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## Biological Effects of Intermittent Compression of the Calf

Early mobilization after surgery appears, in some way, to protect against the development of thromboembolic complications. Despite the introduction of this concept into clinical practice thirty years ago, the incidence of death from pulmonary embolism has continued to rise alarmingly. This is probably due to the increasing age of the population, in whom it is difficult to achieve early postoperative ambulation, and to the increasing severity of the surgery performed. Surgeons have therefore devised ways of simulating exercise artificially by either contracting the calf muscles with repeated electrical stimulation, or compressing them with external intermittent pneumatic pressure.

Using the second method Hills *et al.* (1972) showed that the incidence of postoperative venous thrombosis could be considerably reduced. In a controlled trial the incidence was reduced from 30% to 12%, while if patients with malignant diseases were excluded, there was total protection.

In order to determine the nature of this protection, we studied the effects of the intermittent compression on the venous blood flow. At the beginning of compression, the blood volume flow, measured by an electromagnetic flow probe inserted into the femoral vein at the groin, quickly reached a peak, followed by a depression of flow which was maintained for the rest of the period of compression. The overall effect was a reduction of blood flow. It seems unlikely, therefore, that the beneficial effects of the leggings can be wholly explained by improved blood flow through the veins, since the main effect seems to be that of intermittent occlusion. However, since venous occlusion stimulates fibrinolysis (Clarke *et al.* 1960), it may be that the recurrent venous occlusion results in an accumulative enhancement of fibrinolysis. This view is supported by a controlled trial we conducted in which the patients receiving intermittent compression after operation showed a significant fibrinolytic enhancement compared with their controls.

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## Review of Present Status of Prophylaxis of Venous Thromboembolism

The ideal to aim at is the total prevention of deep vein thrombosis. The method which is to be recommended for general use must fulfil the following criteria: it must be simple, safe and effective; it must cover the period of risk of developing thrombosis, which in surgical patients has been shown to extend from the time of operation until the patient is actively mobile and is discharged from hospital; it must be cheap so that it is within the scope of every hospital.

There is little doubt that the physical methods lessen stasis and lower the incidence of venous thrombosis, except in 'high risk' patients undergoing operation for malignant disease (Table1). However, such physical methods present almost insuperable difficulties as a long-term solution. They must be applied to both legs during certain types of operation; for example, for fractured neck of femur, total hip replacement and where the patient is in the lithotomy position they are either impracticable or extremely inconvenient. These prophylactic measures must be applied not only during operation but at regular intervals for the first ten postoperative days, and perhaps even longer. Some of the methods are uncomfortable for conscious patients, and above all the logistical problem of applying such physical measures on a large scale could strain the resources of even the most lavishly equipped hospital. Experience with less complicated regimens of intensive physiotherapy supports this view. Thus physical methods are unlikely to be the choice for the future.

Recently therefore, there has been great resurgence in the development of chemical methods for the prevention of venous thromboembolism (Table 2). The evidence that drugs such as aspirin and dipyridamole, known to interfere with platelet function, effectively reduce the incidence of deep vein thrombosis is unconvincing. However, the role of dextran is still uncertain and its efficacy in reducing the incidence of fatal pulmonary embolism remains to be determined. There is no doubt that drugs which are known to enhance naturally occurring fibrinolytic activity, such as phenformin and ethylœstrenol, are totally ineffective in preventing deep vein thrombosis in surgical patients. Oral anticoagulant therapy, properly employed (starting before operation or immediately after admission to hospital) is the most effective and proved method of preventing

*Table 1*

**Prophylaxis: effect of elimination of stasis on incidence of postoperative DVT as detected by $^{125}$I-fibrinogen test**

| | *Control group* | | *Treated group* | | |
|---|---|---|---|---|---|
| *Study* | *No. studied* | *DVT* | *No. studied* | *DVT* | *Statistical significance* |
| Intensive physiotherapy (Flanc *et al.* 1968) | 65 patients | 23 (35%) | 67 patients | 17 (25%) | $P=0.25$ |
| Electrical stimulation of calf muscles (Browse & Negus 1970) | 110 limbs | 23 (20.9%) | 110 limbs | 9 (8.2%) | $0.001 < P < 0.01$ |
| Pneumatic compression of calves (Hill *et al.* 1972) | 16 patients ● | 8 (50%) ● | 9 patients | 5 (55.5%) ● | |
| | 34 patients ■ | 7 (21%) ■ | 41 patients | 1 (2.4%) ■ | $P=0.015$ |
| Passive flexion of calf muscles (Sabri *et al.* 1971) | 47 limbs | 13 (27.6%) | 47 limbs | 3 (6.4%) | 5%▲ |

● Patients with malignant disease ■ Patients without malignant disease
▲ Sequential analysis – line of significance corresponds to probability level of 5%

*Table 2*

**Prophylaxis: drugs which affect platelet function and incidence o fpostoperative DVT**

| | *Diagnostic* | *Incidence of DVT* | |
|---|---|---|---|
| *Study* | *technique* | *Control group* | *Treated group* |
| Aspirin: | | | |
| Salzman *et al.* (1971) | Clinical | 23/67 (34%) | 4/43 (9%) |
| MRC (1972) | $^{125}$I-fibrinogen test | 32/150 (22%) | 42/153 (27.5%) |
| Dextran: | | | |
| Johnsson *et al.* (1967) | Clinical | 13/25 (52%) | 1/27 (4%) |
| Sawyer (1968) | Clinical | 5/53 (9.4%) | 3/51 (6%) |
| Brisman *et al.* (1971) | Clinical/autopsy | 14/90 (15.5%) | 11/89 (12.4%) |
| Kakkar (1973, unpublished) | $^{125}$I-fibrinogen test | 14/40 (35%) | 16/43 (27%) |
| Bonnar & Walsh (1972) | $^{125}$I-fibrinogen test | 15/140 (10.7%) | 1/120 (0.8%) |
| Dipyridamole: | | | |
| Browse & Hall (1969) | Clinical | 7/334 (2.1%) | 12/315 (3.8%) |
| Phenformin and ethylœstrenol: | | | |
| Fossard *et al.* (1974) | $^{125}$I-fibrinogen test | 10/45 (20%) | 10/50 (20%) |

*Table 3*

**Prophylaxis: effect of low doses of heparin in incidence of postoperative DVT as assessed in controlled clinical trials**

| | *Control group* | | *Treated group* | | |
|---|---|---|---|---|---|
| *Study* | *No. studied* | *DVT* | *No. studied* | *DVT* | *Statistical significance* |
| Kakkar *et al.* (1971) | 27 | 7 (26%) | 26 | 1 (4%) | $0.05 > P > 0.25$ |
| Williams (1971) | 29 | 12 (41%) | 27 | 4 (15%) | $0.02 > P > 0.01$ |
| Gordon Smith *et al.* (1972) ● | 50 | 21 (42%) | 52 | 7 (13.5%) | $P < 0.003$ |
| | | | 48 | 4 (8.3%) | $P < 0.001$ |
| Kakkar *et al.* (1972) ■ | 39 | 17 (42%) | 39 | 3 (8%) | $P < 0.001$ |
| | | | 133 | 13 (9.7%) | |
| | | | 50 | 20 (40%) | |
| Nicolaides *et al.* (1972) | 122 | 29 (24%) | 122 | 1 (0.8%) | $P < 0.000003$ |
| Gallus *et al.* (1973) | 118 | 19 (16%) | 108 | 2 (2%) | $P < 0.003$ |

● Trial comparing two different regimes ■ Double-blind randomly allocated trial

venous thrombosis. However, in spite of strict laboratory control, the risk of hæmorrhage is real and may even be greater than the dangers of thromboembolism if such therapy was accepted for general use.

Of all the chemical agents which are being investigated at present, low-dose heparin (5000 units subcutaneously begun two hours before surgery and every eight hours thereafter for 7 to 10 days) seems to be the most promising drug for preventing deep vein thrombosis (Table 3). The efficacy of this method has been assessed in a number of controlled clinical trials and these studies have shown clearly that this form of prophylaxis is well tolerated by patients, is devoid of side-effects, requires no special monitoring, except that the patients receive the drug, and

does not seem to result in excessive bleeding during or after surgery. Furthermore, it can be used on an extensive scale without straining hospital resources. However, final judgment on the value of this form of prophylaxis can only be established by unequivocal demonstration of a significant reduction in postoperative deaths from pulmonary embolism. This requires large-scale studies involving thousands of patients and such a multicentre trial is already under way in the United Kingdom and abroad. Fifty-one centres in eleven countries are taking part in this study and a uniform protocol is being followed. Patients over the age of 40 having major operations are being randomly allocated to control or treatment groups. The incidence of fatal pulmonary embolism, confirmed at autopsy, is being recorded in both groups. The results are being analysed by computer. In the first nine months of the trial 2055 patients have been entered – 1020 in the control group and 1035 in the heparin group. Computer analysis of these patients has shown that the two groups are well matched for age, sex, presence of malignancy, type of operation performed and other factors likely to influence the incidence of thromboembolism. Seven patients in the control group and one in the heparin group died due to acute, massive, isolated pulmonary embolism. In another 2 patients in each group pulmonary emboli were confined to the lobar or segmental branches and, though not thought to be the primary cause, did contribute to the patients' death. If these findings are confirmed in large numbers of patients, then low-dose heparin will provide an effective prophylactic method.

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## Intermittent Compression of the Legs During Operation as a Method of Prevention of Deep Vein Thrombosis

Intermittent compression of the legs is effective in reducing deep venous thrombosis (DVT) by increasing the pulsatility of venous flow rather than by increasing mean venous flow (Cotton & Roberts 1973). It need only be applied during the period of the operation. Study of the hæmodynamics of venous flow have defined the optimum parameters for maximal pulsatility. First, the pressure should rise no more than 45 mmHg. The rate of rise should be rapid, at least 8 mmHg per second. This pulse of pressure empties the leg of about 80 ml of blood. It takes at least one minute for the leg to fill with venous blood (Roberts *et al.* 1972).

Intermittent compression as thus defined is provided by the BOC Roberts Venous Flow Stimulator. With this machine a 75% overall depression of DVT was achieved.

In the older age group (40–60 years) the depression was 71% and in cases of malignancy 90% (Roberts & Cotton 1974). The remarkable result in malignant cases was at variance with the conclusions of Hills *et al.* (1972) who found malignant cases unaffected by intermittent compression. An explanation of this contradiction is that almost all cases of DVT in malignancy occur in the first 24 hours after surgery when the machine would be expected to be most effective if it is not to produce maximal pulsatility of venous flow. This is the simplest and cheapest method of prevention of DVT following surgery.

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## Medical Management of Deep Vein Thrombosis

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