This subject, the prevention of deep vein thrombosis, will either stimulate you or bore you. For ease of reading, let's call it DVT. Why discuss DVT? There are four good reasons:

1. It is a subject which brings physicians, surgeons and haematologists together, for all have a vested interest in knowing more about it. Why does liquid blood clot in a vessel? What are the mechanisms? How can it be prevented?

2. The Registrar-General's returns for 1972 stated that 12,000 persons in England and Wales died from pulmonary embolism following a DVT. We don't know why they had DVT but the inference was that these were people who should not have died—an indictment of doctors.

3. There is some evidence that the condition is becoming more common after surgery.

4. Lastly, it is the fastest growing subject in the West, because we have begun to realize what we don't know and have taken steps to rectify this.

In the past, there was a lack of hard facts but much opinion and, probably, wrong interpretations and much speculation. One of the most dangerous things in medicine today is a hypothesis without supporting data.

Venous thrombosis is a serious condition contributing to a large proportion of the country's morbidity and mortality in terms of chronic venous disorders and pulmonary embolism. We are particularly concerned with its prevention during the postoperative period because complications from infection, anaesthesia and biochemical disturbances have been reduced substantially, yet those from thromboembolic disease are increasing at an alarming rate (Roberts, 1971).

The ability of the blood to change from a liquid to a solid state in response to an appropriate stimulus was an important and necessary development in the evolution of a closed circulatory system. However, it is the perversion of this complex mechanism which is usually responsible for the development of venous thrombosis, which can be considered either as an abnormal response to normal stimuli or as a normal response to abnormal stimuli. The nature of these stimuli is not fully known, but Virchow (1856) proposed three, which have subsequently been designated "Virchow's Triad". Recent experimental work suggests that this was an over-simplification (fig. 1) for while the triad of changes, in the vessel wall, in blood flow and in the blood itself, form the foundations of our present knowledge, each can be further extended to cover several independent factors, most of which are affected in varying degrees by surgery.

### Virchow's 'Triad' vs Present Concepts

<table>
<thead>
<tr>
<th>Virchow's 'Triad'</th>
<th>Present Concepts</th>
</tr>
</thead>
<tbody>
<tr>
<td>WALL</td>
<td>collagen, basement membrane, endothelial cell, platelet, coagulation factors, fibrinolysis, plasma proteins, viscosity, velocity, volume, turbulence, eddying</td>
</tr>
<tr>
<td>BLOOD</td>
<td></td>
</tr>
<tr>
<td>FLOW</td>
<td></td>
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</table>

Fig. 1. Virchow's (1856) triad expanded to include modern concepts.

In experimental work on thrombosis, it is usual to study one of these factors in isolation, but to do so denies their complex interrelationships. It seems likely that many factors are operative in any particular individual, but that their relative importance varies from patient to patient. It must be admitted that the aetiology of venous thrombosis is far from clear and it follows that approaches to preventing it must be, for the present, empirical.
WHAT WE DON'T KNOW

We list only four important questions. Of course, we are not totally ignorant: we have clues and some circumstantial evidence.

(1) How does a thrombus develop?

Platelets aggregate, fibrin is deposited and red cells congregate: we know all this, but what is it really that starts the whole thing off so unexpectedly?

Eberth and Schimmelbusch (1886) believed that the underlying cause of venous thrombosis was a change in the venous endothelium combined with a displacement of platelets to the periphery of the blood stream, although Paterson and MacLachlin (1954) were not able to detect any difference in the histology of the vein walls of those with and without thrombi. Sevitt and Gallagher (1961) have shown that thrombi originate independently at well defined points along the venous system of the limb, and it may be that these points represent areas of high stress on the endothelium, as might be expected to occur at valves opposite tributaries. Studies of the vein wall have been made after the artificial application of trauma externally to the vein (Ashford and Freiman, 1967; French, McFarlane and Sanders, 1964; Spaet and Zucker, 1964) and it has been found that platelets adhere to exposed collagen fibres. Baumgartner, Tranzer and Studer (1967), in a more detailed study, applied the trauma internally to the vein wall and found, in fact, that the platelets adhered to the basement membrane exposed by the loss of endothelial cells.

Observations by Born (1956) implied that the damaged endothelial cell released ADP, so initiating the first phase of platelet aggregation. If intimal damage is an important stimulus for thrombus formation, it could be argued that an agent which could strengthen the vessel wall might be a valuable prophylactic agent. Such claims have been made for high molecular weight dextrans (Bloom et al., 1964) for the hydroxyethylrutosides (Felix, 1972) and for vitamin C (Spittle, 1973). Spittle demonstrated a reduction in the incidence of postoperative venous thrombosis (with isotopic detection) after the administration of vitamin C, but only at the 5% level of significance. Our own observations on the hydroxyethylrutosides, previously known as vitamin P, have not been encouraging. In a double-blind controlled trial, a daily injection of a mixture of these rutosides did not reduce the incidence of postoperative thrombosis in patients with malignancy (Calnan, 1972).

(2) Where does a thrombus develop?

A great many seem to start around the cusps of valves in veins, where there is some slowing and turbulence of blood. That is understandable, but others seem to start on the wall of large veins where there may be no valves. Why is this? Is the vein wall damaged in some way and if so, by what?

(3) What are the predisposing factors?

Some are well known (such as age, infection), but in many instances of DVT after surgery, there is little explanation.

(4) What are the normal/abnormal mechanisms?

We now have a better understanding since McFarlane, working in Oxford, collated and unified knowledge at that time in his “cascade” hypothesis (McFarlane, 1964). This can be represented on a chart which is complicated and best studied at length (fig. 2). It does have a kind of inevitability about it, with a sense of mathematical uncertainty which we find difficult to accept easily.

**Fig. 2. Simplified diagram of the “cascade” hypothesis of blood coagulation.**

WHAT WE DO KNOW

Let's consider what we do know, or think we know. Again, we will list only four aspects:

(1) DVT occurs before, and may lead to, pulmonary embolism which, if not fatal, causes anxiety and physical discomfort for the patient (and often for the doctor too).
(2) The clinical diagnosis of thrombosis in the legs is grossly inaccurate. Even today, pulmonary embolism occurs where no signs are present in the legs, even though they have been sought. On other occasions, a diagnosis of DVT has been made and treatment instituted when the condition was not present. So, early detection is not just important, it is vital. In 1968 the $^{125}$I fibrinogen method was introduced by Atkins and Hawkins, and by Negus and colleagues, and to our surprise, the incidence of calf-vein thrombosis was found to be 30% or more in patients after surgery (and also after a coronary thrombosis).

The fibrinogen method is a clever way of detecting the presence of a thrombus. Human fibrinogen is labelled with the isotope iodine-125 and a dose of 100 $\mu$Ci is injected intravenously into the patient, usually immediately after completion of the surgical operation, but it can be given before. The isotope circulates, and if a thrombus forms in the leg there will be a higher level of radioactivity (measured by an external counter) at that site. The legs are scanned every day so that the progress of the thrombus can be monitored. If the thrombus remains the same size, it can probably be ignored; if it enlarges then appropriate therapy can be started to limit further spread.

(3) Prevention is better than cure! This should be self-evident, an axiom for medicine.

(4) Thrombosis can be prevented. For the remainder of this paper we wish to concentrate on this aspect: the various methods, their cost, ease of administration, and safety.

METHODS OF PREVENTION

There are essentially three methods of prevention which have so far shown promise: dextran, mechanical stimulation, anticoagulants.

Dextran.

The antithrombotic properties of dextran were first discovered from animal studies by Borgstrom, Gellin and Zederfelt (1959) but the exact mechanism remains speculative; it was suggested that it might be the result of altered suspension-stability of the blood, and Gruber and Bergentz (1966) thought it was caused by the stabilizing effect on the suspension of red cells. Bloom et al. (1964) showed that dextrans coated the endothelium with a protective layer, while Afors et al. (1968) showed that dextran 70 had a depressive effect on platelet activity at sites of endothelial damage. A suppression of platelet activity has been found both in normal man (Bennett et al., 1966; Bygdeman and Eliasson, 1967) and after surgery in patients with enhanced platelet adhesiveness (Dhall, Bennett and Matheson, 1967). Other possible mechanisms include changes in the red cell electrical charge (Bernstein et al., 1963), expansion of the plasma volume causing an increased local blood velocity (Gelin and Thoren, 1961; Schenk et al., 1964; Schwartz et al., 1964), or a reduction in viscosity due to haemodilution (Dormandy, 1971).

Koekenberg (1961) was the first to show, by a controlled clinical trial, that dextrans could prevent postoperative thrombosis in man. This was followed by similarly enthusiastic reports (Jansen, 1968; London and Crosfill, 1969; Sawyer, 1968; Stadil, 1968). Unfortunately, the value of these trials was limited by the fact that the results were based on a purely clinical diagnosis of the thrombus. Johnsson, Bygdeman and Eliasson (1968) subjected these clinical impressions to a more rigorous assessment using phlebographic confirmation of the diagnosis, and their findings supported the promising results of the previous work. Recent studies have used the more accurate isotopic detection methods. Lambie et al. (1970) found that the protective effects of dextran were significantly better than those of warfarin. However, the anticoagulants were given after the operation and therefore were not present at a critical period in the development of the thrombi. Bronge, Dahlgren and Lindquist (1971) compared dextran 70 with dicoumarol in patients with fractures of the neck of the femur; although the prophylactic measures were started before curative surgery, they were in fact commenced well after the time of the initial injury. The incidence of thrombosis was 30—40% in the controls, a figure not reduced by dextran or by dicoumarol. Recognizing the need to start the prophylaxis as soon as possible after the initial trauma, Bergquist et al. (1972) repeated the study with prophylaxis starting as soon as the patient was admitted to hospital and the clinical diagnosis made. In spite of this, the incidence of thrombosis after surgery was not reduced by a significant amount. Bonnar and Welch (1972) increased the dose of the dextran, and in a double-blind trial for women undergoing surgery for benign gynaecological conditions (a low-risk population because the incidence of thrombosis was only 15% in the abdominal hysterectomy controls and 6% in the vaginal hysterectomy controls), found a significant
reduction in the incidence of postoperative thrombosis in their treated patients. Carter and Eban (1973) reported a trial of dextran which again was administered at an increased dose, but involved a rather cumbersome regimen which necessitated the administration of the agent until the day of the patient's discharge. Again there was reported a reduction in the incidence of postoperative thrombosis, but only at the 10% level in males (and again the overall incidence in the controls was low at 9.9%). This is difficult to explain, but suggested either that the incidence of venous thrombosis varied from district to district (Sripad, Antcliff and Martin, 1971), that techniques of detection varied from hospital to hospital, or that methods of patient selection differed. Perhaps it is true that the incidence of thrombosis also varies at different times (Little and Binns, 1972).

**Mechanical methods.**

There are many reasons for believing that reduced venous blood flow is an important aetiological factor in venous thrombosis during and after surgery. The venous anatomy of man, no doubt resulting from his assumption of an upright posture, is unique in possessing large muscular sinusoids which act as a peripheral pump and in which venous pooling can occur. These are the commonest sites in which early thrombi start. However, thrombi do occur independently along the whole length of the venous tree, including the iliofemoral segment where blood velocities are quite high (Allenby, Jeyasingh and Boardman, 1973).

Ambulation, which apparently reduced venous pooling, appeared to confer protection against thrombus formation (Makin, 1969), but this might be caused by other factors associated with exercise, such as fibrinolytic stimulation. Situations associated with recumbency (and therefore with reduced blood flow), such as surgery and acute illnesses, are also associated with a high risk of development of thrombosis. That there is a reduced velocity in blood flow after surgery has been confirmed by Doran, Drury and Sawyer (1964); the time of the greatest reduction of velocity, however, was not associated with the period when the majority of thrombi are known to form. Dyde and Bethel (1968) suggested that modern anaesthetic techniques may even aggravate the situation; using radioactive tracers to measure venous blood velocity, they found that transit times were increased when the surgery was performed under anaesthesia incorporating intermittent positive pressure ventilation. For these reasons it is customary to try to achieve early ambulation after surgery. However, it should be pointed out that it is probably better to have an ill patient moving his legs in bed than sitting in a chair with the knees bent and the legs dependent, for if "stasis" has any importance in the aetiology of venous thrombosis, this is one of the best ways of achieving it! Likewise, bandaging the legs, on the rationale that it diverts blood from the superficial veins into the deep system and thereby increases blood velocity in the deep veins, is often performed for the prevention or treatment of venous thrombosis. This concept was supported by Makin (1969), but recent work (Spiro, Roberts and Richards, 1970) has shown that such bandaging, depending on the type used, may actually reduce venous flow. Rosengarten et al. (1970) at Hammersmith Hospital, demonstrated that such measures had no protective effect at all, a view supported by Browse et al. (1974). Further, leg elevation and active physiotherapy designed specifically to promote venous blood flow was not found to be particularly helpful (Flanc, Kakkar and Clarke, 1969; Browse et al., 1974).

At Hammersmith Hospital, Calnan and Pflug designed and developed a method of applying external pressure to the leg intermittently to simulate muscular activity. Hills et al. (1972) set up a randomized clinical trial in general surgical patients to find whether the leggins would prevent DVT and pulmonary embolism. The leggins were put on at the time of premedication, and worn in theatre and for 24 hr afterwards until the patient was up and about. The fibrinogen test was used for diagnosis and 100 consecutive patients studied. The results were interesting and are shown in the following tables. The fact that the incidence of thrombosis had been reduced in those using the leggins was encouraging (table I), but disappointing because the leggins were expected to prevent DVT altogether. The case records were then examined in more detail, to reveal that 25 had cancer and these did very badly, although others have found differently; indeed, our leggins had

<table>
<thead>
<tr>
<th>Table I. One hundred consecutive general surgical patients.</th>
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<td>Controls</td>
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<tr>
<td>Total patients</td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Controls</td>
</tr>
<tr>
<td>Treated</td>
</tr>
</tbody>
</table>
not protected them at all (table II). Fortunately, the 75 without cancer showed more promise (table III). When patients over 60 years old and who did not have cancer were inspected, the incidence of DVT in the untreated group was quite high (38%) even though the numbers were small, and thrombosis occurred only in one patient of the treated group.

**TABLE II. Twenty-five cancer patients (from table I).**

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>Treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patients</td>
<td>16</td>
<td>9</td>
</tr>
<tr>
<td>No DVT</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>DVT</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Incidence</td>
<td>50%</td>
<td>55%</td>
</tr>
</tbody>
</table>

**TABLE III. Seventy-five non-cancer patients (from table I).**

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>Treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patients</td>
<td>34</td>
<td>41</td>
</tr>
<tr>
<td>No DVT</td>
<td>27</td>
<td>40</td>
</tr>
<tr>
<td>DVT</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Incidence</td>
<td>21%</td>
<td>2%</td>
</tr>
</tbody>
</table>

Another quite separate trial was set up, limited to those over 60 years without cancer. When all patients in this category were summed (table IV) there was a dramatic improvement: thrombosis can be prevented!

**TABLE IV. Patients over 60 years and no cancer.**

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>Treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patients</td>
<td>36</td>
<td>37</td>
</tr>
<tr>
<td>No DVT</td>
<td>22</td>
<td>36</td>
</tr>
<tr>
<td>DVT</td>
<td>14</td>
<td>1</td>
</tr>
<tr>
<td>Incidence</td>
<td>39%</td>
<td>3%</td>
</tr>
</tbody>
</table>

To reinforce what was found, we have used the leggings prophylactically in a further 16 patients who were due to have a second operation, did not have cancer, but had had either a serious DVT or pulmonary embolism after the first operation. This was not a controlled trial; indeed, it seemed unethical to make it so. In no patient was there trouble after the second operation; we may therefore accept these further results as circumstantial evidence supporting the earlier findings (Clark et al., 1974).

How the leggings work is far from clear. Experimental work had demonstrated a change in the pattern of venous flow, consisting essentially of two parts: an initial increase in venous return followed by a longer period of reduced flow, when pneumatic leggings were applied. Roberts et al. (1972) concentrated attention on this initial increase in flow, and modified the apparatus to produce more rapid and increased peak venous flows, although the mean volume flow remained largely unchanged. However, the presence of an occlusive element in the flow pattern led us to explore the effects of intermittent compression on the fibrinolytic system (Allenby, Boardman and Calnan, 1973).

It was found, in patients with benign conditions and having intermittent compression of the legs, that there was stimulation of fibrinolysis, significantly better than in matched controls (who were experiencing the usual postoperative "fibrinolytic shutdown"). In a similar trial on patients with malignancy—those patients whom Hills et al. (1972) had found not to benefit from intermittent compression—there was no such fibrinolytic enhancement. The source of the plasminogen activator produced by this procedure is not clear; evidence seems to point to the venous endothelium, but Menon (1974) believes it to be derived from the compressed muscles themselves.

Other attempts to prevent postoperative venous thrombosis by increasing venous blood flow have utilized the electrical stimulation of calf muscles. Doran, White and Drury (1970) reduced the incidence of thrombosis using this technique, but their diagnostic criteria were clinical and therefore inaccurate. However, their findings were confirmed by Browse and Negus (1970) using radioactive detection methods, but a later study by Dejode, Khurshid and Wather (1973) was unable to confirm this. It may be significant that the latter group used the patient as his own control by stimulating only one leg, and using the other leg as the control. If then, systemic factors, rather than simply venous flow, were involved, any benefit derived from stimulating one leg would be enjoyed by both legs. Also, the technique of electrical stimulation has the great disadvantage that it can be used only during the period the patient is anaesthetized (because it is painful) while thrombi can, of course, form and extend after this time.

**Heparin.**

Many attempts have been made to establish a prethrombotic state, and so predict those patients with a propensity to develop venous thrombosis after surgery. Changes in the coagulation factors have been identified in patients who have developed venous thrombi, but it is difficult to know if these changes were the result, rather than the cause, of the thrombosis. In a recent study by Gallus, Hirsh and Gent (1973), 14 tests of haemo-
Stasis and fibrinolysis were performed on patients before and after surgery and the presence of venous thrombosis was assessed by radioactive methods. Of these tests, only the partial thromboplastin time was found to be useful in predicting those patients who subsequently developed thrombi. Prospective trials are now required to confirm this. It is interesting that increased antiplasmin levels were found after surgery in those patients who developed thrombi. If a hypercoagulable state does exist in some people, it would be rational to try to correct it with anticoagulants. Unfortunately, until this type of patient can be identified, such a preventive approach cannot be used and all patients must be subjected to the hazards of anticoagulants.

Several trials have confirmed the efficacy of anticoagulants (Sevitt and Gallagher, 1959). When the thrombi were detected by radioactive means, the subsequent use of an anticoagulant was found to be ineffective (Pinto, 1970), but this may have been due to inadequate dosage. Necessarily, the achievement of adequate anticoagulation incurs the dangers of haemorrhage for the patient, and a lot of extra work for the hospital laboratory staff, who have to monitor the anticoagulation. For these reasons, it has not been accepted generally as a means of prophylaxis, but reserved for particularly “high risk” patients.

In an attempt to overcome the recognized dangers of anticoagulation, Sharnoff, Kass and Mistica (1962) administered a smaller dose of the drug to large numbers of patients and later reported its value as beneficial (Sharnoff, 1973), although only clinical assessment of thrombosis was used. Kakkar et al. (1971) overcame these objections by using radioactive detection methods and subcutaneous heparin. The controls and test patients were run consecutively and not concurrently but, even so, the results were encouraging; they have subsequently been confirmed in surgical patients by others (Williams, 1971; Nicolaides et al., 1972; Gordon-Smith et al., 1972), and by Warlow et al. (1973) in medical patients. However, in all these studies the occurrence of venous thrombosis was not totally abolished, and it is not yet known if the regime of subcutaneous heparin will also reduce the incidence of pulmonary embolism. The work of Lahnborg et al. (1974) indicates that it may, but the diagnosis of pulmonary embolism by radioactive lung scanning alone is not entirely satisfactory. Browse, Clemenson and Croft (1974) and Kakkar (1974) have decided to study this problem by observing the effect of subcutaneous heparin on the incidence of death from pulmonary embolism, confirming the diagnosis at postmortems. This clinical trial, involving many centres throughout Europe, is still in progress and its outcome is eagerly awaited. As yet, no significant improvement has been found in the patients receiving heparin (Kakkar, 1974).

Important practical disadvantages to the use of heparin are that there is a small but definite risk of haemorrhage, that it is painful when administered, and that it is in short supply (and is likely to become more difficult to obtain if its use becomes widespread).

Other methods.

Pharmacological methods to increase venous velocity have included the use of digitalis, inhalation of carbon dioxide, and thyroid extract, but these are of historical interest only.

An important development in the understanding of venous thrombosis was the establishment by Fearnley (1965) of the physiological role of fibrinolysins, which are large β-globulins found normally in plasma. By preserving the temperature-labile activator and by removing or diluting the inhibitors, he unmasked the spontaneous fibrinolytic activity of normal blood. It would appear that this activity works in a continuous dynamic equilibrium with the coagulation processes, in order to maintain a patent but intact vascular system. That a disturbance of this system might be involved in the aetiology of thrombosis is supported by the following observations:

(a) Fibrinolysis is depressed after surgery, during the period when thrombosis is known to occur (Chakrabarti, Hicking and Fearnley, 1969; Mansfield, 1972). Gordon-Smith, Hickman and LeQuesne (1972) showed that patients who had already developed postoperative DVT, exhibited significantly lower fibrinolytic activity on the first day after operation than those who had not.

(b) The presence of postoperative venous thrombosis is associated with low preoperative fibrinolytic activity in the blood (Menon, McCollum and Gibson, 1971), and of the vein wall (Pandolfi, Isacson and Nilsson, 1969), and with a high level of antiplasmin from the first day after surgery (Gallus, Hirsh and Gent, 1973).
The fibrinolytic activity of the leg veins, which are notoriously prone to develop thrombosis, is much less than in the arms, in which thrombosis is very rare (Nilsson and Robertson, 1968; Pandolfi et al., 1968).

It may be that simply by preventing the fibrinolytic shutdown which follows surgical operations, the incidence of venous thrombosis could be reduced. To test this hypothesis the authors have performed two trials involving phenformin and ethyloestrenol (Allenby, Jeyasingh and Calnan, 1973). Both of these drugs had previously been shown to be capable of stimulating the fibrinolytic activity of the blood in atherosclerotic patients (Fearnley, Chakrabarti and Hocking, 1967) and in surgical patients (Brown et al., 1971). Unfortunately, significant fibrinolytic enhancement, as measured by the euglobulin lysis time, was not achieved with either drug during the critical postoperative period, which may have been due to an inappropriate drug regime.

A similar failure to maintain fibrinolytic stimulation after surgery, using phenformin, occurred in a trial by Fossard et al. (1974). Thus it has been impossible, so far, to use fibrinolytic stimulants for the short-term prevention of venous thrombosis, such as occurs following surgical operations. It seems more likely that they may find a place in the prophylaxis of arterial thrombosis (Fearnley, Chakrabarti, 1974) where long-term therapy is possible. However, the fact that fibrinolysis is important in the prevention of venous thrombosis is supported by our own observations that intermittent compression, applied to both legs of patients with benign conditions, is effective in stimulating fibrinolytic enhancement and in preventing venous thrombosis in the postoperative period. In patients with malignancy, there is no significant improvement in fibrinolysis and, correspondingly, no protection against postoperative thrombosis. Obviously, much more research is required to establish the importance of fibrinolysis and the factors influencing it; that it is amenable to pharmacological manipulation suggests that anaesthetic agents too may play an important role during the postoperative period.

### THE FUTURE

What of the future? Clearly, there are several facets of the subject which will require further work.

1. The fact that the leggings fail to protect patients with cancer is disappointing. There is some evidence that subcutaneous heparin will do so in some patients and it may be that a combination of therapies will supply the best answer. Comparative costs are shown in table V.

<table>
<thead>
<tr>
<th>Table V. Costs of prevention for one patient.</th>
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<tbody>
<tr>
<td>1. Compression leggings</td>
</tr>
<tr>
<td>Capital cost of motor £32—less depreciation £0.32</td>
</tr>
<tr>
<td>Capital cost of pair leggings £8—replaced every 100 patients £0.08</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>2. Macrodex 540 ml × 2</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>3. Subcutaneous heparin 5,000 unit vial b.d. × 7 days</td>
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(2) We badly need a simple method of detecting those particularly at risk. It would be helpful, for instance, if one could measure two or three elements in the blood before operation and then calculate an “index of susceptibility”. Susceptible people could then be monitored by a “progress meter”, whatever form that might take.

(3) We have to find out more about the indications for each of the three current methods of prevention that we now have.

(4) We require a much simpler method of diagnosis. The fibrinogen technique is expensive in time and materials. It is an excellent research tool but is too complicated for use in every hospital. Detection by a Doppler machine is usually too late; we want an early warning system.

(5) Perhaps, more than anything else, we need a good sieve to separate the wheat from the chaff in current publications, which are running at 100 or more a year. Through these meshes anyone can pass the valueless reports and retain the important for further examination. For instance, in reading of a controlled clinical trial between two treatments, we want to know:

Were the patients in the two groups comparable? (Editors of journals often don't like printing such trivia.)

Was the trial run concurrently? (Several reported trials were not!)

Was it a continuous trial?

How was bias eliminated?

Unfortunately, the literature does not answer these questions in a great many instances. Perhaps the information was available, but not printed. Who knows? In future, editors of journals will have to
impose supervision and codes of compliance (which some do already) if the number of publications is not to exceed the annual toll of victims of DVT.

CONCLUSIONS

There are some people who think that partisan attitudes towards the best method of preventing DVT are wrong. We disagree. The man who promotes a particular technique or method will work hard to support his view, and in this way new information accrues and in the end we all gain. True, we do need to know which is the best method of prevention in a particular situation, but, as stated at the beginning, the very fact that we have a choice is encouraging.

Everyone's views on venous thrombosis have changed radically in recent years. Rather than being a rare condition, occurring in about 5% of patients at about the 7th day after surgery, we now know it to be the common response to surgery in many patients, and occurring during the surgical operation; patients differ only in the degree of thrombus growth and extension. Certainly, the process can be controlled and limited by the prophylactic measures mentioned in this paper, but whether drugs such as subcutaneous heparin, or mechanical methods such as intermittent pneumatic compression are used, there seems to be a hard core of patients (about 10%) who, despite prophylactic measures, form isotopically detectable thrombi. It may be just these patients who inevitably go on to produce clinical pulmonary emboli. Since there is a large population with subclinical deep vein thrombi, it is probable that there is an equally large population of patients with subclinical pulmonary embolii (after surgical operation), but whether they are important is not known. While the widespread introduction of present known prophylactic measures might be expected to reduce the prevalence of late venous and even pulmonary thrombus growth and extension. Certainly, the process can be controlled and limited by the prophylactic measures mentioned in this paper, but whether drugs such as subcutaneous heparin, or mechanical methods such as intermittent pneumatic compression are used, there seems to be a hard core of patients (about 10%) who, despite prophylactic measures, form isotopically detectable thrombi. It may be just these patients who inevitably go on to produce clinical pulmonary emboli. Since there is a large population with subclinical deep vein thrombi, it is probable that there is an equally large population of patients with subclinical pulmonary embolii (after surgical operation), but whether they are important is not known. While the widespread introduction of present known prophylactic measures might be expected to reduce the prevalence of late venous and even pulmonary disease, there is still little evidence that they reduce the incidence of fatal pulmonary embolism. Clearly, much more work is required.

REFERENCES


PREVENTION OF DEEP VEIN THROMBOSIS


