It is only in the past 10 years that clinical studies have suggested that anaesthesia may influence the incidence of deep venous thrombosis (DVT) and also, possibly, pulmonary thromboembolism (PTE). Much of the evidence is far from conclusive, but work on the possible mechanisms of the effects of anaesthetic techniques and drugs has shown some fascinating and often entirely unexpected phenomena.

The method of detection of DVT is crucial to the reliability of the results; the “gold standard” is ascending venography or phlebography [1]. This is highly accurate and reliable, but too invasive, expensive and time consuming for routine clinical use. The fibrinogen uptake test (FUT) uses radio-labelled fibrinogen which is injected before operation and a scan is used non-invasively to detect incorporation of fibrinogen into newly formed thrombus. Unfortunately, while this is accurate for clots below mid thigh, in hip surgery it is associated with a false positive rate of more than 30% [2]. This reduces its role to that of a screening technique. The risk of transmission of hepatitis B is a further disadvantage. In addition, it is of little use for detection of existing thrombi. Detection of DVT by clinical signs is so unreliable as to have no place in research [1].

Not surprisingly, workers in the field have chosen groups of patients at high risk of DVT and PTE, mainly those undergoing surgery for hip replacement and repair of hip fracture. All studies which have reported a difference in incidence of DVT with anaesthetic technique have compared extradural or subarachnoid block (SAB) with general anaesthesia (GA). In 1980, Thorburn, Loudon and Vallance [3] compared the incidence of DVT in patients after hip replacement. Fifty-three per cent of 47 patients in the GA group had DVT, compared with 29% of 38 patients who had SAB (P < 0.05). Patients were considered to have DVT only when clots were found by both FUT and venography. This study was not stated to have been randomized.

Modig [4, 5] has studied extensively patients having hip replacement, comparing the incidence of DVT and PTE (using perfusion lung scan) after GA with that after extradural block continued for 24 h. In both his major studies, Modig did not report the total DVT incidence, but he subdivided the incidence of thrombi into popliteal and femoral vs calf and thigh in the 1983 study [4], and thigh vs thigh and calf in the 1986 study [5]. In every case the incidence was significantly smaller in the extradural groups. Modig used venography 14 days before and 11 days after surgery. Coincidentally, in both studies, the incidence of PTE was shown by perfusion lung scan to be 33% after GA and 10% after extradural block. There were 60 patients in the 1983 study and 94 in the 1986 study. Presumably, even larger numbers would yield a conclusive result, but this author’s verdict on these DVT results must be “highly suggestive but not proven”.

Two studies have compared the incidence of DVT after repair of hip fracture under SAB or GA [6, 7]. Despite using completely different methods of detection, the results were almost identical. The study using FUT [6] found 76% of the GA group (n = 37) to have DVT, compared with 46% of the SAB group (n = 37). Venography was used in the other study [7] and showed DVT in 76% of the GA group (n = 21) and 40% in the SAB group (n = 20). Both of these results are statistically significant. It is an enigma that the FUT results should be almost identical to the venogram results, despite the above comments on FUT.

A study by Hendolin, Mattila and Poikolainen [8] comparing extradural block and GA for incidence of DVT in open prostatectomy should be discounted, as a significant reduction in DVT in the extradural group was shown by FUT but
not by venography; this demonstrates that the FUT had a false positive rate of just over 30%.

The sparse number of positive studies is expanded significantly by the study reported in this issue by Jørgensen and colleagues [9], of patients undergoing knee replacement. DVT incidence (by venography) was significantly smaller in the extradural group; 18%, compared with 59% in the GA group. Two aspects of this excellent study are unique in the area of anaesthesia and DVT. First, the use of a tourniquet leading to total intraoperative stasis and thus denying the assumed intraoperative advantage of extradural block in decreasing stasis. Second, the prolongation of analgesia with low dose bupivacaine for 3 days in the majority of patients. All patients wore graded compression stockings.

Studies yielding negative results may be supremely valuable in many ways. Those comparing the incidence of DVT where thoracic as opposed to lumbar extradural analgesia was used have shown no effect on incidence of DVT [10, 11]. It is also interesting that a study by Fredin and Rosberg [12] found that when all patients received dextran there was no difference in DVT incidence after hip replacement under either extradural or GA. However, the incidence was approximately 45% overall, which is almost that which one would expect in a GA group with no prophylaxis.

Summarizing the clinical evidence, it would seem that SAB is associated with a reduction in DVT in hip replacement and hip fracture repair, but that the evidence for an effect of extradural block in these procedures, while consistently suggestive, is not yet conclusive. Extradural block in knee replacement is, however, associated with a reduced incidence of total DVT.

General anaesthesia has been known for many years to reduce lower limb blood flow by about 50% [13, 14]. However, although in theory positive pressure ventilation should worsen the situation by further impeding venous return, this has not been shown to increase either incidence of DVT [15] or overall mortality [16].

Lumbar (but not thoracic) extradural and subarachnoid block produce vasodilatation of the lower limbs. Modig [17] has shown increased arterial inflow and venous emptying rate associated with extradural block. It is likely that not only vasodilatation but also a reduction in blood viscosity are important in this situation. Patients with SAB or extradural block are commonly given a fluid load, reducing PCV and thus reducing viscosity. Vasodilatation, by decreasing intravascular hydrostatic pressure, further reduces viscosity. SAB has been shown [18] to reduce viscosity still further by increasing the deformability of red cells, white cells, or both. General anaesthesia, however, decreases red cell deformability in vitro, and halothane in vitro does so in a dose dependent manner. An explanation for these changes has not yet been determined.

Modig and colleagues [19] have also shown that extradural block is associated with significantly less inhibition of fibrinolysis than occurs after GA, associated with an increase in concentration of plasminogen activators. In addition, activation of factor VIII was significantly less after extradural compared with GA.

It may be that local anaesthetic agents themselves are important in mediating a prophylactic effect. Cooke and colleagues [20] infused lignocaine 2 mg min⁻¹ for 6 days to patients having hip replacement. No patient developed DVT in this group by 7 days after surgery. By 14 days, only 14% had DVT, compared with 78% in the control group. This extraordinary study surely merits confirmation.

Local anaesthetic agents are known to inhibit platelet adhesion [21], aggregation and release [22], leucocyte migration and aggregation [23], and lignocaine causes a small reduction in blood viscosity [24]. At first sight, the study in this issue [9] appears to cast doubt on the value of intraoperative improvement in blood flow as an important mechanism of prevention of DVT, as all patients had tourniquets. However, tourniquets have been shown not to affect risk of DVT [25] and indeed promote release of plasminogen activators, albeit lasting only for a short time after deflation of the cuff. The prolonged extradural analgesia in this study and in that of Modig and colleagues [19] may be important in reducing DVT risk.

Methods of reducing DVT abound, but only one—full preoperative anticoagulation with phenindione [26] (a warfarin-like compound)—has been shown to reduce overall mortality. Where does regional analgesia stand in this respect? As far as its effect on mortality in hip replacement is concerned, we do not know. A very large study indeed would be needed, as mortality is around 1.6% [27]. In patients with fractured hips, a reduction in early postoperative mortality associated with SAB has been shown by several studies [28–30] and the time course is consistent.
with a reduction in thromboembolic events. However long-term outcome is unaffected [29–31].

Other questions also remain unanswered. Should we use SAB or extradural analgesia in patients receiving low-dose heparin or those receiving aspirin or other anti-platelet agents? If we do, what degree of haematological investigation is sufficient?

Perhaps the topic could be summed up by the depressingly appropriate quotation of Mitchell [32]: “What we have is not what we want; what we want is not what we need; what we need is not what we can obtain.”

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REFERENCES


BRITISH JOURNAL OF ANAESTHESIA

