elevation of serum transaminases (aspartate aminotransferase (SGOT) and alanine aminotransferase (SGPT)) in patients taking propranolol has been reported by Stephen,[5] but in some of his cases other factors could have been responsbile. We therefore consider it important to record our observations in a woman aged 69 years receiving propranolol 80 mg daily.

She has been hypertensive for four years and the diagnosis of phaeochromocytoma was made on the basis of a rise in urinary catecholamine excretion. She was treated first with phenoxybenzamine 30 mg daily for four weeks; then propranolol was added, first 40 mg daily and after two weeks 80 mg daily. She had previously been exposed to propranolol 40 mg daily for one week at another hospital without untoward effect. When receiving only digoxin (because of an episode of atrial flutter) and hydrochlorothiazide (for hypertension) with potassium supplements, transaminases, lactic dehydrogenase (LDH), and alkaline phosphatase were normal, and the addition of phenoxybenzamine 30 mg daily for 3 weeks produced no change. Retesting four weeks after the addition of propranolol showed a rise in these enzymes in two samples drawn on different days (though one LDH sample was within normal limits): SGOT 275 and 275 I.U., LDH 395 and 185 I.U., alkaline phosphatase 275 and 300 I.U. On discontinuing propranolol while continuing other medications serum enzymes returned to normal.

She had longstanding minimal ankle oedema, probably due to impaired venous drainage, and there were no other features of heart failure. Moreover no other evidence of impairment of liver function was detected, including tests for Australia antigen before, during, or after the period of raised enzymes.

The temporal relationship of these abnormalities to propranolol is very suggestive of a causal effect. We did not feel justified in re-exposing her to the drug to prove this, as the phaeochromocytoma has now been removed and she has no further need for propranolol.

Since propranolol is a very useful drug in several conditions and this side effect appears to be uncommon and reversible we do not recommend that its use should be restricted because of it. Nevertheless, it would seem prudent to check serum enzymes from time to time during therapy.—We are, etc.,

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Overdosage of Tetracosactrin in Rheumatoid Arthritis

SIR,—Dr. F. Dudley Hart and others (17 April, p. 165) draw attention to the problem of overdosage of synthetic corticotrophin, tetracosactrin. They state that the preparation they use contains 1 mg of tetracosactrin in 1 ml of a zinc phosphate complex. Recommending smaller doses they end their letter with the plea "the availability of a more dilute solution would make the injection of these small doses somewhat easier".

Cortrosyn Depot is presented in the more dilute solution of 0·5 mg tetracosactrin in 1 ml of zinc salt complex, and we find that it is used by those who, like the Westminster group, require to use doses that are regularly below 0·5 mg tetracosactrin.—I am, etc.,

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Gold for Rheumatoid Arthritis

SIR,—I have read with interest your leading article (27 February, p. 471) and also Dr. H. J. A. Richards's letter (p. 504). In both instances there would appear to be an important omission—namely, the time factor.

For a period of 18 years I had occasion to treat a considerable number of patients with gold, and there were never (and I would stress the word never) any significant side effects. This could, of course, be relative to the size of the dose, but I ascribe it to the fact that after each series of 12 weekly doses the patient was required to have eight weeks rest from the treatment. For a time blood and urine tests were made, but the former were ultimately omitted as being unnecessary.—I am, etc.,

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Dyspareunia

SIR,—In Mr. W. T. Fullerton's article (3 April, p. 31) on "Dyspareunia" although infection was mentioned as being a cause of this disorder I thought its importance was underemphasized. In younger women, especially in large cities, surely such conditions as trichomoniasis, candidiasis, and herpes labialis are often more important causes of dyspareunia than less frequently seen pelvic abnormalities.

The patient with trichomoniasis often has an exquisitely tender vagina and it is quite obvious how painful this. Herpes labialis caused by herpes virus hominis must be a cause of dyspareunia.

The average specimen of vaginal discharge taken in a surgery and sent for laboratory examination, I submit, is a useless investigation unless taken under very careful conditions. In most cases the possibility of gonococcal infection will be overlooked—and poorly treated—with disastrous medical and legal complications later on.—I am, etc.,

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SIR,—Mr. W. J. Fullerton (3 April, p. 31) is to be congratulated on his excellent and emphatic article on dyspareunia in gynaecology in general practice. Many practitioners are not aware of the problems associated with "failure of lubrication." However, in addition there may be a iatrogenic factor brought about by the anti-oestrogenic effect of some of the oral contraceptive preparations. This is particularly prone to develop in those women whose periods tend to be scantier than most or in those whose libido is only fair. This problem especially tends to occur with the formulations containing a higher content of norethisterone and its acetate.

A doctor who is aware of this possibility might often prevent this adverse effect of hormonal contraception by a judicious choice of brand of contraceptive. This problem can also present as recurrent and intractable monilial infection. Furthermore, it would appear that the anti-oestrogenic effect of some of the progestagens in the oral contraceptives might contribute significantly to the alleged disturbances of libido per se, in addition to their "drying" effect on the vaginal secretions. Once these undesirable effects are recognized, they can be dealt with by changing the formulation to a preparation which is more oestrogenic in action or even altering the method of contraception.—I am, etc.,

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Gastrointestinal Bleeding

SIR,—Your leading article entitled "Pharmacological Control of Upper Gastrointestinal Bleeding" (13 March, p. 569) betrayed a rather naive approach to the complexities of the effects of drugs on the gastrointestinal circulation. Reliable data on man are lacking, but some indication of the problems may be gained from animal experiments. In this context studies on the dogs[1] are of questionable value, since the easily-induced constriction of the canine hepatic veins produces responses which are not analogous to those in the human.[2] For this reason, the splanchnic vascular bed of the cat has received intensive investigation. These studies indicate several objections to the infusion of adrenaline and propranolol after haemorrhage from the gastrointestinal tract even if one makes the big assumption that intestinal vasoconstriction reduces bleeding from a ruptured artery.

Stimulation of the alpha-adrenergic receptors in the intestinal vascular bed causes a brief vasoconstriction followed by autoregulatory escape during which intestinal flow recovers to approximately the pre-infusion level.[3-5] This escape occurs within 1-2 minutes and is not blocked by propranolol.[6] Adrenaline itself causes dilatation of the intestinal and splenic arterioles,[7-8] and if the beta-receptors were not adequately blocked by the propranolol a sizeable vasodilatation would occur. Full blockade of the intestinal beta-receptors must inevitably be accompanied by more wide-spread effects and, in particular, by an impaired cardiac response to haemorrhage.

Passage of the mixture into the portal blood would probably cause an elevation of portal venous pressure by constriction of the portal radicles and a reduction in hepatic arterial flow.[2 9] Vasopressin, on the other hand, causes maintained constriction of the intestinal and splenic arterioles and no constriction or even a dilatation of the hepatic arterial bed.[5 8 10] Preservation of flow through the hepatic artery may help to prevent some of the metabolic consequences of haemorrhage.

In conclusion, it appears from animal experiments that local infusion of adrenaline and propranolol would produce a variety of