awoke and vomited. Prochlorperazine 10 mg was given intramuscularly, which relieved her temporarily. By 5 a.m. she appeared delirious and respirations were 36, pulse 96, and blood pressure 150/90. Venous blood drawn at 7 a.m. revealed sodium 132 mEq/l., potassium 5.6 mEq/l., chloride 89 mEq/l., carbon dioxide content 4.0 mEq/l, pH 6.97, PCO₂ 15.6 mm Hg, and lactic acid 246 mg/100 ml. In spite of infusion of fluids containing dextrose and sodium bicarbonate, therapy with digoxin and hydrocortisone, she died at 5 p.m. Necropsy revealed severe pulmonary oedema and moderate, bilateral chronic pyelonephritis.

The patient had been receiving three grammes daily of tetracycline for 10 days and phenformin 100 mg daily for seven days, when suddenly a catastrophic episode intervened under observation in the hospital. Although spontaneous lactic acidosis occurs in diabetics not on phenformin, the frequency of case reports of lactic acidosis in patients on phenformin has prompted suggestions of a causal relationship. Tetracycline may have played a role in this patient by increasing the blood levels of phenformin through its catabolic effects in a patient with impaired renal function.—I am, etc.,

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Ganglion Cysts of Bones

SIR,—In discussing ganglion cysts of bones you state that the pathogenesis of ganglia is obscure (13 November, p. 380).

In 1938 Wilson, Eyre-Brook, and Francis¹ suggested that semimembranous bursae (which contain ganglion-like fluid) might become distended by reason of a valve-like opening into the knee joint. A similar aetiology for ganglia seemed likely but, as you rightly point out, defects in the joint capsule are difficult to substantiate by dissection and injection of ganglia with radio-opaque material fails to show a communication with the joint.²

However, failure to demonstrate flow from ganglion to joint is just what one would expect with a valve-like mechanism; what is needed is evidence of one way flow from joint to ganglion. This has now been convincingly demonstrated by Andrén and Eiken,³ who have been able to show communication between the wrist and adjacent ganglia in 37 out of 59 cases investigated by injecting radio-opaque fluid into the wrist joint under pressure.

There are strong theoretical arguments in favour of ganglia being "blow outs" through valve-like openings in joint capsules and tendon sheaths. They occur in characteristic anatomical sites, they are aggravated by movements and relieved by rest, they recur if excised without operating on the valve opening, and they often exhibit remarkable ramifications and burrow into tendons, nerves, and bones.

For many years I have operated successfully on ganglia on the basis of a valve aetiology. Cure can be always obtained by either closing the opening into the capsule or tendon sheath or, if this cannot be demonstrated, by excising the area of capsule underlying the ganglion. In suitable cases I am now taking this treatment to its logical conclusion by leaving the ganglia in situ and

operating only on the valve mechanism.—I am, etc.,

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¹ Wilson, P. D., Eyre-Brook, A. L., and Francis, J. D., *The Journal of Bone and Joint Surgery*, 1938, **20**, 963.

² McEvedy, B. V., *British Journal of Surgery*, 1962, **49**, 585.

³ Andrén, L., and Eiken, O., *The Journal of Bone and Joint Surgery*, 1971, **53-A**, 299.

Submandibular Gland and Lingual Nerve

SIR,—The necessity for identification of the lingual nerve is a leitmotif in descriptions of removal of the submandibular gland in textbooks of operative surgery. That this particularly applies to removal of the gland for calculi is obvious from the facts of the anatomy of the lesion, the two sites at which calculi calling for the operation impact being at the hilum of the gland as it lies on the hyoglossus just below the lingual nerve, and in the posterior part of the extra-glandular duct at or close to the point at which it is crossed by the lingual nerve. The nerve is 3-4 mm wide, and only rarely are adhesions so dense as to render its identification unduly difficult. In recent years, however, the idea has obtained a certain currency in Britain that it is unnecessary to identify the lingual nerve if the gland is being removed for calculi. The object of this letter is to emphasize that this is a dangerous and mistaken idea, and to try to trace how it has arisen.

Its proximate source would appear to be a misinterpretation of an account of the operation in Farquharson's *Textbook of Operative Surgery*,¹ a popular work among candidates for the final Fellowship. A short paragraph describing the operation terminates with the sentence: "Related to the deep surface of the gland, between it and the hyoglossus, are the hypoglossal and lingual nerves; these should be identified and safeguarded." This is clear and categorical, but the next paragraph continues: "In inflammatory and calculous disease, only the superficial part of the gland requires to be removed. In malignant disease the deep part of the gland extending forwards between the mylohyoid and hyoglossus should be dissected out and included in the excision."

This latter paragraph is an almost literal transposition of a similar paragraph in the first edition of Aird's *A Companion to Surgical Studies*,² which seems to be the original source. The paragraph is capable of being misinterpreted in two ways. The first is in relation to the word "superficial." The "superficial part of the submandibular gland" as anatomically defined is the whole of the gland with the exception of the small portion running forwards deep to the mylohyoid, which is anatomically defined as "the deep part." In both Aird and Farquharson such anatomical details as are given make it clear that they are using the terms as anatomically defined, and that they are not advising a blind cutting through the substance of the superficial part. Again, careful reading of the paragraph in which the warning on the lingual nerve occurs makes it obvious that it is removal of only the anatomical superficial part which is being described, no mention of the deep part being made or implied.

I am writing to the late Mr. Farquharson's

publishers suggesting that in the next edition the pseudo-qualifying paragraph in question should be omitted. Quite apart from its potentialities for misinterpretation, it is on the one hand unsound on the treatment of calculi, and on the other irrelevant to the realities of malignant disease. Exposure, and preferably also removal, of the deep part of the gland is necessary to deal adequately with calculi impacted in the posterior part of the extra-glandular duct, and is desirable, because of the increased access thus provided, for calculi impacted at the hilum of the gland.

In the treatment of the rare malignant disease of the submandibular gland, preservation of the lingual nerve becomes of secondary importance. In fact, since the commonest variety primarily affecting the gland is adenoid cystic carcinoma which has a predilection for spreading along nerve sheaths, resection of the nerve may actually be indicated.—I am, etc.,

DAVID PATEY

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¹ Farquharson, E. L., *Textbook of Operative Surgery*, 4th edn. Edinburgh, Livingstone, 1969, p. 408.

² Aird, I., *A Companion to Surgical Studies*. Edinburgh, Livingstone, 1949, p. 255.

Antileprosy Drugs

SIR,—May I comment on the letters of my good friends, Dr. A. S. Garrett (30 October, p. 300), and Dr. W. H. Jopling (6 November, p. 366) regarding the occurrence of psychosis in leprosy patients under treatment with dapsone? As so frequently happens, when two knowledgeable and sincere persons disagree, both may be right.

It is undeniable that despite social pressures and attitudes, and despite the emotional shock occasioned by the diagnosis of leprosy, psychotic manifestations were quite rare in the developing countries in the pre-sulphone days among leprosy patients undergoing treatment in institutions or at rural dispensaries with the pure hydnocarpus or chaulmoogra oil or their derivatives or esters (iodized or not), or with such salts as sodium gynocardate. It is also true that the widespread use of dapsone at daily doses of 300 or 200 mg (as advocated by Lowe and others), was accompanied by a high incidence of dose-related toxic phenomena in the skin (notably exfoliative dermatitis) and other organs, and of acute psychotic episodes. When, in the earlier '50's, the dose of dapsone in general use was reduced to 100 mg a day, the frequency of acute psychosis diminished. These observations were made in several countries, and in typically rural areas where patients were not taking other drugs or confined in institutions.

A very small proportion of patients, probably less than 1 in 1,000, under treatment for leprosy with even lower doses of dapsone, suffer from insomnia, delusions, and hallucinations, sometimes with manic or suicidal tendencies. When dapsone is stopped the mental state slowly returns to normal. If dapsone is given again—even in very small doses—the psychotic symptoms recur; if a placebo of similar appearance is given, nothing happens.

The 12 leprosy patients reported by Jopling¹ as having mental disturbances (including six who "developed signs of frank schizophrenia, requiring admission to a mental hospital") among 125 admissions to

the Jordan Hospital over the course of 11 years, may represent a typical cross-section of more or less sophisticated patients in a Western institutional setting, and their troubles may indeed be unrelated to dapson. This inference, however, does not invalidate the reports that acute psychosis occurred with some frequency when dapson was given in high dosage in the early days, and that it is seen in a small but definite proportion of patients taking 100 mg or less daily.

It would be interesting to ascertain if psychotic episodes, apparently dapson-related, have been noted in patients taking the drug for such conditions as dermatitis herpetiformis, deep mycetoma, etc.—I am, etc.,

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¹ Jopling, W. H., *London Clinic Medical Journal*, 1963, 4, No. 2, 47.

Prophylaxis of Supraventricular Tachycardia

SIR,—The recent Therapeutic Conference on supraventricular tachycardia (6 November, p. 354, and 13 November, p. 419) prompted me into writing this personal account of the prophylactic use of oral practolol in paroxysmal atrial tachycardia.

I have suffered from this condition since early childhood. It is typically aggravated by ethanol, smoking, lack of sleep, and mental excitement, and is always precipitated by strenuous physical activity. The paroxysms occurred approximately once a fortnight and usually lasted less than an hour, but occasionally persisted for 12 hours or more. E.C.G.s showed atrial tachycardia without any evidence of Wolff-Parkinsonism-White syndrome. The paroxysms could occasionally be curtailed by physical manoeuvres designed to stimulate the vagal nerve, but usually required oral quinidine, digoxin, or phenytoin to abort an attack. The use of these drugs either as a single dose or in a protracted course had no prophylactic effect. Propranolol in a dose of 10 mg t.d.s. resulted in depression and lassitude and only occasionally prevented paroxysms.

Practolol taken as a single dose of 100–150 mg ground to a powder taken two to three hours before strenuous physical activity, such as a game of football or squash, has been almost completely successful in preventing a paroxysm of tachycardia and has not resulted in any symptoms.

For the young patient with predominantly stress-induced paroxysmal atrial tachycardia a prophylactic regimen of this kind is eminently preferable to continuous drug therapy.—I am, etc.,

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Cot Deaths and Deficiency of Vitamin E and Selenium

SIR,—The young of about 40 mammalian and bird species cannot tolerate vitamin E and selenium deficiency. The pathology of their various fatal diseases is very different, species by species, because of variation in the susceptibility of tissues. However, they are all characterized by effusion, haemorrhage, and necrosis of cells.

Low vitamin E blood levels are usual in bottle fed infants, and Millar and Sheppard¹ of this laboratory have recently measured

differences between the selenium content of human and cow milks. There is evidence of respiratory failure in cot death victims² and if the human pulmonary capillary endothelium is first susceptible to the degeneration characteristic of the veterinary deficiencies, sometimes single, and sometimes dual, I have proposed^{3,4} that changed permeability to gases and liquids could prove fatal before there was visible change, even with the aid of light microscopy. In 1949 Owens and Owens⁵ demonstrated a potent vitamin E activity for infants in the prevention of retrolental fibroplasia after they had observed similarity between its pathology and epidemiology and those of vitamin E deficiency diseases of chickens and rats. Their finding lost importance when the role of oxygen in this disease was appreciated, soon afterwards, and has not been justly referred to in the retrolental fibroplasia literature. More male than female infants are affected, as is the case with the sudden infant death syndrome. For both syndromes the age of victims is similar. Patz⁶ has recorded that one-fourth to one-half per cent of retrolental fibroplasia cases occur without oxygen therapy. This is about the incidence of cot death.

In New Zealand, for the first time on a large scale anywhere, infants are now receiving a vitamin E supplement in Karilac (lactose) and in Glaxo formulae. The Meade Johnson and Wyeth ones have long been supplemented but are not very widely used. Future victims will be classified according to their vitamin E nutrition.—I am, etc.,

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- ¹ Millar, K. R., and Sheppard, A. D., *New Zealand Medical Journal*, 1970, 72, 417.
- ² Bergman, A. B., Beckwith, J. B., and Ray, C. G., eds., *Proceedings of the Second International Conference on Causes of Sudden Death in Infants*. Seattle and London, University of Washington Press, 1970.
- ³ Money, D. F. L., *New Zealand Medical Journal*, 1970, 71, 32.
- ⁴ Money, D. F. L., *Journal of Pediatrics*, 1970, 77, 165.
- ⁵ Owens, W. C., and Owens, E. U., *American Journal of Ophthalmology*, 1949, 32, 1631.
- ⁶ Patz, A., *The Sight Saving Review*, 1966, 36, 67.

Preclinical Salaries

SIR,—We share the concern expressed by Dr. B. F. Martin and his colleagues (23 October, p. 236) and other recent correspondents regarding the number of medical graduates on the permanent staffs of preclinical departments in our medical schools. As your correspondents have indicated, this is a double problem. Recruitment of medical graduates to these departments has declined and continues to do so, and also many medical graduates have left these departments for overseas or clinical appointments.

The only way in which many universities can attract medical graduates to preclinical departments is by making appointments at a starting salary higher than the minimum point of the lecturer scale. This has succeeded in bringing into preclinical departments young medical graduates who are willing to undertake some teaching duties while they study for the primary F.R.C.S. examination or, occasionally, for a higher academic degree. However, these people are very much aware that career prospects in preclinical departments compare unfavourably with those elsewhere in the medical profession, and they seldom stay long. On appointment they

usually have little or no experience in either teaching or research and can make only a limited contribution to the teaching and research activities of these departments. Just as they are gaining in experience they depart for more promising or rewarding careers elsewhere.

Any decline in the number of medical graduates holding permanent appointments on the staffs of preclinical departments, coupled with the expansion of medical schools and the reduction in the time available to teach preclinical subjects, must inevitably lead to a change in the orientation of preclinical courses. We believe such a change will be to the detriment of medical education as a whole. The present emphasis on teaching those aspects of preclinical subjects that are of particular relevance in clinical medicine can be maintained only if a sufficient number of medical graduates take up a career in preclinical departments.

In terms of career prospects the gap between preclinical staffs and other sections of the profession widens with every salary review. This gap can be measured not only in terms of immediate financial reward, but in the prospect of achieving a position of highest seniority, responsibility, and status. If, therefore, the medical profession as a whole shares our concern for the quality of preclinical medical education in this country, then it must use its weight to support an urgent campaign for improvement in the career prospects for medically qualified preclinical staff.—We are, etc.,

G. W. ATHERTON	N. T. JAMES
E. J. CLEGG	D. MAYOR
D. J. GOLDSTEIN	F. C. TRING
M. C. HAYES-ALLEN	C. F. A. WHELAN

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Specimens from the Female Genital Tract

SIR,—The purpose of our letter (16 October, p. 170) describing an improved method of specimen collection from the female genital tract seems to have been misunderstood by Dr. W. H. Hughes and Mr. J. M. Davies (13 November, p. 424). We wish to ascertain in the female population the true extent of infection with genital pathogens—including the gonococcus but by no means limited to this organism. At the same time, we certainly have no desire to increase the pressure on our already overworked special clinics. It was for these very reasons that we recommended the use of our convenient new swabbing method in general practice.

Dr. Hughes and Mr. Davies suggest that if a woman's regular male partner has not developed gonorrhoea then she has no reason to fear that she is carrying the infection. This is true as far as it goes, but they do not mention the possibility of a male partner becoming infected, though without symptoms. Even in the male, asymptomatic gonorrhoea is far from rare, and the more carefully it is looked for the more frequently it will be found. One such asymptomatic man was found to be responsible for infecting 22 people.²

In fact, Dr. Hughes and Mr. Davies have indicated the probable high frequency of undiagnosed genital infections according to their results on 1,000 women who were not suspected of having gonorrhoea. Their discovery of a 19% incidence of specific infection, and possibly a similar amount of non-