helping during the survey and Mr A Nunn for his advice on aspects of the statistical analysis.

References

- 1 Maccia CA, Bernstein IL, Emmett EA, Brooks SM. In vitro demonstration of specific IgE in phthalic anhydride hypersensitivity. *Am Rev Respir Dis* 1976; **113**:701-4.
- 2 Zeiss CR, Patterson R, Pruzansky JJ, Miller MM, Rosenberg M, Levitz D. Trimellitic anhydride-induced airway syndromes: clinical and immunologic studies. *J Allergy Clin Immunol* 1977; **60**:96-103.
- 3 Howe W, Venables KM, Topping MD, et al. Tetrachlorophthalic anhydride asthma: evidence for specific IgE antibody. *J Allergy Clin Immunol* 1983; **71**: 5-11.

- 4 Schlueter DP, Banaszak EF, Fink JN, Barboriak J. Occupational asthma due to tetrachlorophthalic anhydride. *J Occup Med* 1978; **20**:183-8.
- 5 Nelder JA, Wedderburn RWM. Generalized linear models. *Journal of the Royal Statistical Society Part A* 1972; **135**:370-84.
- 6 Zetterström O, Osterman K, Machado L, Johansson SGO. Another smoking hazard: raised serum IgE concentration and increased risk of occupational allergy. *Br Med J* 1981; **283**:1215-7.
- 7 Jones JG, Minty BD, Royston D, Royston JP. Carboxyhaemoglobin and pulmonary epithelial permeability in man. *Thorax* 1983; **38**:129-33.
- 8 Hulbert WC, Walker DC, Jackson A, Hogg JC. Airway permeability to horseradish peroxidase in guinea pigs: the repair phase after injury by cigarette smoke. *Am Rev Respir Dis* 1981; **123**:320-6.
- 9 Leskowitz S, Salvaggio JE, Schwarz HJ. An hypothesis for the development of atopic allergy in man. *Clin Allergy* 1972; **2**:237-46.
- 10 Burrows B, Halonen M, Barbee RA, Lebowitz MD. The relationship of serum immunoglobulin E to cigarette smoking. *Am Rev Respir Dis* 1981; **124**:523-5.

(Accepted 8 October 1984)

SHORT REPORTS

Support hose and varicose veins

Despite the successful clinical use of support hose for many years the exact amount of compression required to give maximum benefit to patients with varicose veins is still disputed.^{1,2} Physiological studies have shown that the tension and pressure of support hose should be close to the capillary pressure,³⁻⁵ but as the capillary pressure varies with posture and the distance from the heart this is technically difficult to achieve. We investigated the acceptability of a stocking that is claimed by the manufacturer (Sigvaris, Ganzoni, St Gallen, Switzerland) to provide graduated support with a pressure of roughly 40 mm Hg at the level of the ankle.

Patients, methods, and results

Patients were selected sequentially from a surgical waiting list, starting with those added most recently. They were randomised into two groups and given stockings that provided either 30-40 mm Hg or 40-50 mm Hg pressure. For each patient a history was taken and an examination made for the presence of pain, eczema, and ulceration and the extent of varicosities. The patients were fitted with support hose below the knee and asked to wear the stockings for six weeks. They were then reviewed blind, particular attention being paid to tolerance of the stockings and whether symptoms were better, worse, or unchanged.

Altogether 163 patients were asked to take part in the trial. Twenty five did not reply because they had moved from the area, four had had operations elsewhere, and 30 declined to participate. Thus 104 patients entered the trial, of whom 53 were randomised to wear stockings providing 30-40 mm Hg pressure and 51 stockings providing 40-50 mm Hg pressure. The groups were evenly matched for age, symptomatology, and extent of varicose veins. On review nine patients given the 30-40 mm Hg stockings and 13 given the 40-50 mm Hg stockings asked for their names to be removed from the waiting list because their symptoms had improved. In all, 42 patients given the 30-40 mm Hg stockings and 40 given the 40-50 mm Hg stockings claimed symptomatic improvement (table). Their overall feeling of benefit was not due to improvement in any one particular symptom. An attempt to analyse the effect of the two types of stocking on particular symptoms was unsuccessful because the subgroups were too small.

Results in patients asked to take part in trial

	No of patients	Remained on waiting list	Stockings improved symptoms	Came off waiting list
Non-participants	59	30		29
Participants:				
30-40 mm Hg	53	44	42	9
40-50 mm Hg	51	38	40	13
Total	163	112	82	51

Comment

We reduced our waiting list by 51 patients simply by conducting this trial. Of the 104 patients who took part in the trial, 80 claimed that the stockings were comfortable. In the remaining group of patients the main cause of discomfort was not simply that they were too tight. In answer to the proponents of low pressure stockings, most of our patients found the higher pressure stockings tolerable and roughly one quarter found them sufficiently acceptable that they

decided not to undergo surgery. We could have increased the acceptability of the stockings by varying their weight and length (for example, above knee length or tights), but for consistency within the trial we did not offer different styles to the patients.

We accept that the study was biased towards surgery because patients were taken from the waiting list and therefore may have considered stockings to be second best; but we believe that this bias was probably offset by our giving those patients who were not keen on surgery an alternative method of treatment. Despite these reservations we believe that the trial showed that most patients with simple varicose veins tolerate pressures of about 40 mm Hg and that suggestions that lower pressures are more acceptable are too cautious.¹

We thank Lesley Davies for typing the manuscript, Mr L James, who acted as fitter, and Sigvaris Company for providing the stockings.

- 1 Fentem PH. Claims about compression treatment for venous disease. *Br Med J* 1982; **285**:61.
- 2 Chant ADB. Claims about compression treatment for venous disease. *Br Med J* 1982; **285**:439.
- 3 Chant ADB. The effects of posture, exercise and bandage pressure on the clearance of 24 Na from the subcutaneous tissues of the foot. *Br J Surg* 1972; **59**:552-5.
- 4 Spiro M, Roberts VC, Richards JB. Effect of externally applied pressure on femoral vein blood flow. *Br Med J* 1970; **i**:719-23.
- 5 Jones NAG, Webb PJ, Rees RI, Kakkar VV. A physiological study of elastic compression stockings in venous disorders of the leg. *Br J Surg* 1980; **67**:569-72.

(Accepted 23 October 1984)

Department of Vascular Surgery, Royal South Hants Hospital, Southampton SO9 4PE

A D B CHANT, FRCS, consultant surgeon
P MAGNUSSEN, FRCS, surgical registrar
C KERSHAW, FRCS, surgical registrar

Correspondence to: Mr A D B Chant.

Mixing short and intermediate acting insulins in the syringe: effect on postprandial blood glucose concentrations in type I diabetics

Many diabetics take combinations of short and intermediate acting insulin, and they often mix them in the syringe before administration.¹ We have recently shown that mixing short acting and isophane insulins in the syringe does not affect the absorption kinetics of the short acting insulin, whereas its activity is delayed when it is combined with lente insulin.² This study compared the effects of mixtures of short acting with lente and short acting with isophane insulins on postprandial blood glucose and plasma free insulin concentrations in type I diabetics.

Patients, methods, and results

We studied 13 type I diabetics aged 19-64 who did not secrete endogenous insulin. They were treated with twice daily mixtures of short and inter-

mediate acting insulins and were studied twice with an interval of one week in between. Patients were randomised to receive either human Actrapid plus human Monotard or human Velosulin plus human Insulatard initially and then received the other combination during the second period of study. All insulins were of U40 strength. The tests began at least 30 minutes after cannulation. After an overnight fast the morning dose of short acting (mean 12.6 IU, range 4-36 IU) and intermediate acting insulin (mean 32.2 IU, range 16-52 IU) was administered by one of us. The insulins were injected perpendicularly into the thigh immediately after mixing in the syringe (Plastipak). The mean (range) ratio between short and intermediate acting insulin was 0.39 (0.11-0.90). After 30 minutes a standard liquid meal (2.1 MJ (500 kcal), 56% carbohydrate) was taken. Blood glucose concentrations and plasma free insulin concentrations (measured by radioimmunoassay after plasma extraction with macrogol (polyethylene glycol)) were measured at regular intervals for four hours. Statistical analysis was by Student's paired *t* test and Kendall's rank correlation test. Results are given as means (1 SEM).

Postprandial blood glucose concentrations rose to higher peaks after short acting plus lente insulin than after short acting plus isophane insulin: from 9.9 (1.3) to 16.5 (1.5) mmol/l (178 (23.4) to 297 (27) mg/100 ml) at 130 (9) minutes, compared with from 10.5 (1.2) to 13.6 (1.5) mmol/l (189 (21.6) to 245 (27) mg/100 ml) ($p < 0.01$) at 118 (6) minutes (figure). Blood glucose concentrations were significantly different from 105 to 240 minutes.

Postprandial plasma free insulin and blood glucose concentrations after administration of short acting with lente (●—●) and short acting with isophane (○- - ○) insulin mixtures in 13 patients with type I diabetes.

* $p < 0.05$, ** $p < 0.005$, *** $p < 0.001$.

Conversion: SI to traditional units—Glucose: 1 mmol/l $\approx$ 18 mg/100 ml.

Plasma free insulin concentrations rose faster after short acting plus isophane insulin than after short acting plus lente insulin: from 20 (3) and 20 (3) mU/l to peaks of 91 (8) and 64 (7) mU/l ($p < 0.01$) at 137 (9) and 172 (13) minutes ($p < 0.05$), respectively. Plasma free insulin concentrations were significantly different from 30 to 165 minutes (figure). The initial rate of absorption of insulin (incremental peak concentration divided by the time in which it was reached) was significantly greater after short acting plus isophane insulin than after short acting plus lente insulin (0.54 (0.06) v 0.26 (0.04) mU/l/min ($p < 0.001$)). These values were positively correlated

with the ratios of short to intermediate acting insulins (for short acting plus lente insulin $r = 0.62$, $p < 0.01$; for short acting plus isophane insulin $r = 0.54$, $p < 0.02$).

Comment

This study shows that mixing short acting with lente insulin in the syringe immediately before injection delays absorption of the insulin and causes higher postprandial blood glucose concentrations than a mixture of short acting plus isophane insulins. The results agree with our findings in healthy volunteers.² Retarded absorption is probably caused by the excess of zinc in lente insulin, which binds the added short acting insulin.³⁻⁵ The relation between the rate of absorption of insulin and the ratio between short and intermediate acting insulins in the mixture suggests that the dosage of short acting insulin may be reduced by changing from a combination of a short acting plus lente insulin to a short acting plus isophane insulin.

- 1 Kahn CB. Insulin therapy. In: Kozak GP, ed. *Clinical diabetes mellitus*. Philadelphia: W B Saunders, 1982:72-85.
- 2 Heine RJ, Bilo HJG, Fonk T, van der Veen EA, van der Meer J. Absorption kinetics and action profiles of mixtures of short and intermediate acting insulins. *Diabetologia* (in press).
- 3 Hallas-Møller K, Peterson K, Schlichtkrull J. Crystalline and amorphous insulin zinc compounds with prolonged action. *Ugeskr Laeger* 1951;113:1761-7.
- 4 Grootendorst BC, Jonkers JR, Kruit L. The miscibility of short acting insulins with depot insulins: an in vitro study. *Pharm Weekbl [Sci]* 1983;118:746-51.
- 5 Berger M, Cüppers HJ, Hegner H, Jörgens V, Berchtold P. Absorption kinetics and biologic effects of subcutaneously injected insulin preparations. *Diabetes Care* 1982;5:77-91.

(Accepted 2 October 1984)

Department of Internal Medicine, Free University Hospital, 1081 HV Amsterdam, The Netherlands

R J HEINE, MD, physician
H J G BILO, MD, physician
A C SIKKENK, MD, research associate

Department of Endocrinology, Free University Hospital
E A VAN DER VEEN, PHD, physician

Correspondence to: Dr R J Heine.

Necrotising glomerulonephritis associated with cholesterol microemboli

Embolisation of cholesterol in the kidneys may result in severe, irreversible renal failure.¹ Antemortem diagnosis can sometimes be established by renal biopsy when characteristic crystalline clefts are seen in arterial lumens and ischaemic changes in the renal parenchyma.² Although fibrinoid necrosis of small vessels has been associated with microemboli of cholesterol,^{3,4} necrotising angiitis in the kidney has not been reported as a manifestation of cholesterol embolisation. We describe a case of necrotising glomerulonephritis associated with cholesterol microemboli in an elderly man with extensive aortic atheromatosis.

Case report

A 75 year old man with chronic obstructive pulmonary disease was admitted to this hospital in October 1982 with acute bronchitis. He had a long history of coronary insufficiency and had recently experienced transient right hemianopsia. Results of biochemical tests were unremarkable apart from an increased erythrocyte sedimentation rate (72 mm in the first hour). Serum urea concentration was 3.7 mmol/l (22 mg/100 ml) and creatinine concentration 97 μ mol/l (1.1 mg/100 ml); no proteinuria was found, and the urine sediment was normal. Treatment with antibiotics resulted in a rapid improvement of the pulmonary state. Fundoscopic examination showed three cholesterol emboli in the right retina, and computed tomography of the brain indicated scattered bilateral ischaemic lesions. On 15 November carotid angiography was performed via the femoral artery. It showed an ulcerated atheromatous plaque in the right internal carotid artery and several stenotic lesions of the intracerebral vessels. Severe atheromatous lesions were present in the aorta.

On 21 December he developed oliguria and rapidly progressive renal failure. Blood urea nitrogen concentration was 32.5 mmol/l (91 mg/100 ml) and serum creatinine concentration was 407 μ mol/l (4.6 mg/100 ml). The urine sediment contained +++ red cells, and transient macroscopic haematuria was noted. Proteinuria was 1.5 g/day. On 23 December he was anuric and