nodes. This may well link up with the work done by Hawley *et al.*² and Paile⁵ suggesting that some patients may do better because their cellular immune mechanisms are putting up resistance to the primary, and they may do well even if some metastases have reached a few local nodes.

This is an important problem, because the surgeon at laparotomy who finds some palpable nodes near a resectable gastric tumour may well decide against radical local dissection on the basis of an apparently hopeless prognosis ("glandular metastases"). My study showed that where surgeons reported "malignant glands present," the histological findings in no less than 1:3 patients were of OX or LTH status (and therefore a better prognosis). In other words, there are two reasons to continue with radical lymphatic surgery, even with palpable nodes. Firstly, they may be benign, and secondly, they may represent the minimal invasion and quite good prognosis situation. For those who can stand awful doggerel this may be summarized:

"All that bulge are not maligne,
Even be some so, do not pyne."

May I also point out the fact that early diagnosis of gastric cancer, and greatly improved results in treatment, have been taken a stage further by the use of gastric cytology, with or without fibroscope collecting methods.^{6,7}—I am, etc.,

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¹ Pygott, F., *Gut*, 1964, 5, 118.

² Hawley, P. R., Westerholm, P., Morson, B. C., *British Journal of Surgery*, 1970, 57, 877.

³ Pack, G. T., McNeer, G., *Surgery*, 1948, 24, 769.

⁴ Cantrell, E. G., *British Journal of Surgery*, 1971, 58, 384.

⁵ Paile, A., *Annales Chirurgiae et Gynaecologiae Fenniae*, 1971, 60, Suppl. 175.

⁶ Cantrell, E. G., *Quarterly Journal of Medicine*, 1971, 40, 239.

⁷ Kasugai, T., *Gastroenterology*, 1970, 58, 429.

Antileprosy Drugs

SIR,—In "Today's Drugs" (17 July, p. 174) it is mentioned that it is doubtful if psychosis can be accepted as a toxic effect of dapsone. W. H. Jopling, to whom this statement is attributed,¹ was not in on the early treatment with dapsone in which high dosage was given to large numbers.

In 1950 I was in charge of Oji River Leprosarium, Nigeria. We treated all 15,000 patients with hydnocarpus oil and scarcely ever had any mental trouble. Within six months we changed the 1,800 settlement and 8,000 of the clinic patients to dapsone. Having been warned by the initial toxicity in a much smaller series under Dr. J. Lowe at Uzuakoli receiving a dose of 300 mg/day (1,800 mg/wk), we adopted a dose of 200 mg/day (1,200 mg/wk) in the settlement and 400 mg twice weekly in the clinics. Our idea of the lower dose in the clinics together with a slower induction was to minimize the serious reactions where fewer and less skilled staff were able to cope with the consequences.

We also induced treatment more slowly than at Uzuakoli (12 weeks instead of six weeks to reach the maximum), but still we were faced with many cases of acute psychosis with violence, delusions, and visual and auditory hallucinations together with two suicides within the first few months.

Most of these were in the settlement where we had a higher dose and more rapid induction, so we soon changed our treatment to twice weekly, lowered the maximum, and induced more slowly. In addition, we were alerted to early signs of mental disturbance and took immediate action, thus reducing the rate of psychotic and other drug reactions to a much lower figure.

Dr. Jopling started treatment on much smaller numbers, used lower dosage, and increased more slowly. Modern low dosage treatment must also contribute to minimize this complication.

There was no statistically organized test but I believe the sudden outcrop of psychosis on dapsone treatment can be explained on no other hypothesis.—I am, etc.,

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Reepham,
Norfolk

¹ Jopling, W. H., *Handbook of Leprosy*, London, Heinemann, 1971.

Blood Flow in Ischaemic Feet

SIR,—We would like to respond to one or two points which arise in the letter from Dr. V. C. Roberts and others (9 October, p. 114) commenting on our recently published findings (24 July, p. 220).

They would doubtless agree that there is not necessarily a discrepancy between their observations in atherosclerotic subjects of a lower than normal total limb perfusion as measured in the great vessels and our observations of a higher than normal resting foot blood flow. There may well be a fundamental difference between proximal and peripheral perfusion under these pathological conditions. Our findings and those of Yao¹ indicate that there is a low systolic blood pressure and peripheral resistance in apparently ischaemic feet and therefore the level of femoral artery or vein blood flow is not necessarily a reliable indication of the level of foot blood flow in atherosclerotic subjects. There may, of course, be a simpler explanation for the difference between our findings and those of Dr. Roberts. Our measurements were made in controlled resting conditions where the normal exposed foot vasoconstricts in response to room temperature around 22°C. There is no information about environmental conditions in Dr. Roberts's letter and, therefore, it is difficult to comment on the relative significance of their observations. However, it is certain that both anaesthesia and warm operating theatre conditions would have completely altered our results.—We are, etc.,

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¹ Yao, S. T., *British Journal of Surgery*, 1970, 57, 761.

Predicting Fetal Maturity

SIR,—In their article (25 September, p. 736) Dr. Rosemary A. Underhill and others state that liquor studies were inexact when compared with ultrasound cephalometry and radiology. This is unfortunate. The scoring by Brosens and Gordon¹ should have

attempted a two-week interval in the significant 34-38 weeks period of gestation. Had this been practised, liquor studies would have probably fared better by comparison. Ultrasound studies are more useful in the early stages of pregnancy and liquor studies in the last 6-8 weeks, when more critical decisions are imposed upon the obstetrician.

More recent experience with cytology^{2,4} does suggest a better scoring system can be evaluated by utilizing not only the percentage of orange-staining cells but also the size of clusters, the presence of turbidity and debris, the existence of orange-staining globules, and unstained flakes. Not taking these into account may be responsible for certain spurious readings. As in other investigations, there is a tendency to give them a percentage of accuracy rating which may only reflect the need to improve the technique or interpretation thereof. We feel that in practice the clinician may utilize with benefit the augmented information resulting from a combination of investigations.—We are, etc.,

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¹ Brosens, I., and Gordon, H., *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1966, 73, 88.

² Sharma, S. D., and Trussell, R. R., *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1970, 77, 215.

³ Parkin, F. M., Lind, T., and Cheyne, G. A., *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1969, 76, 673.

⁴ Husain, O. A. N., and Sinclair, L., *Proceedings of the Royal Society of Medicine*, 1971, in press.

Fingerprint Changes in Dermatitis Herpetiformis

SIR,—Dr. T. J. David and colleagues (5 December 1970, p. 594) in a study mainly in adults reported the common occurrence of epidermal atrophy to actual loss of fingerprint patterns occurring on finger digits in coeliac disease, though one of us (Dr. J. Verbov, 2 January, p. 48) advised caution in interpretation of such fingerprint changes and Dr. W. M. McCrae and colleagues (10 July, p. 109) did not find ridge atrophy in six children with untreated coeliac disease.

The occurrence of jejunal mucosal abnormalities in dermatitis herpetiformis was first reported by Marks *et al.*¹ and Shuster and Marks² found from published studies that two-thirds of patients with dermatitis herpetiformis have the enteropathy (coeliac syndrome) and in some cases there is intestinal malabsorption. More recently, Brow *et al.*³ using a multiple biopsy technique, have found the enteropathy to be almost invariably present. The enteropathy usually responds to a gluten-free diet.

Fingerprint changes in dermatitis herpetiformis are obviously of interest in view of the above and we report some preliminary findings. So far, fingers and fingerprints have been examined in 37 patients with dermatitis herpetiformis (12 women and 25 men). The age range of patients was 21-73 years and the mean age was 47.3 years. Intentionally, patients have been examined and prints analysed without prior knowledge of any jejunal biopsy findings. Minor degrees of ridge flattening with some white lines in prints were common, but did not appear to

be more frequent than in normal individuals matched for age and sex. However, a marked degree of fingertip ridge flattening accompanied by white lines, which were usually plentiful, was seen on all fingers in only five patients (3 women and two men). Moreover, in the two males, fingertip changes, including patchy ridge damage, were clearly occupational in origin, and in the females, in whom all prints were readable, appearances were consistent with age and housewifery in two (aged 69 and 71) and long-standing dryness of the hands in the other (aged 51).

These findings seem to be in general agreement with those of Dr. David⁴ who did not find ridge atrophy in dermatitis herpetiformis patients. In addition, in eight patients with dermatitis herpetiformis examined by one of us (R.M.) in whom the rate of uptake of tritiated precursor compounds in the epidermis has been examined no difference has been detected when compared with normal controls. This would indicate a normal rate of synthesis of macromolecules within the epidermis and suggests a normal rate of epidermal replication.

We think it unlikely that fingerprint observation in dermatitis herpetiformis will prove useful as a measure of jejunal pathology in this disease.—We are, etc.,

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- 1 Marks, J., Shuster, S., and Watson, A. J., *Lancet*, 1966, 2, 1280.
- 2 Shuster, S., and Marks, J., *Systemic Effects of Skin Disease*, London, Heinemann, 1970.
- 3 Brow, J. R., Parker, F., Weinstein, W. M., and Rubin, C. E., *Gastroenterology*, 1971, 60, 355.
- 4 David, T. J., in *Proceedings 4th International Congress of Human Genetics*, Paris, 1971, Amsterdam, *Excerpta Medica*, in press.

Uterine Hypotonia

SIR,—Further to the correspondence concerning uterine hypotonia (24 July, p. 251 and 11 September, p. 637) Landesman¹ reported relaxation and cessation of activity of the human uterus in the presence of bradykinin, and Serner² showed a relationship between bradykinin and fibrinolysis.

In 1969 while working at the University of Bradford I repeated the work of Landesman (Fig.) and presented my findings to the Blair Bell Research Society.³ I also suggested⁴ that the presence of bradykinin released as a by-product of the activation of the coagulation system was the cause of uterine atony which occurs with severe antepartum haemorrhage and amniotic fluid embolism. This atony had been described previously by Scott and Reader⁵ as being of greater import than the coagulation defect itself.

Any substance that interrupts the activation of the coagulation system, such as aprotinin (Trasylol) or aminocaproic acid (Epsikapron), will prevent the release of fibrinogen degeneration products⁶ and more

importantly the release of kinins and thus will improve the condition.—I am, etc.,

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- 1 Landesman, R., Campbell, W. L., and Wilson, K., *Nature*, 1963, 197, 1208.
- 2 Serner, G. G. N., Ferrini, P. L. R., Paoletti, P., Pant, A., and Valva, G. d'A., *Thrombosis et Diathesis Haemorrhagica*, 1965, 14, 508.
- 3 Senior, J. B., and Spencer-Gregson, R. N., *Journal of Reproduction and Fertility*, 1969, 18, 551.
- 4 Spencer-Gregson, R. N., Thesis. University of Bradford, 1969.
- 5 Scott, J. S., and Reader, J. G., *British Medical Journal*, 1962, 1, 153.
- 6 Basu, H. K., *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1969, 76, 481.

Mental Deficiency Nursing

SIR,—Mrs. Jean Patey (2 October, p. 50) presents a point of view which is held by many parents and relatives of patients in hospitals for the mentally handicapped.

It is the experience of hospitals that patients who are settled, clean, and happy in hospital (the critics say "institutionalized") often fail to be accepted, become dirty, and present a nuisance outside hospital. With routine supervision patients function in ways which suggest to the visitor that they do not need to be in a hospital.

It is usual and natural for young people to leave home after adolescence, and if the mentally handicapped are to follow a normal pattern of living they too should go away from their parental homes. At present a reduction in hospital places with little immediate expansion in community provision compels many mentally handicapped people to remain at home.

Providing hospitals for the mentally handicapped with better facilities and more staff is expensive, and the argument that these hospitals are not necessary will appeal on economic grounds. Scandinavian services for the mentally handicapped, which claim to be a model, have residential institutions which are hospitals given other names. In planning for the mentally handicapped the doctors, nurses, and parents associated with hospitals will be the least consulted, because they could be imputed to hold biased views.

The organizations which adopt an anti-hospital attitude are composed of only a minority of the parents of the mentally handicapped. A survey of the wishes of the parents and relatives of patients in hospitals for the mentally handicapped would probably show a majority in favour of hospital care.—I am, etc.,

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Agranulocytosis Associated with Trimethoprim-sulphamethoxazole

SIR,—Drs. B. Hulme and D. S. Reeves (11 September, p. 610) report leucopenia associated with a combination of trimethoprim and sulphamethoxazole during immunosuppressive therapy with prednisolone and azathioprine after renal transplantation. They warned against the use of trimethoprim-sulphamethoxazole soon after cadaveric renal transplantation, but they left the pathogenetic mechanism of leucopenia open. In two patients we recently observed agranulocytosis in association with the use of tri-

methoprim and sulphamethoxazole, suggesting an immunological reaction caused by the sulphonamide component.

A 64-year-old woman received sulphamethoxazole for a urinary tract infection during a period from 10 to 24 January 1971, and thereafter ampicillin. This was changed to Eusaprim, a combination of trimethoprim and sulphamethoxazole, on 2 February. On the next day she was febrile, and a rash and a disappearance of neutrophils was noted on 8 February. The treatment with Eusaprim was discontinued, and a spontaneous remission took place seven days later.

The urinary tract infection of a 67-year-old woman was treated with Eusaprim during the period from 13 to 17 November 1970, and the white blood count remained normal. A new course of treatment was started on 25 November with sulphamethoxazole, but stopped on the following day as she became febrile and neutropenic. A remission took place over three days during treatment with hydrocortisone.

The course of the disease in both of our patients was similar; they had received sulphamethoxazole alone or in combination with trimethoprim two weeks earlier, and the new treatment was followed by a rapid neutropenic and febrile reaction. The clinical picture was typical of an immunological reaction. In earlier reports on agranulocytosis due to trimethoprim and sulphamethoxazole^{1,2} the recovery was more delayed than in our cases, and there was morphological support for marrow toxicity.¹

It is evident that in the combination of trimethoprim and sulphamethoxazole it is the sulphonamide component which causes agranulocytosis, probably both immunological and toxic. No evidence is available to support the view that the combination with trimethoprim would cause agranulocytosis more often than the sulphonamide component used alone.—We are, etc.,

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- 1 Evans, D. I. K., and Tell, R., *British Medical Journal*, 1969, 1, 578.
- 2 Paullay, J. W., *British Medical Journal*, 1970, 2, 364.

Chromosome Breakage and Ultrasound

SIR,—Mr. I. J. C. Macintosh's letter concerning chromosome breakage and ultrasound (18 September, p. 703) has prompted my response.

The use of Schlieren photography to examine the shape of Doppler ultrasonic patterns is fraught with the possibility of misinterpretation. I fear that the blame for this rests upon us, the manufacturers, who have promulgated this technique. The Schlieren depicted by Mr. Macintosh in his letter is obtained by alternately vibrating both the transmitting and the receiving crystals. Obviously, when any Doppler ultrasonic unit is used in vivo, this is not the fact. Only one crystal is used for transmission and the other for receiving. Thus, if one takes a Schlieren photograph of a Doppler ultrasonic unit as it is used in actual practice, the picture is as seen in the Figure. Examination of this readily points out that there is no focal point at all in the Doptone fetal pulse detector. The beam is