The observed sex difference suggests the importance of a complex sociocultural variable in the optimum selection of female athletic and sporting talent. It appears that other countries are failing to exploit the sporting potentialities of their women in the way that East Germany has done.

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Anti-inflammatory drugs for rheumatoid arthritis

SIR,—Clinical judgment should be based on fact rather than fantasy. This thought is provoked by the paper by Dr E C Huskisson and others (1 May, p 1048) but more particularly by the recent advert for Naprosyn which appeared as a pull-out supplement in your Journal (3 July). We would dispute the opening premise of this article, namely, that aspirin is no longer treatment of choice in rheumatoid arthritis. Out of the three references for this statement two were by Huskisson himself.

However, our major objections to this paper are not based on a matter of opinion but the following facts: (1) The tablets used were not matched, naproxen being different from the other three. (2) There are no baseline data and, moreover, no placebo group, which is so important in a short-term study. (3) There is the introduction of a new toxicity index which is neither defined nor evaluated. (4) The conclusions drawn do not appear to be justified from the data presented—namely, fenpropfen reduced morning stiffness and joint size better than the other agents, suggesting that fenpropfen was more anti-inflammatory in this study.

We believe that in this paper there are too few facts for too many conclusions and that great care should be taken in its interpretation.

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* * * We sent a copy of the above letter to Dr Huskisson and his colleagues, whose reply is printed below.—ED, *BMJ*.

SIR,—It was not our intention to present evidence that aspirin is no longer the first line of treatment for rheumatoid arthritis. Our introduction merely intended to say that if this were true it would be nice to know which of the propionic acid derivatives might have taken its place. We support the desire for fact in preference to fantasy. The facts put forward in our paper were that two of the drugs tested were more effective than the other two and that two more produced side effects. These facts were supported by statistical significance levels which are unusually high because of the large number of patients treated.

We are not impressed by the specific objections: (1) None of the tablets were matched but all were unrecognisable. We know of no evidence that colour affects the performance

of active analgesics, and for placebo, yellow is the worst colour.¹ Problems of bioavailability prevented us from using identical formulation. (2) Baseline data were collected and are available. However, the principle of a crossover trial is that a patient's state at the end of one treatment period is compared with his state at the end of another, and we cannot see the value of baseline data. Patients in trials always improve, and one could not use this improvement as evidence that the new treatment was better than the old. We did not set out to show that propionic acid derivatives were effective, which has been done, and didn't therefore need placebo. We set out only to compare the drugs. (3) Dr H Berry may remember the study of which he was a co-author,² in which side-effect scores were first used as a measure of toxicity. (4) The differences between fenpropfen and naproxen in morning stiffness and joint size were not statistically significant and there was no justification for the claim that its anti-inflammatory potency was greater.

We have examined the advertisement for Naprosyn and find the facts in it to be accurate. We regret only the omission of what for us was the most important conclusion of the study. Our trial showed for the first time that there is one particular drug which is right for one particular patient, and Dr Clarke and his colleagues may be interested to hear that for this reason some of our patients still take . . . aspirin.

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¹ Huskisson, E C, *British Medical Journal*, 1974, 4, 196.
² Huskisson, E C, et al, *British Medical Journal*, 1974, 1, 176.

Confidence limits

SIR,—In his article "Statistics at Square One, XI—The *t* tests" Dr T D V Swinscow (31 July, p 291) falls into a trap which many of us are at pains to warn our students about. After finding the 95% confidence limits for a population mean to be 120.97 and 109.03 he writes, "We therefore conclude that the chance of the population mean lying below 109.03 or above 120.97 is only 5% or less." The "or less" is, on any interpretation, redundant and misleading, but the major point is that the standard theory of confidence limits does not allow this conclusion. The correct interpretation is that if the unknown population mean were to lie below 109.03 or above 120.97 then, on his data, an event with a chance of only 5% must have happened: either the mean lies between those limits, or something rather improbable has happened, and we usually prefer to assume the former.

In fact there is a very ingenious argument, known as the fiducial argument, advanced by Sir Ronald Fisher from 1930 onwards, which purports to justify statements of the kind made by Dr Swinscow. But it is not generally accepted by statisticians, least of all those who advocate confidence limits. Oddly enough its origins can be traced back to the very paper by "Student" that Dr Swinscow quotes, but

in general it is prudent to avoid making any statement about the probability of the population mean lying in an interval and to warn students away from it. There is deep water all round.

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* * * Dr Swinscow writes: "Dr Edwards is correct in his interpretation. The lapse is theoretical rather than practical in its implications but will be repaired when the article is revised for publication in book form later this year. I am grateful for the correction—italics and all."—ED, *BMJ*.

Accidental injection of Immobilon

SIR,—A few weeks ago the product licence for Immobilon—a potent veterinary neuroleptanalgesic combination of the opiate etorphine hydrochloride and a phenothiazine, acepromazine or methotrimeprazine—was suspended on the advice of the Veterinary Products Committee following the death, due to accidental self-injection of Immobilon, of a member of the veterinary profession.¹ In this case the recommended accident procedure, which involves the injection of a narcotic antagonist, was not followed. In other cases when accidental injection has been promptly treated by injection of a suitable antagonist recovery has been uneventful.²⁻⁵

After consideration of the circumstances of this accident and the evidence on the use of Immobilon during the past six years the Veterinary Products Committee has now recommended the reinstatement of the product licence and the recommendations for the treatment of accidental injection have been revised. The product is now again available.

It is possible that doctors may be called to treat cases of accidental administration of Immobilon and it is therefore essential that all doctors are aware of the correct treatment and have the appropriate antagonist to hand. The revised procedure recommends the use of naloxone but allows for the emergency use of nalorphine and Revivon (diprenorphine hydrochloride), the veterinary antagonist which always accompanies Immobilon. The following accident procedure appears on the reverse of the pack and also in the product literature.

ACCIDENT PROCEDURE—IMMOBILON

Immobilon is a very potent neuroleptanalgesic with a high toxicity in man. In the event of accidental administration to man, or if there is a possibility that absorption may have occurred, the procedure given below should be adopted. Symptoms caused by Immobilon are dizziness, nausea, and pin-point pupils, followed by respiratory depression, fall in blood pressure, and cyanosis. In extreme cases loss of consciousness and cardiac arrest occur.

SUMMON MEDICAL HELP IMMEDIATELY

If there is any danger that absorption of Immobilon may have occurred INJECT A REVERSING AGENT IMMEDIATELY.

(1) *Spillage on skin or splashing of eyes.* Wash immediately with copious quantities of water.

(2) *Accidental injection.* Inject one of the following reversing agents: (i) 1 ml Narcan (0.4 mg naloxone) intravenously or intramuscularly. Repeat at 2–3-min intervals if symptoms are not reversed. (ii) If Narcan is not available inject 1 ml Lethidrone (10 mg nalorphine) intravenously or intramuscularly. Repeat at 5-min intervals if necessary up to a total of 4 ml. There are Lethidrone formulations