

## Graduated compression and its relation to venous refilling time

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### Abstract

Graduated compression is important in improving venous function, but the pressure profiles of different brands of stockings in situ and effects on a direct measure of venous function have not been investigated. The pressure profiles of 15 different types of below knee compression stockings were established with a medical stocking tester in 13 healthy volunteers. Analysis of variance was performed for each stocking separately, considering the factors of size of stocking, site of measurement, and their interaction. The criteria used to define satisfactory function were that the stockings should have a significant linear trend with site—that is, graduation—and no other significant effects. Only five types of stockings met these standards. Venous function was then assessed by photoplethysmography in 19 patients with defined venous abnormalities. For each patient the effect on venous refilling time of three satisfactory and three unsatisfactory stockings was assessed. The three satisfactory stockings gave refilling times that were not significantly different from normal in patients with both superficial and deep vein incompetence, while refilling times with the three unsatisfactory stockings remained significantly below normal in all patients with deep vein incompetence; one stocking had no significant effect on refilling times in either group.

Functional testing of compression hosiery should form part of future British Standards specifications.

### Introduction

The use of compression on the legs as a treatment for venous disorders can be traced to the ancient Egyptians. The first true elastic stocking was developed in Nottingham in the early 1840s by

Taberer,<sup>1</sup> and elastic stockings have been used to treat venous disorders since then. Previous work emphasised the need to obtain graduated compression on the leg to improve venous function.<sup>2,5</sup> Most studies looked at the effect of a garment on venous function without measuring the pressure profiles.<sup>6,7</sup> When pressure profiles were obtained a mechanical model was used for measurement.<sup>2,8</sup> The Borgnis medical stocking tester enables clinicians to investigate the compression effect of any stocking in situ.<sup>9</sup> A stocking can truly be said to produce graduated compression only when matched with a patient's leg as the compression depends not only on the stocking's tension but also on the way it matches the leg in size and shape.

To investigate the relation between graduation and venous function we studied a selection of below knee compression stockings available in hospital practice in patients with venous disease and normal subjects.

### Methods

The study was divided into two. In the first part we measured the pressure exerted on normal legs by a range of appropriately fitted stockings with a Borgnis medical stocking tester. Subjects were chosen so that the full range of manufactured sizes could be tested. We analysed the results to give a functional classification (satisfactory or not) for each stocking based on the presence or absence of statistically significant linear graduation and of unwanted and inappropriate effects related to size of stocking and site of measurement. Because of the considerable time spent obtaining the numerous measurements we arbitrarily chose six stockings for the second part of the study; three of these had given what we considered to be satisfactory results and three unsatisfactory. We established the pressure profiles of these stockings on the legs of a series of patients with venous disease. Subsequently, we used photoplethysmography to measure the venous refilling time in each subject both with and without stockings, thus allowing an assessment of the measured profiles of the stockings and their effect on venous function.

### FIRST STUDY

We measured the pressure exerted at three separate sites beneath 15 different types of below knee stockings. Thirteen normal volunteers were chosen so that each of the manufacturers' standard sizes could be tested on legs of the appropriate size. The stockings tested were Sigvaris types 601, 503, 504, and 505; Venosan types 2002 and 2003; Scholl Superlastic, Duoten, and Softgrip stockings; Thrombex; Supreme antiembolism; and

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Tubigrip in both its tubular and shaped form and as a single and double layer.

The pressure exerted under each stocking was recorded with a medical stocking tester developed by Borgnis.<sup>9</sup> This device consists of a thin plastic tube with four paired electrical contacts on its inner surface, which is connected to a small air pump and an electric pressure transducer. The plastic tube is placed between the leg and stocking on the midline of the medial aspect of the calf. Pressure exerted by the hosiery closes the contacts, and an indicator lamp lights up on the measuring device. Air is pumped slowly into the tube, and as soon as the inner pressure at a contact point is higher than the pressure exerted by the hosiery the electrical contact is interrupted. The lamp goes out and the pressure is recorded digitally in mm Hg. The recording sites were 2.5 cm above the malleolus; the gaiter area; and the widest diameter of the calf. Previous (unpublished) studies have shown that these points along the medial aspect of the calf provide the most reliable and reproducible sites for measuring the pressure.

TABLE I—Calf and ankle circumferences (cm) of normal subjects (first study) and patients (second study), with corresponding size of compression stockings

Manufacturers' size	No of subjects	Ankle circumference (cm)			Calf circumference (cm)		
		Mean	SD	Range	Mean	SD	Range
<i>Normal subjects</i>							
Small	5	21.0	0.7	20-22	32.8	1.5	31-35
Medium	4	23.8	1.7	22-26	37.0	0.8	36-38
Large	4	27.8	1.5	26-29	40.3	1.3	39-42
<i>Patients</i>							
Small	6	21.8	0.4	21-22	34.8	1.0	34-36
Medium	8	23.8	1.2	23-26	36.6	1.2	35-39
Large	5	25.6	1.7	24-28	40.8	1.9	38-43

TABLE II—Summary of *p* values from analysis of variance of pressure measurements for 15 brands of stocking in 13 normal subjects

Stocking	Site			Size and site interaction			Conclusion
	Linear trend	Deviation from linearity	Size	Different linear trend	Different deviation from linearity		
Single shaped Tubigrip	<0.001	0.19	0.84	0.29	0.16		Satisfactory
Double shaped Tubigrip	0.001	0.09	0.59	0.56	0.33		"
Venosan 2002	<0.001	0.03	0.22	0.60	0.32		"
Venosan 2003	<0.001	0.03	0.74	0.90	0.49		"
Sigvaris 504	<0.001	0.06	0.26	0.79	0.02		"
Single Tubigrip	0.80	0.02	0.07	0.93	0.18		Unsatisfactory
Double Tubigrip	0.46	0.04	0.44	0.82	0.42		"
Sigvaris 601	0.50	0.73	0.34	0.77	0.07		"
Duoten	0.09	0.18	0.10	0.07	0.74		"
Superlastic	0.20	0.06	0.001	0.14	0.22		"
Supreme antiembolism	0.30	0.36	0.01	0.56	0.56		"
Thrombex antiembolism	<0.001	<0.001	0.93	0.52	0.49		"
Sigvaris 503	0.005	0.003	0.01	0.96	0.10		"
Sigvaris 505	<0.001	0.02	0.004	0.36	0.002		"
Softgrip	0.003	0.05	0.008	0.03	0.07		"

Measurements just below the knee were not included because the readings were not reproducible owing to the nearness of the device's bulky connection box to the top of the stocking. We confirmed that the system registered pressure accurately by immersing the probe in a water column; the coefficient of variation of repeated measurements was 1.6%.

The volunteers were studied while sitting with both feet resting on the floor. Their ankle and calf circumferences were measured before appropriate sizes of the 15 types of stocking were fitted (table I); the stockings were tested in random order. For each garment five recordings were made and then averaged. We defined a satisfactory garment as having a significant ( $p < 0.01$ ) linear trend with site (that is, graduation) and no other significant effects (that is, no significant differences between sizes or interactions between size and site of measurement).

## SECOND STUDY

From the results from the first part of the study we selected six types of stocking to measure the effects of a varying degree of compression and graduation on venous refilling time. Nineteen patients were studied: nine

had deep venous insufficiency and 10 superficial vein incompetence confirmed by Doppler ultrasound and photoplethysmography.

Ankle and calf circumferences were measured before testing in each patient; patients were fitted with "off the shelf" stockings (six small, eight medium, and five large; table I). The pressure profile of the six types of stockings was established for each patient with a medical stocking tester.

We measured the venous refilling time both with and without the stockings with photoplethysmography, using a modification of the technique described by Abramowitz *et al* and subsequently by Miles and Nicolaides.<sup>10,11</sup> The patients were studied while sitting with both feet resting on the floor. The transducer was attached to the skin with double sided adhesive tape 2.5 cm above the medial malleolus. The calf was squeezed vigorously five times and the refilling time recorded; this was repeated after applying a tourniquet to the calf and then to the thigh. The tourniquet was a 2.5 cm pneumatic cuff used at a pressure chosen to occlude only the superficial and not the deep veins.<sup>12</sup> We classified patients as having deep vein damage with popliteal incompetence when the refilling time (by photoplethysmography) failed to become normal when either the calf or the thigh tourniquet was applied; superficial vein incompetence was diagnosed when the refilling time was normal when either the thigh or the calf cuff was applied. To measure refilling time with the stocking in situ a 1 cm hole was cut in each stocking to accommodate the photoplethysmography probe, and the edges of the hole were darned to prevent the stocking from laddering. Refilling time was measured for all 19 patients with each of the six types of stockings tested in random order; five readings were taken on each occasion and the mean recorded.

## STATISTICAL METHODS

In the first part of the study we performed analyses of variance on the pressures recorded for each of the 15 types of stockings separately, factors being the size of the stocking (small, medium, or large) and the site of the measurement. The effect of site was divided into two orthogonal

components testing for either the presence of a linear trend (graduation) or deviations from the linear trend (non-linearity). The effect of size was tested against the variation between subjects, and the effect of site and its interaction with size were tested against the within subject variation.

For those stockings tested in the second study we performed similar analyses of variance on the pressure measurements with the additional factor group normal, superficial vein incompetence, or deep vein damage. An analysis of variance was performed for refilling time with the factors group (superficial or deep vein incompetence) and brand of stocking (including measurements made without the stocking and with the calf tourniquet). Group was a between subject comparison while stocking and its interaction with group were within subject comparisons.

## Results

### FIRST STUDY

The coefficient of variation of repeated pressure measurements in situ was 4.2%. Table II summarises the results of the analysis of variance performed on the pressure measurements. Only five garments had satisfactory pressure

profiles, while 10 garments were unsatisfactory. Table III summarises the mean pressure profiles of each garment, grouping together satisfactory and unsatisfactory stockings.

## SECOND STUDY

Three of the six stockings selected for study had satisfactory pressure profiles (Venosan 2002, Venosan 2003, and two layers of shaped Tubigrip) and three had unsatisfactory profiles (Softgrip, Superlastic, and Duoten

range). We found no differences in the pressure profiles of these six types of stockings between the patients and the normal subjects; thus the hole cut in the garments did not alter the pressure profile.

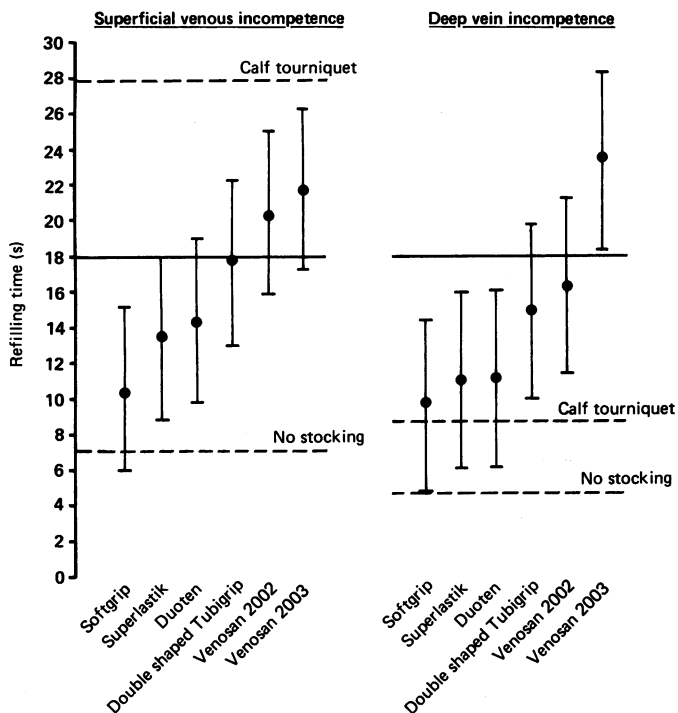
The figure shows the mean photoplethysmographic refilling times for each of the six stockings in patients with superficial and deep vein incompetence. Significant differences ( $p < 0.05$ ) existed whenever the confidence interval did not include the value with which the measurement was being compared (normal, value obtained when calf tourniquet applied, or value obtained without a stocking). Thus the three satisfactory garments all gave refilling times that were either not significantly different from or significantly greater than the lower limit of the normal refilling time of 18 seconds in both

TABLE III—Mean pressure profiles (mm Hg) for each type and size of stocking by site (B, B1, C)\*

Stocking	Small			Medium			Large			Standard error of difference between means†
	B	B1	C	B	B1	C	B	B1	C	
<i>Satisfactory</i>										
Single shaped Tubigrip	11	9	8	10	10	8	10	11	9	1.2
Double shaped Tubigrip	21	18	15	19	20	15	20	22	17	2.7
Venosan 2002	24	21	18	23	22	15	21	19	15	2.0
Venosan 2003	29	26	20	28	29	19	28	25	18	3.1
Sigvaris 504	35	33	30	31	35	26	31	29	27	2.8
<i>Unsatisfactory</i>										
<i>No graduation:</i>										
Single Tubigrip	7	8	7	7	7	7	9	10	9	1.1
Double Tubigrip	14	15	14	14	15	14	16	18	16	2.1
Sigvaris 601	19	17	18	15	17	14	15	15	15	2.5
Duoten	18	18	18	20	21	20	22	21	19	1.5
<i>No graduation and compression varied with size:</i>										
Superlastic	11	11	11	12	13	12	17	17	16	1.2
Supreme antiembolism	12	13	12	11	12	12	16	16	17	1.4
<i>Non-linear graduation:</i>										
Thrombex antiembolism	16	16	12	16	16	12	15	17	12	1.7
<i>Non-linear graduation and compression varied with size:</i>										
Sigvaris 503	22	28	26	23	24	21	23	25	21	1.7
Sigvaris 505	46	35	31	36	40	25	33	31	19	3.2
<i>Compression varied with size:</i>										
Softgrip	11	10	10	15	15	15	18	15	16	1.7

\*B=2.5 cm above malleolus; B1=gaiter area; C=widest diameter of calf.

†Standard error of difference between two site means of different sizes.



Mean refilling times for six types of stocking in patients with superficial and deep vein incompetence. Vertical lines indicate 95% confidence intervals for difference between two means; broken horizontal lines indicate mean values when no stocking was worn and after a calf tourniquet had been applied; solid horizontal line indicates lower limit of normal range (18 s). Significant ( $p < 0.05$ ) differences exist whenever confidence interval does not overlap normal value, value with calf tourniquet, or value without stocking.

superficial and deep vein incompetence. The three unsatisfactory garments produced refilling times significantly below normal in patients with deep vein incompetence. All stockings except Softgrip resulted in refilling times that were significantly greater than those obtained without stockings. In the patients with superficial vein incompetence all stockings resulted in refilling times that were significantly below those obtained when a calf tourniquet was applied.

## Discussion

Previous studies concentrated on a single type of stocking and its effects on either venous function or limb compression, or both. Horner *et al* established a pressure-girth profile for an unnamed type of stocking on a test rig<sup>8</sup> and subsequently reported a relation between graduated compression, as measured by this device, and improvement in ambulatory venous pressure.<sup>2</sup> Partsch showed a graduation of pressure from lower to upper calf with a medical stocking tester but did not analyse the effect of different sizes of stockings.<sup>4</sup> He concluded that, in general, the expelled volume on foot volumetry increased with the pressure exerted on the leg. Norris *et al* evaluated fitted compression stockings of a single brand with quantitative photoplethysmography but did not refer to pressure-girth profiles.<sup>5</sup>

In this study we compared a stocking's pressure profile and linear graduation with its resultant effect on a measure of venous function—namely, the venous refilling time as measured by photoplethysmography. Photoplethysmography is a simple, non-invasive method of assessing venous function; measurements correlate closely with ambulatory venous pressures.<sup>10,11</sup> Subsequent work showed that this correlation was maintained in studies of compression hose.<sup>13</sup> The new British Standards specification, which is based on use of the Hosiery and Trades Research Association hose



pressure tester mark II, does not include any functional testing of compression hosiery.<sup>14</sup>

We found only a few stockings to be effective. The criteria for satisfactory stockings are important for venous function—namely, they should show a significant linear trend with site of measurement, no systematic difference between sizes, and no interaction between size and site. These criteria were applied only within the manufacturers' size specifications. Only five of the 15 types of stocking tested reached the fairly basic standards we had set. In the second part of the study all six stockings tested (with the exception of Softgrip) significantly improved venous refilling time in patients with both superficial and deep vein incompetence. Refilling time more nearly approached normal values, however, when the stocking met our criteria for being satisfactory, particularly in patients with deep vein incompetence.

In practice, patients' acceptance of compression hosiery is better when the stockings are selected from those shown to have appropriate linear graduation. Functional testing should be an integral part of any future British Standards specification. This would lead to a more satisfactory prescribing policy in both hospitals and the community and to a greater benefit to patients.

We thank Mrs Claire Llewellyn Williams, formerly blood flow technician at this hospital, for her help and Mrs P A Jones for secretarial help.

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(Accepted 6 August 1987)

# Quantitative DNA analysis of low grade cervical intraepithelial neoplasia and human papillomavirus infection by static and flow cytometry

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## Abstract

Quantitative deoxyribonucleic acid (DNA) analysis of cervical biopsy specimens from 26 women with cytological, colposcopic, and histological evidence of mild cervical atypia consistent with cervical intraepithelial neoplasia grade I, reactive atypia, or human papillomavirus infection alone or in combination was performed in a comparative evaluation of Feulgen microspectro-

photometry, the fast interval processor image analysis system, and flow cytometry. The fast interval processor image analysis system showed a distinct advantage over the other methods, being faster and allowing the operator to see the cells that were selected for measurement. The three methods of measurement together showed that the DNA content of at least 2% of the cells measured exceeded 5C (C being the haploid amount of DNA in a normal cell and 2C representing the diploid complement of a normal cell) in all cases of cervical intraepithelial neoplasia grade I and reactive atypia and in 87% of those reported as showing human papillomavirus infection alone. In contrast, the DNA content of cervical biopsy specimens from the transformation zone of 11 normal controls did not exceed 4C.

This study shows the value of using a DNA threshold—that is, the "5C exceeding rate"—to distinguish between normal and neoplastic appearances of the cervix. These results support the view that cervical infection by human papillomavirus is a true precursor of neoplasia.

## Introduction

Recent developments in techniques of quantitative deoxyribonucleic acid (DNA) analysis by flow and static cytometry have renewed interest in the use of ploidy analysis and morphometry in diagnosis and the evaluation of tumour behaviour, prognosis, and response to chemotherapy.<sup>1</sup>

Many invasive intraepithelial neoplasms are associated with an aneuploid nuclear DNA content. The aneuploid nature and

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