interaction between oral contraceptives and other drugs

SrN,—I should like to make some comments concerning the paper by Drs Janet F Bacon and Gillian M Shenefield (2 February, p 293). They have suggested that the decreased blood levels of steroids associated with coadministration of rifampicin and oral contraceptives is due to an interference in the enterohepatic circulation of steroids. However, administration of rifampicin causes proliferation of the smooth endoplasmic reticulum of the hepatocytes and inducement of drug-metabolising enzyme systems in the liver (the cytochrome P450 content of the liver is increased). Steroid hormones are eliminated mainly by metabolism in the liver. Hence the hepatic clearance (or rate of removal from the body) of steroid hormones is increased when these are given in conjunction with enzyme-inducing agents such as rifampicin (and other barbiturates) and theophyllin.\(^1\) An increase in hepatic clearance results in decreased plasma levels of the drug. This mechanism of drug interaction is a common one and may explain the reported results.

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Multiple sclerosis: what can and cannot be done

SrN,—The difference between the poor result (75% success) obtained with the erythrocyte electrophoretic mobility (E-UFA) test\(^1\) in Göttingen referred to by Drs S Poser and W Poser (19 January, p 184) in their comments on our paper (25 December, p 1901) and the excellent results of coded trials in England,\(^2\) Italy,\(^3\) and America\(^4\) led us to conclude that the difference must lie in the biological material. Since many German patients with multiple sclerosis (and most errors were among this group) were currently, or recently had been, under heavy medication with adrenocorticotropic hormone (ACTH), as well as other drugs, while we ourselves always worked with cases currently free from corticosteroid treatment, we made a specific study of the effect of ACTH on the E-UFA test result. This has shown that a positive result in multiple sclerosis is converted into a negative one after a few days\(^5\) treatment and that this false result persists for about three weeks after cessation of the steroid course. On the other hand, a patient not having multiple sclerosis initially giving a negative result with the E-UFA test converts to a positive one, which again persists for three weeks.\(^6\) This phenomenon, incidentally, affords an explanation for the very short life (5-10 minutes) of the pseudopods in the blood of patients being given rapid adsortion on to the red blood cell surface. Early or untreated cases were not available in Göttingen, nor were mothers for confirmatory testing.

The Posers alone advance Thompson's heuristic proposition\(^7\) to the status of a "proved fact." Our own results can only be interpreted as supporting it. Dr J H D Millar (19 January, p 194) points out that the value of y-linolenate is only on the supposition, now discarded,\(^8\) of its immunosuppressive activity—is not yet substantiated. There is no doubt that y-linolenate alters the character of the red blood cell membrane,\(^9\) and the original anomaly is not due to a plasma factor.\(^10\) The positive value of the E-UFA test lies largely in early diagnosis, and above all in prophylaxis\(^11\) and the possibility of setting up a controlled trial among children single out as "multiple sclerosis candidates" before myelin is fully laid down. Encouraged by the confirmations cited above, we formally propose that a positive E-UFA test be added to the Schumacher criteria for diagnosis of multiple sclerosis.

The Posers pass over the critical analysis by Seaman et al\(^12\) of recorded false results and choose to ignore Claude Bernard's warning\(^13\) about the importance of all the details of investigative procedures. They take a very selective and unsophisticated view of myelin constitution, neglecting all-important steric considerations. So far as the inability of Seaman et al to pick up a few patients with (unspecified) "minimal neurological findings" is concerned, note should be taken of Fog's opinion\(^14\) that "the percentage of false diagnosis of multiple sclerosis is about 20% ... and in both directions," and the similar uncertainties expressed by Bauer at the same symposium. Dr Millar was present at this symposium and acknowledged his assent. We too have patients referred by both general practitioners and consultants who cannot make up their minds early in the disease (and sometimes late).

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8 Joyce G, Gutenberg 1979;ii:1012-3.

Treatment of meningitis

SrN,—Dr P J Geiseler (23 February, p 566) in making a case against the administration of antibiotics before lumbar puncture to patients with clinically diagnosed meningitis quotes his review\(^1\) of 1316 cases of community-acquired purulent meningitis. This is a most impressive number of cases and the study could yield some worthwhile information. As his paper is in press, perhaps Dr Geiseler would be good enough to say whether in his study he looked at the effects of corticosteroids on the survival rate in bacterial meningitis. It would be very interesting and most useful to know what percentage in his study were treated with corticosteroids, and at what dosage. The percentage of the 103 fatal cases had been given corticosteroids before death.

Some clinicians are not convinced that any advantage from the administration of corticosteroids in severe life-threatening meningitis has been demonstrated\(^2\) and Dr Geiseler's review might provide that evidence.

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*We sent a copy of this letter to Dr Geiseler, whose reply is printed below.—Ed, BMJ.*

SrN,—In response to Dr Cargill's inquiry, we did not study the effects of corticosteroids on survival in our review of 1316 cases of community-acquired bacterial meningitis. It would have required a controlled study, which was not performed.