).

The plethysmograph (Christopoulos et al., 1988) is a 35 cm long PVC air chamber that fits around the leg with a zip fastener. It is inflated with air to a low resting (bias) pressure of 6 mmHg. A pressure sensor detects pressure changes within the plethysmograph and relays these to a chart recorder. After calibration and a period of time has elapsed to allow for development of a stable air/chamber/leg temperature gradient, measurements equating to volume changes can be made.

On standing erect (from the supine position), the studied leg non-weight bearing, the volume in the chamber (lower limb) increases (due to a combination of venous reflux if present and arterial inflow in all cases). The maximum increase in volume reached is known as the Venous Volume. Tip toe movements are performed 2-3 times, the drop in volume representing the Ejection Volume of the limb (Figure 2.2). From this the Ejection Fraction can be calculated as follows:

\[
\text{Ejection Fraction} = \frac{\text{Ejection Volume}}{\text{Venous Volume}}
\]

The overall function of the venous calf pump is assessed over a period of 10 tip toes; the final minimum volume is the Residual Volume. This allows calculation of the Residual Volume Fraction (RVF):

\[
\text{Residual Volume Fraction} = \frac{\text{Residual Volume}}{\text{Venous Volume}}
\]
Welkie (Welkie et al., 1992) has shown the RVF correlates with the AVP.

A quantification of the venous reflux combined with arterial inflow is known as the Venous Filling Index and is calculated as follows:

Venous Filling Index = 0.9 x (Venous Vol.) / time to reach this volume.

APG has been used to study the effects of venous surgery and compression therapy, and the risk of ulceration occurring has been associated with a VFI > 10ml/s (van Bemmelin et al., 1994a). The uses of APG are confined to assessing venous function from the volume perspective but it gives no anatomical information to help in planning specific details of proposed surgery.

Figure 2.2 Diagram adapted from Belcaro et al., 1992, illustrating the manoeuvres and methods of deriving the airplethysmographic measurements. VV = Venous Volume, VFT = Venous Filling Time, VFI = Venous Filling Index, EV = Ejection Volume, EF = Ejection Fraction, RV = Residual volume, RVF =
Residual Volume Fraction. $a = \text{supine}, b = \text{erect}, c = \text{one tip toe movement}, d = 10 \text{ tip toe movements}, e = \text{resting erect}$.

2.3biv  Straingauge Plethysmography (SPG)

Mercury in rubber and latterly silastic tubing (Coleridge-Smith, 1996) increases its electrical resistance when stretched. When applied circumferentially to the lower leg investigation of venous obstruction (Barnes et al., 1973b) and venous reflux (Barnes et al., 1973a; Holm, 1976) can be performed, as well as providing a measure of calf pump efficiency (emptying) and venous refill times. SPG has been demonstrated to have a high sensitivity and specificity for the detection of deep venous thrombosis (Hallbrook et al., 1971). Unfortunately only a very narrow section of the calf is assessed by this technique.

2.3bv  Foot Volumetry

This measures the change in foot volume following exercise. The subject stands with each foot in a ‘bath’ containing a known volume of water, the level of which indicates the foot volume and any changes thereof. Calculations of expelled volume and refill times can be made.

2.3bvi  Ultrasonography

Ultrasound scanning, in particular colour coded duplex scanning has revolutionised the investigation and subsequently management of venous disease in recent years. Colour duplex scanning is rapidly threatening to replace venography as the ‘gold standard’ in venous imaging (Neglen et al., 1992). Section 2.3bvi describes the use of hand held Doppler and colour duplex imaging.
Doppler Ultrasound

A simple and cheap method used during the measurement of ABPI as well as initial investigation of venous disease. Examination of the venous system testing for reflux can be performed in the supine or erect positions. When supine three characteristics of venous flow are described: spontaneous flow, variation in flow with respiration and the augmentation of flow with distal compression of the limb (Barnes et al., 1975; Barnes et al., 1976). Examining for reflux when erect relies on the compression of the calf distal to the vein being examined i.e. the superficial femoral vein in the groin. The augmented flow of blood up the femoral vein is heard and on relaxation of the compression a competent vein will demonstrate no reversed flow whereas a refluxing vein will show reversed flow of varying duration. The maximum duration of reversed flow in normal limbs is <0.5 seconds (van Bemmelen et al., 1989; Evans et al., 1995). The popliteal fossa can similarly be examined but here there is a great limitation in the anatomical accuracy as the hand held Doppler gives no indication as to which vein possesses reflux (Coleridge-Smith, 1996). The use of superficial tourniquets to isolate the superficial and deep systems has been advocated as a method to improve the accuracy of hand held Doppler testing (Folse et al., 1970). The advantage of the hand held Doppler is the ease with which it can be incorporated into the physical examination of the patients’ limbs.
**Colour Coded Duplex Scanning**

Duplex combines B mode imaging with pulsed Doppler; colour coding provides a very clear indication of direction and velocity of blood flow. Direct visualisation of the veins allows identification and separation of reflux in the deep and superficial veins with ease, especially in the popliteal fossa where numerous veins can produce confusing results with the hand held Doppler alone. The use of colour coded duplex scanning has provided the basis for modern venous imaging and management with precise anatomical data being obtained completely non-invasively. Unfortunately, duplex provides little numerical information regarding overall venous function. Images are produced by scanning with either a rotating or multi-element transducer producing images in 'real time'.

Venous duplex scanning is probably the best non-invasive method of detecting reflux in various venous segments (Nicolaides et al., 1990; Bays et al., 1994). When compared with descending venography duplex was more successful in detecting reflux (Baker et al., 1993; Harrison et al., 1994) in particularly in the distal veins (Valentin et al., 1993). In addition, attempts to quantify venous reflux based on duplex scanning have demonstrated that reflux >10 ml/s is associated with a 66% incidence of skin changes (Vasdekis et al., 1989).

2.4 CONSERVATIVE TREATMENT OF VENOUS ULCERATION

There are two aspects to the treatment of venous ulceration, one is to heal the ulcer itself and the second is prevention of recurrence. Assuming that there is no significant arterial component to the ulceration, or any pre-existing arterial lesion has been corrected, virtually all venous ulcers can be healed by eliminating the abnormally
high ambulatory venous pressure with bed rest and elevation, possibly over the course of a number of months. This is obviously impractical and so alternative methods of treatment that allow ambulation must be employed. According to Mayberry et al. (1992) the ideal treatment option should: allow ambulation, heal the ulcer in a reasonable time period, be tolerated by the patient thus ensuring compliance, and equally importantly prevent ulcer recurrence.

In striving for this ideal a number of conservative and operative therapeutic regimens have been employed with varying degrees of success; these methods are examined below.

2.4a. Elevation

Elevation has been used for centuries in the treatment of venous ulcers. Hippocrates felt that 'in the case of an ulcer it is not expedient to stand, more especially if the ulcer be situated on the leg' (Browse et al., 1988) and bed rest either at home or in hospital was recommended by John Hunter (Hunter, 1835). Dodd and Cockett (Dodd, 1976a) noted that venous ulcers would heal with bed rest and (maximal) elevation alone and, as with Mayberry (Mayberry et al., 1992), they included a period of bed rest and elevation as part of their management of venous ulcers as a pre-operative/ pre-compression requirement or as part of a ‘rescue package’ in the case of an early ulcer recurrence. However, this policy has the obvious disadvantages of cost in terms of hospital bed occupancy, economic and social disadvantages for the patient and the significant risks of joint stiffness and deep vein thrombosis. Bearing these factors in mind most clinicians aim to manage venous ulcers on an outpatient basis as far as possible. The therapeutic actions of elevation follow the reduction in hydrostatic
pressure exerted on the gaiter skin and include the re-absorption of oedema fluid and improved capillary microcirculatory function.

2.4b. Compression Therapy

Compression ‘bandages’ have been used to treat leg ulcers since the time of Celcus in AD 25 (Browse et al., 1988) who described a linen and paste wrapping (a very early variation of Unna’s Boot). Although initially used in the 18th century (Browse et al., 1988) the efficacy of elastic bandages was first clearly documented by Dickson-Wright in 1931 (Mayberry et al., 1992), however, the general use of elastic bandages was delayed until the development of elastic webbing in 1948 by Bisgaard (Browse et al., 1988). An alternative method of providing compression, used extensively in Europe, is graduated elastic compression stockings. Richard Wiseman in 1676 initially described a lace up leather stocking capable of providing graduated compression to legs of varying profile. However, it was not until the 1940s and the development of graduated elastic stockings by Conrad Jobst (Mayberry et al., 1992) that the use of these garments became common. However, despite the present ubiquitous use of compression therapy and its proven efficacy it is not without complications (Callam et al., 1987) and must be used with adequate patient assessment and supervision.

‘Graduated compression’ refers to a decreasing compressive force exerted by the bandage varying with the distance from the ankle, i.e. maximal at the ankle and minimal at the knee. This is required to reduce oedema by altering the balance of Starling’s Law, and in addition increase the velocity of deep venous blood flow (Sigel et al., 1975); enhance fibrinolytic activity (Clarke et al., 1960) and provide symptomatic relief possibly by reducing venous distension (Arcelus et al., 1993) and ultimately enhancing the efficiency of the calf muscle pump as determined by venous pressure and refill time.
These beneficial features are lost if inadequate compression is applied (Ruckley, 1992; Myers et al., 1972). In order to fulfil the above roles, compression bandages once applied need to exert a minimum of 40 mmHg pressure at the ankle (Fentem, 1986). Unfortunately, there is a significant degree of interbandager variation in achieving this pressure (Dale et al., 1983) which is also dependent on the bandage itself, the technique of bandage application and on the individual limb characteristics (Barbenel et al., 1994). To reduce this variation adequate training (Nelson et al., 1995b) making use of a bandage pressure tester to monitor sub-bandage pressure is advisable (Fentem et al., 1976; Pattison et al., 1987).

The ideal bandage should fill the following criteria (Fentem, 1994): provide safe, reproducible, effective compression; maintain graduated compression over a primary dressings for a reasonable length of time; be unaffected by ulcer exudate and remain effective after laundering; and in addition it must be comfortable enough and not so bulky as to reduce patient compliance.

2.4c Bandage Classification

The materials used in the manufacture of extensible bandages are available with varying physical properties defining their response to extension (Fentem, 1994). These variable properties are a relatively recent development and are dependent on the yarns used in the manufacturing process and whether the bandage is knitted or woven. These factors allow the 'power' of a bandage to be predetermined and controlled to fulfil the various clinical uses to which it may be put.

The science of bandages and bandaging, has resulted in the following terminology (Thomas, 1994):
The extensibility of a bandage dictates the change in length produced by an extending force. It is measured by extending the bandage at a constant rate and recording the tension produced and expressing this as the percentage change of the stretched and unstretched bandages. If a point is reached beyond which no further extension is possible, lock out is said to have occurred.

The power (modulus) dictates the force necessary to produce a set increase in bandage length.

Elasticity describes the resistance to extension of a bandage and its ability to return to its original length on cessation of the extending force.

The frequently used term compression is used to describe the application of pressure to produce a purposeful clinical effect. With regard to compression bandages/hosiery applied to the leg (or any cylindrical body) the sub-bandage pressure is determined by the law of Laplace (Reicher, 1994) thus:

\[ P = \frac{TN.c}{rW} \]

where \( P = \) sub-bandage pressure

\( T = \) bandage tension

\( N = \) number of layers

\( r = \) radius of curvature of the limb

\( W = \) bandage width

\( c = \) constant depending on the units used

It can therefore be seen that by applying a bandage with constant tension and constant degree of overlap to a limb the sub-bandage pressure is determined by the limb
circumference and in most limbs will result in the highest pressure at the ankle
decreasing towards the knee i.e. graduated compression.

**Support** is the retention and control of tissue without compression.

**Conformability** describes the ease with which a bandage is able to follow the
contours of a limb and is greatest in a bandage with the ability to stretch in two planes
(parallel and perpendicular to its length).

Two other terms are commonly used in the literature: **long stretch** refers to a
bandage that once applied retains the ability to stretch further with muscle contraction,
i.e. lock out has not been reached, this type of bandage is typically applied with 50% -
90% stretch; **short stretch** bandages allow no further increase in length once applied i.e.
they are applied at their lockout length and as such behave relatively inelastically. These
two concepts are important when considering the working pressure of an individual
bandage system.

Using these terms Thomas (1994) has classified bandages as follows:

**Type I**  *Lightweight conforming bandages* used simply for retaining
dressings with a sub-bandage pressure of only a few mmHg.

**Type II**  *Light support bandages* for the prevention of oedema and
support of minor sprains. These posses limited elasticity with early lock out and include
Crevic and Crepe BP.

**Type III**  *Compression bandages* this bandage type includes most of the
bandages used in the treatment of venous ulceration and they are further classified
depending on their ability to exert a predetermined pressure on laboratory testing. They
can produce ranges of sub-bandage pressure at the ankle corresponding to the three
classes of compression stockings defined by the British Standards Institution (BS 6612)
(1985).
**IIIa  Light compression bandages** equate to Class I compression hosiery of the Drug Tariff (producing 14 - 17 mmHg at the ankle) and include J-Plus and K-Crepe.

**IIIb  Moderate compression bandages** correspond to Class II hosiery (18 - 24 mmHg) and include Granuflex Adhesive and Veinopress.

**IIIc  High compression bandages** (Class III hosiery, generating 25 - 35 mmHg) and include Setopress and Tensopress.

**IIId  Extra High compression bandages** such as Blue Line Webbing generate upto 60 mmHg compression and as such are suitable for use on very large oedematous limbs.

It must be emphasised that these pressure groupings refer to testing on a laboratory mannequin and in clinical practice may vary from limb to limb and with time.

For the treatment of venous disease a relatively inelastic bandage has been advised as this generates the broadest range of sub-bandage pressures on ambulation (the working pressure) with minimal resting pressure thus ensuring adequate compression without compromising the perfusion of skin and extra fascial tissues (Stemmer et al., 1980). The relative efficacies of elastic versus non-elastic bandages regarding ulcer healing are not yet proven (Dale, 1994) despite the possibility of a greater margin of safety offered by an inelastic bandage when recumbent as the residual compression in this position is less then an elastic bandage (Callam et al., 1991). The Drug Tariff Technical Specification Number 40 recommends the following sub-bandage pressures for various clinical conditions: early varicose veins 14-17 mmHg; varices of medium severity and the treatment of venous ulcers 18-24 mmHg and severe varices and post thrombotic syndrome with/ without ulcers 25-35 mmHg. Stemmer (Stemmer et al., 1980), however, recommends pressures upto 50% higher than these.
There is a broad range of compression products available to the clinician and an even larger range of primary dressings. When deciding on compression the choice essentially lies between bandages or stockings in the first instance. It is important to remember that bandages will generally have to be applied by a nurse whereas patients can often apply their own stockings so long as they are not too frail. For some patients stockings are impossible to put on without help. There is variability in sub-bandage pressure depending on how the bandage is applied, although a bandage is more adaptable to different limb dimensions a stocking requires skilled limb measurement and sizing which may need reviewing as the limb dimensions change. Finally, bandages can absorb large volumes of exudate from open ulcers unlike stockings and as such may be more suitable in cases of severe active ulceration. Having said this, however, excellent results can be obtained with compliant use of compression stockings (Mayberry et al., 1991b; Samson et al., 1996), and the compliant use of stockings to prevent ulcer recurrence cannot be overstressed (Samson et al., 1996).

Of the available bandages the characteristics of an ideal bandage are most likely to be met by a multi-layer design (Ruckley, 1992) capable of providing high, evenly distributed compression over a reasonable time span. Single layer bandages often fail to maintain adequate compression within a few hours of application (Raj et al., 1980; Wright et al., 1988b); may exert dangerously high pressures over bony prominences and inadequate compression over natural hollows in the limbs' profile.

2.4d Four Layer Bandaging

Within the last ten years the use of an elasticated four layer bandage (The Charing Cross bandage) has become widespread within the hospital setting. This method of bandaging may provide a more even pressure distribution and durability over
a seven day period and although it provides a lower level of compression than a purely inelastic bandage its pressure characteristics may give it a higher margin of safety (Callam et al., 1991). As far as I am aware no published work exists characterising the working pressure profiles of the Charing Cross bandage, and so it is not known whether it behaves in an overall elastic or inelastic manner. The application of more than one layer provides some degree of compensation if the preceding layer is applied with insufficient extension which if uncompensated would provide inadequate compression (McCollum, 1992). The components of each individual layer of a Charing Cross type bandage vary according to the ankle circumference (Figure 2.1) (Moffatt et al., 1992b; Freak et al., 1992).
<table>
<thead>
<tr>
<th>Ankle Circumference (cm)</th>
<th>Bandage Regimen</th>
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<tbody>
<tr>
<td>&lt;18</td>
<td>2 or more Velband/ Sofban</td>
</tr>
<tr>
<td></td>
<td>1 Crepe</td>
</tr>
<tr>
<td></td>
<td>1 Elset</td>
</tr>
<tr>
<td></td>
<td>1 Coban</td>
</tr>
<tr>
<td>18 - 25</td>
<td>1 Velband/ Sofban</td>
</tr>
<tr>
<td></td>
<td>1 Crepe</td>
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<tr>
<td></td>
<td>1 Elset</td>
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<tr>
<td></td>
<td>1 Coban</td>
</tr>
<tr>
<td>25 - 30</td>
<td>1 Velband/ Sofban</td>
</tr>
<tr>
<td></td>
<td>1 Plastex 23+</td>
</tr>
<tr>
<td></td>
<td>1 Coban</td>
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<tr>
<td>&gt;30</td>
<td>1 Velband/ Sofban</td>
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Figure 2.1. Bandage components used in the four layer system (Moffatt et al., 1992b; Freak et al., 1992).

Without compression, healing rates of venous ulcers have been reported at 30% at ten weeks (Stewart et al., 1987; Browse, 1983) rising to 45% at 12 weeks with simple elastic bandage compression. Encouraging results achieved with the Charing Cross bandage compared to an adhesive plaster bandage were reported in the British Medical Journal in 1988 (Blair et al., 1988). This study reported two relevant aspects of compression bandaging: the sub-bandage pressure profiles and efficacy. The four layer system provided a mean medial maleolar pressure of 42.5 mmHg and maintained a pressure of 36.3 mmHg seven days later. The plaster bandage provided 29.8 mmHg medial maleolar pressure falling to 10.4 mmHg by 24 hours. From this it appears that a
four layer bandage can provide adequate and sustained compression. Unfortunately, efficacy was not examined within the confines of a prospective randomised trial, the results being reported as part of an ongoing study examining the role of various primary dressings. However, 148 ulcerated limbs with mean ulcer areas of 15.4 cm$^2$ had received adhesive bandages for a mean of 27.2 months before crossing over to the Charing Cross regimen. During the 12 week duration of the study, 110 (74%) of the ulcers healed in a mean of 6.2 weeks. By applying the same bandaging methodology in district nurse run community clinics to 477 venous ulcers of median area 4.2 cm$^2$ the Riverside Project Group (Moffatt et al., 1992b) achieved complete healing in 69% of ulcers at 12 weeks rising to 83% at 24 weeks. The underlying aim of this latter study was to primarily assess the setting up of a community based ulcer project rather than bandage efficacy as such it was non-randomised and used historical control data obtained from the published literature. In comparison, the controlled application and monitoring of a single layer short stretch bandage can achieve a 71% healing rate at 12 weeks (Charles, 1991). Travers et al. (1992) examined the efficacy of a single layer of adhesive bandage versus a 3 layer bandage system in a randomised, prospective manner and found no difference in healing rates of venous ulcers. Unfortunately he did not report the numbers of ulcers successfully healed, so comparisons with other published data are difficult.

One prospective, randomised trial (Duby et al., 1993) exists comparing a short stretch bandage (Comprilan), four layer Charing Cross bandage after Blair et al.(1988) and a paste bandage (Icthopaste) with outer support. Over a 12 week period the short stretch bandage completely healed 40% of ulcers; the four layer 44% and the paste bandage 23%. Initial mean ulcer areas were 13.1 cm$^2$, 11.9 cm$^2$ and 12.3 cm$^2$ respectively. Although there has been little demonstrable benefit of four layer over short stretch bandages this study clearly demonstrates that paste bandages (Unna’s Boot) are
less efficacious than other available methods of applying compression. More recently Nelson (Nelson et al., 1994) reported the results of a randomised trial of four layer Charing Cross bandaging (FLB) versus a single layer bandage (SLB) (Granuflex Adhesive Compression Bandage) in which 69% of ulcers had healed in 24 weeks with FLB and 49% healed with SLB; this was a significant difference. However, the initial ulcer area was 11 cm² in the SLB group versus 7.7 cm² in the FLB group; it is not known whether this difference is significant nor any data provided about the duration of ulceration prior to compression. Finally, a systematic review published in the BMJ examined the available research into compression bandaging as treatment of venous ulceration and concluded that the optimal bandage would provide high compression using multiple layers (3 or 4) (Fletcher et al., 1997).

2.4e Unna’s Boot (non-elastic zinc based paste bandages)

Has been used extensively in the past to provide compression and relieve the symptoms of venous eczema. The principle is to apply a bandage that provides maximum compression when ambulant but with minimal residual compression when recumbent. The original ‘boot’ had glycerine incorporated into the paste to ensure they set hard like a boot. Nowadays, this component is omitted so the bandage is flexible but inelastic. Reported healing rates vary between 23% to 46% at 12 weeks (Blair et al., 1988; Jopp-McKay et al., 1991; Cordts et al., 1992), to 73.7% at 6 months (Jopp-McKay et al., 1991) and 70% over 78 weeks (Hendricks et al., 1985). These bandages were left in place for a number of weeks at a time.
2.4f The Physiological Effects of Graduated Compression

Application of the gold standard test of venous function (ambulatory venous pressure measurement, AVP) to limbs with varicose veins and symptoms of CVI (but not ulceration) found that wearing compression stockings improved both symptoms and AVPs (Christopoulos et al., 1991) but these improvements were dependent on the continued use of stockings, returning to pre-compression values within 5 months of discarding the stockings (Somerville et al., 1974). Non-invasive measures of venous function have demonstrated the haemodynamic benefit of compression stockings as defined by airplethysmography (APG) (Christopoulos et al., 1991) and photoplethysmography (PPG) (Cornwall et al., 1987; Noyes et al., 1987). PPG refill times have been found to normalise for the duration of stocking use, but return to pre-compression levels on discontinuing compression hosiery (Noyes et al., 1987) and although APG parameters improved, as may be expected, venous reflux is not abolished by stockings but can be reduced to a level at which further skin damage is unlikely to occur (Christopoulos et al., 1991). However, these findings are not always reproducible; in post-thrombotic limbs the wearing of 30-40 mmHg compression stockings had no effect on either the AVP or the RT90 (O'Donnell, et al., 1979; Mayberry et al., 1991a), but it was noted that the maximum foot vein pressure achieved and the range of pressure changes during exercise were both decreased by the use of stockings (O'Donnell, et al., 1979). This may be one of the haemodynamic effects contributing to the clinical benefit of compression stockings.

It has been suggested that compression stockings exert their effect on the superficial venous system with no compression of the deep veins. However, the action of compression hosiery on the deep system is unclear; external compression enhances deep venous blood flow (Sigel et al., 1973; Sigel et al., 1975) and Mayberry et al.
(1991a) detected an increase in both deep venous flow velocities and deep venous
diameters on duplex scanning limbs with compression stockings. Although others have
detected a reduction in deep venous diameters with compression (Lewis et al., 1976; Husni et al., 1970b). Mayberry’s finding may represent the increased deep
venous blood flow following compression of the superficial system; since compression
stockings did not improve AVPs Mayberry et al. concluded that the effect of
compression stockings may influence the microcirculation dynamics via Starlings’ Law.

Using foot volumetry, below knee compression stockings have been shown to prolong
the venous 50% restitution time (seconds) and the rate (ml/min) at which refilling occurs
(Jones et al., 1980) when applied to post-thrombotic limbs. On a microcirculatory level
the balance of Starlings’ forces are altered in favour of enhanced clearance of
subcutaneous fluid (Jones et al., 1980; Bates et al., 1995; Nehler et al., 1993). Sarin
(Sarin et al., 1992b) applied variable external compression to limbs with venous reflux
and found that it was possible to abolish venous reflux in the saphenous and non—
thrombotic popliteal veins before occlusion occurred. It was interesting to note that at 40
mmHg (the suggested therapeutic ankle pressure of compression garments) only 5/19
(26%) of the refluxing LSVs became competent. The reason for this may be that the
valvular defect in varicose veins is such that on coaption of the valve cusps some reflux
still occurs at the valve commissures (Van Cleef, 1993). Obviously, therefore,
compression hosiery acts without necessarily restoring venous competence. Although 40
mmHg have been recommended as the ideal pressure at the ankle, no prospective trials
have been conducted to examine this statement. Stemmer (Stemmer et al., 1980) advises
the use of higher pressures (in the absence of contraindications) whereas Lawrence
(Lawrence et al., 1980) demonstrated an impairment of subcutaneous tissue blood flow
with sub-bandage pressures of 30 mmHg.
2.4g Intermittent Pneumatic Compression (IPC)

Originally intended for the prevention of post-operative deep venous thrombosis (DVT) (Hills et al., 1972) IPC boots can improve the symptoms of the post-thrombotic syndrome (Caprini et al., 1993), enhance the rate of ulcer healing (Coleridge-Smith et al., 1988a; Smith et al., 1990; Pekanmaki et al., 1987; Mulder et al., 1990) and overall success when used in combination with standard class II compression stockings. IPC is created by wearing a pneumatically inflatable boot with multiple chambers that are inflated with compressed air at variable rates, pressures and for variable durations. The order of inflation is distal to proximal giving a massaging effect as well as a compressive one. As well as enhancing ulcer healing, IPC is associated with improved transcutaneous oxygen tensions in the gaiter skin (Pekanmaki et al., 1987).

2.5 OPERATIVE TREATMENT OF VENOUS ULCERATION

Since venous ulceration results from venous hypertension it would seem logical to correct the venous hypertension as far as possible by ligating/ excising refluxing venous segments and a number of authors have advocated this (Scurr, 1996; Goren, 1993), however, two editorials in leading journals have dismissed the role of venous surgery in the management of venous ulceration (Anonymous, 1977; Allen, 1990). However, De Friend (DeFriend et al., 1992) takes a more cautious approach recommending that superficial venous surgery should only be performed ‘where the evidence for potential benefit is strong’ met by the following criteria:
1) A fall in the AVP of at least 30 mmHg must follow calf pump exercise.

2) The refill time must be improved by the application of tourniquets occluding the superficial veins to at least 12 seconds. Thus demonstrating potential surgical improvement.

3) The PRI must at least double.

No matter which approach the individual clinician employs, it has become apparent that the outcomes vary depending on the exact distribution of venous reflux between the deep, perforating and superficial systems. The efficacy of various surgical interventions in varying patterns of reflux will be examined below.

2.5a Saphenous Venous Surgery

2.5ai Superficial Venous Surgery Associated with Normal Deep Veins

In those ulcerated limbs with isolated long or short saphenous vein (LSV or SSV) reflux disconnection from the deep system is both haemodynamically (Burnand et al., 1977) and clinically effective. Sethia and Darke (1984) performed sapheno-femoral junction (SFJ) disconnections in combination with LSV stripping to the knee and they found that this procedure resulted in a significant improvement in the drop in foot vein pressure with exercise compared with pre-operative values. It is noteworthy that all the limbs operated upon also had incompetent calf perforating veins that were not ligated, implying that the contribution of the perforating veins to venous hypertension may be minimal. Addressing the clinical aspect of ulcer healing further work by Darke and Penfold (1992) demonstrated that of 54 ulcerated limbs with LSV or SSV reflux in combination with perforator reflux 49 (91%) healed their ulcers following saphenous ligation and stripping of the LSV to the knee without any perforator surgery followed by postoperative compression in some patients. This is an important finding as it further
questions the role of perforator incompetence in the aetiology of ulceration.

Unfortunately, assessing the role of surgery alone in this paper is hampered by the fact that up to 1/3 of the patients applied an unspecified form of compression hose/bandages on an ad hoc basis in the postoperative period before the ulcers had healed. These findings were reproduced by Wright (Wright et al., 1988a) confirming that superficial venous surgery is effective if the deep veins are normal. This is in agreement with the pressure and flow studies performed by Bjordal (Bjordal, 1988).

Whilst in theory, SFJ disconnection alone will reduce venous hypertension, stripping the LSV to the knee in order to prevent recurrent reflux into the LSV remnant has been recommended (DeFriend et al., 1992) and McMullin has shown that SFJ ligation alone may fail to adequately control LSV reflux (McMullin et al., 1991a).

2.5a ii  Superficial Venous Surgery associated with deep venous reflux

Although it was stated in 1992 that ‘the benefit of varicose vein extirpation in cases of combined superficial and deep venous insufficiency is at present unknown’ (Mayberry et al., 1992), Scurr and Goren (Scurr, 1996; Goren, 1993) have since advocated saphenous vein surgery in this group of limbs, and The Alexander House Group Consensus Paper on Venous Leg Ulcers (1992) recommend the correction of superficial and perforating vein reflux before any deep venous procedures are contemplated. Support for this rational is provided by Åkesson et al., (1990) who described improvements in AVP measurements after LSV stripping but not after perforator vein ligation in limbs with combined deep and superficial vein reflux associated with a good clinical outcome at 3.5 years (Åkesson, 1993) follow up. Further evidence supporting the role of superficial venous surgery in limbs with associated deep venous reflux is provided by Padberg et al. (1996) who demonstrated improved venous
haemodynamics as measured with air plethysmography following saphenous and perforating vein ligation in limbs with deep reflux confined to the popliteal vein and above. However, in limbs with deep reflux extending below the popliteal segment no improvement was noted and in fact the two limbs reported on deteriorated with respect to venous function. In view of the ‘gatekeeping’ role of the popliteal vein, limbs with deep reflux above this level may have insignificant femoral vein reflux that is not contributing to overall calf pump dysfunction.

It has been suggested that in a proportion of cases deep venous reflux of a non-thrombotic nature may be a secondary event brought about by entry of refluxing LSV blood through the perforating veins into the deep system, thus causing deep vein dilatation and ultimately reflux (Walsh et al., 1994). A number of authors have described the resolution of femoral and popliteal (Walsh et al., 1994; Goren, 1993) vein reflux after saphenous vein ligation and stripping supporting the above ‘volume overload theory’. However, Sottiurai (1990) in a prospective study comparing superficial venous surgery alone with superficial surgery and femoral vein valve reconstruction found that in the absence of valve reconstruction the ulcer recurrence rate was 56% compared to 13% if femoral valve reconstruction was performed. From this he concluded that superficial venous surgery was inadequate to heal ulcers if the deep veins are refluxing and recommended compression therapy in the first instance in this group of patients, employing surgery for those who fail to improve with conservative management.

2.5b Perforating Vein Surgery

For many years venous ulcers were attributed to incompetent calf perforating veins (Cockett et al., 1953; Dodd et al., 1976b) and that ulcer healing and recurrence
rates could be improved by ligating incompetent perforators by various methods. These included Cockett's extrafascial approach (Cockett, 1955), Linton's subfascial approach (Linton, 1953), Dodd's 'radical subfascial ligation' method (Dodd et al., 1957) and variations thereof (Felder et al., 1955; Healey et al., 1979). All these techniques involve a long incision through either ulcerated or liposclerotic skin and as such were associated with a high rate of post-operative wound infections and delayed healing. To try and avoid such problems a modified method of ligating perforating veins through multiple individual incisions was introduced by De Palma (1974), and Edwards (1976) described an instrument for the blind division of perforating veins through a single incision in relatively normal skin reporting good venographic results with his method. More recently minimally invasive methods of performing subfascial perforator division involving various endoscopic techniques have been developed including fibre-optics (Fischer, 1989), rigid endoscopes (Hauer, 1985; Paraskeva et al., 1996) and bronchoscopes (Couto et al., 1991), laparoscopes (Conrad, 1994; Gloviczki et al., 1996), mediastinoscopes (Pierik et al., 1995) or purpose built endoscopic equipment (Jugenheimer et al., 1992).

Despite the advent of these endoscopic techniques, the role of perforating vein surgery needs clarifying. It is associated with a recurrence rate of > 50% at 5 years (Johnson et al., 1985) and has been described as only a palliative measure (Hyde et al., 1981) as approximately 1/3 of ulcers will recur. In 1976 Burnand et al. reported in the Lancet that in the presence of deep venous damage (as assessed by ascending venography) perforating vein ligation was unable to prevent ulcer recurrence, whereas in those patients who did not suffer an ulcer recurrence the deep veins were venographically normal. Burnand concluded that the perforator incompetence was secondary to the deep venous abnormalities. Stacey et al., (1988a) reported similar
findings in limbs with deep venous reflux, but in order to detect any improvement in venous function in limbs without associated deep venous reflux it was necessary to apply compression stockings in addition to the surgery.

Negus (Negus et al., 1983; Negus, 1985), however, advocated that all perforating veins ought to be ligated in combination with saphenous ligation as necessary and that the reason for the recurrences in those with refluxing deep veins was the lack of post-operative compression hosiery. Using this regimen Negus was able to heal over 80% of venous ulcers and prevent recurrence at 3 years follow up in 76%, but the additional use of saphenous ligation and compression hosiery fails to test the significance of perforator ligation alone and any perceived benefit may be due to the compression/ concomitant saphenous surgery. However, as outlined in the preceding paragraphs Darke (Darke et al., 1992) has shown that in the presence of normal deep veins it is the saphenous ligation that provides the impetus to healing and not the perforator surgery. In fact, if the deep veins are normal then perforating reflux may be abolished in a significant proportion of cases by saphenous vein surgery alone (Campbell, 1995; Stuart et al., 1998).

Deep venous reflux has been implicated in ulcer recurrence after thorough saphenous and subfascial perforator surgery (Bradbury et al., 1993a; Bradbury et al., 1993b) in that the initial improvement in venous function following surgery is not maintained. Bradbury and Ruckley (Bradbury et al., 1993a) suggested this may occur following the opening of small, previously undetected perforating veins or by true neovascularisation, but it is equally likely that the ulcer recurrences may be accounted for by the presence of extensive deep to superficial venous anastomoses in the region of the ankle joint and the metatarsals.
Unfortunately, many of the reports maintaining the benefit of perforating vein ligation are poorly controlled in that in addition to perforating vein surgery the authors have simultaneously performed saphenous vein (long and/or short) extirpations (Thomas et al., 1986; Wilkinson et al., 1986; Bowen, 1975), applied postoperative compression (Lim et al., 1970; Wilkinson et al., 1986) or delayed surgery until the ulcers had healed pre-operatively (Lim et al., 1970; Wilkinson et al., 1986; Bowen, 1975). These additional procedures make interpretation of the efficacy of perforating vein ligations difficult as it is possible that either the compression or saphenous ligation plays the pivotal role in ulcer healing/prevention of recurrence rather than the perforator ligations themselves. In their original operative descriptions Linton (1953) and Cockett (1955) relied on either previous or simultaneous saphenous vein surgery and elastic compression was used for variable periods post-operatively by Linton, Cockett and Dodd (Dodd et al., 1957). De Palma (1974, 1979) enforced two weeks bed rest before mobilisation with permanent support hose as part of a treatment regimen for venous ulceration. From these frequently cited papers it is clear that perforating vein ligation alone is unlikely to be beneficial.

2.5c Deep Venous Surgery

Various surgical techniques are available to render previously refluxing veins competent or to bypass obstructed deep veins; these are described below. The application of individual methods is dependent on the state of the venous valves (McMullin, 1990) i.e. valves destroyed by previous thromboses (unlike cases of primary valve failure) are unsuitable for a reparative procedure (valvuloplasty) and in these limbs some form of valve replacement (transfer/transplant) will be required (Wilson et al., 1991).
2.5c  Primary Valve Failure

Valvuloplasty

First performed by Kistner in 1968 (Kistner, 1980), but initially reported in 1975 (Kistner, 1975) this procedure tightens the floppy valve cusps allowing apposition and as such competency. Essentially, reefing sutures are used to shorten the valve cusps and can be inserted in a closed manner or more usually via a longitudinal or transverse (Raju, 1983) venotomy. Jones (Jones et al., 1982) described a similar technique - 'triangular venous valvuloplasty' which combined shortening the valve cusps with narrowing the vein immediately proximal to the operated valve. Kistner recommended repair of the most proximal valve in the femoral vein. In his original series of 16 patients with 19 ulcerated limbs Kistner (1975) reported excellent clinical results (healing of 90% of ulcerated limbs maintained for 7 years) with postoperative venographic competency in 9/14 limbs, however, he performed a two stage procedure with femoral vein valvuloplasty being undertaken 3-7 days after ligation and stripping of superficial and perforating veins making evaluation of the valve repair difficult. Despite the clinical improvement and prolongation of RT90, ambulatory venous pressures did not improve (Kistner, 1980; Schanzer et al., 1982; Huse et al., 1983). Raju (Raju, 1983), however, demonstrated good clinical results from valvuloplasty alone with improved but not normal post-operative ambulatory venous pressures in 10/15 limbs operated upon. When used in combination with saphenous and/or perforating vein surgery 85% of limbs can remain reflux free and 68% maintain normal venous pressures with an ulcer recurrence rate of 9% 12 months after surgery (Cheatle et al., 1994).
**External Band Valvuloplasty**

In 1972, by placing a Dacron cuff around a dilated, incompetent femoral vein valve site Hallberg (Hallberg, 1972) reduced the diameter of the vein resulting in a competent venous valve and a healed ulcer. This method of external banding valvuloplasty has been adapted with the development of a device called the ‘Venocuff’ (Vaso Products Inc., Somerville, New Jersey, USA) and can correct femoral vein reflux in up to 90% of cases (Guarnera et al., 1994). The Venocuff has also been applied to the treatment of primary varicose veins (Lane et al., 1994) with the abolition of SFJ reflux in 75% of limbs at 2 months post implantation.

**2.5cii Post-thrombotic Venous Reflux**

This can be corrected by one of three surgical procedures; vein transposition, transplant or insertion of a prosthetic valve. Surprisingly, SFV ligation has been used as a therapeutic manoeuvre in the post-thrombotic limb with a improvement in AVP and RT90 (Huse et al., 1983) despite it having being abandoned by Linton by 1953 because of its failure to heal ulcers in the majority of patients (Linton, 1953).

**Vein Transposition**

Vein transposition was initially described by Kistner (1979) (Kistner et al., 1979) and requires a competent venous valve in one of the thigh veins (most commonly the profunda vein). The incompetent deep vein (usually the SFV) is divided distal to the profunda confluence and the proximal end of the SFV is ligated. The remaining SFV is anastomosed end to side or end to end to the competent thigh vein either the profunda vein or LSV. In this manner blood passing cephalad in the SFV reaches the iliac veins via a competent valve in either the profunda/LSV. Results using this method have been
mixed, Ferris and Kistner (Ferris et al., 1982) reported good clinical outcomes with an associated improvement in AVP, however, superficial venous surgery was performed as well as vein transpositions in these cases obscuring the effect of vein transposition alone. In fact Ferris and Kistner recommended correction of all venous abnormalities if optimal results were to be achieved. Johnson (Johnson et al., 1981) performed vein transposition without associated surgery and found the outcome less encouraging. Only 25% were free of elastic compression or ulcer recurrence postoperatively and although venous RT90 was improved in 75% of limbs by 18 months this objective measure of venous function had deteriorated and they concluded that perforating vein reflux was central to the ulceration process.

Valve Transplantation

This procedure is employed when there are no competent suitable valves in the lower limb. Taheri (1982) published a technique to transplant a segment of brachial vein containing a competent valve into the SFV (Taheri et al., 1982b) or popliteal vein (Taheri et al., 1985) which achieved symptomatic and haemodynamic improvement sustained at 2 years follow up with 6/13 ulcers healed (Taheri et al., 1982a). All his original patients had undergone previous superficial venous surgery and deep reflux was the only remaining venous abnormality. In essence, a segment of SFV is excised and the competent arm vein segment is inserted in an end to end manner. One year later Raju described a larger series using axillary vein with similar clinical and haemodynamic results (Raju, 1983). However, in this series there were 8/23 failures due to the smaller diameter of the upper limb veins compared to those of the leg and because of progression of reflux to involve the transplanted vein segment. Reviewing his 5 year experience in 64 limbs undergoing vein valve transplantation in isolation, Taheri (Taheri
et al., 1985) performed postoperative venography in 31 limbs and found that 28/31 transplanted valves remained patent and competent without the routine use of postoperative anticoagulation. Of the 3 failures, 1 had an occluded valve and the remaining 2 had incompetent valves suggesting that these may dilate with time and exposure to venous hypertension. Perhaps combining this procedure with a proximal valvuloplasty if a suitable valve is present or transplanting 2 or more valves may prevent this, an alternative would be external support of the valve with Teflon for example (McMullin, 1990). It is interesting that only one transplanted valve occluded as valve transplantation in a canine model found that without an additional arteriovenous fistula thrombotic damage occurred in all transplanted valves rendering them incompetent with 2 weeks of surgery (Dalsing et al., 1994).

Prosthetic Venous Valves

An artificial venous valve was constructed in dogs by Eiesman (Eiseman et al., 1953) in 1953 by invaginating the existing vein wall into the lumen to create valve leaflets. Postoperatively, venography confirmed function of the valve without thrombosis but the method progressed no further. The vein walls of post-thrombotic limbs are not suitable for this type of procedure and as such prosthetic mechanical devices have been developed. Taheri (Taheri et al., 1995) implanted bicuspid, platinum or titanium based valves into the inferior vena cava or femoral veins of 9 dogs. Two valves failed within 3 months of surgery because of technical errors in insertion, the remaining 7 remained venographically patent and functioning at this time. However, by two years all 7 animals developed signs of venous insufficiency and at post-mortem all 7 valves had failed due to the ingress of intimal hyperplasia preventing the mechanical
action of the leaflets. Thrombosis was not a problem, the only ‘anticoagulant’ used being a single aspirin tablet daily until animal sacrifice.

**Extravascular Valve Mechanisms**

As an alternative to constructing an intravenous valve Psathakis (1968) employed the tendon of gracilis passed between the popliteal vein and artery and secured to biceps femoris to occlude the popliteal vein when the knee flexes. Unfortunately his initial clinical successes also had saphenous and perforator ligations performed. Of those limbs with the gracilis procedure performed in isolation 5/6 experienced postoperative ulceration. Since adapting his method by lengthening the gracilis tendon with silastic rubber (Psathakis et al., 1985) 23/34 procedures have had good clinical and haemodynamic outcomes (Psathakis et al., 1986).

2.5ciii Deep Venous Obstruction

Warren (Warren et al., 1954) transferred the long saphenous vein from its subcutaneous position to the deep muscle compartment of the ipsilateral leg and located alongside the deep femoral veins with or without an associated sapheno-popliteal vein anastomosis. The theory behind this was to enhance venous return through extra vessels. Although of limited success Warren set the scene for surgically relieving venous outflow obstruction.

To bypass ilio-femoral venous obstruction Palma (Palma et al., 1960) developed the eponymous cross-over bypass procedure of anastomosing the contralateral LSV to the ipsilateral femoral vein distal to the point of obstruction, thus allowing enhanced venous drainage of the symptomatic limb via the contralateral iliac veins. This
procedure produced good results (Husni, 1971; Dale, 1979) and was adapted for use in limbs with obstructed popliteal veins (Husni, 1970a) with good results (Dale, 1982).

The use of synthetic grafts in the low pressure, high thrombotic venous system has been less successful than in the arterial system, and even using autologous vein patency rates in animal models are at best 55%. The use of anticoagulants, external graft supports to prevent collapse and the construction of arteriovenous fistulae remain contentious (McMullin, 1990).

2.5civ Experimental Procedures

Endovenous Surgery

To obviate the need for an open procedure and extensive dissection vein valve transfers have been carried out using an endovenous approach. Initially modelled in goats (Hughes et al., 1996) the first report of deployment of such a device in humans was presented by Richer de Forges et al. (1996). Essentially, this device combines an autologous axillary vein transfer with state of the art endovascular stent technology. Axillary vein was harvested in the usual manner retrieving a length of vein containing a competent valve. A Palmaz balloon expandable stent was sutured to each end of the vein segment and the entire stent - vein - stent device mounted onto an angioplasty balloon catheter. At the time of sapheno - femoral disconnection the balloon catheter (with stent) was passed through the saphenous ostium in the common femoral vein down into the superficial femoral vein where the two stents are expanded thus anchoring the device in place. Obviously, the vein to be transferred needs to be mounted on the balloon catheter in such a way to render the valve open to conventional cephalad flow of blood in the SFV but closed to blood flow in the refluxing direction thus returning competency to the SFV. It has been suggested that this type of device may be resistant to dilatation of the
transferred valve segment. Long term efficacy studies have yet to be presented but if the outcome is favourable then the ability to reliably repair the deep venous system will greatly improve the outlook for those patients with venous ulceration.

Experimental Valve Technology

Many animal models of deep venous valve reconstruction have been examined in an attempt to correct deep venous reflux but none have proved to be of any benefit largely because of thrombosis induced in the reconstructed segment despite anticoagulation. Hill (Hill et al., 1985) described a bicuspid flutter valve which occluded within 48 hours or 8 days depending on whether the valves were manufactured from tanned human umbilical vein or polyethane polymer. Similarly, Kaya (Kaya et al., 1988) implanted glutaraldehyde preserved autografts into dog external jugular vein with occlusion at 7 weeks. In an attempt to induce the ‘growth’ of a valve Warmenhoven (Warmenhoven et al., 1985) implanted a Silastic mandrel into dogs and removed it once a collagen sheath had grown into the shape of a valve which was subsequently transplanted autologously into femoral/jugular veins without anticoagulation- all had thrombosed within 16 weeks. Cardiac bioprosthetic xenografts (Phifer et al., 1989) were implanted into dog IVC but despite initial success 10/22 valves had thrombosed at 28 months, 9 giving rise to pulmonary emboli! A more successful result has been achieved by implanting monocusp valves fashioned from preserved bovine pericardium in a patient with SFV and LSV reflux (Garcia-Rinaldi et al., 1986) and postoperative anticoagulation for 6 months. Follow up was by Doppler and PPG and at 14 months the valves were patent and competent and the patients ulcers had healed without compression hose.
Summary

In summary, overall in non-obstructed refluxing systems valvuloplasty has been found to be the better of the above methods if a suitable valve is present (Raju, 1983; Raju et al., 1988) and although despite a 'curative' clinical outcome and a functioning valve venous pressures only improve in approximately 2/3 of limbs. In this study, long term oral anticoagulation was commenced 3 days postoperatively and no episode of thrombosis of valvuloplasty sites were reported beyond the immediate postoperative period. This has also been documented by others without the need for formal anticoagulation. As for obstructed deep veins bypass using either the Palma or Husni method is preferable to synthetic graft material. Although this will not render the deep veins necessarily competent it relieves the disabling symptoms of venous obstruction.

2.5d Skin Grafting

Recently published guidelines (Douglas et al., 1995) recommend that skin grafting be withheld until ulcers have had 12 months of unsuccessful compression therapy. Pinch grafts (Poskitt et al., 1987) are more robust than split skin grafts and can be applied on an outpatient basis. More recently cultured keratinocytes have been used but at present offer no advantage to conventional methods (Leigh et al., 1987). Silver described extensive debridement of the ulcer and in some cases the entire medial or lateral subcutaneous compartments (including the deep fascia) combined with perforator, long and short saphenous vein ligations followed by split skin grafting (SSG) or by covering the exposed muscle with the skin flaps raised by the procedure (Silver et al., 1971). Skin grafting, however, does not necessarily confer a cure with recurrence rates remaining high (Sebastian, 1994). This may be because of ongoing β-haemolytic
streptococcus or *Pseudomonas* infection or because the underlying venous disorder is inadequately corrected and so the grafted skin is ultimately exposed to the same underlying venous hypertension as the native ulcerated skin. SSG combined with superficial venous surgery only managed to maintain 63% of ulcers free from 'significant' recurrence at a mean of 42 months (Robison et al., 1992). Although skin grafting achieves ulcer healing the longevity of the graft will be purely temporary unless the underlying venous defect is corrected.

2.6 PHARMACOLOGICAL THERAPY OF VENOUS ULCERATION

It is an interesting concept to attempt to treat the sequelae of venous hypertension by pharmacological means, however, there are clearly documented microcirculatory abnormalities that may be pharmacologically manipulated to enhance lower limb skin blood flow. Since the primary venous abnormality may not be fully corrected (especially in the presence of deep venous reflux) manipulation of the local microcirculation may be the way forward in certain instances.

There are four main classes of drug that have been examined to date with specific reference to ulcer healing and they all exert their action via the skin microcirculation, specifically at the fibrin cuff or leukocyte (Colgan et al., 1992); they are detailed below.

*Fibrinolytic Therapy*

The anabolic steroid Stanozolol was developed to reverse the hypoxic effect of the pericapillary fibrin cuff. When used in combination with standard compression methods Stanozolol provided symptomatic relief and reduced the area of LDS (Browse
et al., 1977b) but did not influence the rate of ulcer healing (Layer et al., 1986) nor the AVP (Burnand et al., 1980). A newer profibrinolytic agent Defibrotide has been found to enhance ulcer healing again when used in combination with elastic stockings (Belcaro et al., 1989).

**Hydroxyrutosides**

O-(β-Hydroxyethyl)-rutoside (HR) reduces capillary permeability and oedema formation (Negus, 1992a) and, in combination with compression hose, has been found to improve transcutaneous partial pressure of Oxygen (tcpO₂) and venous refill times (Neumann et al., 1990). However, their role in improving the symptoms of chronic venous insufficiency or preventing ulcer recurrence is unproved (Anderson et al., 1990; Wright et al., 1991).

**Prostaglandins**

Prostaglandin E₁ acts via vasodilatation, inhibition of platelet and neutrophil activation and has been used for the treatment of peripheral vascular disease. By way of a placebo controlled trial Rudofsky (1989) demonstrated improved tcpO₂, symptoms and ulcer healing with intravenous PGE₁ and compression. Unfortunately an equivalent oral preparation is not available.

**Methylxanthines**

Having been used previously for the treatment of peripheral vascular disease, Pentoxifylline was examined in a multi centre, double blind, placebo controlled randomised trial as an adjunct to compression therapy (Colgan et al., 1990). Used in this way oral pentoxifylline significantly improved the rate of ulcer healing from 34% ulcers
healed at six months in the placebo and compression group to 64% with pentoxifylline and compression.

Several recently developed agents are under investigation including Gingo biloba (Colgan et al., 1993), Daflon (Nicolaides, 1994) and urokinase (Belcaro et al., 1989).

**Antibiotics**

These are not indicated in the absence of cellulitis or septicaemia, in which case they should be administered systemically (Eriksson, 1988). However, if an ulcer is failing to respond to otherwise adequate treatment a specific search for β-haemolytic streptococci is indicated followed by appropriate antibiotic therapy (Schraibman, 1990). Necrotic, sloughy ulcers are best treated by debridement. However, the case for Metronidazole is an exception. Ulcers infected with anaerobes may heal quicker if treated with oral or topical Metronidazole (Cheatle et al., 1991b).

**Zinc**

Supplements are indicated in those patients with dietary insufficiencies that have caused a low serum zinc level. The routine use of zinc supplementation in venous ulceration is not required as zinc deficiency in patients with venous ulceration is rare (Schraibman et al., 1985).

**Diuretics**

In cases of significant lower limb oedema a cause other than CVI must be sought and treated in its own right. The oedema of CVI usually responds to elevation and compression and the routine use of diuretics is not indicate. Care must be exercised in
the mobilisation of dependent oedema in the elderly or those with incipient heart failure
to avoid inducing pulmonary oedema by increasing the circulating volume too rapidly.

**Aspirin**

Aspirin used in combination with compression has been shown to enhance ulcer healing rates (Layton et al., 1994; Ibbotson et al., 1995).

Other therapeutic modalities that enhance the healing rate of venous ulcers are silver sulphadiazine cream (Bishop et al., 1992), ultrasound therapy (Callam et al., 1987b) and more recently the use of *Lucilia sericata* (green bottle maggots) has been resurrected for the debridement of infected necrotic ulcers (Thomas et al., 1996).
CHAPTER THREE

CHARACTERISATION OF THE VENOUS ABNORMALITIES IN ULCERATED LIMBS

3.1 GENERAL INTRODUCTION

3.2 REVIEW OF THE INITIAL EXPERIENCE OF A DEDICATED SINGLE VISIT VENOUS ULCER ASSESSMENT CLINIC
   a. Introduction
   b. Patients and Methods
   c. Results
   d. Discussion
   e. Summary

3.3 CONCLUSIONS AND IMPLICATIONS REQUIRING FURTHER INVESTIGATION
3.1 GENERAL INTRODUCTION

Venous leg ulcers are currently managed according to variable regimes and by a variety of clinicians including general practitioners, dermatologists, general, plastic and vascular surgeons. The common denominator in terms of actual ‘hands on’ ulcer management is usually the district or practice nurse, usually applying one of numerous primary dressings to the ulcer followed by various forms of bandage. It is not surprising that with the involvement of so many varied practitioners that ulcer management is variable and has varying degrees of success.

In order to effectively manage patients with venous ulceration it is necessary to offer a reliable, convenient and appropriate therapy (Morrell et al., 1998; Ghauri et al., 1998). This can only be achieved by accurately identifying an individual ulcer’s aetiology. This chapter achieves this by investigating the range of ulceration referred to a dedicated venous ulcer out patient clinic illustrating the varied pathophysiology encountered and thus posing a number of questions relating to the most appropriate treatment of an individual venous ulcer.

3.2 A REVIEW OF THE INITIAL EXPERIENCE OF A DEDICATED SINGLE VISIT VENOUS ULCER ASSESSMENT CLINIC

3.2a Introduction

Compression bandaging as the principle therapy for venous leg ulcers assumes that all venous leg ulcers will respond to external compression. This is not an unreasonable assumption as the underlying venous abnormality is raised ambulatory venous pressure for whatever reason and a broad range of methods to reduce venous
pressure have been used extensively in the past (Browse et al., 1988; Hunter, 1835; Dodd et al., 1976a; Mayberry et al., 1992). However, can it be assumed that compression bandaging is the optimal treatment for all venous leg ulcers? Before attempting to answer this question it is necessary to ascertain the underlying vascular abnormalities in ulcerated limbs. This requires accurate assessment of venous anatomy and function.

Recent advances in colour duplex scanning now allow rapid, non-invasive functional and anatomical assessment of both the arterial and venous systems of the lower limb. This facility, therefore, offers an ideal method of assessing patients with an ulcerated lower limb. Based on this imaging modality a single visit venous ulcer assessment clinic was established and this chapter reports the results of the first year. This is relevant not only to the effective planning of venous ulcer treatment for each individual patient but also gives valuable information that can be applied to the venous ulcer ‘population’ nationwide.

3.2b Patients and Methods

Patients who attended the Leicester Royal Infirmary Venous Ulcer Assessment Clinic during the period 1st May 1994 to 30th April 1995 were prospectively studied. All patients underwent a full clinical assessment and in particular, were questioned about previous venous thrombosis and venous surgery. In addition, the ankle brachial pressure index (ABPI) was measured and a venous duplex scan was performed. An arterial duplex scan was performed if the ABPI was less than 0.8. Ulcers in limbs with normal arterial and venous scans were biopsied under local anaesthetic in the clinic if they appeared atypical, or if a ‘venous type’ ulcer failed to respond to treatment as anticipated. As part of the general assessment of the patients presenting to the single
visit ulcer assessment clinic all patients had the following blood tests performed: full blood count, random glucose, urea and creatinine and albumin.

Ulcers were classified as venous if the only demonstrable abnormality was venous reflux; arterial if the ABPI was <0.8 with normal veins on duplex scanning and mixed if the ABPI was <0.8 with reflux in one or more venous systems.

The ABPI was measured in the standard manner (Negus, 1992b) using a continuous wave Doppler and mercury sphygmomanometer and was considered to be abnormal if <0.8 (Figure 3.1). Colour duplex scans were performed using either an ATL Ultramark 9 HDI (Advanced Technology Laboratories UK Ltd, Letchworth, Herts., UK) or a Diasonics Masters (Sonotron Ltd., Bedford, UK) machine (Figure 3.2). Arterial scans were performed as previously described by Sensier et al., (1996) and a significant stenosis was defined by the presence of a peak systolic velocity increase across the lesion of more than two-fold. The deep and superficial venous systems were examined with 5 MHz and 10 MHz linear array probes respectively. Patients were examined with the limb dependent and venous reflux was defined as the presence of reversed blood flow for more than 0.5 seconds after release of a calf squeeze distal to the segment of vein under examination (van Bemmelin et al., 1989). Figure 3.3 demonstrates the spectral image of a competent venous segment during calf squeeze and subsequent release. As can be seen after an initial period of reversed flow during which time the venous valves are closing no further reversed flow is present. An incompetent venous segment is shown in Figure 3.4 demonstrating prolonged reversed venous flow following release of the calf squeeze, a colour coded image of an incompetent sapheno-femoral junction is depicted in Figure 3.5 illustrating the clarity of definition of blood flow obtained using colour coded duplex.
Post-thrombotic damage was inferred from the following characteristics on duplex scanning: old intraluminal thrombus (incompressible vein); thickened/scarred vein walls; stenosis of the vein; shrunken and scarred valve cusps (Negus, 1992b). Venous obstruction was defined as no forward flow in the vein after a calf squeeze distal to the segment under examination with/without visible thrombus. We have defined the superficial venous system as the long and short saphenous and perforating veins; the deep system includes any vein deep to but not traversing the lower limb deep fascia.

Ulcer areas were determined at the time of consultation by taking tracings of the ulcer perimeter onto transparent acetate sheets with a fine-tipped permanent marker. Subsequent analysis by computerised planimetry provided the area of each individual ulcer seen. If more than one ulcer was present on a single limb the areas were combined to provide the total area of ulcerated limb.

Figure 3.1. Measurement of the Ankle Brachial Pressure Index (ABPI). The patient is positioned supine and a sphygmomanometer cuff used to occlude the dorsalis pedis artery. A continuous wave Doppler probe and amplifier is used to detect the disappearance and reappearance of the pulse.

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Figure 3.2. The portability of colour duplex equipment makes it ideally suited to the outpatient investigation of venous disease.

Figure 3.3. Doppler analysis of the response of a competent venous segment to a distally placed calf squeeze. C = cephalad flow during the calf squeeze, R = brief reversed flow following release of the calf squeeze during which time the normal venous valves close and A = absent flow during release of calf squeeze because of the closed competent venous valves.
Figure 3.4. Doppler analysis of the response of an incompetent venous segment to a distally placed calf squeeze. C = cephalad flow during the calf squeeze, R = reversed flow flowing the calf squeeze.

CFV = Common Femoral vein, SFJ = Sapheno-femoral Junction, LSV = Long Saphenous Vein. N.B. the probe orientation has been reversed between figures 3.3 and 3.4. Thus the direction of blood flow in the two figures appears to be in opposite directions.

Figure 3.5. The addition of colour coding to the direction of blood flow (blue = cephalad, red = reversed) adds clarity of interpretation to the duplex images. Here an incompetent sapheno-femoral junction is scanned during and on release of a distally placed calf squeeze.
3.2c Results

*Patients and Ulcers*

During this initial twelve month period, 88 patients presented with 104 ulcerated limbs. The median (range) age of the patients was 71 (36-93) years and 47% were male. As would be expected patients in this age group possessed a number of co-morbid diseases; eight (9%) patients were diabetic, one (1%) suffered from rheumatoid arthritis, one (1%) had scleroderma and one (1%) had a combination of diabetes and ankylosing spondylitis. The major source of referral was general practitioners (61, 69%), followed by dermatologists (16, 18%), other surgeons (9, 10%) and physicians (2, 3%).

The median (range) ulcer duration prior to referral was 2 years (6 weeks to 47 years) with a median (range) initial ulcer area of 9.6 (1.9 - 332) cm².

*Ulcer Aetiology*

The ABPI was <0.8 in a total of 15 (14%) limbs, and based on the combination of this criterion and duplex venous scanning, 82 (79%) were classified as venous, 2 (2%) as arterial and 13 (12%) as mixed. Of the remaining 7 ulcers, 4 were secondary to lymphoedema, 1 was a basal cell carcinoma and 2 were of uncertain aetiology.

*Distribution of Venous Reflux*

Ninety-five limbs demonstrated venous reflux. In ten (11%) limbs there were post-thrombotic deep vein changes apparent on duplex scanning, the remaining 85 (89%) limbs had no apparent post-thrombotic deep vein changes and were, therefore, assumed to have primary venous reflux.

In 54 (63%) of the 85 limbs with primary venous reflux this was confined to the superficial venous system, 1 (1%) had deep reflux only and 30 (35%) had combined
deep and superficial reflux. The distribution of reflux in those limbs with superficial reflux only is detailed in Table 3.1. In those 30 limbs with primary combined reflux the deep reflux was in combination with saphenous reflux in 28 (93%) and with perforating veins in 2 (7%). Of the 41 limbs with deep venous reflux (primary or secondary) all had involvement of the popliteal vein and the deep reflux was distributed as follows: deep and saphenous reflux combined 33/41 (80%); deep and perforating vein reflux combined 2/41 (5%) and deep reflux alone 6/41 (15%).

<table>
<thead>
<tr>
<th>Refluxing Veins</th>
<th>Number of Limbs (n=54)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long Saphenous Only</td>
<td>30</td>
<td>56</td>
</tr>
<tr>
<td>Short Saphenous Only</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>Long and Short Saphenous</td>
<td>13</td>
<td>24</td>
</tr>
<tr>
<td>Perforating Veins Only</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Saphenous (Long &amp;/or Short) and Perforating Veins</td>
<td>4</td>
<td>7</td>
</tr>
</tbody>
</table>

Table 3.1 Patterns of venous reflux in the 54 limbs with primary superficial reflux only.

**Deep Vein Thrombosis**

In 22 (23%) of the 95 limbs with duplex confirmed venous reflux there was a history of deep venous thrombosis (DVT). Of these 22 limbs, 13 (59%) had deep vein reflux and 9 (41%) had normal deep veins. Examination of the remaining 73 limbs, in which the patient did not give a history of DVT, 28 (38%) had deep vein reflux. Three (3%) limbs demonstrated deep venous obstruction and in all three cases the patient gave a history of previous DVT.
Varicose Veins

Of the 54 limbs with superficial reflux only (detailed in Table 3.1), 21 (39%) limbs had no clinically apparent varicose veins. Of the remaining 33 (61%) limbs with clinically apparent varicose veins, 5 (15%) limbs had not been considered for varicose vein surgery and 28 (85%) were awaiting surgery. Thus, 26 of the 54 (48%) limbs with superficial reflux only had not been offered superficial surgery.

Haematological and Biochemical Investigations

Of the 88 patients referred 12 patients (14%) were anaemic, 10 male (Hb <13.5 g/dL) and 2 female (Hb < 11.5 g/dL); 5 of these 12 patients were iron deficient. Two patients had a random glucose >11.1 mmol/L, one was already known to be an insulin dependent diabetic and the other patient with a random glucose of 14.3 mmol/L was not. Seven patients (8%) had a serum creatinine >120 μmol/dL, 5 male (creatinine levels of 124, 124, 128, 172, 193 μmol/dL) and 2 female (creatinine levels of 138 and 189 μmol/dL). No patient was found to have a low (<32 g/L) serum albumin concentration.

4.2d Discussion

A single visit venous ulcer assessment clinic with its accompanying nursing staff is advantageous for a number of reasons: it minimises the number of hospital attendances and enables a diagnosis to be made and appropriate treatment planned and instituted on the same occasion. In addition, before the commencement of the clinic patients with venous ulcers posed substantial practical problems for the vascular technologists and the vascular studies unit. This was because there was no trained nursing staff attached to the unit and the complete removal of bandages (essential for complete assessment) was either avoided or else the patient had to wait while a nurse
was located. The single visit clinic, however, is located in the outpatient department with a trained nurse continually present. This has obvious cost savings for the health service and is more appropriate to the elderly population requiring the service. This is born out by the finding that the median age of patients referred to the venous ulcer assessment clinic was 71 years with an upper limit of 93 years. Similarly the chronic debilitating nature of the condition is illustrated by the size of the ulcers referred (up to 332 cm²) and the duration of ulceration before referral (47 years in one instance). These findings re-enforce the indications for accurate assessment and subsequent appropriate therapy. Referrals were predominately made by general practitioners reflecting the large pool of community managed ulcers.

As a diagnostic service it provides the information necessary for the appropriate initial management of a leg ulcer. During the first year 12% of ulcerated limbs referred had significant co-existing arterial disease in addition to venous reflux, and more importantly 2% of limbs had purely arterial disease. It is particularly important to accurately identify this 14% of ulcerated limbs presenting with an arterial component not only because many will heal with correction of the arterial abnormality but because inappropriate compression bandaging of these limbs can have disastrous consequences (Callam et al., 1987). Seven percent of ulcerated limbs had neither a venous nor an arterial abnormality. The aetiologies in these limbs were 1 basal cell carcinoma, 4 primary lymphoedema and two cases in which no aetiology could be identified. A number of co-morbid factors were identified in the patients described but were not primarily responsible for ulceration. In particular all of the diabetics studied had an ABPI > 0.8 excluding significant arterial disease and no diabetic patient had evidence of a peripheral neuropathy.
Nutrition and wound healing are closely related, and a low dietary intake of protein (Breslow et al., 1994) and Vitamin C (Goode et al., 1992) are associated with the development of pressure sores. Despite the elderly age of the patients referred during the first year only 14% were anaemic and none were hypoalbuminaemic. This contrasts with recent work by Busari-Alabi et al. (1994) who examined 40 consecutive elderly (average age 76 yr.) patients with leg ulcers. They found 25% of these patients were anaemic and approximately 55% were hypoalbuminaemic. The experience described in this chapter would suggest that the routine examination of serum albumin would not alter the management of these patients and of the factors examined one new diabetic was discovered but no major deficiencies that would influence wound healing were highlighted.

Sixty-three percent of limbs with venous ulcers and no evidence of previous DVT had reflux confined to the superficial system only. This figure is higher than the 28-39% reported in studies using continuous wave hand held Doppler (Sethia et al., 1984; Hoare et al., 1982; Darke et al., 1992), but is in close agreement with the 52 and 53% described in other colour coded duplex studies (Lees et al., 1993; Shami et al., 1993; Grabs et al., 1996). This may reflect the diagnostic inaccuracy of continuous wave Doppler especially when used in the popliteal fossa (Coleridge-Smith, 1992 & 1994; Lane, 1996) rather than any change in the underlying pattern of venous disease. It has recently been suggested that isolated superficial venous reflux as the sole aetiological factor in venous ulceration is more common than previously thought (Shami et al., 1993) putting to rest the previously held belief that ulceration occurs only in the presence of post-thrombotic deep venous damage. With this finding in mind it is important to note that 39% of limbs in this study with gross duplex detected isolated superficial venous reflux did not have visible varicose veins despite many of these limbs
being thin with no oedema. In accord with others (Coleridge-Smith, 1992, & 1994) it is important, therefore, that all ulcerated limbs are adequately assessed not only to identify those patients who may benefit from superficial venous surgery but to adequately assess the aetiology of ulceration. This statement is re-enforced by the finding that clinical history alone is a poor indicator of deep venous function. Thus, of those 22 limbs in which the patient gave a history of a definite previous DVT, deep venous function was normal in 9 (41%), implying that 41% of DVTs recanalise with fully functional venous valves or that the original diagnosis given to the patient was incorrect. The former is not unreasonable as valve destruction is not a universal consequence of DVT (Meissner, 1995) and complete resolution of venous function as defined by duplex scanning is recognised (Johnson et al., 1995). The incidence of deep venous reflux two years after an acute DVT has been found to be 63% (Markel et al., 1992) which correlates with the finding that 40% of venous segments with previous DVT do not develop venous reflux on recanalisation (Van Haarst et al., 1996). Conversely, of the 73 limbs in the Leicester series with a history of no DVT 28 (38%) had abnormal deep veins. The clinical importance of this is that many patients with venous ulcers and a history of DVT (41% in this series) may benefit from superficial venous surgery, whilst an equal number (38%) without a history of DVT may not benefit from superficial venous surgery. This is an important point when contemplating surgery in this group of patients.

A further feature highlighted by this study was the small number, 6 (11%), of refluxing perforating veins identified by duplex scanning. This is important when considering the possible surgical treatment of venous reflux, and highlights the fact that only 1 in 10 ulcerated limbs have evidence of perforating vein reflux suggesting that in the majority of patients perforating vein surgery may not be required. However, the role of perforating vein surgery in venous ulceration needs its own evaluation.
3.2e Summary

This study has highlighted a number of important issues in the management of venous ulceration, not least in the degree of vigilance required in the initial investigation of an ulcerated limb. Firstly arterial disease must be excluded as the incidence of significant arterial impairment was found to be 14% in this series of 104 limbs. Second, in the absence of arterial or venous disease another pathology must be actively sought and histological examination is recommended to confirm or refute the suspicion that an ulcer may be malignant. Third, an accurate assessment of the deep, superficial and perforating veins is required in order to identify those limbs that may benefit from superficial venous surgery and to establish the state of the deep veins prior to disregarding surgical intervention on the basis of a clinical history of DVT alone. Finally, the absence of visible varicose veins must not lead to the assumption that superficial venous incompetence is absent when it is possibly the only venous abnormality giving rise to ulceration.

3.3 CONCLUSIONS AND IMPLICATIONS FOR FURTHER INVESTIGATION

This chapter has reported the findings encountered in clinical practice and has raised a number of questions that require further investigation in order to optimise the range of therapies applied to venous ulcers. The most important point to be answered involves the role of venous surgery in the management of venous ulceration. I have demonstrated that in limbs with venous ulceration and primary venous reflux 63% of limbs had superficial reflux only and 35% have deep and superficial reflux combined. The role of superficial venous surgery in these two groups of limbs needs evaluating. It
is also apparent that the degree of deep venous reflux is variable and if simple surgery is efficacious then defining the value of such surgery would be of benefit to patients with venous ulceration of all aetiologies. The prevalence of perforating vein reflux is small in this study bringing into question the role of perforating vein reflux in ulceration and consequently the value of perforating vein surgery.
CHAPTER FOUR

EXAMINATION OF TWO COMMONLY USED COMPRESSION BANDAGES
FOR THE TREATMENT OF VENOUS ULCERATION

4.1 GENERAL INTRODUCTION

4.2 A PROSPECTIVE RANDOMISED TRIAL OF SHORT STRETCH VERSUS
FOUR LAYER (CHARING CROSS) COMPRESSION BANDAGES FOR
THE TREATMENT OF VENOUS LEG ULCERS
a. Introduction
b. Patients and Methods
c. Results
d. Discussion
e. Summary

4.3 AN EXAMINATION OF THE PRESSURE PROFILES OF SHORT STRETCH
AND FOUR LAYER COMPRESSION BANDAGES
a. Introduction
b. Patients and Methods
c. Results
d. Discussion
e. Summary
4.4 THE DEVELOPMENT OF A PRESCRIBABLE FOUR LAYER COMPRESSION BANDAGE FOR THE TREATMENT OF VENOUS ULCERATION

a. Introduction

b. Patients and Methods

c. Results

d. Discussion

e. Summary

4.5 CONCLUSIONS
4.1 GENERAL INTRODUCTION

Venous leg ulceration in the U.K. is predominately managed in the community using various types of compression bandaging. The chronic, recurrent nature of venous ulceration and the financial costs necessitate the optimisation of any treatment used. Two commonly used methods of applying lower limb compression are short stretch and four layer (Charing Cross) bandages. However, there are few studies in the literature comparing the efficacy of these two bandage systems. This chapter examines the efficacy of short stretch (Rosidal K) and four layer (Charing Cross) bandages in the form of a prospective randomised clinical trial. In addition, the pressure profiles beneath the two bandaging systems have been recorded.

At the time these studies were performed neither four layer nor short stretch bandages were available on prescription (FP10) and with this in mind the development of an alternative four layer compression bandage is described using components available via an NHS prescription. Some of the physical properties of this alternative four layer system relevant to clinical practice are outlined as well as the potential cost advantages.
4.2 A PROSPECTIVE RANDOMISED TRIAL OF SHORT STRETCH VERSUS
FOUR LAYER (CHARING CROSS) COMPRESSION BANDAGES FOR THE
TREATMENT OF VENOUS LEG ULCERS

4.2a Introduction

Compression bandaging is the established method of treatment for venous ulcers
and two frequently used bandage systems are the short stretch and four layer regimes.
Initial non-randomised uncontrolled trials reported by Blair et al. (1988) and Moffatt et
al. (1992b) suggested that approximately three-quarters of ulcerated limbs would heal by
12 weeks using the four layer system. Duby et al. (1993) compared four layer and short
stretch bandages in a prospective randomised manner and found healing rates of 44%
and 40% respectively at 12 weeks although the number of limbs in this trial was small
(only 25 legs per limb of the study). Only one study has reported improved efficacy
using multi-layered bandages in a prospective, randomised manner (Nelson et al.,
1995a) with healing rates among 200 legs using multi-layer and single layer bandages of
69% and 49% respectively at 24 weeks. Thus, from the available evidence it remains
unclear which of the two commonly used compression bandages, short stretch or four
layer is more efficacious. In order to address this clinically and economically important
issue I report the results of a prospective, randomised trial comparing four layer and
short stretch compression bandages.

4.2b Patients and Methods

Patients

Fifty-three patients with active lower limb ulceration were identified from those
attending the Venous Ulcer Assessment Clinic at which each limb underwent a full
assessment as described in Chapter 3. Ulcers were identified as venous if the only
demonstrable abnormality was venous reflux of >0.5 seconds duration and an ankle brachial pressure index (ABPI) of >0.8.

**Study Design**

The study was designed to examine the safety and efficacy of four layer (FLB) and short stretch (SSB) compression bandages when used to heal venous ulcers in a prospective, randomised manner with the approval of the local ethical committee. Limb randomisation was performed at the first attendance for bandaging and was achieved using sealed envelopes naming the type of bandage to be applied determined by a block randomisation method (Altman, 1996); in addition limbs were stratified within each arm of the trial by initial ulcer area into two groups; 10 cm\(^2\) or less and over 10 cm\(^2\). Patients with bilateral disease had each ulcerated limb randomised separately, thus it was possible for a single patient to be prescribed different bandages for each leg. The type of bandage remained unchanged until the ulcers had healed. However, if by 12 weeks there was no evidence of ulcer healing or the ulcers deteriorated within that time then that limb was deemed to have failed with the allocated bandage and was withdrawn from the trial. After withdrawal, the alternative bandage was applied in an attempt to achieve ulcer healing. At the initial hospital visit for commencement of bandaging the size of each ulcer was measured and leg volume recorded. This was repeated every two weeks until that individual limb had completed the trial protocol or had been withdrawn.
**Colour Duplex Scanning**

A colour duplex scan of the deep and superficial veins was performed at the assessment clinic visit to define venous anatomy and function with particular reference to the pattern of venous reflux in each limb. Venous reflux was defined as the presence of reversed blood flow for more than 0.5 seconds on release of a calf squeeze distal to the segment of vein under examination. The superficial venous system was defined as the saphenous veins, their tributaries and the perforating veins; the deep venous system included any vein deep to but not traversing the lower limb deep fascia. Evidence of previous deep vein thrombosis (DVT) was inferred from the following features on duplex scanning: old intraluminal thrombus (incompressible vein), thickened and/or scarred vein walls, stenosis of the vein and shrunken and scarred valve cusps.

**Ulcer Area**

Ulcer areas were obtained by computerised planimetry of tracings of the ulcer perimeter made onto transparent acetate sheets taken at the time of first bandaging attendance and at two weekly intervals thereafter. Ulcer healing was determined by inspection and deemed to be complete if full re-epithelialisation had occurred.

**Leg Volume**

Leg volume was calculated using the ‘multiple disk model’ (Badger, 1993; Tierney et al., 1996). The limb circumference was measured (in centimetres) at 4 cm intervals from the tip of the medial maleolus to the tibial tuberosity. Where the tibial tuberosity fell between measurement points the final disk circumference was recorded at the closest point distal to the tuberosity. The volume is calculated thus:
where: \( C = \) circumference corresponding to each 4 cm interval

\[
\sum_{i=1}^{n} \frac{C_i^2}{\pi}
\]

\( n = \) the number of 4 cm segments (this will vary in proportion to the limb length)

Volumes were calculated from measurements taken at 2 weekly intervals at the time of bandage changes with the patient in a supine position. The 4 cm intervals were marked on the skin, and I personally performed all measurements to ensure consistency throughout the study period.

**Bandages and Dressings**

A standardised method of ulcer dressing was adopted throughout the study period and was carried out by trained nursing staff with many years experience in the techniques of compression bandaging thus ensuring reproducible bandage application for the duration of the study period. The primary dressing throughout the study period consisted of simple non-adherent NA dressings (*Johnson & Johnson Ltd., UK*) (Blair et al., 1988) followed by a layer of sterile gauze. The compression bandages were applied on top of this as follows: the FLB (Figure 4.1) was applied in the standard manner (Moffatt et al., 1992b; Freak et al., 1992) defined by the ankle circumference and consisted of Velband (*Johnson & Johnson*), Crepe, Elset (*Seton*) and Coban (*3M*). The SSB (Figure 4.2) was Rosidal K (*Lohmann*) and was applied in accordance with the manufactures recommendations of 50% stretch with 50% overlap between turns. A minimum of 2 layers of wool (Velband) was applied around the ankle and along the tibial crest to protect these bony prominences from local pressure effects. Unfortunately, our early experience with this bandage before the commencement of the trial found it necessary to apply a cohesive retaining layer overlying the Rosidal K in order to prevent
it from slipping down towards the ankle rendering it ineffective as a compression bandage. This layer was in the form of Coban applied without any stretch such that its contribution to the overall compression was minimal whilst ensuring retention of the Rosidal K.

Compression pressure was measured as the sub-bandage pressure using a Talley II Oxford Pressure Monitor (Talley Group Ltd., UK.) (Figure 4.3). A small flat plastic ‘envelope’ (Figure 4.4) is located between the bandage and the primary dressing and the attached tubing brought to the bandage surface by a suitable route between the bandage layers (Figure 4.5). The free end of the tubing is connected to the Oxford Pressure Monitor. Pressure readings were taken twenty minutes after application of the bandage components (to allow the bandage to settle on the leg) at a point 4 cm proximal to the medial maleolus representing the sub-bandage pressure at the ankle. Data to be reported in Section 4.3 found the median (range) increase in sub-bandage pressure at the ankle caused by the additional layer of Coban was 11.5 (-1 to 18) mmHg. Bandages were changed once weekly, or occasionally more frequently if clinically indicated by excessive exudate and bandage soiling. The FLB was replaced with all new components at each visit whereas patients in the SSB arm of the trial were supplied with two Rosidal K, one to be used and the other washed by the patient for use at the next bandage change. After 20 washings the bandages were replaced. Once healed, the limb was measured by an orthotist and a Class II below knee compression stocking was fitted.
Figure 4.1 (a-d). The four layer bandage (FLB). a) All components shown, NA dressing, Wool, Crepe, Elset, Coban, b) layer 1 of wool, c) layer 2 of Crepe, d) layer 3 of Elset. The completed bandage possesses an additional layer (4) of Coban.
Figure 4.2 (a-d).  a) All components of the short stretch bandage (SSB), NA dressing, Wool, Rosidal K, complete layer of Rosidal K, b) Wool applied to pressure points, c) Rosidal K (50% stretch, 50% overlap) d) completed bandage with covering layer of Coban.
Figure 4.3. Talley II Oxford Pressure Monitor configures to measure pressure at three sites sequentially.

Figure 4.4. Close up view of the plastic pneumatic ‘envelope’ placed beneath the bandage to measure sub-bandage pressure. The small plastic tube courses between bandage layer to reach the surface. (Visible in Figure 4.2b,c,d).
Figure 4.5. The final appearance of a short stretch compression bandage with the OPM sensors in position. As can be seen the measurement of sub-bandage pressure can be done with minimal invasion and disruption of the bandage.

Analysis of Data

Ulcerated limbs were analysed on an intention to treat basis and efficacy was determined for each of the two trial arms. Data were analysed using non-parametric statistics as appropriate. Continuous variables within the two arms of the trial were directly compared using the Mann Whitney U statistic, and healing rates were examined in the form of Kaplan-Meier plots comparing trial arms with the log rank test. Data from the two trial arms were combined and the following factors were examined using $\chi^2$ for an association with complete ulcer healing: initial ulcer area $>10\, \text{cm}^2$, ulcer duration $>6$ months, evidence of a previous DVT, and the presence of deep venous reflux. The computer software Statistical Package for Social Sciences (SPSS, Chertsey, U.K.) was used for the analysis.
4.2c. Results

Randomisation

Fifty-three patients (64 ulcerated limbs) were randomised to receive either FLB or SSB. Of these patients, 20 were male and the median (range) age for all 53 patients was 73 (36-93) years. Forty-two patients had unilateral ulcers (26 left leg and 16 right) randomised thus, FLB 22 limbs and SSB 20 limbs. Eleven patients had bilateral ulcers randomised as follows; FLB to one leg and SSB to the other 7 patients, SSB to both legs 2 patients and FLB to both legs 2 patients. Thus of the 64 ulcerated limbs 32 were allocated FLB and 32 SSB. The proportion of limbs with initial ulcer areas >10 cm² in each arm of the trial was as follows: FLB 21/32 and SSB 14/32 ($\chi^2 = 2.20$, df = 1, P = 0.14).

During the study period one patient died after two attendances and two patients repeatedly failed to attend and ultimately defaulted from follow up to the community nursing service. These latter two patients represented two ulcerated limbs randomised FLB one limb and SSB one limb. They were subsequently considered as treatment failures and are thus included in the analysis of results on an intention to treat basis.

The characteristics of the two trial arms are detailed in Table 4.1. The two groups were comparable for each of the features examined.
Table 4.1. Details of the two arms of the trial. Values are reported as median (range), # Mann-Whitney U Test, *χ²=2.20, df=1.

<table>
<thead>
<tr>
<th></th>
<th>Short Stretch Limb (n=32)</th>
<th>Four Layer Limb (n=32)</th>
<th>Significance Level (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>73 (36 - 93)</td>
<td>70 (45 - 91)</td>
<td>0.34#</td>
</tr>
<tr>
<td>Initial Ulcer Area (cm²)</td>
<td>8.3 (2 - 104)</td>
<td>13.3 (2 - 378)</td>
<td>0.05#</td>
</tr>
<tr>
<td>Number of Limbs with Ulcers &gt;10 cm²</td>
<td>14</td>
<td>21</td>
<td>0.14*</td>
</tr>
<tr>
<td>Ulcer Duration (months)</td>
<td>21 (3 - 360)</td>
<td>13 (1-480)</td>
<td>0.47#</td>
</tr>
<tr>
<td>Initial Ankle Circumference (cm)</td>
<td>25.3 (26 - 32)</td>
<td>24.5 (20 - 32)</td>
<td>0.29#</td>
</tr>
<tr>
<td>Initial Limb Volume (L)</td>
<td>2.75 (1.37 - 4.22)</td>
<td>2.44 (1.40 - 4.48)</td>
<td>0.16#</td>
</tr>
</tbody>
</table>

Ulcer Healing

Overall ulcer healing rates for each arm (SSB and FLB) of the trial are shown in the form of a Kaplan-Meier plot (Figure 4.6). The ulcer healing rate at 1 year was 55% for the FLB group and 57% for the SSB group, Log Rank analysis found no difference in efficacy (χ²= 0.0, df 1, P = 1.0).
Figure 4.6. Kaplan-Meier Plot of Ulcer Healing by Bandage. FLB= Four Layer Bandage, SSB= Short Stretch Bandage. For all data points the standard error is <10%.

Since both bandages demonstrated equal efficacy, data from the two arms of the trial were combined and the following characteristics were examined for any influence on complete ulcer healing: initial area >10 cm², duration of ulcer >6 months, duplex evidence of previous DVT, presence of deep venous reflux. These data are outlined in Table 4.2. None of the above mentioned factors showed an association with complete ulcer healing.
Healing Rate for FLB and SSB combined

<table>
<thead>
<tr>
<th>Ulcer Area</th>
<th>Healing Rate</th>
<th>$\chi^2$</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>$&gt; 10 \text{ cm}^2$</td>
<td>17/35 (49%)</td>
<td>1.17</td>
<td>0.28</td>
</tr>
<tr>
<td>$&lt; 10 \text{ cm}^2$</td>
<td>18/29 (62%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ulcer Duration &gt; 6 months</td>
<td>27/47 (57%)</td>
<td>0.27</td>
<td>0.60</td>
</tr>
<tr>
<td>&lt; 6 months</td>
<td>8/17 (47%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Evidence of Previous DVT</td>
<td>8/11 (72%)</td>
<td>1.74</td>
<td>0.19</td>
</tr>
<tr>
<td>No Evidence of Previous DVT</td>
<td>27/53 (51%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deep Venous Reflux</td>
<td>15/31 (48%)</td>
<td>0.96</td>
<td>0.33</td>
</tr>
<tr>
<td>No Deep Venous Reflux</td>
<td>20/33 (61%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 4.2. The influence of initial ulcer area, ulcer duration, previous DVT and deep venous reflux on complete ulcer healing. For each characteristic one degree of freedom exists. Data from both arms of the study combined.

**Effect of Compression on Leg Volume**

Leg volumes in each of the trial arms at the initial visit, four weeks after commencing bandaging and the percentage reduction in volume at four weeks are shown in Table 4.3. Both bandages dispersed oedema to an equal degree.

<table>
<thead>
<tr>
<th></th>
<th>SSB</th>
<th>FLB</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vol 0 (L)</strong></td>
<td>2.75</td>
<td>2.44</td>
</tr>
<tr>
<td></td>
<td>(1.37 - 4.22)</td>
<td>(1.40 - 4.48)</td>
</tr>
<tr>
<td><strong>Vol 4 weeks (L)</strong></td>
<td>2.33</td>
<td>1.92</td>
</tr>
<tr>
<td></td>
<td>(1.31 - 4.24)</td>
<td>(1.33 - 3.47)</td>
</tr>
<tr>
<td><strong>Percentage reduction (%)</strong></td>
<td>13.1 #</td>
<td>8.8 #</td>
</tr>
<tr>
<td></td>
<td>(73.4 to -1.4)</td>
<td>(48.2 to -53.1)</td>
</tr>
</tbody>
</table>

Table 4.3. Leg volumes at first attendance, 4 weeks later and the percentage reduction in volume after four weeks of compression therapy. Values are expressed as median (range). # P = 0.34 (Mann Whitney U).
Complications

Of the 32 limbs randomised to receive four layer bandages only one limb (3%) sustained any complication. This consisted of minor haemorrhagic blistering of the toes distal to the bandage which fully resolved without sequelae. The initial ankle circumference in this case was 25 cm.

Of the 32 limbs receiving short stretch bandages 4 limbs (13%) sustained clinically significant complications as follows: Exposure of tibialis anterior tendon at the level of the ankle joint crease (ankle circumference 21.8 cm) and one limb experienced necrosis of the heel in association with patchy necrosis of the skin overlying the tibial crest (ankle circumference 20 cm); these limbs were two of the thinnest of all limbs studied. Two further limbs suffered significant skin maceration (ankle circumferences 24.5 and 29 cm); one of these limbs was the most oedematous in the SSB arm.

4.2d Discussion

The optimal non-surgical treatment of chronic venous ulceration is graduated compression bandaging (Ruckley, 1992) rather than a noncompressive bandaging such as a paste based bandage. The most efficacious compression bandage has not been identified.

This study compared the efficacy of two compression bandages, FLB and SSB, in a prospective, randomised, stratified manner. The end point of a completely healed ulcer was chosen to eliminate the potential difficulty of interpreting rates of wound closure for ulcers of varying contour. Although methods have been described to standardise the rate of advancement of a wound edge (Gilman, 1990) a healed wound is a definitive and incontrovertible end point. The components and method of application of the FLB have been previously described (Blair et al., 1988). However, in this study the SSB (Rosidal K) required an additional layer of Coban as a retaining layer. Without this extra
retaining layer the SSB failed to remain in place on the leg for seven days. Others have also found maintaining an SSB in position difficult without recourse to an extra retaining layer (Duby et al., 1993). The Coban described in this instance was applied without tension to minimise any additive compressive force. Although this produced an increase in compression of 11.5 mmHg due to the Coban this could only act to enhance the compression rather than detract from it, thus this does not alter the validity of the findings (see Chapter 4.3).

The characteristics of the two arms of the trial are comparable (Table 4.1) although the median ulcer area was slightly larger in the FLB arm. This is explained by the broad range of ulcer areas included in the study and that no upper limit of ulcer area was enforced as an exclusion criterion. Furthermore, the study was stratified by initial ulcer area into two groups; 10 cm² or less, and >10 cm²; examining the proportions of ulcers in each study limb confirmed an even distribution of ulcers size across the two study arms. It is noteworthy that the median areas reported here exceed those appearing elsewhere in the literature (Blair et al., 1988; Moffatt et al., 1992b) more recently, others have reported mean ulcer areas (Duby et al., 1993; Charles, 1991) which will give the impression of larger ulcers having been studied. In this report the mean ulcer areas were as follows; FLB 49.6 cm² and SSB 19.1 cm² misleadingly exaggerating ulcer size because of the range in ulcer areas recruited to the study. It is possible that the ulcer dimensions seen in our ulcer clinics are greater than those in the community as many patients referred for a vascular surgical opinion may be a select group by nature of their reluctant ulcer healing and hence stage of disease. Furthermore, this study was performed during the early stages of the Venous Ulcer Assessment Clinic; it is thus possible that many of the patients were referred because the General Practitioners responsible for them recognised a ‘difficult’ ulcer and thus referred onwards.
No significant difference in the ability of either bandage to heal ulcers was found. Stratifying by ulcer area demonstrated no greater ability for FLB over SSB to successfully heal large or small ulcers. In view of this clinicians and patients can be encouraged that even large ulcers can be successfully treated by adequate outpatient compression bandaging.

Although efficacy was not dependent on the bandage type, four significant complications occurred in the SSB arm and one minor complication in the FLB arm. Interestingly, the most serious complications occurred in the SSB arm and involved pressure induced ulceration in non-oedematous limbs with small ankle circumferences and significant maceration in limbs with larger, more oedematous legs. In fact, the iatrogenic ulceration occurred in two of the three smallest limbs studied and one of the macerated limbs was the most oedematous in the study. No such pressure induced complications were found in the small limbs in the FLB group, likewise maceration was less problematic in oedematous limbs treated with FLB. This is most likely related to the composition of the bandages. Short stretch bandages having fewer layers will exhibit a reduced absorptive capacity when compared to FLB hence the increased maceration as leaking tissue fluid will be held in contact with the non-ulcerated surrounding skin rather than being draw into the bandage keeping the skin relatively dry. Similarly having fewer layers seems to enhance any local pressure effects despite the recommended wool padding giving rise to more iatrogenic ulceration. This has been recently highlighted by Stockport et al (1997) who reported high poorly graduated pressures from the use of single layer compression bandages. Four layer bandages on the other hand exert a more evenly distributed pressure profile (Callam et al., 1991; Stockport et al., 1997), reducing iatrogenic ulceration in small limbs and the extra layer of crepe and complete layer of wool seemed to absorb tissue fluid resulting in absence of severe maceration in this study arm.
Limb volumes were indirectly obtained from the summation of 4 cm deep disks between two fixed points (medial maleolus and tibial tuberosity). Water displacement techniques are considered to be the 'gold standard' method (Tierney et al., 1996) but this would be impractical for the often elderly patients with ulceration who are of limited mobility. Leg volumes behaved as expected i.e. most of the oedema was dispersed in the initial month of bandaging, this period corresponds to the period during which legs can appear to exude larger quantities of fluid. Once the excess tissue fluid has been either absorbed into the circulation (compression increases the extravascular hydrostatic pressure) or lost via the ulcer base into the bandages subsequent leg volumes changed little and the leg volume at healing was similar to that after one month compression. The two concerns of patients experiencing this fluid loss into the bandage was the odour associated with the wet bandage which disappeared on removal of the bandage where the ulcer itself was not found to be malodorous; in addition the exudate coagulated in the bandage causing it to set hard like a plaster cast in a small number of cases. These two factors were pivotal in deciding to change the bandages twice weekly rather than once per week.

One major criticism of this study is the sample size of 64 limbs. Studies of similar size comparing bandage efficacy have failed to identify any significant difference between the two types of bandage they studied (Duby et al., 1993; Cameron et al., 1996). The only study to report a statistically significant result of one bandage type over an other reported a sample size of 200 limbs (Nelson et al., 1995a). As such it must be considered that a Type II statistical error may have occurred in the study. This can only be corrected by extending the sample size by a further study.

In comparing two treatments the cost of each is becoming an increasingly important and influential factor in prescribing. The cost of all components (January 1998 prices) in the four layer bandage used here obtained from a high street retail
pharmacy was £15.10 and assuming that each limb is bandaged once per week and takes twenty six weeks to heal the total cost of bandages is £392.60. Considering the short stretch bandage priced from the same pharmacy, two short stretch bandages were supplied at the initial visit and changed after 20 washes, these two bandages would therefore last for 40 weeks. Changing the short stretch bandage weekly only required replacement dressings, wool and Coban thus this regime costs £7.10 and over a six month period the cost is £184.56. These calculations take no account of the hidden costs such as ambulance transport to and from the hospital and staff salaries but for the purpose of comparing costs of two bandages these can largely be ignored as these costs are common to both arms of the study.

However, despite the inference that SSBs are cheaper than FLBs the cost of treating any ensuing complications must be borne in mind. In this study we report two major and two lesser complications in legs treated with SSBs. Obviously the management of such complications will probably offset any financial gains resulting from the use of a cheaper bandage technique.

Most of the complications experienced in this study occurred in the SSB arm of the study in limbs at the extremes of leg circumference (i.e. the thinnest or most oedematous). Thus, it would be reasonable to suggest that short stretch bandages would be adequate for most limbs of typical dimensions whereas very thin or oedematous limbs may benefit from four layer bandages in an empirical attempt to reduce iatrogenic complications.

4.2e Summary

This study describes the efficacy of short stretch and four layer compression bandages used to treat venous ulceration. Both bandages were found to be equally effective but the SSB required external support by a retaining layer of cohesive bandage
and was associated with complications in limbs with dimensions at the extremes of those studied.

4.3 AN EXAMINATION OF THE PRESSURE PROFILES OF SHORT STRETCH AND FOUR LAYER COMPRESSION BANDAGES

4.3a Introduction

Section 4.2 described the efficacy of two commonly used compression bandages (short stretch and four layer) and found there was no advantage of one over the other. The two bandages differed significantly in their construction i.e. four layers versus two, and the short stretch bandage required an additional layer of cohesive material to ensure the bandage remained in the desired position on the leg. This additional layer converted an intended single layered bandage into a two layer bandage which would presumably have an influence on the pressure profile of the bandage. As efficacy between these two bandages is comparable, the contribution of the various individual components of each bandage to the sub-bandage pressure is of interest considering the differences in bandage construction. Furthermore, maintaining the bandages insitu on the ulcerated limb for seven days is convenient for both patients and nursing staff but this would only be of therapeutic benefit to the patient if the sub-bandage pressure is maintained over this seven day period. The sub-bandage pressure for both four layer (Blair et al., 1988) and short stretch (Charles, 1991) bandages can be maintained for 7 days. The pressure profile of the SSB and FLB used at The Leicester Royal Infirmary have yet to be documented in terms of the maintenance of graduated pressure and a low resting pressure. In addition, the overall behaviour of four layer compression bandages remains unknown; no reports have appeared in the literature describing whether four layer
bandages behave as a long stretch or short stretch device, the two commonly described profiles of elastic compression bandages.

The ambulant measurement of sub-bandage pressure is made possible by the use of an Oxford Pressure Monitor (Talley UK Ltd.). This instrument uses small plastic envelopes, inflated by a pneumatic device from which the pressure in the envelope is determined to a tolerance of +/- 4 mmHg (personal communication Talley UK Ltd.).

This study aims to investigate: the individual contribution of the various layers of the SSB and FLB to the sub-bandage pressure developed; the pressure profiles of the SSB and FLB used in this study over seven days and to attempt to classify the FLB used here in terms of long/short stretch characteristics.

4.3b Patients and Methods

Study Design and Methodology

This study aimed to investigate three aspects of compression bandaging:

First, how do the individual layers of the four layer and short stretch bandages contribute to the sub-bandage pressure and does the application of these bandages in the outpatient department of The Leicester Royal Infirmary produce adequately graduated pressure with a low and hence safe resting pressure? In addition, the short stretch bandage used at The Leicester Royal Infirmary required an additional retaining layer of Coban; the influence of this layer on the sub-bandage pressure needs clarification. This investigation was performed by recruiting 10 healthy volunteers from the hospital staff. Ten legs were bandaged with FLB and 10 legs with SSB, overlying three pressure sensors located at the ankle, calf and knee. Pressures were measured both supine and standing erect after the application of each bandage layer to document the contribution of each layer to the developing sub-bandage pressure. Each newly applied layer was allowed to ‘settle’ for 20 minutes before the pressure was recorded. The components
used in the FLB consisted of wool, crepe, Elset, and Coban. The components of the SSB included a localised layer of wool over pressure points, Rosidal K and one of two retaining layers (Stockingette or Coban). Two retaining layers were examined to ensure the most appropriate component was used in the definitive SSB.

Second, the pressure profiles of each bandage is investigated over seven days to ensure that an adequate pressure at the ankle is maintained along with graduation of compression and a safe resting pressure. Twenty patients with ulcerated limbs having previously been randomised to receive either FLB (10 limbs) or SSB (10 limbs) (section 4.2 above) were recruited. When attending for bandage changes, the three pressure sensors were placed in the ankle, calf and knee positions prior to application of the FLB or SSB as appropriate. Pressures were recorded in both supine and erect positions at 20 minutes, 4 hours, 24 hours and then at 24 hourly intervals for seven days. Pressures were recorded in the morning and as far as possible the same time each day to allow for any changes in limb dimension over the day (Coleridge-Smith et al., 1986). This study was performed only after the subjects had undergone bandaging for at least one month to allow for the initial dispersion of leg oedema and hence pressure measurements were carried out on a limb of stable dimensions.

Third, an attempt is made to define how the four layer bandage behaves during simulated ambulation. Simulated ambulatory sub-bandage pressures were recorded for Tubigrip, SSB, FLB and a long stretch bandage (LSB) (BP blue line webbing). Ten volunteers were recruited and pressure sensors were located in the usual three sites and the bandages applied. With the subject standing, pressures were recorded over a one minute period whilst the subject performed tip toe exercises at a rate of approximately one every 2 seconds. At the end of 1 minute the minimum and maximum pressures recorded beneath the bandage were noted producing a working range of sub-bandage pressure. The nature of compression bandages is such that a short stretch bandage has a
limited maximum elongation with an applied force and thus the sub-bandage pressure range ought to be large as once the elongation limit is reached sub-bandage pressure must rise; a long stretch bandage possess a much greater maximum elongation with force and thus can accommodate greater elongation before the sub-bandage pressure must rise. Thus a long stretch bandage would be expected to demonstrate a small pressure range on ambulation.

*Oxford Pressure Monitor*

This equipment permits the portable measurement of sub-bandage pressure. The Talley 2 device (*Talley Group Ltd., UK.*) was used throughout these studies (Figure 4.3) and is reported by the manufactures to record pressures to an accuracy of +/- 4 mmHg. Pressure is measured using small plastic envelopes (Figure 4.4) placed beneath the bandage and connected to the Talley 2. A known volume of air is forced into the envelope and from the degree of envelope filling the pressure exerted on the envelope can be measured. Being battery powered and portable it is safe to use and allows measurement of pressures in the patients' own homes, thus avoiding the inconvenience and expense of transporting patients to the hospital for pressure recordings to be made. The quoted therapeutic working pressure of a compression bandage is the pressure exerted at the level of the ankle, and the graduation of pressure must be reducing towards the knee. To assess this the sites chose for pressure measurements were 4 cm above the tip of the medial maleolus (ankle), 4 cm below the tibial tuberosity (knee) and half way between these 2 sites (calf). Placing the sensor in close proximity to an active ulcer was avoided, and the closest non-ulcerated area used if necessary.
4.3c Results

Investigation of the Contribution of Bandage Layers to Sub-bandage Pressure

Sub-bandage pressures taken both supine and erect for the SSB at the ankle, calf and knee sites are summarised in Table 4.4. All data are shown as median (range); changes in sub-bandage pressure brought about by the two retaining layers examined are calculated with reference to the basal pressure without any retaining layer. The data demonstrate that the Rosidal K without any cohesive layer exerts a pressure at the ankle of 27 (10-43) mmHg. This is inadequate for use as a compression bandage but is associated with graduation of pressure towards the knee and supine pressures are low and hence safe when at rest. Application of a layer of Stockingette has minimal effect on sub-bandage pressure and would initially appear a good choice of retaining layer, however, it failed to remain in situ for more than a few minutes of ambulation and thus is of no practical value in compression bandaging. Coban increased the median (range) sub-bandage pressure when erect by 11.5 (-1 to +18) mmHg to an ankle pressure of 41 (27-54) mmHg. This working pressure is adequate for use in a compression bandage and is associated with good graduation of pressure (41 - 20 mmHg) and a low, graduated supine resting pressure (23 - 9.5 mmHg).

Sub-bandage pressures taken both supine and erect for all four layers of the FLB at the ankle, calf and knee sites are summarised in Table 4.5. All data are shown as median (range). Changes in sub-bandage pressure brought about by the various layers are calculated with reference to the pressure due to the previous layer. Thus the crepe pressure change is calculated as crepe pressure minus wool pressure, Elset pressure change as Elset pressure minus crepe pressure and Coban pressure change as Elset pressure minus Coban pressure.

The data demonstrate that the layers of wool and crepe exert a minimal erect sub-bandage pressure of 7 (1-16) and 16.5 (3-38) mmHg respectively. The addition of
the elastic Elset produces a high compression bandage, 53.5 (18-88) mmHg erect at the ankle, with good graduation of reducing pressure towards the knee and a graduated lower resting supine pressure. The retaining Coban layer increased the erect ankle pressure by 9.5 (-4 to +25) mmHg to 66 (34-85) mmHg, the graduation of pressure (66 - 29 mmHg) was maintained as was the lower, graduated resting pressure (30 - 20 mmHg).
<table>
<thead>
<tr>
<th>SSB Layers</th>
<th>Ankle</th>
<th>Calf</th>
<th>Knee</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal SSB Supine</td>
<td>15.5 (2-29)</td>
<td>11.5 (0-36)</td>
<td>12 (0-30)</td>
</tr>
<tr>
<td>Basal SSB erect</td>
<td>27 (10-43)</td>
<td>14 (8-39)</td>
<td>14.5 (4-34)</td>
</tr>
<tr>
<td>Pressure</td>
<td>Pressure Change</td>
<td>Pressure</td>
<td>Pressure change</td>
</tr>
<tr>
<td>Stockingette supine</td>
<td>16 (5-28)</td>
<td>-2.5 (-5 to +7)</td>
<td>11.5 (0-37)</td>
</tr>
<tr>
<td>Stockingette erect</td>
<td>27.5 (12-42)</td>
<td>0 (-12 to +4)</td>
<td>14 (7-38)</td>
</tr>
<tr>
<td>Coban supine</td>
<td>23 (14-34)</td>
<td>6 (-1 to +17)</td>
<td>20.6 (7-49)</td>
</tr>
<tr>
<td>Coban erect</td>
<td>41 (27-54)</td>
<td>11.5 (-1 to +18)</td>
<td>25 (10-47)</td>
</tr>
</tbody>
</table>

Table 4.4.  SSB Sub-bandage pressures (mmHg) reported as median (range). The three sites examined were ankle, calf, knee, pressures recorded are supine and erect for SSB without cohesive layer (basal SSB), SSB plus stockingette (stockingette) and SSB plus Coban (Coban). Pressure changes refer to the change in pressure (mmHg) with application of the Stockingette / Coban with reference to the basal SSB (without any cohesive retaining layer). Number of limbs = 10.
<table>
<thead>
<tr>
<th>FLB Layers</th>
<th>Ankle</th>
<th>Calf</th>
<th>Knee</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wool Supine</td>
<td>5 (0-13)</td>
<td>0 (0-4)</td>
<td>3.5 (0-8)</td>
</tr>
<tr>
<td>Wool erect</td>
<td>7 (1-16)</td>
<td>0.5 (0-14)</td>
<td>3 (0-9)</td>
</tr>
<tr>
<td>Crepe supine</td>
<td>Pressure 7.5 (1-12)</td>
<td>Pressure Change 1 (-3 to +12)</td>
<td>Pressure 5 (0-14)</td>
</tr>
<tr>
<td>Crepe erect</td>
<td>Pressure 16.5 (3-38)</td>
<td>Pressure Change 5.5 (-2 to +26)</td>
<td>Pressure 8 (1-10)</td>
</tr>
<tr>
<td>Elset supine</td>
<td>Pressure 24.5 (12-44)</td>
<td>Pressure Change 14 (5 to 61)</td>
<td>Pressure 19 (7-34)</td>
</tr>
<tr>
<td>Elset erect</td>
<td>Pressure 53.5 (18-88)</td>
<td>Pressure Change 33.5 (9 to 64)</td>
<td>Pressure 22.5 (13-56)</td>
</tr>
<tr>
<td>Coban supine</td>
<td>Pressure 30 (21-90)</td>
<td>Pressure Change 9 (1 to 18)</td>
<td>Pressure 26 (10-52)</td>
</tr>
<tr>
<td>Coban erect</td>
<td>Pressure 66 (34-85)</td>
<td>Pressure Change 9.5 (-4 to +25)</td>
<td>Pressure 32.5 (22-67)</td>
</tr>
</tbody>
</table>

Table 4.5. FLB Sub-bandage pressures (mmHg) reported as median (range). The three sites examined were ankle, calf, knee, pressures recorded are supine and erect for Wool, Wool + crepe (crepe), Wool + crepe + Elset (Elset), Wool+ crepe + Elset + Coban (Coban). Pressure changes resulting from the addition of a layer are calculated with reference to the immediate preceding layer. Number of limbs = 10.
Investigation of Sub-bandage Pressure over Seven Days

Median sub-bandage pressures for FLB and SSB recorded over seven days are shown in Figure 4.7. After an initial drop in sub-bandage pressure at the four hour stage (most marked in the SSB) pressures are maintained over the seven day period. For each time point the pressure beneath the FLB is greater than that of the SSB.

![Graph showing median sub-bandage pressures for FLB and SSB over seven days.]

Figure 4.7. Sub-bandage pressure for SSB (-----) and FLB (........) (mmHg) measured at the ankle standing erect over a seven day period. Data points shown are medians of 10 legs per bandage.

Pressures for each bandage type 20 minutes after application and seven days after application in the erect and supine positions at the ankle, calf and knee are shown in Table 4.6. Twenty minutes after application both SSB and FLB exerted a comparable therapeutic pressure at the ankle 47 and 44 mmHg respectively ($P = 0.65$) with graduation towards the knee. Both SSB and FLB possessed a comparable graduated resting pressure. After 7 days insitu on the leg under investigation the FLB maintained a high compressive pressure at the ankle but the SSB ankle pressure had fallen.
significantly compared to the FLB (33 and 51.5 mmHg respectively (P = 0.02)). Both SSB and FLB maintained graduated working and resting pressures.

<table>
<thead>
<tr>
<th>Site of measurement of sub-bandage pressure</th>
<th>SSB Pressure (mmHg)</th>
<th>FLB Pressure (mmHg)</th>
<th>Mann Whitney U level of significance (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ankle 20 mins (supine)</td>
<td>26 (14-52)</td>
<td>30 (20-73)</td>
<td>0.37</td>
</tr>
<tr>
<td>Ankle 20 mins (erect)</td>
<td>47 (27-79)</td>
<td>44 (31-93)</td>
<td>0.65</td>
</tr>
<tr>
<td>Calf 20 mins (supine)</td>
<td>27 (5-48)</td>
<td>31.5 (22-51)</td>
<td>0.24</td>
</tr>
<tr>
<td>Calf 20 mins (erect)</td>
<td>30 (8-74)</td>
<td>42 (27-58)</td>
<td>0.39</td>
</tr>
<tr>
<td>Knee 20 mins (supine)</td>
<td>21 (9-33)</td>
<td>24.5 (18-52)</td>
<td>0.05</td>
</tr>
<tr>
<td>Knee 20 mins (erect)</td>
<td>26.5 (14-55)</td>
<td>33 (19-73)</td>
<td>0.16</td>
</tr>
<tr>
<td>Ankle 7 days (supine)</td>
<td>21 (4-38)</td>
<td>32 (21-56)</td>
<td>0.05</td>
</tr>
<tr>
<td>Ankle 7 days (erect)</td>
<td>33 (16-60)</td>
<td>51.5 (34-80)</td>
<td>0.02</td>
</tr>
<tr>
<td>Calf 7 days (supine)</td>
<td>21 (9-28)</td>
<td>27 (16-40)</td>
<td>0.08</td>
</tr>
<tr>
<td>Calf 7 days (erect)</td>
<td>23.5 (10-46)</td>
<td>35.5 (24-48)</td>
<td>0.02</td>
</tr>
<tr>
<td>Knee 7 days (supine)</td>
<td>14 (0-29)</td>
<td>21.5 (14-30)</td>
<td>0.13</td>
</tr>
<tr>
<td>Knee 7 days (erect)</td>
<td>20 (0-42)</td>
<td>30 (15-51)</td>
<td>0.08</td>
</tr>
</tbody>
</table>

Table 4.6. Sub-bandage pressure measurements for SSB and FLB taken at the knee, calf and ankle sites after 20 minutes and after 7 days in the erect and supine positions. Data appear as median (range) mmHg. Statistical comparisons made by non-parametric Mann Whitney U Test. Ten limbs per bandage were examined.
Investigation of the in situ Behaviour of Compression Bandages

Four ‘bandages’ were examined in situ on ten volunteer legs, Tubigrip, FLB, SSB, Long Stretch (Blue Line). The median (range) range of sub-bandage pressure for the ten subjects obtained during simulated ambulation at the level of the ankle when erect are shown in Table 4.7 as medians (range). Values are compared with non-parametric Mann Whitney U Test.

<table>
<thead>
<tr>
<th>Bandage Examined</th>
<th>Minimum Pressure (mmHg)</th>
<th>Maximum Pressure (mmHg)</th>
<th>Pressure Range (max. - min.) (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSB</td>
<td>19.5 (12-50)</td>
<td>34 (15-89)</td>
<td>9.5 (3-40)</td>
</tr>
<tr>
<td>FLB</td>
<td>16.5 (8-72)</td>
<td>28 (16-88)</td>
<td>12.5 (5-23)</td>
</tr>
<tr>
<td>Tubigrip</td>
<td>6.5 (0-13)</td>
<td>14.5 (6-29)</td>
<td>5.5 (4-18)</td>
</tr>
<tr>
<td>Long Stretch</td>
<td>62 (14-89)</td>
<td>72 (8-25)</td>
<td>12 (8-25)</td>
</tr>
</tbody>
</table>

Table 4.7. Simulated ambulation sub-bandage pressures recorded at the ankle in mmHg. Data appears as median (range). Statistical comparisons as follows (Mann Whitney U): α P = 0.76, θ P = 0.45, ϕ P = 0.88. The pressure ranges beneath the Tubigrip were significantly lower than SSB P = 0.04, FLB P = 0.02, and LSB P = 0.01. 10 limbs per bandage were examined.

The data demonstrate that the range of sub-bandage pressure beneath SSB, FLB and Long Stretch bandages (LSB) are comparable suggesting that all three types of bandage function in a similar manner when in situ on a leg. The range of pressure beneath a Tubigrip bandage is significantly less than either SSB, FLB or LSB suggesting a larger degree of compliance and as such behaviour akin to a very long stretch bandage.
4.3d Discussion

This study set out to examine various aspect of sub-bandage pressure using a Talley 2 Oxford Pressure Monitor, one of the various forms of ‘bandage tester’ recommended for assessing the bandaging skills of those responsible for applying compression bandages. The margin of error inherent in the Talley 2 is +/- 4 mmHg which for clinical purposes would be satisfactory, however, some of the pressures recorded in this study in particular the wool layer of FLB records a low pressure the accuracy of which could be questioned as the proportional error of measurement is high in these instances.

Specifically, the sub-bandage pressure recorded beneath the SSB suggested that this bandage alone would be inadequate for use as a compression bandage based on accepted criteria. This is interesting as the manufacturers recommend the use of Rosidal K without any overlying cohesive layer when used in the manner of this investigation (50% stretch with 50% overlap between layers). In the randomised trial described in section 4.2, Coban was used as the cohesive retaining layer rather than Stockingette. Although the Stockingette had no influence on sub-bandage pressure it failed to be of any practical use in keeping the Rosidal K in position, and although Coban increased the sub-bandage pressure the size of this increase can and has been documented and acts merely to enhance the compressive effect of the Rosidal K. Importantly, the addition of the Coban layer did not decrease the graduation of pressure and furthermore the resting pressure supine was low and graduated. Thus the use of Coban over the Rosidal K is justifiable and is effects definable.

Considering the FLB data, as may be expected the wool created minimal compression and the addition of crepe although almost doubled the compressive force still exerted no significant compression. This is understandable as these two layers function predominately as protective padding of the bony prominences, to ensure an
even distribution of the compression provided by the Elset and importantly as an absorptive layer for any exudate leaking from the ulcer bed. A pressure increase to therapeutic levels is only achieved by the addition of the elastic Elset layer and the retentive Coban added a small additional degree of compression. The completed bandage demonstrated good graduation of pressure from ankle to knee with a lower graduated resting pressure.

Thus, at the outset, both SSB and FLB systems adequately meet the criteria for use as a compression bandage for the treatment of venous ulceration. However, the SSB only reached this standard with the addition of an extra layer of retaining Coban.

The ability of a compression bandage to remain therapeutic over the course of seven days is important; changing the bandages when convenient for both patient and nursing staff is acceptable only if the sub-bandage pressure is adequate to allow this practice. Should a bandage lose its therapeutic properties after say 3 or 4 days then days 5, 6 and 7 are of no value in ulcer healing terms. Both SSB and FLB pressures fell over the initial 4 hours of use; this is understandable as the bandage components will adjust themselves to some degree after application. Thereafter the minimum pressure remains stable but the FLB maintains a higher pressure throughout the 7 day study period suggesting it may be more beneficial and that its multi-layer construction accommodates any wide pressure changes. Despite the fall in pressure beneath the SSB, the pressure gradients both at rest and erect were preserved. This confirms that although the degree of compression may be reduced in the SSB limbs no detrimental effects attributable to pressure gradients should occur. This fall in sub-bandage pressure may be a feature of the bandage itself or may be a phenomenon of the limbs examined. Thus, the volume of more oedematous limbs would reduce by a greater degree than less oedematous limbs resulting in a looser and thus less compressive bandage over the 7 day period. However, this effect is unlikely as all limbs recruited to this aspect of the study had undergone
compression bandaging for at least one month and section 4.2 of this thesis clearly
demonstrates that the leg volume does not change significantly after one month of
bandaging. I suspect therefore, that the fall in pressure is an inherent feature of the SSB.
This is borne out by the casual observation the the SSB would be more likely to displace
from its original position on the leg than the FLB irrespective of leg dimensions.

The examination of the in situ behaviour of the bandages during simulated
ambulation produced disappointing results in that the data suggested that SSB, FLB and
LSB behaved in a comparable manner. There are a number of reasons to account for
this: 1) my hypothesis about the behaviour of each bandage during simulated ambulation
may be wrong. Bandage characteristics were originally defined in a laboratory situation
based on a mannequin which may not translate into the clinical situation. 2) the model
used for simulated ambulation may be inappropriate and perhaps a treadmill would have
been a better option, however, tip toe exercises are accepted for the measurement of
ambulatory venous pressures and ankle dorsiflexions are used during
photoplethysmography so I feel that the simulation of ambulation is in fact appropriate.
3) the tolerance of the Talley 2 OPM may be too low to allow this type of measurement
at the pressures encountered and finally 4) having only 10 legs in each group may have
resulted in a Type II statistical error.

This study, however, has clearly demonstrated that Tubigrip exerts minimal
compression and stretches to accommodate changes in leg dimension with minimal
increase in pressure 5.5 (4-18) mmHg.
4.3e Summary

This section has confirmed that the SSB alone is inadequate for use as a stand alone compression bandage but with the addition of a layer of Coban graduated adequate compression can be achieved. Most of the FLB compressive force comes from the Elset with a lesser degree from the Coban and is maintained with graduation over seven days, the usual period of use before changing the bandage. Although probably adequate, the sub-bandage pressure at the ankle of the SSB was significantly less than the FLB. Finally, I was unable to clarify the behaviour of FLB in terms of long or short stretch but demonstrated that Tubigrip exerts minimal compression.

4.4 THE DEVELOPMENT OF A PRESCRIBABLE FOUR LAYER COMPRESSION BANDAGE FOR THE TREATMENT OF VENOUS ULCERATION

4.4a Introduction

A recent systematic review in the BMJ (Fletcher et al., 1997) concluded that the healing of venous ulcers is improved when compression is applied and that high compression applied in three or four layers performs better than low compression and is possibly better than single layer systems. The review concluded that the use of correctly applied high compression bandaging should be promoted. One of the major obstacles to the widespread use of currently used multiple (four) layer high compression bandaging systems, such as that described by Charing Cross Hospital (Moffatt et al., 1992b), is that many of the bandage components are not available on the Drug Tariff and they cannot therefore be freely prescribed (Blair et al., 1988; Freak et al., 1995; Moffatt, 1992a). The purpose of this study was to develop a four layer graduated compression bandaging
system with similar properties to the Charing Cross system using components that are available on the Drug Tariff.

4.4b Patients and Methods

The British National Formulary and Drug Tariff were examined to identify FP10 prescribable bandaging components. The following bandaging components were thought to be possible alternatives to those used in the Charing Cross system: Gamgee as a replacement for the various forms of orthopaedic wool used in the first layer of the four layer bandage; Surepress, Tensopress and Setopress are all elastic compression bandages suitable for use as an alternative to Elset (the third layer of the four layer system); Elastoplast, Lestreflex and Tubigrip are possible bandage components possessing a retentive/securing property to maintain the position of the bandage once applied to the leg (Coban was used by the Charing Cross group). The second layer of the Charing Cross bandage being Crepe is freely prescribable and no alternative component was therefore examined.

In determining the suitability of a bandage combination, three important characteristics must be accommodated, 1) a sub-bandage pressure of at least 40 mmHg at the ankle when standing erect with graduation to a lower pressure towards the knee, 2) a low and hence ‘safe’ resting pressure when supine and 3) the ability of the bandage to maintain position on the leg and this graduated pressure for a reasonable period of time, usually seven days. A safe resting pressure refers to a low sub-bandage pressure at the ankle when supine. In this position, venous pressure is low and thus not likely to act in a pathological manner, thus, compression in this position is of little benefit. Likewise, arterial perfusion may be reduced when in the supine position and although compression bandages are not recommended in patients with occlusive arterial disease complications involving pressure ulceration have been reported. However, compression bandages are
designed to be worn for 24 hours per day and as such must exert as low a pressure as possible when counteraction of venous hypertension is not required i.e. when in the supine position sub-bandage pressure must be less than in the erect position.

To investigate these characteristics, two studies were performed: A *static* investigation of various bandage components to establish a bandage combination producing an adequate graduated sub-bandage pressure, and a *dynamic* study comparing the pressure exerted at the ankle by FP10 prescribable and Charing Cross bandages over seven days. The static study of bandage components involved the application of various combinations of bandage components to the non-ulcerated legs of 10 healthy volunteers without vascular disease. The sub-bandage pressures were measured in the supine and erect positions 20 minutes after bandaging to allow the bandages 'to settle' on the leg. Pressures were measured at three sites on the leg; 4 cm above the medial maleolus, 4 cm below the tibial tuberosity and midway between these two sites. These sites are referred to as ankle, knee and calf respectively. Two important aspects of the bandage were assessed. Firstly, the ambulatory working pressure; this was measured with the subject standing erect and weight bearing on the contralateral leg to that under investigation. Secondly, the resting pressure, this was measured with the subject in the supine position and reflects the 'safety' pressure of the bandage when the subject is lying down with minimal venous pressure at the level of the ankle. The most appropriate bandage combination must exert an adequate and graduated pressure whilst erect and equally importantly a low pressure when supine (Stemmer et al., 1980).

Once a suitable bandage combination was identified twenty subjects with venous ulceration (Ankle Brachial Pressure Index > 0.8) underwent the dynamic study for seven days. Ten legs were bandaged with the new FP10 combination and 10 legs with the Charing Cross system. Sub-bandage pressures were measured 20 minutes, four hours, 24 hours and then at 24 hour intervals for seven days at which time the bandages were
changed. Pressure measurements were made in the morning and as far as possible at the same time each day.

Sub-bandage pressure was measured using a Talley II Oxford Pressure Monitor (Talley Group Ltd., UK.) to an accuracy of ±/− 4 mmHg. A small flat plastic 'envelope' is located between the bandage and primary dressing and the attached tubing brought to the bandage surface by a suitable route between bandage layers. The free end of the tube is left free to allow connection of the Oxford Pressure Monitor each day thus permitting full ambulation of the patient. All bandaging was applied by the same two experienced bandagers thus ensuring uniformity of application. The Charing Cross bandage was applied as previously described (Blair et al., 1988).

4.4c Results

*Static Study to Determine the Ideal Bandage Combination*

Three bandage combinations were examined. Three components were common to each combination and included a complete single layer of Gamgee cut from a larger sheet, a layer of Crepe as in the standard four layer bandage and an outer layer of cohesive Lestreflex. The third layer was variable and consisted of one of the following: Setopress, Surepress or Tensopress.

The ‘working pressure’ of the bandage combinations was assessed by the ability to produce an adequate and graduated pressure. These data are shown in Table 4.8a. Statistical comparisons were made by non-parametric Wilcoxon Signed Rank Testing (Table 4.8b).
Table 4.8a. Median (range) of sub-bandage pressures (mmHg) taken at the three sites studied (ankle, calf and knee) for the three bandages tested with the subject standing erect. n=10

<table>
<thead>
<tr>
<th>Site</th>
<th>Sub-bandage pressure (mmHg) by elastic bandage, median(range)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tensopress</td>
</tr>
<tr>
<td>Ankle</td>
<td>62.5 (38-100)</td>
</tr>
<tr>
<td>Calf</td>
<td>39 (10-67)</td>
</tr>
<tr>
<td>Knee</td>
<td>33 (18-64)</td>
</tr>
</tbody>
</table>

Table 4.8b. Wilcoxon Signed Rank Analysis of the working pressure of the three bandages tested and the sites of comparison of pressures. Values shown are levels of significance (‘P’ value). n=10.

<table>
<thead>
<tr>
<th>Sites Compared</th>
<th>Wilcoxon Signed Rank Significance for each Bandage Tested</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tensopress</td>
</tr>
<tr>
<td>Ankle vs Calf</td>
<td>0.001</td>
</tr>
<tr>
<td>Calf vs Knee</td>
<td>0.73</td>
</tr>
<tr>
<td>Ankle vs Knee</td>
<td>0.001</td>
</tr>
</tbody>
</table>

The ‘resting pressure’ as previously described was measured and compared in a similar manner at the same sites with the subject supine. Results are shown in Figure 4.9a and b.
<table>
<thead>
<tr>
<th>Site</th>
<th>Sub-bandage pressure (mmHg) by elastic bandage, median(range)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tensopress</td>
</tr>
<tr>
<td>Ankle</td>
<td>36 (26-84)</td>
</tr>
<tr>
<td>Calf</td>
<td>26 (10-41)</td>
</tr>
<tr>
<td>Knee</td>
<td>27 (7-48)</td>
</tr>
</tbody>
</table>

Table 4.9a. Median (range) of sub-bandage pressures (mmHg) taken at the three sites studied (ankle, calf and knee) for the three bandages tested with the subject lying supine. n=10.

<table>
<thead>
<tr>
<th>Sites Compared</th>
<th>Wilcoxon Signed Rank Significance for each Bandage Tested</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tensopress</td>
</tr>
<tr>
<td>Ankle vs Calf</td>
<td>0.003</td>
</tr>
<tr>
<td>Calf vs Knee</td>
<td>1.0</td>
</tr>
<tr>
<td>Ankle vs Knee</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Table 4.9b. Wilcoxon Signed Rank Analysis of the working pressure of the three bandages tested and the sites of comparison of pressures. Values shown are levels of significance ('P' value). n=10.

The pressure studies using the prescribable bandaging components described above revealed that the most suitable combination of FP10 components was an initial layer of Gamgee followed by a layer of Crepe applied in the same manner as used in the Charing Cross bandage. The third layer was Tensopress applied with 50% stretch and 50% overlap between turns, finally these layers were secured in place by a layer of cohesive Lestraflex applied with 50% overlap and minimal stretch. All layers were secured to each other with adhesive tape. (Figure 4.8). The combination using Tensopress was selected as the above data demonstrate an adequate and graduated working pressure and equally importantly a low, safe resting pressure. The median (range) static sub-bandage pressures (mmHg) obtained using the FP10 combination were as follows: ankle 62.5 (38-100), calf 39 (10-67), knee 33 (18-64) mmHg.
Figure 4.8 (a–f). a) The components used in the FP10 bandage described, b) The complete layer of Gamgee, c) A second layer of Crepe, d) The Tensopress representing layer 3, e) The fourth layer of Lestreflex, f) The final appearance.
Dynamic Study of Sub-bandage Pressure over Seven Days

The sub-bandage pressures obtained with the FP10 bandage (Gamgee, Crepe, Tensopress, Lestreflex as determined in the previous section) over seven days are illustrated in Figure 4.9. The same data obtained from a standard Charing Cross bandage is shown for comparison. Analysis of variance comparing the sub-bandage pressure exerted by these two bandages over the seven day period of the study showed no significant difference, Kruskal-Wallis $\chi^2 = 0.59$, df=1, P=0.44. The median (range) sub-bandage pressure (mmHg) exerted at initial application by the two bandage systems was as follows: FP10 62.5 (38-100) vs Charing Cross 44 (31-93), Mann-Whitney U Test P = 0.20; and after seven days FP10 33 (10-67) vs Charing Cross 46 (34-80) Mann-Whitney U Test P = 0.22. No complications resulted from the use of either of these bandage combinations, the bandages stayed in place for 7 days in all subjects and no patient reported any subjective problems with the FP10 combination.

Figure 4.9. Median erect sub-bandage pressure (mmHg) over seven days at the ankle for the FP10 (---) and Charing Cross (----) bandage systems. Pressures were measured over 7 days in 10 limbs for each bandage type. Kruskal-Wallis $\chi^2 = 0.59$, df = 1, P = 0.44.
4.4d Discussion

This study describes the physical properties of a four layer FP10 prescribable compression bandage for use as a possible alternative to Charing Cross or short stretch compression bandages. The bandaging described produces graduated and sustainable compression that is similar over a seven day period to that produced by the Charing Cross system. The median initial ankle pressure exerted by this bandage was 62.5 mmHg and therefore, as with all high compression bandages, it is essential that the ankle brachial pressure index is confirmed to be greater than 0.8 before the bandaging is applied.

The data suggest that the Setopress combination ought to be rejected as it possessed a lower initial working pressure with poor graduation of pressure up the leg and resting pressures of similar degrees. The Tensopress and Surepress combinations both demonstrated good graduation of sub-bandage pressures with Tensopress commencing with a higher working pressure than the Surepress combination. The Tensopress combination possessed a lower resting pressure than the Surepress combination. The Tensopress combination was chosen over the Surepress combination for two reasons. First, the working pressure was slightly higher, this is an advantage in that allowance can be made for the initial reduction in pressure in the first 24 hours of use. Second, the lower resting pressure of the Tensopress combination gives a higher margin of safety. However, the range of pressures recorded beneath the Tensopress combination demonstrated that one limb experienced very high pressures both when standing erect and more worryingly when in the supine position. Likewise the median working pressure was initially higher in the Tensopress than Charing Cross limbs. This data acts to re-enforce the fact that these bandages must be applied by trained personnel to limbs without arterial disease (ABPI > 0.8) and once applied the patient need careful monitoring and information about the recognition of possible complications.
The total cost of all the components (using January 1998 prices) of the Charing Cross four layer bandage described above, when obtained from a high street retail pharmacy is £15.12. The total cost of the FP10 prescribable bandage system described in this study is £13.17 when obtained from the Drug Tariff. The crucial issue of course is that the majority of venous ulcers occur in the elderly who could therefore receive the bandaging system described here free of charge to themselves via an FP10 prescription.

4.4e Summary

Although this study has described a multi-layer compression bandage system comprising prescribable components for use in the treatment of venous ulcers, this bandaging system needs to be compared with the Charing Cross system in prospective clinical trials of adequate power. Nonetheless, this prescribable system represents a possible alternative to Charing Cross bandages and as such, it could be used in parts of the UK where at present patients with venous ulcers are denied effective compression therapy because of lack of funding for non-prescribable high compression bandaging systems.

4.5 CONCLUSIONS

This chapter has examined the efficacy of SSB and FLB and found them to be comparable in terms of ulcer healing, however, more complications were recorded in the SSB group. It may be possible to recommend SSBs to patients with ulcerated limbs of 'standard' dimensions and use FLBs in those limbs likely to suffer complications of bandaging i.e. very thin or very oedematous limbs. I have demonstrated that both SSB and FLB as used in this thesis exert adequate graduated compression with a good
margin of safety, however, the SSB required an additional layer of Coban to raise the sub-bandage pressure to an adequate level and to keep the bandage in place on the leg. Both SSB and FLB maintain their compression for seven days making changing the bandages once per week unless otherwise indicated a sensible option. Finally, a fully FP10 prescribable alternative multi-layer bandage is described for use where funding for Charing Cross or short stretch bandaging is not available.
CHAPTER FIVE

INVESTIGATION OF THE ROLE OF SAPHENOUS VEIN SURGERY IN THE
TREATMENT OF VENOUS ULCERATION

5.1 GENERAL INTRODUCTION

5.2 THE CLINICAL AND HAEMODYNAMIC EFFECTS OF SAPHENOUS
VEIN SURGERY
   a. Introduction
   b. Patients and Methods
   c. Results
   d. Discussion
   e. Summary

5.3 THE ABILITY OF PNEUMATIC CUFFS TO OCCLUDE THE
SUPERFICIAL VENOUS SYSTEM AND THE ROLE OF CUFFS IN
PREDICTING THE OUTCOME OF SUPERFICIAL VENOUS SURGERY
   a. Introduction
   b. Patients and Methods
   c. Results
   d. Discussion
   e. Summary

5.4 CONCLUSIONS
5.1 GENERAL INTRODUCTION

Chapter three identified that in ulcerated limbs with venous reflux, the reflux was confined to the saphenous veins in 56% of limbs and involved the deep and saphenous venous systems combined in 33% of limbs. It would seem logical to attempt to reduce ambulatory venous pressures by surgically correcting any venous reflux present in an ulcerated limb. This approach has been advocated (Scurr, 1996; Goren, 1993) despite leading articles dismissing the role of surgery in the treatment of venous ulceration (Anonymous, 1977; Allen, 1990) whilst others take a more circumspect approach (Mayberry et al., 1992) and suggest diagnostic criteria on which to base the indications for surgery (DeFriend et al., 1992). De Friend (1992) relied on the use of pneumatic tourniquets to indicate any potential surgical improvement. Tourniquets are also used to delineate reflux in the deep and/or superficial venous systems. If the decision to operate on a limb is taken according to the result of 'tourniquet tests' then this test must be valid in order to prevent inappropriate surgery.

This chapter investigates the role of saphenous vein surgery in limbs with saphenous reflux alone and limbs with deep and saphenous reflux combined in the treatment of venous ulceration and also examines the ability of a pneumatic tourniquet to compress the superficial venous system and thus indicate the possible outcome of superficial venous surgery.
5.2 THE CLINICAL AND HAEMODYNAMIC EFFECTS OF SAPHENOUS VEIN SURGERY

5.2a Introduction

Recent studies have reported the relative involvement of the superficial and deep venous systems in ulcerated limbs (Table 5.1). It is clear that the majority of limbs with venous ulcers have superficial venous reflux either in isolation or in combination with deep venous reflux. There are clearly two groups of patients for which saphenous vein surgery needs to be considered: those limbs with isolated saphenous reflux and those with saphenous reflux combined with deep venous reflux.

<table>
<thead>
<tr>
<th></th>
<th>Superficial Reflux</th>
<th>Combined Reflux</th>
<th>Deep Reflux</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Only (%)</td>
<td>Only (%)</td>
<td>Only (%)</td>
</tr>
<tr>
<td>Darke &amp; Penfold (1992)</td>
<td>43</td>
<td>35</td>
<td>22</td>
</tr>
<tr>
<td>Shami et al. (1993)</td>
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<td>15</td>
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<tr>
<td>Myers et al. (1995)</td>
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<td>48</td>
<td>8</td>
</tr>
<tr>
<td>Grabs et al. (1996)</td>
<td>51</td>
<td>39</td>
<td>7</td>
</tr>
<tr>
<td>Scriven Chapter 3</td>
<td>57</td>
<td>32</td>
<td>11</td>
</tr>
</tbody>
</table>

Table 5.1. The patterns of venous reflux identified in ulcerated limbs using hand held Doppler or colour duplex scanning. Superficial reflux includes limbs with ankle perforating vein reflux alone or combined with saphenous vein reflux. Deep reflux only refers to limbs with predominately post thrombotic disease and combined reflux includes limbs with deep (usually primary) and saphenous reflux in combination. These classifications correspond with Darke and Penfold types II, III, IV (Darke & Penfold, 1992).

Darke and Penfold (1992) have reported medium term healing of 90% of ulcers in limbs with normal deep veins and isolated superficial reflux. This was achieved by sapheno-femoral/ popliteal disconnections as appropriate combined with stripping of the
long saphenous vein to the knee. Postoperatively up to one third of the patients used compression hose at their own discretion. Importantly perforating veins were not disconnected in any limb. Saphenous vein surgery in limbs with isolated saphenous reflux is also associated with improved venous haemodynamics in terms of improved ambulatory venous pressures (Sethia et al., 1984; Wright et al., 1988a). It thus appears that sapheno-femoral/popliteal disconnection combined with long saphenous vein stripping to the knee and variable use of postoperative compression is indicated in ulcerated limbs with isolated saphenous vein reflux.

More controversial is the role of 'stand alone' saphenous vein surgery in limbs with combined saphenous and deep vein reflux. The consensus paper on venous leg ulcers (Alexander House Group, 1992) recommends that: "Full correction of insufficiency of superficial veins and/or perforating veins should always be carried out prior to considering surgery for deep venous insufficiency". Stand alone superficial venous surgery is advocated as an initial procedure by Jamieson (1993) and Scurr (1996), whereas Goren (1993) in a letter to the Journal of Vascular Surgery suggests that primary deep venous reflux seen in this group of patients is a secondary phenomenon consequent upon volume overload of the calf muscle pump caused by severe saphenous vein reflux. The avoidance of such surgery in post-thrombotic limbs is advocated by Burnand et al. (1976) who found that in patients with venographic evidence of deep vein damage saphenous vein ligations in limbs with healed ulcers failed to prevent ulcer recurrence in 95% of cases whereas 100% of limbs remaining healed had normal deep veins. Others remain uncertain about the role of saphenous vein surgery in these limbs (Mayberry et al., 1992).

The principle of treating venous ulceration is to reduce venous hypertension and as such it is likely that stripping the long saphenous vein is not a mandatory manoeuvre,
although this must be balanced by consideration of the recurrence rate of saphenous reflux (and hence possible ulcer recurrence) if the LSV is not stripped. In addition all previous reports have involved saphenous vein stripping with or without postoperative compression in addition.

Thus the aims of this chapter are to assess the clinical and haemodynamic effects of saphenous vein surgery in limbs with isolated superficial venous reflux and deep and superficial reflux combined.

5.2b Patients and Methods

Patients

Patients with active lower limb ulceration were identified from those attending the Venous Ulcer Assessment Clinic at which they underwent a full assessment as previously described in Chapter 3. Ulcers were defined as venous if the only demonstrable abnormality was venous reflux of > 0.5 seconds duration with an ABPI of > 0.8.

Study Design

The study was designed to investigate the role of local anaesthetic saphenofemoral and/or saphenopopliteal disconnection in a total of 40 limbs, 20 with superficial reflux only and 20 with superficial and deep reflux. The study received local ethical committee approval. Limbs underwent pre-operative colour duplex scanning and ambulatory venous pressure (AVP) measurements and these were repeated immediately after surgery (within one hour) and at three months. Venous ulcer size was measured pre-operatively and at one and three months postoperatively. Patients were followed up for 24 months postoperatively.
To assess whether the final AVP was influenced by not stripping the saphenous vein the difference between the pre-operative and follow up AVP (expressed as a percentage of the resting pressure) in the limbs with normal deep veins was examined according to the status of the saphenous vein remnant at follow up. Each limb was classified into one of two groups. Group 1 (no reflux) which included those limbs with thrombosed and/or competent saphenous veins, and group 2 (reflux) which included those limbs with reflux still present in the venous remnant. Limbs that underwent surgery to both the LSV and SSV were included in group 1 only if both venous remnants were either competent or thrombosed. This grouping was chosen because it represents the functional effect of saphenous vein stripping i.e. an absent vein possesses no reflux and therefore cannot contribute to the AVP. In a similar manner reflux is also absent in a thrombosed or competent vein and therefore these remnants cannot contribute to the AVP either.

Measurement of AVP

Ambulatory venous pressure (AVP) was measured in the standard manner (Nicolaides, 1986). A dorsal foot vein was cannulated with an 21 gauge intravenous cannula and flushed with heparinised saline and via a sterile, flexible PVC tube the cannula was connected to a sterile pressure transducer (P23XL, Spectromed, Omedia, UK), and thence amplifier and chart recorder (Gould Electronics Limited, Ilford, UK) (Figures 5.1 and 5.2). The connecting tube and transducer were similarly primed with heparinised saline and any air bubbles were expelled from the system. Before commencing pressure recordings the transducer was calibrated to read atmospheric pressure as zero. The recordings of AVP were performed with the patient standing, bearing weight on the opposite leg and with the pressure transducer located at the level
of the cannulated foot vein. After standing still to obtain a basal resting pressure a
standard exercise of 10 heel raises at 1 second intervals was performed followed by a
further stationary period to allow the venous pressure to return to the pre-exercise level.
AVPs were recorded immediately pre-operatively, immediately postoperatively (within
one hour of surgery) and at a follow up visit 3 months following surgery. The cannula
remained in situ between the pre- and immediate postoperative recordings.

From the pressure tracing obtained (Figure 5.3) the resting venous pressure (RP)
(mmHg), AVP (mmHg) and time (seconds) to return to 90% of the resting pressure
(RT90) were measured. An overall assessment of venous calf pump function, the
Pressure Relief Index (PRI) (Greenwood et al., 1995) was calculated thus:

\[ PRI = RT90 \times (RP - AVP) \]

At each time point the following data were collected: AVP (expressed as a
percentage of RP); RT90 (seconds) and the PRI.
Figure 5.1  The equipment used to measure AVP, consisting of an intravenous cannula, connecting tubing, heparinised saline, pressure transducer and amplifier with chart recorder.

Figure 5.2  Illustration of positioning of the cannula in a dorsal foot vein of a non-ulcerated leg
Figure 5.3 An AVP tracing obtained from a leg with no apparent venous or arterial abnormality.

RP, resting pressure (mmHg); AVP, ambulatory venous pressure (mmHg); RT90, return time 90 (seconds); PRI, pressure relief index = RT90 x (RP - AVP); T, ten tip-toe movements; R, standing at rest.

In this instance RP = 85 mmHg, AVP = 23 mmHg, RT90 = 17.2 s, thus PRI = 1066.

**Colour Duplex Scanning**

A full colour duplex scan of the deep and superficial veins was performed pre-operatively and at the follow up visit. Colour duplex scans were performed using either an ATL Ultramark 9 HDI (Advanced Technology Laboratories UK Ltd., Letchworth, Herts., U.K.) or a Diasonics Masters (Sonotron Ltd., Bedford, U.K.) machine. The deep and superficial venous systems were examined with 5 MHz and 10 MHz linear array probes respectively and patients were examined with the limb dependent. Venous reflux was defined as the presence of reversed blood flow for more than 0.5 seconds on release of a calf squeeze distal to the segment of vein under examination.
Ulcer Area

Ulcer areas were obtained by computerised planimetry from tracings of the ulcer perimeter on transparent acetate sheets taken on the day of surgery and at one and three months postoperatively. Ulcer healing was determined by inspection at the follow up visits and deemed to be complete if full re-epithelialisation had occurred.

Surgery

All saphenous ligations were performed under local infiltration anaesthesia. Reflux at the sapheno-femoral junction (SFJ) was treated by standard flush ligation and division of the SFJ with formal exploration, identification, ligation and division of all tributaries. Sapheno-popliteal reflux was treated by flush ligation and division of the sapheno-popliteal junction (SPJ). Limbs with reflux at both the SFJ and SPJ had both junctions disconnected in the one procedure. Postoperatively the ulcers were dressed with a simple non-adherent NA dressing (Johnson and Johnson Ltd, U.K.), a layer of gauze, and a graduated below knee Tubigrip (Seton Health Care Group plc., U.K.). No compression bandages were applied postoperatively unless, after one month healing had not commenced then the above regimen was replaced by a four layer compression bandage. There was no mortality or morbidity associated with the surgical procedures.

Statistics

Data were analysed using two tailed non-parametric paired (Wilcoxon Matched Pairs) and unpaired (Mann-Whitney U) testing as appropriate with the aid of a IBM compatible computer and SPSS for Windows version 6 software (SPSS, Chertsey, U.K.). All statistical comparisons assume significance with $P < 0.05$. 

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5.2c Results

Patients

The study was terminated after a total of 25 limbs had been studied. This was because it was not felt ethical to continue because of the poor outcome in limbs with combined superficial and deep reflux. A total of 24 patients with 25 actively ulcerated limbs were therefore studied. Sixteen ulcerated limbs had isolated saphenous vein reflux distributed as follows: long saphenous vein (LSV) only 9 (56%) limbs; short saphenous vein (SSV) only 4 (25%) limbs and long and short saphenous veins (L/SSV) combined 3 (19%) of limbs. Nine limbs had venous reflux in the deep and long saphenous systems combined, in all of these limbs the deep venous reflux extended distally beyond the below knee popliteal vein. The patients’ ages, initial ulcer areas and duration of ulceration at the time of surgery are given in Table 5.2.

<table>
<thead>
<tr>
<th>Saphenous Reflux Only (n=16)</th>
<th>Initial Ulcer Area (cm²)</th>
<th>Ulcer Duration Prior to Surgery (years)</th>
<th>Patient Age (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>8.5</td>
<td>2</td>
<td>73</td>
</tr>
<tr>
<td></td>
<td>(2.7 - 14.4)</td>
<td>(0.9 - 5.8)</td>
<td>(56 - 77)</td>
</tr>
<tr>
<td>Deep and Superficial Reflux Combined (n=9)</td>
<td>18</td>
<td>1.5</td>
<td>77</td>
</tr>
<tr>
<td></td>
<td>(9 - 92.3)</td>
<td>(0.7 - 2.8)</td>
<td>(63 - 85)</td>
</tr>
</tbody>
</table>

| Significance Level (Mann Whitney U Test) | P = 0.02 | P = 0.59 | P = 0.41 |

Table 5.2. Initial characteristics of the two groups of patients and ulcers. Values are expressed as median (range).
Operative Procedures

All patients underwent local anaesthetic sapheno-femoral (SF)/ popliteal (SP) disconnections as described. Eighteen limbs underwent SF disconnection, four SP disconnection and three limbs SF and SP disconnections combined. All patients requiring SP disconnections had pre-operative marking of the SPJ guided by colour duplex scanning.

Ulcer Healing

All 16 ulcerated limbs with isolated saphenous venous reflux began to heal within one month of surgery, and all 16 ulcers went on to heal completely at a median (range) of 81 (14 - 253) days. None of these 16 limbs required compression bandaging.

None of the nine ulcerated limbs with combined deep and saphenous venous reflux had begun to heal by one month. The median (range) ulcer areas had increased from 18 (9 - 92.3) cm² to 24.3 (14.8 - 126) cm² (Wilcoxon Matched Pairs P = 0.01). All nine limbs were subsequently treated with four layer compression bandaging. After a median (range) follow up of 16.5 (10-24) months 3 ulcers had healed at 136, 168, and 196 days the remaining 6 ulcerated limbs remained unhealed.

These findings are most clearly illustrated by a male patient who underwent long saphenous vein surgery to both limbs; one of which (left) had superficial venous reflux only and the other (right) had superficial and deep venous reflux combined (Figure 5.4).
Figure 5.4. A photograph taken 4 months post operatively a healed left leg (saphenous reflux only) and an unhealed right leg (deep and superficial reflux combined) belonging to a male patient who underwent simultaneous bilateral long saphenous vein surgery.

Venous Function

The Pressure Relief Index (PRI) (Figure 5.5) increased significantly immediately following surgery and at the follow up visit in those limbs with isolated saphenous reflux. In those limbs with deep and saphenous reflux combined the PRI remained unchanged immediately after surgery and at the follow up visit.
The Refill Time to 90% (RT90) (Figure 5.6) lengthened significantly immediately following surgery in those limbs with isolated saphenous reflux. This lengthening in the RT90 was maintained but not improved upon at the follow up visit. In limbs with combined deep and saphenous reflux there was no change in the RT90 after surgery or at the follow up visit.
Figure 5.6. The 90% Refill Time (RT90) pre- and postoperatively and at 3 months follow up (Review). SO - saphenous reflux only, SD - saphenous and deep reflux combined. Bars - medians, Box - interquartile range, Whiskers - range. Statistical comparisons are made with Wilcoxon Matched Pairs Testing.

The Ambulatory Venous Pressure (AVP) (Figure 5.7) was unchanged postoperatively in the limbs with saphenous reflux only but at the follow up visit had significantly decreased. The AVP remained unchanged throughout the study period in those limbs with combined deep and saphenous reflux.
The Distribution of Venous Reflux at Follow Up

Of the 16 limbs with isolated saphenous vein reflux, 12 long and 7 short saphenous veins were disconnected. At the follow up visit all 12 LSVs had been adequately disconnected at the SFJ and of the unstripped remnant 5 LSVs had thrombosed, 3 remained incompetent, 3 had become competent and 1 LSV was not fully visualised. Of the 7 SPJ disconnections, all had been disconnected, 2 SSV remnants had thrombosed, 3 regained competency, 1 remained incompetent and 1 was found to have a recurrent connection with the deep venous system. All of the deep veins in this group of limbs remained fully patent and competent.
Considering those limbs with combined deep and saphenous venous reflux, all 9 LSVs were adequately disconnected at the SFJ and all deep veins remained patent and incompetent. The states of the LSV remnants were: 4 had thrombosed, 3 remained incompetent, 1 had recurrent reflux from the groin, 1 was inadequately visualised and none had regained their competency.

The Haemodynamic Effect of Residual Saphenous Vein Reflux

The median (range) difference in pre-operative and follow up AVP in those limbs with normal deep veins was as follows: Group 1 (no reflux) 16.5 (5 - 37)\% and group 2 (reflux) 10 (-2 - +30)\%, (Mann Whitney P = 0.44). This is shown graphically in Figure 5.8.

![Graph showing comparison of haemodynamic effect of residual saphenous vein reflux](image)

**Figure 5.8** Comparison of the haemodynamic effect of the saphenous remnant demonstrating no significant detrimental effect is produced by not stripping the saphenous trunk. Group 1 (no residual reflux present) n = 8, Group 2 (residual reflux present) n = 4.
5.2d Discussion

This study examined the efficacy of sapheno-femoral/ popliteal disconnection alone without stripping the saphenous vein and without postoperative compression for three reasons. First, if correction of venous hypertension is of prime importance in achieving ulcer healing, then stripping the LSV is unnecessary. Second, saphenous ligation alone lends itself to local anaesthetic day case surgery and does not carry the morbidity nor cost associated with LSV stripping. This is an important consideration because 70% of venous ulcers occur in those aged over 70 years (Cornwall et al., 1986). Third, the application of postoperative compression was avoided to allow full evaluation of the surgical procedure in isolation.

In the absence of deep venous reflux saphenous disconnection alone results in a healing rate of 100% without the need for compression hose/ bandages. This clinical finding was accompanied by an improvement in the PRI in the immediate postoperative period and a further improvement 3 months following surgery. Of note, the parameters that constitute the PRI behaved differently. The RT90 lengthened immediately following saphenous disconnection and although this prolongation of the RT90 was maintained at 3 months it did not improved further. The AVP, however, failed to improve immediately after surgery but at 3 months follow up was significantly lower than either the preoperative or the post operative value. This adds support to the volume overload theory in that saphenous disconnection immediately removes the source of venous reflux (reflected in the lengthening of the RT90) but it takes time for the AVP to drop to a significantly lower value. This suggests that in order for the calf muscle pump to regain its function some degree of recovery and accommodation to the reduced reflux load is required, hence the delay in obtaining a reduced AVP. It is also noteworthy that 3 of the 7 LSV remnants regained competency suggesting that reducing the refluxing volume
allows the veins to regain their natural tone, allowing the opposition of valve cusps once again.

Based on the haemodynamic changes demonstrated by this study, saphenous vein stripping is unnecessary to achieve ulcer healing and improved venous function if the deep veins function normally. There was no detrimental haemodynamic effect of leaving a refluxing LSV remnant behind. However, it has been shown that the incidence of recurrent reflux at the SFJ (McMullin et al., 1991a; Bollinger et al., 1982) is greater if the SFJ is ligated compared to ligation and stripping. Simple SFJ/SPJ disconnection may be suitable for use in elderly patients but because of the associated higher incidence of recurrence of deep to superficial connections ligation and stripping under general anaesthesia may be the preferred option in the younger patient with venous ulceration and isolated superficial reflux.

It has been suggested that in the absence of post-thrombotic damage superficial femoral (SFV) and popliteal vein (PV) reflux may occur secondarily to LSV reflux as a consequence of volume overload on the calf muscle pump (Walsh et al., 1994). Varying degrees of saphenous vein surgery in this situation have corrected reflux in the SFV and PV (Walsh et al., 1994; Sales et al., 1996). It has been recommended that in the presence of coexisting deep venous reflux saphenous reflux should be corrected as far as possible in the treatment of venous ulceration (Scurr, 1996). Unfortunately, saphenous disconnection had no significant effect on venous haemodynamics in those limbs with combined deep and saphenous vein reflux. Ulcer healing occurred in only 3 limbs after the introduction of four layer compression bandages, in fact without any compression the ulcer areas enlarged following saphenous vein ligation. Duplex scanning at the follow up visit did not demonstrate reversal of deep venous reflux in any of the 9 ulcerated limbs. Bradbury et al. (1993a) documented improvement in deep
venous function assessed by foot volumetry which was short lived and recurrence of ulceration followed deterioration in venous function possible due to dilatation of pre-existing small perforating veins or neovascularisation. Ultimately, superficial venous surgery does not provide a long term solution to venous hypertension if full length deep venous damage is present.

5.2e Summary

Local anaesthetic, day case saphenous disconnection is a safe procedure in the elderly and that providing the deep veins are normal, 100% of ulcers heal without the need for postoperative compression bandaging. Improvements in venous function are apparent postoperatively and continue to improve at 3 months following surgery. If, however, there is deep venous reflux extending below the knee then saphenous ligation has no effect on venous haemodynamics and all ulcers failed to heal without compression bandages. Extrapolating from the data regarding the function of the venous remnant, suggests that stripping the LSV is not required to achieve these outcomes in limbs with isolated saphenous reflux. In the light of these findings we would encourage local anaesthetic day case saphenous vein ligation in the elderly patient with venous ulceration and normal deep veins, and recommend the avoidance of such surgery in the presence of deep vein reflux extending below the knee. There appears to be no role for saphenous surgery alone in limbs with full length deep venous reflux.
5.3 THE ABILITY OF PNEUMATIC CUFFS TO OCCLUDE THE 
SUPERFICIAL VENOUS SYSTEM AND THE ROLE OF CUFFS IN 
PREDICTING THE OUTCOME OF SUPERFICIAL VENOUS SURGERY 

5.3a Introduction

Tourniquets are frequently used for the clinical assessment of varicose veins to 
confirm the source of superficial venous reflux and identify any perforating veins 
(Scurr, 1996). This form of assessment relies on the abolition of venous filling by reflux 
down the superficial system under investigation, the inference being that on abolition of 
reflux distal to the tourniquet, the source of reflux must be proximal to the level of 
tourniquet application. The tourniquets used consist of variable materials and 
dimensions and are applied in various manual ways to limbs of various dimensions 
containing veins of clinically indeterminate diameters. Thus, it is very difficult to be 
certain that the superficial veins under examination are occluded (the assumed action of 
the tourniquet) and to ensure that no deep venous narrowing or occlusion has occurred 
that may complicate the situation further. Such is the basis on which clinical tourniquet 
testing is carried out.

Pneumatic tourniquets are often described as a method to distinguish between 
deep and/ or superficial venous reflux usually by applying cuffs of various widths 
inflated to various pressures to the upper thigh thus occluding the LSV or below the 
knee occluding the SSV (Coleridge-Smith, 1996a; Gretz et al., 1995; Nicolaides et al., 
1971; Nicolaides et al., 1987; Coleridge-Smith, 1990; Baker et al., 1993). As 
demonstrated in Section 5.2 superficial venous surgery is ineffective as a therapeutic 
manoeuvre to heal venous ulcers if full length deep venous reflux is present. If the basis
of offering or withholding possibly beneficial surgery is based on the results of cuff
tests, then the cuff tests themselves must be accurate.

McMullin et al. (1991b) reported variability in the ability of pneumatic cuffs to
occlude the LSV in the thigh at a standard pressure indicating the broad range of
pressures at which a cuff will occlude the saphenous vein in limbs of varying size. If this
is indeed the case then using cuffs to distinguish deep from superficial reflux may be
unreliable with important therapeutic implications. With this in mind the value of
pneumatic tourniquets to control the superficial veins is examined below with respect to
two issues: one, can pneumatic tourniquets accurately compress the superficial venous
system and two, can either pneumatic tourniquets or direct manual compression of the
saphenous veins predict the haemodynamic outcome of saphenous vein surgery.

5.3b Patients and Methods

Study Design

This study was designed to examine the ability of pneumatic tourniquets to
occlude the long saphenous vein in the thigh or the short saphenous vein below the knee
and hence their usefulness in distinguishing deep from isolated superficial venous
reflux.

The success of an occluding cuff can be directly assessed by colour duplex
scanning detecting the presence or absence of occlusion of the superficial veins and also
any occlusion of the deep veins at this same level. This demonstrates the effect a
pneumatic cuff has on the superficial and deep venous systems.

All patients with venous ulceration at The Leicester Royal Infirmary undergo a
colour duplex scan as an integral part of their management; during this investigation it is
very easy to directly compress the main saphenous vein by applying manual pressure to
occlude the vein with the scanning head at the time of diagnostic scanning. The pressure exerted by the examining hand/scanning head can be controlled by observing the scans for occlusion of the vein under study. This permits accurate and total occlusion of the superficial vein under investigation along with confirmation of the state of the deep veins subsequent upon compression.

In addition, the effect on venous function of these manoeuvres can be assessed by photoplethysmography (PPG). Thus, PPG refill times to 90% of the resting level (PPG RT90) are measured pre-operatively without any venous compression, with the application of a pneumatic tourniquet to the leg, with manual compression using the duplex scanner head and postoperatively to assess the PPG RT90 after SFJ/SPJ disconnection. Duplex scanning repeated at the time of the postoperative review reassessed the SFJ/SPJ for completeness of disconnection and also to re-examine the deep venous system and the saphenous remnant if stripping had not been performed. This allows assessment of the ability of tourniquets or manual compression to predict the postoperative PPGRT90 and thus possibly predict the efficacy of venous surgery.

Patients

Patients with venous ulceration and/or varicose veins were recruited from the Venous Ulcer Assessment and General Vascular Outpatient Clinics. Two groups were studied: those with saphenous reflux only and those with saphenous and deep venous reflux combined. All limbs studied had an ABPI >0.8 and venous reflux was defined as previously described.
**Pneumatic Tourniquet**

A 2.5 cm wide pneumatic cuff was used in all cases inflated to a pressure of 120 mmHg at the upper thigh level or 80 mmHg below the knee (Nicolaiides et al., 1987), pressures commonly used in practice are similar (Gretz et al., 1995; Nicolaiides et al., 1987; Coleridge-Smith, 1990; Baker et al., 1993). The inflation pressure was created and monitored by a mercury sphygmomanometer attached to the cuff via a three-way tap.

**Duplex Scanning**

Colour duplex scanning, was performed in all limbs at the pre- and postoperative visits. At the pre-operative visit the ability of the pneumatic cuff to occlude the saphenous systems was assessed by scanning the LSV or SSV as appropriate in such a manner as to demonstrate the length of vein immediately above and below, and directly beneath the cuff. The images and spectral analysis obtained confirm whether venous occlusion had occurred. Simultaneously obtained images of the SFV or popliteal vein ascertain that this vein was not occluded by the cuff. Following this manoeuvre, manual compression of the saphenous vein under investigation with the duplex scanning probe was performed. The position of the probe adjusted to allow simultaneous imaging of the deep veins without moving the probe from the segment of saphenous vein being compressed. Photoplethysmography determined the effect each of the above manoeuvres had on venous function.

**Photoplethysmography (PPG)**

Photoplethysmographic 90% refill times, a non-invasive test of venous function that correlate with AVP measurements with the subject seated (Abramowitz et al.,
1979), were used to assess venous function. Measurements were made using a Scimed PVL-50 photoplethysmograph (Scimed, Bristol, UK.) (Figure 5.9) with the subject seated, legs dependent over the edge of an examining couch. The knees were relaxed and flexed to 90 degrees with the knee joints clear of the edge of the examining couch to prevent inadvertent compression of the popliteal vein (Figure 5.10). The infra-red probe of the PPG unit (Figure 5.11) was secured to the dorsum of the foot using transparent double sided tape thus ensuring that the local dermal vascular plexuses were not compressed by a circumferential bandage or length of tape. Recordings were made after a period of initial stabilisation to obtain a resting recording; the subject was then asked to perform five ankle dorsiflexions at one second intervals whilst keeping the knee flexed and relaxed. Thereafter the leg was left to 'dangle' freely until the recording returned to the pre-exercise base line. If the pre-exercise level was not regained then the post exercise level was used as the baseline for the whole investigation and all measurements of RT90 were made with reference to this post exercise level. PPG was performed pre-operatively without any compression and then with cuff then manual compression; postoperative PPG recordings were made at three months postoperatively.
Figure 5.9  The Scimed PVL 50 Photoplethysmograph.

Figure 5.10  Photograph demonstrating the typical positioning of the PPG probe with the leg dependent.
Surgery

Those limbs with varicose veins and no ulceration underwent sapheno-femoral disconnection with formal groin exploration and division of all tributaries of the SFJ, the LSV was stripped to the knee and below knee varicose veins were avulsed through small 'stab' incisions, all performed under general anaesthesia. In cases of SSV varicose veins, sapheno-popliteal disconnection was performed, the SSV trunk was not stripped but obvious varicosities were avulsed in a similar manner. The sapheno-popliteal junction was identified by duplex scanning and marked on the skin pre-operatively. Limbs with venous ulceration underwent full sapheno-femoral/ popliteal dissection and disconnection without associated venous stripping or avulsions usually under local infiltrative anaesthesia.

Data Analysis

Assessment of the ability of the cuff to occlude the saphenous veins was performed by a simple tally method. To assess the effect of compression the lengthening
of RT90 was measured with the application of the cuff/probe. The ability of pneumatic cuff and manual probe compression of the saphenous veins to predict the postoperative venous refill time (RT90) was assessed. To do this, the difference between postoperative RT90 and pre-operative basal RT90 is considered to be the ‘gold standard’ with respect to this study. The lengthening of RT90 is measured for each method of compression with reference to the basal RT90 (without any compression) and this result is compared with the lengthening of RT90 achieved with saphenous vein surgery. In assessing the ability the two methods of saphenous vein occlusion (cuff/manual compression) to ‘predict’ the postoperative RT90, a ‘Bland - Altman Plot’ was used (Bland & Altman, 1986).

5.3c Results

Patients

Twenty-nine patients (29 limbs) were recruited to the study. Twenty-two limbs demonstrated superficial venous reflux, 16 limbs with saphenous reflux alone (13 LSV only, 3 SSV only); and 6 limbs possessed saphenous and perforating vein reflux. Seven limbs demonstrated deep and superficial venous reflux combined, 5 deep and saphenous reflux and 2 deep, saphenous and perforating vein reflux. All 7 limbs with deep and superficial venous combined had ulceration, whereas, 17 limbs with superficial reflux only had ulcers; the remaining 5 had uncomplicated varicose veins. All 29 subjects completed the duplex assessment of the effect of the pneumatic cuff on the saphenous and deep venous systems. One patient with saphenous and perforating vein reflux refused to allow any additional form of compression to be applied to the limb because of discomfort and was therefore withdrawn from further analysis. Thus 28 limbs completed the PPG assessment protocol.
**Colour Duplex Scanning Beneath the Pneumatic Cuff**

Table 5.3 reports the results of duplex scanning beneath the pneumatic tourniquet (cuff) for all 29 limbs examined. Whilst the cuff caused no compression of the deep system, only seven of the 29 (24%) saphenous veins were successfully occluded by the cuff. Manual compression using the scanner probe occluded all of the saphenous and none of the deep veins.

<table>
<thead>
<tr>
<th>Occlusion by Pneumatic Cuff</th>
<th>Saphenous System</th>
<th>Deep System</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>No</td>
<td>22</td>
<td>29</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Occlusion by Hand Held Probe</th>
<th>Saphenous System</th>
<th>Deep System</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>29</td>
<td>0</td>
</tr>
<tr>
<td>No</td>
<td>0</td>
<td>29</td>
</tr>
</tbody>
</table>

Table 5.3. Effect of pneumatic cuff and manual compression on the saphenous and deep venous systems in the 29 limbs examined.

**Assessment of Ability of the Cuff and Manual Compression Methods to Predict Postoperative RT90**

The raw data derived from the 28 limbs completing both duplex and PPG examination are shown in Table 5.4. From this data the lengthening of PPGRT90 obtained by cuff (cuff – resting) and probe (probe – resting) compression and the difference in such RT90 lengthening with these methods when compared with that obtained from surgery (cuff – surgery, and probe – surgery) can be calculated (Table 5.5). Examination of the data in Table 5.5 suggests that PPG RT90 lengthens by the application of the pneumatic cuff but to a lesser degree than that produced by manual (probe) compression. This is a significant difference on non-parametric paired Wilcoxon testing ($z = -4.4$, $P = 0.000$)
<table>
<thead>
<tr>
<th>Limb</th>
<th>Pattern of Venous Reflux, Vein occluded by cuff (Y/N)</th>
<th>S, SP, SD</th>
<th>Resting PPGRT90 (s)</th>
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Table 5.4. Table demonstrating the raw data forming the basis of the Bland-Altman Plots in Figures 5.12a and 5.12b. For each limb detailed the PPGRT90 refill times in seconds obtained pre-op without saphenous vein compression (resting), with cuff (cuff) or probe (manual) compression of the saphenous vein and the postoperative PPGRT90 resultant upon saphenous vein disconnection are shown. Pattern of Venous Reflux, S = Saphenous Reflux Only, SP = Saphenous and Perforating Vein Reflux, SD = Saphenous and Deep Venous Reflux.
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| Mean  | 2.4*                      | 9.3*                        |
| 95% CI | -4.3 to 9.1               | -2.9 to 21.5               |

Table 5.5. Table demonstrating the data derived from Table 5.4 used in the Bland – Altman Plots in Figures 5.12a and 5.12b. Cuff – Resting = lengthening of PPGRT90 by application of a pneumatic cuff, Manual – Resting = lengthening of PPGRT90 by manual compression using the duplex probe. These data are summarised as mean (95% CI). Cuff – Surgery = difference in lengthening of PPGRT90 obtained by surgery compared with that obtained using a cuff, Manual – Surgery = difference in lengthening of PPGRT90 obtained by surgery compared with that obtained using manual probe compression. These data are summarised as mean (95% limits of agreement). (* Wilcoxon Paired test z= -4.4, P = 0.000).
To illustrate the association between saphenous vein compression by pneumatic cuff and surgery with the effect on RT90 a Bland-Altman Plot is shown (Figure 5.12a). From this it is clear that the data show a wide degree of scatter and there is little agreement between the increase in RT90 obtained by each method (cuff and surgery).

![Bland-Altman Plot](image)

**Figure 5.12a.** Bland-Altman Plot (Bland & Altman, 1986) comparing the improvement in PPG RT90 obtained by pneumatic tourniquet compression of the saphenous veins and the improvement obtained by saphenous disconnection. n = 28.

A similar analysis is shown in Figure 5.12b to demonstrate the agreement between RT90 lengthening by manual compression and surgery. This plot demonstrates a better agreement between the two methods of saphenous vein control especially for increases in RT90 below 10 seconds. Above this level of RT90 increase the agreement
is less sound (demonstrated by the widening scatter in the differences between the methods used). However, again the scatter of the data is very wide suggesting that for practical clinical purposes there is no agreement.

Expressing this data in the form of a Bland-Altman plot (Figure 5.12), demonstrates a lack of agreement between the measures of venous function produced by the two methods of venous compression (cuff and probe) when compared with the 'gold standard' (surgery). Notably, the range of the differences are wide (-16.6 to +6 seconds.
using cuff compression and -8.4 to +12.6 seconds for manual compression) suggesting that these methods cannot be used in practice to predict postoperative RT90.

5.3d Discussion

Pneumatic tourniquets are frequently used to identify limbs with superficial reflux only from those with deep and superficial reflux combined and based on this limbs without deep venous reflux may be offered superficial venous surgery. However, the main issue pertaining to cuff tests and venous ulceration is not necessarily the correct identification of limbs with a particular pattern of reflux because this can be done using colour duplex scanning. The salient point is will venous haemodynamics improve (thence ulcers heal) by saphenous vein surgery. The purpose of this study was to investigate the ability of pneumatic cuff tourniquets to predict the likely haemodynamic outcome of saphenous vein surgery in limbs with saphenous reflux alone and in combination with deep reflux.

Most publications relying on 2.5 cm wide pneumatic cuffs to control the superficial venous system refer to a paper by Nicholaides in The British Journal of Radiology published in 1971 (Nicholaides et al., 1971). He described a technique for performing ascending deep venous venography for the imaging of the soleal plexus and other deep veins affected by deep vein thromboses. In this paper Nicholaides actually described the application of 5 cm wide cuff using inflation pressures of 120 mmHg at the ankle to occlude the superficial veins at that level and a pressure of 200 mmHg at the mid thigh level to occlude the femoral vein itself. No reference to 2.5 cm wide cuffs is made in Nicholaides’ paper but he is quoted by many authors as describing such cuffs and is referred to when justifying the use of 2.5 cm cuffs. I am thus unable to identify any published data demonstrating that 2.5 cm wide cuffs can occlude the saphenous vein.
in the thigh and as McMullin (1991b) has clearly shown the range of pressures required in a 2.5 cm wide cuff to prevent reflux in the saphenous vein is variable.

Of the 29 limbs examined in total only 7/29 (24%) demonstrated occlusion of the saphenous vein by the cuff implying that 2.5 cm cuffs inflated to 120 mmHg are totally unreliable as a method of occluding the saphenous venous system in the thigh.

Both manual and cuff compression cause lengthening of the PPGRT90 (Table 5.5) but the manual method does so to a greater degree. This can be explained by the fact that cuff compression does not successfully occlude the saphenous vein in many limbs (Table 5.3).

Considering the ability of these two methods of venous compression to predict the haemodynamic outcome of saphenous vein surgery I have demonstrated that neither method shows a reliable agreement with surgical vein 'occlusion'. Figure 5.12a suggests that cuffs under predict the improvement with surgery and Figure 5.12b suggests that the manual method over predicts this. The under prediction is understandable (ineffective venous occlusion/ calf muscle pump accommodation) but an explanation for the ability to over predict the outcome surgery remains less obvious. It must be remembered that the data presented here were obtained from limbs with both superficial reflux only and superficial and deep reflux combined, and that the aim was not to predict the degree of PPGRT90 improvement but to demonstrate whether or not an improvement exists using cuffs or manual compression methods (a finding on which subsequent saphenous vein surgery could be advised/ withheld).

What can be concluded from this data is that neither method shows adequate levels of agreement with surgery to be used in clinical practice. The range of the 95% levels of agreement are so wide they encompass the range of PPGRT90 readings
encountered in the clinical situation. In addition, the mean differences (-4.1 s and 2.2 s) in improved RT90 are distant from the point of equivalence (0 s)

5.3e Summary

The use of 2.5 cm wide pneumatic cuffs inflated to 120 mmHg is an unreliable method to occlude the saphenous vein. The 95% levels of agreement with surgery for both cuff and manual compression methods are so wide that neither method is of value in predicting the outcome of superficial venous surgery on PPGRT90.

5.4 CONCLUSIONS

This chapter has demonstrated the inaccuracy of pneumatic cuffs to isolate the deep and superficial venous systems. The use of cuffs in planning the management of ulcerated limbs by trying to predict the improvement in venous refill times by surgery is of no value. Those ulcerated limbs with superficial reflux only will benefit from superficial venous. Superficial venous surgery is not recommended in the presence of deep reflux. The calf muscle pump volume overload theory is supported by the improvement in venous function demonstrated in those limbs with superficial reflux alone.
CHAPTER SIX

INVESTIGATION OF THE ROLE OF CALF PERFORATING VEIN SURGERY
IN THE TREATMENT OF VENOUS ULCERATION.

6.1 GENERAL INTRODUCTION

6.2 THE CLINICAL AND HAEMODYNAMIC EFFECTS OF CALF
PERFORATING VEIN SURGERY IN PATIENTS WITH ULCERATED
LIMBS AND DEEP VENOUS INCOMPETENCE.

a. Introduction
b. Patients and Methods
c. Results
d. Discussion
e. Summary

6.3 CONCLUSION
6.1 GENERAL INTRODUCTION

Venous ulcers occur most commonly on the supramalleolar medial aspect of the calf in close proximity to incompetent medial calf perforating veins. This anatomical proximity has lead to a pathophysiological association between incompetent perforating veins and venous ulceration, and perforating vein surgery has therefore been proposed as a treatment for venous ulceration (Anonymous, 1977; Allen, 1990). However, the role of perforating vein surgery in patients with venous ulceration remains uncertain (Ruckley, 1996), the main problem being difficulty in the interpretation of studies with many confounding methodological factors. Limbs with deep and perforating vein reflux remain a difficult clinical problem to manage, whereas limbs with normal deep veins and superficial reflux in isolation have been discussed in the literature and Chapter 5 above. By removing confounding factors and with the accurate definition of the venous anatomy the following study examines the role of perforating vein surgery in ulcerated limbs with coexisting deep venous reflux.

6.2 THE CLINICAL AND HAEMODYNAMIC EFFECTS OF CALF PERFORATING VEIN SURGERY IN PATIENTS WITH ULCERATED LIMBS AND DEEP VENOUS INCOMPETENCE

6.2a Introduction

The uncertainty of the role of perforating vein surgery (PVS) in the treatment of venous ulceration (Ruckley, 1996) is compounded by difficulty in interpreting the various studies in the literature. Thus, in many studies superficial venous surgery has
been combined with PVS (Linton, 1953; Cockett et al., 1953; Thomas et al., 1986; Burnand et al., 1976; Negus et al., 1983; Gloviczki et al., 1996; Stacey et al., 1988a; Bradbury et al., 1993a) and the distribution of venous incompetence in the superficial and deep veins has not been documented (Linton, 1953; Thomas et al., 1986; Negus et al., 1983; Stacey et al., 1988a; De Palma, 1979; Pierik et al., 1995). This latter information is particularly important in view of studies showing that in ulcerated limbs with perforator and superficial venous incompetence and normal deep veins, superficial venous surgery alone, without PVS, will lead to ulcer healing in the majority of cases (Sethia et al., 1984; Darke et al., 1992). The interpretation of the role of PVS in ulcer healing is further hampered by additional peri-operative procedures, including operating only after ulceration has healed (Linton, 1953; Cockett et al., 1953; Burnand et al., 1976; Negus et al., 1983; Gloviczki et al., 1996; Stacey et al., 1988a; Bradbury et al., 1993a; Cockett, 1955), and using prolonged postoperative bed rest, elevation and/or compression (Linton, 1953; Negus et al., 1983; Gloviczki et al., 1996; Stacey et al., 1988a; Bradbury et al., 1993a; Lim et al., 1970; Pierik et al., 1995).

The advent of colour duplex scanning has revolutionised the investigation of patients with venous ulceration and it is now possible to rapidly and accurately define the distribution of venous incompetence in affected limbs. The purpose of this study was to investigate the role of PVS in patients with venous ulceration and incompetent deep veins. Limbs were purposefully identified that had previously undergone saphenous vein surgery so that the only remaining venous abnormalities were calf perforating vein and deep venous incompetence. The effect of PVS was examined without pre-operative ulcer healing and without postoperative bed rest, elevation or compression, thereby allowing the specific role of PVS to be assessed.
6.2b Patients and Methods

Patients and Study Design

The Venous Ulcer Assessment Clinic identified ulcerated limbs having a combination of calf perforating vein incompetence and deep venous incompetence extending from the common femoral vein distally into the below knee calf veins which were entered into the study. All patients had previously undergone long saphenous vein surgery in an unsuccessful attempt to achieve ulcer healing and were receiving four layer compression bandaging at the time of recruitment. Each limb under investigation had an ABPI >0.8, excluding significant peripheral arterial disease. The influence of PVS was measured by its effects on ulcer healing and local venous reflux. Thus, pre- and one month postoperatively ulcer areas were measured and photoplethysmography (PPG) performed at three sites on the ulcerated limb. No postoperative compression was applied. If however at one month there was no evidence of ulcer healing or the ulcer size had increased, then a four layer compression bandage was applied.

Ultrasonography

Colour duplex scanning used either an ATL Ultrasound (HDI) (Advanced Technology Laboratories UK Ltd.) or a Diasonics Masters (Sonotron Ltd) machine with linear array 5 MHz and 10 MHz probes to examine the deep and superficial venous systems respectively. Limbs were examined in the dependent position and venous reflux was defined as reversed blood flow of more than 0.5 seconds on release of a manual calf squeeze distal to the segment of vein under examination. Colour duplex scanning was used to mark the site of refluxing calf perforating veins pre-operatively and to re-examine the operated limb at the follow up visit to assess the completeness of PVS. Perforating veins were defined as possessing venous reflux if they could be made to
exhibit deep to superficial blood flow in response to manual compression. Post-thrombotic deep vein damage was inferred from the following characteristics on duplex scanning: old intraluminal thrombus (incompressible vein), thickened/scarred vein walls, stenosis of the vein, shrunken and scarred valve cusps.

**Ulcer Area**

Ulcer areas were obtained by computerised planimetry of tracings of the ulcer perimeter taken onto transparent acetate sheets immediately pre-operatively and one month postoperatively. Ulcer healing was defined as complete re-epithelialisation of the ulcer base determined by inspection.

**Photoplethysmography**

Local venous reflux were assessed by photoplethysmography (PPG) (Van Bemmelin et al., 1994c). In order to detect any localised abnormality in venous reflux 90% refill times (RT90) were measured at three sites in the lower limb: the dorsum of the foot (5 cm distal to the ankle joint crease), the medial and lateral gaiter regions 5 cm proximal to the tip of the respective malleolus. If the preferred sites of RT90 measurement were involved in ulceration, extensive lipodermatosclerosis or atrophie blanche then the nearest area of skin to the preferred site was used to obtain the measurements. PPG measurements were made using a Scimed PVL-50 photoplethysmograph (*Scimed, Bristol, UK*) with the legs dependent. The knees were relaxed and flexed to ninety degrees and the knee joints and popliteal fossae were clear of the edge of the couch to ensure the popliteal vein was not compressed. Recordings were made after a stable resting reading was obtained by the PPG and the subject was asked to perform 5 dorsiflexions of the ankle whilst keeping the knee relaxed and
flexed. The dorsiflexions were made at one second intervals and thereafter the knee and ankle joints were left fully relaxed and dangling free until the tracing returned to the pre-exercise baseline reading. If the pre-exercise level was not regained then the post-exercise level was used as the baseline for the whole investigation and all measurements of RT90 were made with reference to this level.

_Surgery_
Perforating vein surgery was performed in one of three ways; via individual 2-3 cm skin incisions at the pre-operatively marked (duplex guided) sites, subfascial endoscopic perforating surgery (SEPS), or radiologically deployed coil embolisation. Postoperatively limbs were dressed with NA dressings *(Johnson and Johnson Ltd.)* sterile gauze and a graduated Tubigrip *(Seton)* to keep the dressings in place.

_Data analysis_
Photoplethysmographic data were analysed using ANOVA techniques to test for site dependent variations in RT90. Thus, if refluxing medial calf perforating veins do give rise to venous abnormalities in their immediate vicinity then one would expect to find a more rapid RT90 in association with the medial perforating veins than at the pedal and lateral gaiter sites. If, however, there is no local venous abnormality then no such site dependent abnormality in RT90 will be detected. All limbs were examined in this manner pre-operatively and one month postoperatively. If PVS does alter local venous reflux then one would expect the postoperative RT90 to show a prolongation at the medial site compared to the other two points. Pre- and postoperative readings were not compared because temporal variations in skin perfusion do not allow such comparisons *(Tenland et al., 1983; Sundberg, 1984).*
6.2c Results

Patients, Limbs and Ulcers

Seven patients with seven ulcerated limbs were investigated, four were male and
their median (range) age was 70 (36-90) years. All 7 limbs had previously undergone
sapheno-femoral disconnection with long saphenous vein stripping to the knee at least
12 months prior to entry into this study. None of the limbs had undergone short
saphenous vein surgery and none had short saphenous vein reflux. Only one patient
gave a history of deep vein thrombosis (DVT) and this was the only limb with duplex
evidence of a DVT, the remaining six limbs had neither a history nor colour duplex
evidence of previous DVT. No limb studied possessed any duplex demonstrable deep
venous valves.

Five limbs had medial ulcers (all with refluxing medial perforating veins only),
one had a lateral ulcer (with reflux in four medial and one lateral perforating vein and
duplex evidence of a previous DVT) and one limb had medial and lateral ulcers
(refluxing medial perforating veins only). The median (range) ulcer duration prior to
surgery was 2 (0.5-6) years with a pre-operative median (range) area of 31 (7-685)cm².
Pre-operative colour duplex scanning identified a median (range) of 2 (1-5) perforators
per limb that were disconnected as follows: direct open division five limbs, SEPS one
limb, coil embolisation one limb.

At operation there was complete agreement between the pre-operative duplex
identification of perforating veins and the operative findings. This was corroborated by
the postoperative duplex scanning that confirmed the absence of persisting refluxing
perforating veins in any of the limbs studied.

One month postoperatively none of the ulcers had begun to heal and the median
(range) ulcer area had increased to 35.5 (7-796)cm² (Wilcoxon Matched Pairs testing
P=0.07) and consequently all 7 limbs were treated by four layer compression bandaging thereafter.

**Venous Haemodynamics**

Figure 6.1 demonstrates the duration of the pre-operative RT90 for all 7 limbs at the three sites investigated. All three sites in all 7 limbs demonstrated a more rapid RT90 than normal (20 seconds) (Negus, 1992b). Interestingly, one limb with a medial ulcer (refluxing medial perforators) displayed a more rapid RT90 in the lateral gaiter area (4.0s) compared to the pedal (8.8s) and medial gaiter areas (6.4s), and the limb with a lateral ulcer (four medial and one lateral perforators) had a medial RT90 of 2.5s and pedal and lateral RT90 of 4.9s and 6s respectively. The five remaining limbs, four with medial ulcers and one with a medial and lateral ulcer (all with refluxing medial perforating veins) demonstrated no meaningful pattern to the distribution of RT90. Repeated measures ANOVA found no site dependent variation in RT90 (F=0.57, df=2, P=0.58).
Figure 6.1. Pre-operative PPG RT90 refill times for the 7 limbs studied.

Postoperatively (Figure 6.2) the RT90s remained abnormally rapid in all three sites in all 7 limbs and there was no site dependent variation in RT90 within any of the limbs examined ($F=1.57, \text{df}=2, P=0.27$). In particular, of those limbs with medial ulcers and medial refluxing perforating veins there was no prolongation of RT90 at the medial site compared with the pedal and lateral sites.
Figure 6.2. Postoperative PPG RT90 refill times for the 7 limbs studied.

6.2d Discussion

This study was designed to investigate the role of calf perforating vein surgery in ulcerated limbs with combined deep and perforating vein incompetence and to document any local venous abnormality associated with incompetent perforating veins that may implicate them in the pathogenesis of venous ulceration. In order to assess the role of calf PVS in isolation limbs were purposefully selected with perforating and deep venous reflux only, thereby avoiding the complicating factor of saphenous reflux. Limbs that fall into this category are relatively uncommon (7/239 in this series) and no more patients are anticipated at The Leicester Royal Infirmary because, based on the findings described in Chapter 5, saphenous surgery is no longer performed in the presence of deep venous incompetence extending from the common femoral into the below-knee popliteal vein. However although there were only seven patients in this
study, if PVS was of any clinical or haemodynamic benefit then this would have been apparent.

To put these 7 limbs into context, they represent a select group of 239 consecutive patients with ulcerated limbs examined over a 2 year period. Of these 239 patients perforating vein reflux was present in combination with deep and superficial reflux in a further 7 limbs and in combination with superficial reflux alone in a further 21 limbs. In 3 limbs perforating vein reflux was the only detectable venous abnormality and 2 limbs exhibited perforator and deep reflux only. As indicated above surgery is no longer offered to patients with ulcerated limbs possessing superficial, deep and perforating vein reflux in combination.

Pre-operatively the predominant pattern of perforating vein reflux was medial with only one lateral refluxing perforator identified. Of the limbs with medial perforating vein reflux only, five limbs had a medial ulcer and one limb had medial and lateral ulcers implying that ulceration can occur at sites on the leg distant from any refluxing perforating veins. Likewise the limb with a combination of four medial and one lateral refluxing perforating vein had a lateral ulcer despite a predominately medial perforator abnormality. These findings suggest a global abnormality of venous function in the ulcerated limb rather than focal abnormalities at the sites of perforating vein reflux.

Ambulatory venous pressures reflect the venous pressure within the deep and superficial veins of the entire limb and cannot, therefore, be used to detect localised venous abnormalities. Photoplethysmography was chosen to assess venous haemodynamics because it allows cutaneous venous reflux to be assessed locally (Rosfors, 1990). Although PPG is an indirect measure of venous function RT90 times correlate well with AVP refill times in the sitting position (Abramowitz et al., 1979).
The pre-operative PPG studies (Figure 6.1) demonstrated a global abnormality of venous function and did not show that the medial gaiter area was any worse than the other two sites. At the postoperative examinations (Figure 6.2) the RT90s still remained globally abnormal and in particular the medial RT90s had not lengthened when compared to the other two sites. This finding shows that PVS does not improve the local venous haemodynamics in limbs with coexisting deep venous reflux.

6.2e Summary

The laterality of calf perforating vein incompetence does not dictate the location of venous ulceration in the presence of below knee deep venous incompetence and PPG confirmed a global abnormality of venous reflux in the calf extending onto the clinically normal dorsal foot skin. Following calf PVS, none of the ulcers began to heal and indeed the ulcer areas enlarged, PPG RT90s failed to return towards normal at any site, remaining globally abnormal with no preferential improvement at the medial gaiter site. Calf perforating vein surgery has previously been shown to be ineffective in limbs with post-thrombotic deep venous incompetence and in limbs with superficial venous incompetence. This study demonstrates similar findings in limbs with primary deep venous incompetence concluding that perforating vein surgery has no role in the management of such ulcerated limbs.

6.3 CONCLUSION

The role of perforating vein surgery needs careful appraisal highlighted recently by the advent of SEPS (Ruckley, 1996). There appears to be no indication for perforating vein surgery in the presence of normal deep veins and saphenous vein
reflux: Bjordal in 1972 demonstrated that in this situation ambulatory venous pressures were normalised by proximal saphenous occlusion and that perforating vein reflux had no influence on venous pressure (Bjordal, 1972). Subsequently, Sethia (1984) and Darke (1992) have clearly demonstrated both clinical healing and venous haemodynamic improvement in limbs undergoing saphenous ligation alone (without PVS) in limbs with saphenous and perforating vein reflux but normal deep veins. Furthermore, it has recently been demonstrated that incompetent perforating veins can regain competence after saphenous vein surgery in limbs with normal deep veins (Campbell et al., 1995; Stuart et al., 1998). Likewise, the role of PVS in limbs with superficial and deep reflux combined is difficult to justify. Burnand (Burnand et al., 1976; Burnand et al., 1977) has demonstrated that perforating vein surgery can neither prevent ulcer recurrence nor improve ambulatory venous pressures in limbs with post thrombotic deep venous reflux. This has been supported more recently by Stacey et al. (1988a), Åkesson et al. (1990) and Bradbury (Bradbury et al., 1993a; Bradbury et al., 1993b). One surgical option remaining in this situation is deep venous valve repair (Raju et al., 1988) if any detectable valves are present or valve transplantation/ transposition (Taheri et al., 1985; Kistner et al., 1979) if no deep venous valves are suitable for repair. Since reflux of the popliteal venous segment is pivotal in the development of venous ulceration (Bradbury et al., 1996) this is an important area for future investigation.
CHAPTER SEVEN

THE EFFECT ON ULCER HEALING BY TREATMENT BASED ON THE
PATTERN OF VENOUS REFLUX

7.1 GENERAL INTRODUCTION

7.2 THE EFFECT OF ADOPTING A SELECTIVE POLICY OF SURGERY OR
COMPRESSION BANDAGING FOR THE TREATMENT OF VENOUS
ULCERATION
   a. Introduction
   b. Patients and Methods
   c. Results
   d. Discussion
   e. Summary

7.3 CONCLUSION
7.1 GENERAL INTRODUCTION

This chapter amalgamates the findings of Chapters 3, 4, 5 and 6. It has been demonstrated that 63% of ulcerated limbs with primary venous incompetence have superficial venous reflux in isolation and that these limbs benefit from simple superficial venous surgery. Furthermore, there appears to be no role for perforating surgery in this group of patients (Darke et al., 1992; Sethia et al., 1984). The remaining limbs with primary venous reflux had superficial and deep incompetence combined and in the presence of full length deep venous reflux superficial venous surgery is of no benefit either clinically or haemodynamically. Perforating vein surgery appears to have no role in this situation either. To date, therefore, compression therapy is the only practical therapeutic manoeuvre in this situation. Four layer and short stretch compression bandaging demonstrate comparable efficacy but four layer bandages appear to be associated with fewer complications and could therefore be recommended for general use if surgery is not indicated.

It is possible to tailor the individual management of an ulcerated limb based on the findings during initial colour duplex scanning that forms an integral part of the management of all ulcerated limbs. This chapter describes an audit performed of the results obtained by adopting a practice of offering superficial venous surgery to patients with venous ulceration due to superficial venous reflux alone and offering four layer compression bandaging to those patients whose limbs demonstrate deep and superficial venous reflux combined based in the setting of a Single Visit Venous Ulcer Assessment Clinic.
7.2 THE EFFECT OF ADOPTING A SELECTIVE POLICY OF SURGERY OR COMPRESSION BANDAGING FOR THE TREATMENT OF VENOUS ULCERATION

7.2a Introduction

Superficial venous surgery affects both clinical and haemodynamic improvements in ulcerated limbs with normal deep venous function and duplex scanning can rapidly and accurately identify this group of limbs. Similarly, limbs with full length deep venous reflux extending below the knee can also be easily identified by colour duplex scanning. With this knowledge surgery can be withheld from this group of patients and compression bandaging be offered at the outset, thus avoiding an unnecessary surgical procedure which although minor and can be performed under local anaesthetic on a day case basis is not without its complications.

This chapter aims to examine the effect of adopting such guidelines over a one year period at The Leicester Royal Infirmary.

7.2b Patients and Methods

Patients

All patients referred to the Venous Ulcer Assessment Clinic between 1st April 1996 and 31st March 1997 who following the standard full assessment were found to have an ulcerated leg, an ABPI > 0.8 and venous reflux of > 0.5 seconds duration were recruited to the study.

Informed consent was obtained and each patient with superficial reflux in isolation was offered superficial venous surgery as previously described, those patients declining the offer of surgery were treated by four layer compression bandaging.
Patients whose limbs demonstrated full length deep venous reflux were not offered surgery and were treated by four layer compression bandaging only.

Study Design

The study was designed to audit such a selective approach to superficial venous surgery in ulcerated limbs.

Those limbs treated by surgery attended on the day of surgery where initial ulcer areas were recorded as described previously; following surgery the leg was dressed with a simple NA dressing (Johnson & Johnson) squares of overlying gauze and a graduated Tubigrip to keep this dressing in place. Patients were reviewed once as an out patient to assess the postoperative course and contact was maintained with the patient by myself until the ulcer healed, the time taken to heal being recorded. Healing was confirmed by one further out patient visit as far as possible.

Those limbs treated by four layer compression bandaging had an initial ulcer area measurement performed when attending for the first bandaging visit to the out patient department and at that time a standard four layer compression bandage was applied. This was changed in the out patient clinic on a weekly basis unless more frequent changes were indicated. Again, ulcer healing was determined by inspection and the time to healing recorded.

Methods

Colour duplex scanning, measurement of ulcer area compression bandage application and the surgical techniques used were carried out as previously describe in this thesis. In particular post-thrombotic damage was inferred from the following characteristics on duplex scanning: old intra-luminal thrombus (incompressible vein),
thickened and/or scarred vein walls, stenosis of the vein, and shrunken and scarred valve cusps.

7.2c Results

Patients and Ulcers

During the 12 month period studied 104 patients with 116 ulcerated limbs were recruited to the study. The distribution of subjects between surgery and compression bandaging is shown in Table 7.1. The proportion of limbs with superficial reflux alone 71/116 (61%) is in accord with previous experience. The age of the patients, initial ulcer area and ulcer duration at presentation are comparable between the two groups.

Of the 71 limbs demonstrating superficial venous reflux; 54 (76%) demonstrated LSV reflux only, 5 (7%) SSV reflux only and 12 (17%) LSV and SSV reflux combined. Thus 76% of limbs underwent LSV surgery, 7% SSV surgery and 17% LSV and SSV surgery combined.
Table 7.1. Details of the two groups of patients treated. Limbs treated by compression bandaging based on a pattern of deep and superficial venous reflux combined (FLB) and those treated by superficial venous surgery having superficial venous reflux with normal deep veins (surgery). Non-parametric statistics (Mann Whitney) are used to compare the two groups where appropriate, proportional differences are compared using Chi Squared Test.

**Ulcer Healing**

The healing rate of those ulcerated limbs with deep and superficial reflux (treated by FLB) was 70% at 1 year, that for those limbs with superficial venous reflux alone (treated by simple superficial venous surgery) was 80% at 1 year. The overall healing rate is demonstrated in the form of a Kaplan-Meier plot (Figure 7.1). Log Rank analysis showed no significant difference between the two groups, $\chi^2 = 0.23$, df = 1, $P = 0.60$. 

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Treatment</th>
<th>Mann Whitney</th>
</tr>
</thead>
<tbody>
<tr>
<td>FLB</td>
<td>Surgery</td>
<td>U Test</td>
</tr>
<tr>
<td>No. of Patients</td>
<td>34</td>
<td>70</td>
</tr>
<tr>
<td>No. of Limbs</td>
<td>45</td>
<td>71</td>
</tr>
<tr>
<td>Proportion Male (%)</td>
<td>47</td>
<td>26</td>
</tr>
<tr>
<td>Age (years) median (range)</td>
<td>75 (27-91)</td>
<td>72 (46-94)</td>
</tr>
<tr>
<td>Ulcer Area at Presentation (cm²) median (range)</td>
<td>12.5 (2-181.6)</td>
<td>9.7 (2-500)</td>
</tr>
<tr>
<td>Ulcer Duration at Presentation (months) median (range)</td>
<td>24 (1-720)</td>
<td>23 (2-960)</td>
</tr>
<tr>
<td>Duplex Evidence of Previous DVT at presentation</td>
<td>13/45 (29%)</td>
<td>6/71 (8%)</td>
</tr>
</tbody>
</table>
Factors Influencing Healing Rates

In a similar manner to Chapter 4 data from the two arms of this audit were combined because there was no significant difference in overall healing rates as demonstrated in Figure 7.1 to examine for the presence of influential factors on healing. The factors examined were initial area of 10 cm² or less and initial area >10 cm²; initial duration of 6 months or less and >6 months and the presence or absence of duplex evidence of previous DVT. This data is demonstrated in Table 7.2.
Stratifying the healing rate by ulcer size (10 cm² and less, >10 cm²) demonstrates that smaller ulcers (10 cm² and less) heal quicker than larger ulcers (>10 cm²). This difference in healing rate is significant by Log Rank testing, $\chi^2 = 23.32$, df = 1, P =0.00 (Figure 7.2).
7.2d Discussion

Ulcer healing rates using compression bandaging alone for ulcerated limbs with venous reflux in any system (deep or superficial) has been demonstrated at 55% - 69% depending on the type of compression bandage used (SSB or FLB) (Chapter 4). At The Leicester Royal Infirmary healing rates using four layer bandages were 55% at one year. By applying selected modes of treatment to venous leg ulcers based on the underlying pattern of venous reflux it was hoped to optimise the management of venous ulceration within the setting of a Single Visit Venous Ulcer Clinic. This approach is recommended.
(Ruckley, 1998) and confers a number of benefits to patients with leg ulceration. Firstly, the ABPI can be accurately assessed by experts thus identifying those patients with significant arterial disease for whom compression therapy is contra-indicated; secondly, on the basis of colour duplex scanning definitive treatment can be offered by this superficial venous surgery or compression bandaging and finally a specialist vascular surgical opinion can be obtained at the outset to advise on optimal management.

This audit has demonstrated improved healing rates of 70% (FLB) and 80% (selective surgery) for limbs with deep venous reflux and isolated superficial venous reflux respectively. This is a noteworthy advance in the management of venous ulceration and reflects the benefit of accurately identifying the underlying pattern of venous reflux and selecting the most appropriate treatment on an individual patient basis. It is tempting to advocate the routine use of colour duplex scanning in all ulcerated limbs along the lines described in this thesis, however, this can only be done when clear evidence exists demonstrating benefits in terms of costs to the health service, quality of life to the patient and in association with this a clear and sustained reduction in ulcer recurrence rates. This can only be demonstrated by a prospective, randomised trial examining the influence of colour duplex scanning on these aspects of leg ulceration.

Ulcer recurrence remains a significant problem and any advance in ulcer management must address reducing this as well as increasing the healing rate. Follow up in this study is too short (2.5 years) to given meaningful data about recurrence rates.

It is encouraging that such healing rates can be achieved but it appears that there remains a proportion of limbs (approximately 20%) that did not heal despite 2 years of treatment in this instance. This figure may be indeed prove to be higher when ulcer management in the community is considered (Callam et al., 1987a). It is difficult to explain why 70% of ulcerated limbs healed with compression bandaging in this study.
compared with the 55% healing rate obtained by the FLB limb of the randomised trial reported in Chapter 4. Initial patient age, ulcer area and duration are comparable and the nursing staff applying the bandages were constant in both these studies. Comparing those limbs treated surgically with those treated by compression bandaging is an artificial comparison as the two groups are not composed of similar subjects, but since both healing rates are so similar this exercise suggests that ulcer healing can be hindered in approximately 20% of cases irrespective of the pattern of venous reflux and of treatment offered. This finding may be explained using the concept of 'calf muscle pump failure'. Thus, although surgery has corrected the venous reflux venous hypertension persists because of pump failure preventing ulcer healing. The same argument can be applied to those limbs treated by compression bandaging for the same reason.

As may have been predicted, the proportion of limbs displaying evidence of previous DVT was significantly higher in those limbs receiving compression bandaging as this mode of treatment was selected on the basis of deep venous reflux. Unlike Chapter 4, healing rates were influenced by ulcer area, with 89% of limbs with a small ulcer (10 cm² or less) ultimately healing. It is possible that a longer follow-up period would find that more of the large ulcers ultimately healed. It is interesting that the presence of a previous DVT did not adversely effect ultimate ulcer healing as one may have anticipated.
7.2e Summary

Improved healing rates of 70% to 80% at 1 year can be achieved using appropriate simple surgical techniques where indicated and standard compression bandages where surgery is not indicated. Colour duplex scanning is pivotal in selecting patients who may be suitable for surgery.

7.3 CONCLUSION

This chapter has illustrated one possible advantage of a Single Visit Clinic in terms of improved healing rates of venous ulcers by applying simple surgical techniques where appropriate. The indications for surgery are based on the findings of colour duplex scanning but before this method of venous investigation can be recommended as standard practice it must be proven to be of benefit within the confines of a prospective, randomised clinical trial.
CHAPTER EIGHT

THE DEVELOPMENT OF AN ENDOVENOUS BIO-PROSTHETIC DEVICE
FOR THE CORRECTION OF DEEP VENOUS REFLUX

8.1 GENERAL INTRODUCTION

8.2 LABORATORY STUDIES OF A BALLOON EXPANDABLE STENT/VENOUS VALVE COMBINATION FOR USE IN AUTOGENOUS ENDOVENOUS VALVE TRANSPLANTATION
   a. Introduction
   b. Materials and Methods
   c. Results
   d. Discussion
   e. Summary

8.3 APPLICATION OF AN ENDOVENOUS DEVICE IN A PATIENT WITH DEEP VENOUS REFLUX
   a. Introduction
   b. Patient and Method
   c. Result
   d. Discussion

8.4 CONCLUSIONS
8.1 GENERAL INTRODUCTION

Chapters Five and Six of this thesis demonstrate that the presence of full length deep venous reflux (primary or secondary) precludes any benefit from superficial venous surgery in the treatment of venous ulceration. It is, thus, necessary to address the issue of correction of deep venous incompetence as a therapeutic manoeuvre.

Various open procedures have been described for the treatment of deep venous reflux. Primary valve failure (where incompetent valve leaflets can be identified) can be corrected by Plication Valvuloplasty (Kistner, 1975; Kistner, 1980; Raju, 1983; Jones et al., 1982) or External Band Valvuloplasty (Hallberg, 1972; Guarnera et al., 1994). Post-thrombotic valve failure where no repairable venous valves are present requires the introduction of a competent valve by way of Venous Transposition (Kistner et al., 1979; Ferris et al., 1982); Autogenous Valve Transplantation (Taheri et al., 1982b) or prosthetic valve surgery (Taheri et al., 1995).

All these procedures are hampered by variable clinical outcomes (Johnson et al., 1981; Wilson et al., 1994) and require extensive dissection often through scarred and fibrotic tissues. Experimental valve transplants/implants have been performed in animal models which have in general failed because of thrombosis and delayed valve dilatation (Hill et al., 1985; Kaya et al., 1988; Warmenhoven et al., 1985; Phifer et al., 1989; Raju et al., 1988).

The advent of endovascular technology for the treatment of both venous and arterial stenoses and aneurysm has permitted the manipulation of devices within the vascular tree distant from the site of vascular access. Open surgery and thus dissection at the site of valve failure where the post-thrombotic perivascular tissues are scarred and fibrotic could be minimised if such technology were applied to venous reflux disease.
To date three groups have reported their experience with endovascular venous valve transplantation in the literature, initially in goats (Hughes et al., 1996; Ofenloch et al., 1997), dogs (Dalsing et al., 1997; Burkhart et al., 1997) and also in post-thrombotic human limbs (Richer de Forges et al., 1996). At the time that this study began no human studies had been reported in the literature. These reports outline the feasibility of the technique using both balloon and self expanding metallic stent devices and have suggested that the intra-luminal location of the valve/stent device may prevent the late valve dilatation and incompetence reported in open valve transplantation. In addition, this approach avoids extensive dissection and theoretically may thus reduce the risks of thrombosis of the transplanted segment of vein.

Endovascular stents have an established role in the management venous obstruction from thrombosis (Lindsay et al., 1994; Roy et al., 1994), or compression (Sawada et al., 1992). Encouraged by early reports (Hughes et al., 1996; Richer de Forges et al., 1996; Dalsing et al., 1997) the bio-prosthetic valve/stent device described below was envisaged for the correction of deep venous reflux.

The underlying principle is the endovascular placement and anchorage of a competent venous valve in the proximal popliteal/distal superficial femoral vein to reconstitute a functional ‘gatekeeper’ mechanism. A system of two balloon expandable stents was envisaged, one stent sutured to each end of a length of harvested axillary vein containing a competent valve (Figure 8.1).

Axillary vein would be the preferred source of transplantable tissue as harvest of this vein is already an established procedure for use during open surgery and has not been found to result in significant clinical effect on upper limb venous return (Raju, 1992). In addition the diameter of axillary vein approximates to that of the popliteal vein into which it would be transplanted. This is important to prevent the introduction of
stenosis (and possible obstructive effects) into an otherwise patent but refluxing lower limb venous system. The intention to use balloon expandable stents was felt appropriate because they are available in suitable dimensions and previous experience using such stents within the Departments of Surgery and Radiology at The Leicester Royal Infirmary would ensure accurate and reliable deployment.

Construction of the bio-prosthetic device was planned as follows; having obtained a suitable length of axillary vein containing a competent valve a partly expanded stent (matched for diameter) would be passed over the vein such that the vein lay inside the 'lumen' of the stent and protruded from each end of the stent by 4 to 5 millimetres. Two stents would be mounted in this manner with the valve leaflets located between the stents. The protrusion of vein beyond the end of the stent was felt to be important so that this length of vein could be everted to cover the ends of the metal stent and when sutured in position enclosing the end of the stent completely. This would ensure that when deployed no part of the metallic stent would be in contact with blood and thus perhaps reduce its thrombogenic potential (Figure 8.2).

Figure 8.1. Diagrammatic illustration of the principle of the proposed valve/stent endovenous device. A balloon expandable stent is sutured over the each end of the segment of vein to be transplanted and the entire construction is deployed within the segment of refluxing popliteal vein undergoing reconstruction. The intended orientation here is, foot to the left, head to the right.
Construction of the device would be aided by performing all the described steps with the vein and stents mounted on the shaft of the angioplasty balloon catheter (distant from the balloon itself so as not to puncture it during suture and manipulation of the device). Obviously the balloon would need to be passed across the venous valve in a ‘retrograde’ manner i.e. against the conventional direction of blood flow so that once deployed via a superficial femoral venotomy the balloon and guide wire could be withdrawn from the limb leaving the valve correctly oriented. Construction of the device on a bench would allow the passage of a guide wire in the conventional direction across the valve to aid the retrograde passage of the balloon.

Once constructed the intention was to located the vein/ stent device in the above knee segment of the popliteal vein. This would be achieved by formally exposing the superficial femoral vein in the femoral triangle and via a venotomy pass a guide wire down the femoral vein into the below knee popliteal vein and to follow this with the device mounted over the balloon catheter and retained by crimping the distal stent onto the balloon between its shoulders. Radiological screening would be used to monitor progress throughout.
Once in position the intention was to deploy the distal stent under screening and when fully expanded withdraw the balloon to relocate within the proximal stent such that a small degree of tension was applied to the valve segment to ensure deployment of the proximal stent without crumpling or folding the valve mechanism. With both stents deployed the balloon and guide wire could be withdrawn.

The following sections describe the early development and laboratory testing of such an autogenous endovenous valve/stent device for use in correction of deep venous incompetence. Finally the first deployment of such a device in a patient is described.

8.2 LABORATORY STUDIES OF A BALLOON EXPANDABLE STENT/ VENOUS VALVE COMBINATION FOR USE IN ENDOVENOUS AUTOGENOUS VALVE TRANSPLANTATION

8.2a Introduction

Section 8.1 described the intended endovenous device. However, before performing clinical studies the device requires evaluation to ensure that the transplanted valve is competent and patent once deployed. In addition, the method of deployment requires study to determine whether the entire device with both stents could be deployed by one long angioplasty balloon acting on the complete device or two shorter balloons deploying proximal and distal stents separately.

This section describes a cadaveric model of the bio-prosthetic endovenous device examining the ability of a harvested venous valve to withstand the necessary manipulations and maintain a physiological pressure gradient once deployed. In addition, the method of deploying the two stents is examined.
8.2b Materials and Methods

Vein Harvesting

With the co-operation of the Leicester Royal Infirmary Department of Pathology, human cadaveric saphenous and femoral vein segments were obtained at the time of post-mortem examination. The LSV was harvested from the ankle to SFJ with ligation of all tributaries. Valved segments of the LSV of suitable calibre would be used as the model valve for transplantation. The SFV was also harvested with ligation of its tributaries for use as the model segment of vein to receive the LSV valved segment. If the proximal LSV was of adequate calibre than this was also used as the recipient length of vein. Once removed from the cadaver the lengths of vein were rinsed with saline to expel any blood from within the lumen and transported to the laboratory in 0.9% saline.

Hydrostatic Pressure Testing the Vein

A custom built jig was devised (Figure 8.3) to allow the lengths of vein to be mounted securely during the hydrostatic pressure tests. Each end of the vein/stent combination was mounted over the end of a three way tap which was connected to a pressure transducer and bag of 0.9% saline as shown. The purpose of the saline columns were two fold: firstly) to produce a nominal basal pressure within the system of 20 mmHg representing a background filling pressure to maintain the open state of the valve and secondly) to produce a physiological head of pressure across the valve of 100 mmHg which approximates to the resting venous pressure obtained in the human when standing at rest. A sphygmomanometer cuff was used to create the 120 mmHg pressure at the cephalad side of the valve and the 20 mmHg at the distal side was created by raising the bag of saline above the vertical height of the vein under test.

Two questions were to be answered by the laboratory experiments:
Experiment 8.2a) could the vein/ stent combination device remain competent and able to support a pressure gradient of at least 100 mmHg, and what maximum pressure would such a manipulated valve sustain? In doing so this would confirm the ability of the valved venous segment to tolerate the manipulation and handling required in construction of the valve/ stent device.

Experiment 8.2b) would a competent venous valve tolerate dilatation to 10 mm by an angioplasty balloon and remain competent? This question is relevant to the technique used to deploy the final vein/ stent device.

These two questions were addressed using individual lengths of vein containing competent valves. Experiment 8.2a involved constructing a vein/ stent device as previously described and mounting it on the jig as shown in Figure 8.3. The pressure gradient was created across the valve, and maintenance of such a gradient as determined by the pressure transducers (one on each side of the valve leaflets) was used as an indicator of a competent valve. If on applying the pressure gradient the valve could not sustain a gradient of 100 mmHg, the valve was deemed to have failed and been rendered incompetent by the handling involved in its construction. On completion of this test the pressure gradient was increased in the system until the valve failed giving an indication of the maximum sustainable pressure.

Experiment 8.2b was performed by creating a pressure gradient across the valve to confirm its competency, then after disconnecting the ‘distal’ end of the vein from its three way tap, passing an angioplasty balloon across the valve in the direction of normal blood flow so as to minimise the risk of traumatising the valve mechanism and then inflating the balloon to 10 mm diameter using saline. This dilatation was maintained for thirty seconds and then the balloon was fully deflated and removed from the vein. The
vein was then re-attached to the three way tap and the pressure gradient re-applied.

Similarly, if the gradient was maintained the valve was deemed to be competent.

![Diagram of the jig used in the bench testing of the vein/ stent devices. Once the valve stent device has been deployed in a length of recipient vein, each end of the recipient vein is tied to a three-way tap thence a pressure transducer and source of hydrostatic pressure as shown. For clarity the valve/ stent device is depicted here as a single valve leaflet oriented to allow flow from distal (foot) to proximal (head). Varying lengths of vein can be accommodated. The valve leaflets appear in the centre of the vein.](image)

**Figure 8.3.** Diagram of the jig used in the bench testing of the vein/stent devices. Once the valve stent device has been deployed in a length of recipient vein, each end of the recipient vein is tied to a three-way tap thence a pressure transducer and source of hydrostatic pressure as shown. For clarity the valve/ stent device is depicted here as a single valve leaflet oriented to allow flow from distal (foot) to proximal (head). Varying lengths of vein can be accommodated. The valve leaflets appear in the centre of the vein.

**Creating the Pressure Gradient used in Experiment 8.2a**

The pressure gradient across the valve was created thus. Initially both three way taps are closed to the vein but open to both the pressure transducers and hydrostatic column. The hydrostatic pressure on the ‘distal’ side of the valve is increased to 20 mmHg (this will open the valve and so long as an outlet is available on the ‘proximal’ side of the valve flow will follow in the anatomical direction distal to proximal). Having established this basal pressure, the proximal pressure is increased by inflating the sphygmomanometer cuff to 120 mmHg (producing a 100 mmHg cross valve gradient). Once both pressure gradients are established the three way taps are opened to all three
ports (hydrostatic column, vein and pressure transducer) commencing with the distal tap. On completing this part of the experiment, the maximum sustainable pressure was determined.

Experiment 8.2b utilised an identical pressure gradient but the measurements were interrupted as previously described to allow dilatation of the valve with an angioplasty balloon. A 10 mm balloon was used as this is a typical diameter of a popliteal vein in situ in the leg.

8.2c Results

Ten cadaveric limbs underwent LSV and SFV harvest and eight limbs provided suitable lengths of saphenous vein containing a competent valve segment.

Experiment 8.2a

Seven 39 mm Balloon - Expandable Peripheral Palmaz Stents (Cordis, Johnson & Johnson, Berkshire, UK.) were made available by Cordis, allowing the manufacture of seven vein/ stent devices by cutting the stents into two halves. This dimension stent was expandable to a range of diameters 4 to 9 mm when used with an appropriate balloon. Seven devices were thus constructed as described without difficulty. All seven devices were mounted on the jig (Figure 8.3) and all seven valves were found to be competent and capable of sustaining a 100 mmHg pressure gradient (Figure 8.4). The median (range) maximum sustainable pressure was 200 (172->300) mmHg (Figure 8.5). Two valves remained competent upto the maximum available pressure as determined by the sphygomanometer (300 mmHg). Only one valve failed abruptly at 212 mmHg, the remaining four demonstrated a gradual leakage resulting in a non-sudden equalisation of the pressure across the valve at pressures of 172, 183, 190 and 200 mmHg (Figure
8.6). All devices remained competent after inflation of the 10 mm angioplasty balloon across the valve ring.

Figure 8.4. A pressure recording obtained during experiment 8.2a demonstrating a competent vein/stent device. Proximal = pressure recording taken proximal to the valve, Distal = pressure recording taken distal to the valve. The range in pressures are 0 mmHg to a maximum of 120 mmHg. D = opening of the distal tap, P = opening of the proximal tap. Note on opening the distal tap pressure equalises across the valve and on opening the proximal tap a small 'flick' of pressure is seen in the distal trace corresponding to the closure of the valve. The proximal pressure trace demonstrates the maintenance of 100 mmHg gradient across the valve. Time scale, each large square = 1 second.
Figure 8.5. Histogram demonstrating the burst pressure for the seven devices constructed. Note two devices exceed a burst pressure of 300 mmHg and all devices exceed the important pressure of 100 mmHg encountered in the ambulant lower limb.

Figure 8.6. A pressure recording demonstrating leakage failure of a valve at 172 mmHg. Demonstrated is the gradual drop in proximal pressure with a concomitant small rise in distal pressure the test was terminated before full equalisation of pressure was recorded. Note the upper trace is the distal recording unlike Figure 8.4. P = opening of the proximal tap, the distal tap being already open. Time scale, each large square = 1 second.
The functional importance of a competent 'gatekeeper' mechanism is widely acknowledged. These two studies have investigated the feasibility of constructing and the relevant mechanical properties of a bio-prosthetic device for endovascular use by way of laboratory studies to allow progression to studies in a human subject. Human cadaveric vein was used because it shares the dimensions of in vivo vein that is required for the second phase of the study. Some post mortem changes will have taken place and thus some of the physical properties of the vein will have been lost.

The main aim was to establish a method of constructing the device. This has been achieved. In addition the vein/ stent device can maintain the required pressure gradient encountered in an ambulant human limb. When the venous valves did fail this occurred at supra-physiological pressures and as such need not be a concern in the anticipated clinical role of this device. The nature of subsequent valve failure was one of a gradual leakage rather than sudden rupture of the valve mechanism. This may not be representative to the behaviour of normal valves as those used here were cadaveric and had sustained extensive manipulation during the study.

The ability of venous valves to withstand dilatation by an angioplasty balloon suggests that the valve rings possess a significant degree of compliance without valve failure. This finding is interesting considering that venous reflux can occur with apparently minor valve dilation in the in situ state in limbs with venous disease. This aspect of the study was performed to investigate ways of deploying the final valve/ stent device i.e. could a single long (10 cm) balloon be used to deploy both stents simultaneously or would the proximal and distal stents need to be deployed separately. On the basis of these results it would seem possible to deploy both stents simultaneously.
8.2e Summary

Section 8.2 has demonstrated the physical properties and feasibility of constructing a bio-prosthetic device for use in endovascular deep venous reconstructive surgery. The bio-prosthetic device can be easily constructed and manipulated without functional impairment to the valve leaflets \textit{in vitro} and is capable of maintaining valve function under the range of pressure gradient encountered in the ambulant human lower limb. The next stage in the development of the device is its deployment in a human subject.

8.3 APPLICATION OF AN ENDOVENOUS DEVICE IN A PATIENT WITH VENOUS ULCERATION AND BELOW KNEE DEEP VENOUS REFLUX.

8.3a Introduction

Section 8.2 of this thesis described the laboratory development of an endovenous bio-prosthetic device for the treatment of deep venous reflux in the lower limb. This section describes the first deployment of such a device in a patient. At the time this study was begun, no accounts of endovenous valve transplantation had been reported. It was felt that the first patient to receive an endovenous valve transplant would undergo such a procedure as a final therapeutic option to try to gain ulcer healing. The degree of ulceration in the patient chosen was of such a degree that the only alternative was amputation.
8.3b Patient and Method

Patient

A 57 year old female with intermittent venous ulceration of her right leg for 10 years and a continuous ulcer for 2 years at presentation was selected. Twenty-six years previously she had undergone right sided high ligation, stripping of the LSV to the calf and avulsion of calf varicosities for varicose veins. Three years later she sustained a right leg DVT treated with warfarin for six weeks. She was a non-smoker and was not diabetic. The ABPI in the ulcerated leg was 1.0 and initial venous investigation by colour duplex scanning and functional venography demonstrated deep venous reflux without obstruction involving the common femoral vein down to the calf veins at the ankle. In addition there was recurrent long saphenous reflux from a SFJ to the calf with reflux in six calf perforating veins. These abnormalities were treated by recurrent SFJ disconnection and calf perforating vein surgery via a ‘mini’ Cocketts’ incision and at the time of diagnostic venography three perforating veins were successfully embolised with metal coils rendering them obstructed and thus none refluxing. Thereafter, despite a period of hospital inpatient bed rest the ulcer deteriorated from an initial area of 105 cm² to 256 cm² (Figure 8.7). Further investigations demonstrated the following blood results: Hb 11.6 g/dL, glucose 4.9 mM, albumin 40 g/L, urea 4.8 and creatinine 92 thus excluding any major systemic abnormality. A full thrombophilia screen including examination of Anti-thrombin III, Protein S and Protein C was normal.
Pre-operative Imaging and Assessment

Prior to endovenous stenting, further duplex and venographic studies clarified the venous anatomy demonstrating numerous axillary and subclavian vein valves within suitable lengths of vein (Figure 8.8). The right axillary vein proximal and distal to a suitable valve had a diameter of 8.0 mm and 7.5 mm respectively. Dimensions of the right popliteal vein were examined with the limb dependent at rest and on performing a Valsalva manoeuvre to assess any degree of dilatation with raised venous pressure (Table 8.1). Lower limb venography demonstrated no further superficial venous reflux, deep venous reflux along the full length of the CFV into the distal crural veins and no obvious venous valves precluding any attempt at valve repair (Figure 8.9). Duplex examination of the left leg demonstrated no suitable venous valves to use for the transplant.
<table>
<thead>
<tr>
<th>Segment of Popliteal Vein Examined</th>
<th>Diameter Dependent at Rest (mm)</th>
<th>Diameter Dependent with Valsalva (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Above Knee</td>
<td>10.4</td>
<td>11.3</td>
</tr>
<tr>
<td>Level of Knee Joint Line</td>
<td>6.2</td>
<td>6.2</td>
</tr>
<tr>
<td>Below Knee</td>
<td>8.2</td>
<td>8.6</td>
</tr>
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</table>

Table 1. The diameter (mm) of the right popliteal vein in the dependent limb at rest and performing a Valsalva manoeuvre as assessed by Colour Duplex scanning.

The above findings dictated the use of 9 mm balloon expandable stents to be deployed using 5 mm balloons to stabilise each stent in position separately followed by full deployment with 10 mm balloons.

Figure 8.8. Upper limb venogram demonstrating a bifid proximal brachial and single axillary vein with valve sinuses full of contrast medium.
8.3c The Operative Procedure and Result

Full informed consent and local ethical committee approval were obtained. Under general anaesthesia the patient was positioned supine with the right arm abducted to 90 degrees at the shoulder on a supporting arm board. Skin preparation and drapes left the right leg (ulcerated distal part enclosed in drapes) and right arm and shoulder exposed. A longitudinal incision was made in the right axilla exposing the axillary and proximal brachial veins (Figure 8.10). The external diameter of the exposed axillary vein was measured at 10 mm. A suitable valve was identified using the ‘strip test’ to demonstrate unidirectional flow and this valve was excised with 3 cm of axillary vein on each side of the valve ring (Figure 8.11). The divided ends were ligated and the wound closed over a single vacuum ‘Redivac’ drain. Synchronous exposure and control of the
common femoral vein below the entry of the profunda vein and construction of the vein stent device followed. The endovenous device was constructed as described in the preceding sections of this chapter on the shaft of a 5 mm diameter balloon (Figures 8.12, 8.13). After the intravenous administration of 5000 units of Heparin a transverse venotomy was created in the common femoral vein and under X-Ray screening a guide wire passed through the popliteal vein to the below knee venous confluence. The endovenous device, pre-mounted and crimped by the ‘distal’ stent onto the balloon catheter was passed over the guide wire and ‘screened’ to a suitable site (Figure 8.14). This ensured the device would not be deformed on knee flexion. Initial stabilisation of the distal stent was obtained using the 5 mm balloon on which the device had been constructed. This was then withdrawn under screening a short distance and relocated under the proximal stent which was similarly stabilised. This part of the procedure was performed with some degree of tension in the device to prevent any folding or rotation of the device during deployment as this would probably render the valve mechanism ineffective. This balloon was replaced by a 10 mm diameter balloon and the stents fully deployed (Figure 8.15). A completion venogram performed before removal of the catheter and guide wire demonstrated the patency and competence of the device. The venotomy and wound were closed over a ‘Redivac’ drain. A colour duplex scan on completion of the procedure with the legs dependent demonstrated a patent and fully competent venous valve. The patient was fully anticoagulated with intravenous heparin initially at 1000 units per hour and subsequently warfarinised to an International Normalised Ratio (INR) of 2 to 3. At seven days postoperatively a colour duplex scan confirmed the patency and competence of the device. Duplex scanning on day 13 after surgery found the device had occluded and from then on a conservative course of
compression therapy was followed with an initial good response for four months. Thereafter the ulcer enlarged and a below knee amputation had to be performed.

Figure 8.10. Operative Photograph illustrating the bifid brachial vein draining into the axillary vein.

Figure 8.11. Operative photograph of the segment of axillary vein used for the transplant. Unequal marking sutures identify proximal/distal orientation of the valve. Tributaries are ligated with silk.
Figure 8.12. Operative photograph demonstrating the passage of the guide wire across the valve.

Figure 8.13. Operative photograph demonstrating the method of suturing the vein segment onto the two stents. Note the partially inflated angioplasty balloon and the eversion of the vein ends over the stents struts excluding these from the circulation once deployed.
Figure 8.14. Operative photograph showing the guide wire passing into the superficial femoral vein via a venotomy. Slings isolate the tributaries of the SFV.

Figure 8.15. Screening X-Ray demonstrating the final position of the device in the popliteal vein. The shoulders of the angioplasty balloon are identified by the radiopaque markers either side of the distal stent.
8.3d Discussion

This first experience with such a bio-prosthetic device and endovenous approach to deployment of such a device has demonstrated the feasibility of this technique. The procedure successfully deployed a competent autogenous venous valve into the popliteal vein abolishing deep venous reflux. The patency of the device was only two weeks but during this time the patient described significant subjective symptomatic relief with less pain.

This early experience with endovenous stent devices is encouraging, however, the reasons for device occlusion remain unclear. The patient was systemically anticoagulated and duplex examination demonstrated marked ‘hyperaemic flow’ in the deep veins most probably because of the large inflamed ulcer, with these factors in mind mechanical occlusion followed by thrombosis or native venous endothelial damage are the most likely events to have precipitated thrombotic occlusion. Others (Ofenloch et al., 1997) have reported valve patency in goats at 6 weeks after transplantation.

This patient was chosen to be the first subject because of the degree of ulceration such that an amputation may have been the only form of symptom control available to us. It is possible that had a patient with a non-thrombotic history (despite a negative thrombophilia screen) been used then the end result may have been an intact and healed leg. It is possible that the choice of a patient with ‘end stage venous disease’ introduced a degree of bias away from ultimate success and healing as it is possible that such a damaged limb would not have healed with any form of treatment.
This chapter has identified the need for deep venous surgery and suggested a novel technique of performing such surgery. A cadaveric model has been devised to establish a new endovenous procedure which has been characterised in the areas relevant to the deployment of the final device in a human subject. The model has been applied in its intended role by abolishing deep venous reflux in a human subject. This work acts to encourage further such procedures in the future within the confines of a research programme. The technique is not yet recommended for routine use in clinical practice.
CHAPTER NINE

SUMMARY, CONCLUSIONS AND PROSPECTS FOR FUTURE RESEARCH

The experimental work described in this thesis commenced with an examination of the patterns of vascular abnormalities encountered in those patients referred for specialist management of 'venous ulceration'. This consecutive series of 88 patients (104 legs) demonstrated that 14% of ulcerated limbs had arterial insufficiency (ABPI <0.8) including 2% with purely arterial disease. Using colour duplex scanning, I confirmed the work of others (Darke & Penfold, 1992; Shami et al., 1993; Myers et al., 1996; Grabs et al., 1996) demonstrating that ulceration results from superficial venous reflux alone in over 50% of cases. This finding suggests that venous reflux could be abolished by simple saphenous vein disconnection in limbs with normal deep veins which may result in ulcer healing. In addition, deep venous reflux and perforating vein reflux was found to occur less commonly than previously thought (42% and 11% of limbs with venous reflux respectively).

The effects of saphenous vein disconnection on ulcer healing and venous pressures were examined in 25 ulcerated limbs (Chapter 5), and I concluded from this that saphenous vein disconnection in legs with normal deep veins resulted in ulcer healing without the application of postoperative compression therapy, whereas this was of no benefit in legs with full length deep venous reflux and in this group of patients superficial venous surgery should not be recommended. Following this finding, the role of pneumatic tourniquets in identifying limbs that may benefit from saphenous vein surgery has been explored. The use of such cuffs to identify limbs with superficial venous reflux in isolation (that would benefit from saphenous vein surgery) from those...
with associated deep venous reflux (that do not benefit from saphenous vein surgery) continues to be recommended (Scurr, 1996). However, McMullin et al., in 1991 cast doubt on the validity of this technique and using colour duplex scanning I have demonstrated that the use of a pneumatic cuff to occlude the saphenous vein was successful in only 7/29 limbs tested implying that this method cannot reliably separate the superficial from the deep venous systems. This finding aside, comparing the predicted improvement in PPGRT90 obtained by cuff or manual probe compression with surgery suggested that neither manual compression nor cuff compression conferred any benefit to the clinical management of these patients. I would recommend that the use of cuffs/tourniquets in the planning of venous surgery in ulcerated limbs be abandoned.

Perforating vein reflux has been implicated in the aetiology of venous ulceration and the recent use of SEPS advocated as a therapeutic manoeuvre for venous ulceration. Darke and Penfold (1992) have demonstrated that venous ulcers heal in legs with normal deep veins after saphenous ligation and leaving refluxing perforating veins alone. The role of perforating vein surgery in legs with full length deep venous reflux is not clear. In a small number of limbs possessing such a pattern of venous reflux, a global cutaneous venous abnormality has been demonstrated pre-operatively which remained unchanged following perforating vein ligation suggesting that perforating vein disconnection in limbs with full length deep venous reflux offers no haemodynamic benefit hence questioning the clinical value of this procedure.

Limbs with extensive deep venous reflux do not appear to benefit from superficial venous surgery as such; either deep venous reconstruction or compression bandaging is required. The relative efficacies of four layer (Charing Cross) and short stretch bandages were examined and found to be comparable although the four layer
system was associated with fewer complications in very oedematous or very thin limbs. At the time this work was performed four layer systems were not available via an FP10 prescription representing a major obstacle to their use. With this in mind, Chapter 4 outlines the development of a four layer system using components that are fully available via an FP10 prescription and a combination of bandages providing comparable physical properties is suggested.

The final experimental chapter of this thesis illustrates the development and clinical use of an endovenous device for the correction of popliteal vein reflux. The laboratory work in Chapter 8 demonstrated that construction of the proposed device was feasible and once constructed and deployed possessed the physical properties necessary to support a hydrostatic pressure of 100 mmHg. This pressure is significant because it is the upper limit of likely pressures encountered in the popliteal vein; in fact all devices tested supported a higher pressure than this. Although the clinical efficacy of this device was of limited success, popliteal vein reflux was abolished on deploying the device. This is encouraging and requires further evaluation by way of ongoing clinical studies.

Finally, the clinical value of selecting ulcer treatment based on the underlying pattern of venous abnormality is clearly demonstrated by Chapter 7. Basing the method of treatment on the principles suggested by Chapters 3, 4, 5 and 6 healing rates of venous ulcers at one year of 70% with surgery and 80% with compression bandaging were achieved. This is a significant improvement on the healing rates previously obtained at our hospital (55% using compression bandaging).
PROSPECTS FOR FUTURE RESEARCH

A range of issues relating to the surgical and conservative treatment of venous ulceration have been explored in this thesis and a number of points need further clarification and a number of newly raised questions need answers.

The sub-bandage pressure characteristics of an FP10 prescribable bandage are described but the important factor is the safety and efficacy of this bandage once in clinical practice. A study comparing this FP10 bandage with the four layer (Charing Cross) bandage is currently underway at The Leicester Royal Infirmary as a prospective randomised trial.

Subfascial Endoscopic Perforating Vein Surgery is under close examination as an isolated procedure or often in combination with synchronous saphenous vein surgery. The small study in this thesis suggests there is little value in this procedure in limbs with full length deep reflux. However, the true worth of this new technique can only be evaluated by way of a rigorous, scientifically constructed prospective randomised clinical trial.

I have demonstrated the clear benefit of saphenous vein surgery and optimal compression therapy in correctly selected cases on ulcer healing. This is only one aspect of ulcer management. Ulcer recurrence rates are equally important in terms of patient satisfaction, treatment efficacy and local and national economic health care planning. Recurrence rates have not been addressed in this thesis at all. Extensive work is required in the follow up of patients treated by the techniques I have described; this will need prospective studies spanning a minimum of 5 years. The data-base initiated by this thesis is ongoing and data relating to ulcer recurrence will be available in the future.

Finally, I have merely scratched the surface in the field of endovenous surgery.
This is an exciting area with potential to correct popliteal vein reflux thus rendering an ulcerated limb free of venous reflux. This needs full evaluation in human subjects to assess the clinical efficacy regards healing and recurrence rates. The reasons for valve thrombosis need examining. There are two aspects to this, one is haemodynamic, the other concerns the cell biology of the transplanted valve segment. Both need full evaluation.
CHAPTER TEN

PEER REVIEWED PUBLICATIONS BASED ON THE WORK PRESENTED IN
THIS THESIS


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