Statistical evaluation of trials is usually based on the testing of the null hypothesis; the effects of an intervention in relation to the measured endpoint can be interpreted as "probably beneficial," "no statistically discernible effect," or "probably harmful." The truly negative results would be in the third category, but this category is usually lumped with the more common middle one, which contains large numbers of trials which are simply too small to detect a modest benefit. Hence the current vogue for pooling the results of studies. Hence also the logical absurdity that by adding up the results of a series of "negative" trials one not infrequently comes up with a "positive" result. In such cases the results of most of the trials were not negative but the outcome of each one, taken alone, was indistinguishable from zero because the confidence limits (Dr Stuart Pocock, 5 January, p 41) included zero. It is time for a change in our shorthand way of describing results to one more consistent with statistical interpretation. Even a tripartite classification may be unjust to studies close to an arbitrary cut off point at a p value, but "null" or "zero" result would make more arithmetical sense than "negative."

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Circadian changes in anticoagulant effect of heparin infused at a constant rate

SIR,—The study of Dr H A Decousus and colleagues (2 February, p 341) seems to confirm the results we reported at the Eighth International Congress on Thrombosis (Istanbul, June 1984) about circadian variations of plasma heparin activity during low dose heparin treatment.

Using coagulation factor Xa inhibition assay we measured, every two hours for 24 hours, plasma heparin activity in 13 patients treated by low doses of calcium heparin to prevent postoperative deep vein thrombosis. We found the same mean circadian variations as Dr Decousus and colleagues, but with individual aspects that allow us to interpret our findings in a rather different way.

Our patients, all in the late postoperative period after intestinal surgery, received calcium heparin 250 IU/kg/24 h in three subcutaneous injections (at 1800, 0200, 1000) according to the method of Kakkar *et al.*[1] They were all resting in bed, taking meals at fixed times (0700, 1200, and 1900), and received no oral anticoagulants, antiplatelet drugs, dextran, or any other treatment. Venous blood was taken at 2400 and then every two hours for 24 hours. Blood withdrawal and preservation were identical with the methods used by Dr Decousus and colleagues. The plasma samples were assayed for activated partial thromboplastin time, fibrinogen antithrombin III activity, and factor Xa inhibition assay, according to the method of Yin *et al.*[2]

In these 13 patients we detected a mean circadian rhythm for factor Xa inhibition assay values expressed as a percentage of an individual 24 hour mean. Maximum values were achieved in the first part of the night, more precisely during the first two hours of sleep (2200 to 2400), while the minimum values were early in the morning (0400). Differences between night and morning values reached almost 45% of the mean. In a given patient, for example, we found morning values to be less than 0·1 IU/ml plasma (no antithrombotic effect of heparin), diurnal values to be 0·1-0·2 IU/ml (correct antithrombotic effect of heparin), and night values to be over 0·2 IU/ml (anticoagulant effect of heparin, correlated to increase in activated partial thromboplastin time, and so to bleeding risk).

However, some of the patients went to sleep during the day; their factor Xa inhibition assay values immediately increased in the same way as described during their night sleep. More precisely, such correlation between the beginning of sleep and increase in plasma heparin activity was found in each individual curve whatever the hour at which the subject began to sleep, day or night. In other words each time we found plasma heparin activity to be raised the patient had fallen asleep.

We believe that these sleep dependent variations could explain the incidence of bleeding and perhaps failures in prophylactic low dose heparin treatment.

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1 Kakkar VV, Field ES, Nicolaides AN, Flute PT, Wessler S, Yin ET. Low doses of heparin in prevention of deep vein thrombosis. *Lancet* 1971;ii: 669-71.
2 Yin ET, Wessler S, Butler J. Plasma heparin: a unique, submicrogram sensitive assay. *J Lab Med* 1973; **81**:298-310.

General versus spinal anaesthesia

SIR,—The sideswipe aimed by Drs Peter J Mackenzie and Hugh Y Wishart at spinal anaesthesia (16 March, p 856) may satisfy those anaesthetists who have never acquired competence in that art and may indeed reflect a prevailing British point of view, but it will surely provoke amusement in other centres.

In the Städtischen Kliniken, Osnabrück, a medium sized West German hospital, some 17% of all operations requiring an anaesthetic are performed under spinal anaesthesia (1192 out of 7022 anaesthetics in 1983). Although in this centre I would on occasions give as many spinal anaesthetics in a single day as I did during three years in Oxford, I cannot recall a single case in seven years of a patient being admitted to intensive care for the management of complications of a spinal anaesthetic. In Derby, on the other hand, we have admitted at least four patients since May 1984 to the intensive care unit solely because of complications related to a general anaesthetic, two of which had been administered by holders of the FFARCS diploma, after operations that could have been performed under spinal anaesthesia. Though all the patients survived their hospital stay, this represents a totally unacceptable morbidity.

Space prevents me from replying in detail to their comments on confusional states and chest complications, though I would note that in disallowing Professor Sikorski's references to better fibrinolytic function and fewer thromboembolic problems after epidural anaesthesia, they disqualify themselves from citing evidence related to bronchopneumonia after inguinal hernia repairs.

Their final paragraph would read better if the terms spinal and general anaesthesia were interchanged: "While a useful technique, general anaesthesia is potentially dangerous in the hands of inexperienced anaesthetists and for inappropriate patients. . . ." The evidence is less than convincing that general anaesthesia offers any advantage at all over spinal anaesthesia for the repair of fractured neck of femur. It is more expensive and inherently prone to more complications. It is high time that all anaesthetists were trained to the same extent in giving spinal anaesthetics as they are in giving general anaesthetics, to avoid this peculiar prejudice in the choice of technique and to spare their patients any further risks.

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Syringes for diabetics

SIR,—We welcomed the leading article by Dr Arnold Bloom (9 March, p 727) in which he asked (yet again) that the DHSS reconsider its position on the reuse of plastic syringes. As in many other units, it has been our policy to encourage diabetics to continue to use their fixed needle plastic syringes until the needle becomes blunt or until the markings on the barrel become indistinct. In pursuing this practice at the City Hospital for over five years and for an estimated 1 400 000 outpatient injections we are unaware of any instances of injection site infection. Moreover, in the changeover of 3000 insulin treated diabetics to U100 insulin the coordinating hospital physicians in Nottingham opted to disregard DHSS advice in not prescribing two new glass syringes and spiritproof case to every patient. In this way they saved over £30 000 in a single year. However, we wanted to obtain further evidence of the safety of our practice by performing a detailed prospective microbiological survey of the risk of contamination of syringes, needles, or insulin that may result from this policy. In particular we sought to answer the criticism made by Allwood[1] of the work by Collins and colleagues[2] that the preservative 0·1% wt/vol methyl-p-hydroxybenzoate used in certain insulin preparations may permit the growth of bacteria, including *Staphylococcus aureus*.

Eleven insulin treated diabetics aged 12-62 years (mean 35 years) were studied over four weeks. They all used highly purified porcine insulins; six used a total of nine phials containing methyl-p-hydroxybenzoate as preservative. Their usual injection practices were noted and minimally modified. Six kept neither syringe nor insulin refrigerated. Fresh phial(s) and syringes were provided at the start of the study period. Patients were seen weekly, at which time their syringe was changed and the following microbiological samples collected: (*a*) impression cultures of the phial cap; (*b*) skin injection site(s); (*c*) 0·1 ml of insulin; (*d*) a nutrient broth flush of the syringe; and (*e*) a roll culture of the needle. On entry nose swabs and impression cultures of the fingers were also taken to establish the normal flora. All samples were cultured aerobically on blood agar and all isolates speciated. In addition phage typing and biotyping of all *Staph epidermidis* isolates were performed and antibiograms determined since this was the predominant isolate.

A total of 120 skin samples were collected in addition to 222 cultures from the insulin phials, syringes, and needles. As expected *Staph epidermidis* was the most common isolate from the skin sources and was occasionally present in low counts on the external surface of the phial caps although these isolates were usually of a dissimilar type. From the total of 222 other cultures *Staph epidermidis* was isolated from both the syringe wash and insulin on a single occasion, when only four colony forming