fibrosing alveolitis"[8] with the addition of giant cells. In immune disease stimulation and later failure of affected endocrines may be a by-product of the antibody response.

Preliminary studies by me of three thyroid patients showed reversal of hyperthyroidism on 15 mg daily of prednisone. The first case, with sarcoid hyperthyroidism, remains euthyroid three months after prednisone was withdrawn. Massive doses of steroids are not always necessary to "block" the thyroid overaction. Hyperthyroidism complicated by temporary myasthenia is rare, but early investigation is important because it may be caused by sarcoidosis. Steroid treatment of myasthenia gravis may be more effective if started sooner.—I am, etc.,

G. A. MACGREGOR

Chilworth, Surrey

1 Goldstein, G., *Lancet*, 1962, **2**, 119.
2 Karlish, A. J., and MacGregor, G. A., *Lancet*, 1970, **2**, 330.
3 Mitchell, D. N., and Rees, R. J. W., *Lancet*, 1969, **2**, 81.
4 Palmer, H. P., and Michael, I. E., *Archives of Internal Medicine*, 1965, **116**, 444.
5 Burke, J. S., Medline, N. M., and Katz, A., *Archives of Pathology*, 1969, **88**, 359.
6 MacGregor, G. A., *Lancet*, 1970, **2**, 1257.
7 Miller, W. V., Senhauser, D. A., and Martt, J. M., *Missouri Medicine*, 1966, **63**, 811.
8 Mason, A. M. S., McIllmurray, M. B., Golding, P. L., and Hughes, D. T. D., *British Medical Journal*, 1970, **4**, 596.

SIR,—As your unsigned leading articles tend to acquire the authority of holy writ I hope you will permit me to comment on your first leading article (3 April, p. 1) to correct some misunderstandings which have appeared elsewhere. You kindly refer to my paper[1] giving the first fully formulated autoimmune hypothesis but infer that this was confirmation of earlier work by demonstrating clinical relationships with other autoimmune diseases. In 1960 this was hardly possible (and Miller's paper on the thymus was still a year off). It showed that myasthenia gravis was probably a multisystem disease with some resemblances to the natural history of systemic lupus erythematosus. An autoimmune hypothesis was presented to account for this. In the next decade many of the associated conditions have subsequently been recognized as autoimmune.[2]

Reference to the original paper will show that it reported the conclusions of five years of clinical and experimental work, freely discussed in teaching and research seminars. The passing reference of Smithers,[3] a few months before final publication, to the possible implication of autoimmunity in the thymic changes of myasthenia gravis was referred to, but that paper offered no concept of the nature of the neuromuscular disorder.

It is not possible to decide whether Smithers considered that the thymic pathology was the cause or the result of autoimmune disease. This is a critical point in current thinking about myasthenia. It is unfortunate that your leading article ignored the valuable symposium at the New York Academy of Sciences in December 1970. It quotes the only group of workers supporting Goldstein's experimental work. To the longer list of negative findings[4] will be added a paper (in press) from an Australian group which includes Goldstein's original collaborator. My original hypothesis was that a breakdown of immunological tolerance resulted from a thymic disorder (genetic or acquired). The Goldstein hypothesis considers that the thymus is damaged immunologically without indicating where the primary immunological disorder may occur and the theory requires a neuromuscular blocking substance, which is against all the evidence.[5] The theory lacks the heuristic value of the original hypothesis, for which no incompatible evidence has yet been produced, as it does not predict involvement of other tissues—the very reason for conceiving an autoimmune theory.—I am, etc.,

J. A. SIMPSON

Southern General Hospital,
Glasgow, S.W.1

1 Simpson, J. A., *Scottish Medical Journal*, 1960, **5**, 419.
2 Simpson, J. A., In *Muscle Diseases*, Ed. J. N. Walton, N. Canal, and G. Scarlato, Amsterdam, Excerpta Medica, 1970, p. 14.
3 Smithers, D. W., *Journal of the Faculty of Radiologists*, 1959, **10**, 3.
4 Vetters, J. M., Simpson, J. A., and Folkarde, A., *Lancet*, 1969, **2**, 28.
5 Simpson, J. A., In *The Biological Basis of Medicine*, Vol. 3, Ed. E. E. Bittar, and N. Bittar, New York, Academic Press, 1969, p. 345.

Carcinoma in Pleomorphic Adenomas

SIR,—Pleomorphic adenomas (mixed tumours) sometimes undergo carcinomatous change; in a recent study[1] roughly half of the more malignant types of carcinoma had arisen in this way. The only known predisposing factor is a long history, the average time before the development of the carcinoma in the above series being 19 years. The risk in the individual case is impossible to determine from these figures, since the size of the population of pleomorphic adenomas from which the carcinomas developed is unknown. Nor, so far as I am aware, are there any other pertinent figures. Under these circumstances the following experience may be worthy of reporting.

I have operated on altogether eight cases of the rare dumb-bell pleomorphic adenoma of the parotid, which because of its origin deep in the gland remains latent until it attains a large size, and therefore presumably for many years. In two of these eight cases carcinoma, from which the patients subsequently died, had developed. The figures are obviously too small to serve as anything more than the roughest index of the risk of carcinomatous change in a pleomorphic adenoma left indefinitely. They may however indicate the way in which this question might be solved.—I am, etc.,

D. H. PATEY

London W.1

1 Patey, D. H., Thackray, A. C., and Keeling, D. H., *British Journal of Cancer*, 1965, **19**, 712.

Air Filtration for Asthma

SIR,—Some preliminary results of an investigation into the prevention and treatment of asthma are reported. This treatment consists of the removal from the inhaled air of pollens and mould spores to which the individual is sensitive by the simple process of filtration.

The sizes of individual fungal spores are generally in the range of 2-20 μm, although some are much larger, and pollen grains usually range from 10-50 μm. Air-conditioning has been tried in the past to treat asthma, but has usually been ineffective because the degree of filtration achieved has been inadequate. However, an effective, simple air filtration unit has now been made in Adelaide (Pureair filter). An efficacy of 99% or greater in excluding particles of 2 μm and above is claimed for this filter, and the unit is easily installed in a bedroom window. This means that while in the bedroom the patient can breathe air from which nearly all the offending allergens are removed.

This filter was originally used in 1967 by a man for his 7-year-old son, who was a chronic invalid from asthma. An improvement in the child was noticed immediately and within six months he was able to lead a normal life. Following this more filtration units were made which were then advertised commercially. Favourable reports of the use of this filter for asthma prompted me to send a questionnaire to all the 75 individuals who had bought the filter for asthma, and used it for longer than six months. Fifty-four replies—from 29 men and 25 women—were received. The majority considered that their asthma was markedly improved by using the filter, and that they were now able to lead a normal life after many years of ill-health. The patients had had chronic severe asthma for periods from three to 41 years (mean 14·5 years).

After using the filter for periods from six months to three years three patients considered that they were cured, 36 were markedly improved, 10 were slightly improved, four were unchanged, none was worse, and one did not know whether the filter had helped or not. Twelve had stopped all medication, 21 had reduced their intake of drugs, 15 were on the same therapy, and six were taking more drugs than before. Twenty-two had noticed immediate improvement in their asthma when the air filter was installed, but in others the improvement was not obvious until a varying period of anything up to six months had elapsed.

The answers to this questionnaire strongly suggest that the Pureair filter had produced considerable relief from asthma in the majority of individuals who have used it. These observations are being extended by a double-blind controlled trial of air filtration which is now in progress. It is interesting that although the improvement is often noticed immediately the air filter is installed, there is sometimes a delay before its beneficial effect is evident. This may be due to the chronically over-reactive bronchial mucosa still responding to the small amount of antigen which is not removed by filtration.

It is also interesting that although the most relief from asthma by filtration is noticed by individuals while they are in the filtered room, once improvement has started many individuals have noticed that their asthma becomes progressively less severe when away from the filtered environment. Perhaps the continuing exposure to a very much reduced dose of the relevant antigens enables the patients to develop tolerance to these antigens by the same mechanisms which apply in normal individuals.—I am, etc.,

M. A. DENBOROUGH

University of Melbourne Department of Medicine,
Royal Melbourne Hospital,
Victoria, Australia

Serum Enzymes and Propranolol

SIR,—Most studies on the use of propranolol report no effect on the levels of transaminase or alkaline phosphatase.[1-4] An

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.,

ROBERT WILKINSON
JOHN A. LUETSCHER
ROBERT H. GOLDMAN

Department of Medicine,
Stanford University School of Medicine,
Palo Alto, California, U.S.A.

1 Waal, H. I., *Clinical Pharmacology and Therapeutics*, 1966, **7**, 588.
2 Richards, F. A., *American Journal of Cardiology*, 1966, **18**, 384.
3 Richardson, D. W., Freund, J., Grear, A. S. Mauck, H. P., and Preston, L. W., *Circulation*, 1968, **37**, 534.
4 Frohlich, E. D., Tarazi, R. C., Dustan, H.P., and Page, I. H., *Circulation*, 1968, **37**, 417.
5 Stephen, S. A., *American Journal of Cardiology*, 1966, **18**, 463.

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.,

A. F. TAYLOR
Medical Director,
Organon Laboratories Ltd.
Morden, Surrey

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.,

F. E. GRAHAM-BONNALIE
Edinburgh 9

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.,

MICHAEL A. WAUGH
Department of Venereology,
West London Hospital,
London W.6

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.,

MAX ELSTEIN
University of Southampton

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