Tolerance of Rifampicin

SIR,—One of the virtues of rifampicin is said to be a good patient tolerance which, as you have noted (30 August, 1969, p. 487), should be particularly valuable in treatment of tuberculosis where tolerance is poor.

To demonstrate objectively whether this good tolerance extends to domiciliary ambulant therapy we have used a simple urine test for rifampicin on patients attending the Dagenham Chest Clinic, consecutively during June, July, August, and September last year (Table). During the same period we examined urines of all patients on P.A.S., using Phenistix.¹

	No. of patients	Positive	Negative
Rifampicin (Butanol)	23	23	Nil
P.A.S. (Phenistix)	68	57	11

Butanol test for rifampicin.—This is derived from the biochemical method for estimation of rifampicin in urine, given in *Lepetit Handbook*.² The depth of colour, which varies from salmon pink to dark orange, is a guide to urinary concentration of rifampicin.

If rifampicin 10 mg./kg. of body weight has been ingested on an empty stomach two to eight hours previously, it is likely that the supernatant layer will be light orange or darker. The salmon pink colour may be found at 12 hours or even 24. A light orange corresponds to about 25 µg./ml. rifampicin; salmon pink to 2.5 µg./ml. We base this statement on 240 urine samples taken from 11 patients over a period of three to five days, at two-hourly intervals from 7.30 a.m. to 7.30 p.m. False positives may occur in the presence of excess urinary bile pigments.

Pines *et al.*³ suggested that rifampicin is obvious in untreated urine, but the colour is, in our experience, more orange than brown. However, simple inspection proved misleading to seven nurses in 82 out of 189 observations on eight "positive" and 19 control urines. Using the butanol test on these same urines reduced the error to 12 out of 189 observations.

Although we agree that patient tolerance of rifampicin appears so far to be good, we suggest it may be wise to check from time to time that the drug is being taken. The above simple butanol test may help in this connexion.—We are, etc.,

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J. PRASAD.

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REFERENCES

- 1 Simpson, J. McD., *Tubercle*, 1961, 42, 107.
- 2 *Lepetit Handbook*, 1968.
- 3 Pines, A., Reafat, H., and Bundi, R., *Tubercle*, 1967, 48, 281.

Digoxin-Phenytoin Interaction

SIR,—We would like to draw attention to what appears to be a toxic interaction of digoxin with phenytoin. Cardiac glycosides inhibit the Na,K-ATPase which is closely related to the metabolic "sodium pump". The inhibiting effects of ouabain and phenytoin on the Na,K-ATPase enzyme system are additive.¹ Phenytoin causes bradycardia² as well as digoxin.

A man with Down's syndrome, aged 53, began to get *grand mal* seizures once per month. Because he also had mitral insuf-

ficiency 0.25 mg. of digoxin and 200 mg. of phenytoin were administered daily. After having this medication two months he again had a seizure. At that time his serum phenytoin level was 11.0 µg./ml. only and thus the dosage of the drug was increased to 300 mg. daily. Within two weeks the patient became lethargic and rigid, his cardiac rate fell to 34/min. and the E.C.G. showed a complete heart block. At first this was suspected to be due to digoxin, which was discontinued. The dosage of phenytoin was also reduced to 200 mg. daily. Two days later the patient was comatose with Cheyne-Stokes respiration; cardiac rate 40/min.

In the next few days he began to improve, and a week after the dosage of phenytoin had been decreased from 300 to 200 mg. the serum phenytoin level was 20.2 µg./ml. and the cardiac rate 34/min. The dosage of phenytoin was further decreased to 100 mg. daily. Ten days later the cardiac rate was still 34/min. and phenytoin was discontinued. Within one month without phenytoin, the cardiac rate returned to 60-70/min., and the E.C.G. showed a normal sinus rhythm again. However, the patient is still unable to walk and has ataxia, slight nystagmus, and rigidity suggesting permanent cerebellar damage.

This case, with a nearly fatal outcome, suggests that the combination of digoxin with phenytoin or the treatment of digitalis-induced cardiac dysrhythmias with phenytoin may be hazardous. It is conceivable that the toxicity of phenytoin is due to the inhibition of Na,K-ATPase and the physiological sodium transport, which are impaired further by digoxin. However, cardiac glycosides increase, and phenytoin decreases, the intracellular sodium concentration.—We are, etc.,

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REFERENCES

- 1 Rawson, M. D., and Pincus, J. H., *Biochemical Pharmacology*, 1968, 17, 573.
- 2 Livingston, S., *Postgraduate Medicine*, 1956, 20, 584.

Childhood Urinary Tract Infection

SIR,—Dr. N. C. Mond and his colleagues (7 March, p. 602), in their study of childhood urinary tract infection in general practice, successfully emphasize that pyuria and proteinuria do not prove useful in the prediction of asymptomatic bacteriuria. The findings do, however, illuminate the doubtful value of the present emphasis on bacteriuria itself as a guide to the presence of preclinical urinary tract infection. In their findings approximately ten times as many children displayed pyuria as were found to have bacteriuria. As most of the children may be assumed to have been prepubertal, and the specimens themselves were collected after effective local cleansing had taken place, is it not reasonable to assume that the source of the pus cells was the urinary tract?

In my experience as an obsessive urine microscopist in general practice, the continued presence of pyuria during follow-up of cases of treated overt urinary infection is

an indication that an exacerbation will occur sooner or later, despite the finding of sterile urine over the same period.

In studying the early history of urinary tract infection is there not perhaps some justification for emphasizing pyuria rather than bacteriuria in the search for pre-clinical infection?—I am, etc.,

T. G. S. CAMERON.

Heywood, Lancs.

Entrapment Neuropathies

SIR,—In your leading article on entrapment neuropathies (14 March, p. 645), the list of diagnostic criteria is headed by pins and needles. But it is well to realize that paraesthesia is absent in many cases of pressure on the external aspect of a nerve—for example, with pressure on the lower trunk of the brachial plexus from a cervical rib the only complaint may be wasting of the thenar eminence without any sensory change. In sciatica, where the nerve root is trapped at the intervertebral foramen, or in meralgia paraesthetica pins and needles are often absent.

The criteria that were originally put forward for a diagnosis of "perineuritis" (as I called it in 1942¹) were simply: pain referred to a region obviously corresponding to the cutaneous area of supply of a peripheral nerve, without loss of conduction, in a case where no pain could be elicited on testing the non-nervous tissues. No particular attention was paid to my "medium perineuritis" until the classic paper of Brain, Wright, and Wilkinson,² which certainly should figure in the otherwise extensive bibliography of your leading article.—I am, etc.,

JAMES CYRIAX.

London W.1.

REFERENCES

- 1 Cyriax, J., *British Medical Journal*, 1942, 1, 578.
- 2 Brain, W. R., Wright, A. D., and Wilkinson, M., *Lancet*, 1947, 1, 277.

Pulmonary Sensitivity to Nitrofurantoin

SIR,—Your leading article (20 December 1969, p. 704) mentions confusing this condition with pulmonary oedema or pneumonia. The following case demonstrates another differential diagnosis—pulmonary embolus.

A woman aged 24 years was given nitrofurantoin 100 mg. q.d.s. for a urinary infection. Three weeks later she developed pretibial erythema and pruritus, aching pains in calves and thighs, and general malaise. She had tightness in the chest and a non-productive cough. She vomited once and later that day fainted while waiting for a bus. On recovering consciousness the difficulty in breathing was more severe.

On admission that evening her temperature was 102°F. (39°C.), pulse rate 124. She was not breathless nor cyanosed. There was a pink papulo-urticarial rash over both shins. Both calves were tender but Homan's sign was negative. Chest examination and x ray were normal. She had been taking a contraceptive pill, Lyndiol, for 18 months. This fact, together with calf tenderness, respiratory distress, and the collapse, suggested the possibility of pulmonary

embolus. However, the rash and pyrexia suggested a sensitivity reaction to nitrofurantoin. Withdrawal of the drug resulted in prompt relief of all her symptoms.

Such mild reactions are probably commoner than only 24 reported cases would suggest. Since the publication of your leading article your correspondents have added four more cases (24 January, pp. 235 and 236).—I am, etc.,

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Dartford, Kent.

Cost of Anaesthetic Agents

SIR,—Dr. J. S. Patterson (21 March, p. 755) asks someone to explain why domiciliary oxygen costs twenty-five times as much as the piped supply in hospitals. The answer is surely simple. The cost of filling and delivering oxygen greatly exceeds the cost of the material itself. In a National Health Service where manpower costs of one sort or another make up well over two-thirds of the total expenditure, it is distressing that this obvious fact should have to be spelled out.

The implicit assumption that people's time is an "overhead" of negligible cost is perhaps responsible for much of the wasteful use of resources in the Service.—I am, etc.,

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London W.1.

Recurrent Virus Meningitis

SIR,—My inexcusable failure (27 December, 1969, p. 786, and 28 February, p. 564) to notice the article by Klemola and Lapinleimu¹ is doubly incomprehensible since it appeared in a volume of the *B.M.J.* from which I quoted. My regret is accentuated by previous personal appreciation² of Professor Klemola's work³ in cytomegalovirus infections.

But at least I have been in good company in overlooking previous relevant communications, since Bagshawe⁴ had to take our distinguished Finnish colleagues themselves to task on this account.—I am, etc.,

J. P. ANDERSON.

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Taunton, Somerset.

REFERENCES

- 1 Klemola, E., and Lapinleimu, K., *British Medical Journal*, 1964, 1, 1087.
- 2 Anderson, J. P., and Stern, H., *British Medical Journal*, 1966, 1, 672.
- 3 Klemola, E., and Kääriäinen, L., *British Medical Journal*, 1965, 2, 1099.
- 4 Bagshawe, K. D., *British Medical Journal*, 1964, 1, 1380.

Employment Medical Advisory Service

SIR,—Your leading article (28 February, p. 517) raises some vital points. There are few who will regret the passing of the appointed factory doctor service which, due to neglect, was generally regarded as useless, but it is a pity the baby has been thrown out with the bathwater. A service

primarily for the benefit of young people has been discarded in favour of a departmental bid to establish a rudimentary occupational health service. In the process the interests of young people have been almost completely disregarded.

The idea of pre-selection on leaving school and the imposition of a "red-card," precluding the unfortunate recipient from employment until authorized by the E.M.A., has been dropped. There is now no indication how medical information can be passed to the Careers Advisory Service (late Youth Employment Service). There is no likelihood that any persons apart from the mentally retarded and the grossly physically handicapped will get any help—that is, those who would have been on the old Disabled Register. The C.A.S. will notify the E.M.A. (on what grounds) who will then notify the employer that an examination is necessary. The employer will then notify the individual (young person) that he or she is "free to attend." The E.M.S. may then send to the local education authority for medical records. What an ordeal for the young person. What a sledgehammer to crack a nut! Presumably, also, the young person is "free" to refuse. This mechanism almost guarantees that those most in need, as the relative importance of psychological problems increase, will be least likely to respond.

The employer is now instructed to notify the C.A.S., in place of the A.F.D., when employing a young person under 18. This is based on the assumption that, in fact, the A.F.D. has in the past been notified. Unfortunately this assumption is false. Notifications are made in only about 60% of cases, and for the most part by the "better"

firms employing the "better" young people. The C.A.S. will, since no additions to staff or powers have been made, be little the wiser or more useful than in the past.

The C.A.S. is potentially a vital extension of the education service into the early years at work, corresponding to the function of a tutor at a university. Its relationship to the employee should be one which stimulates and helps to stabilize changing individuals in changing circumstances in a time of accelerating technological change. It could produce an attitude of tolerance and understanding in the employers and link the difficult phasing out process between school and work.

If the C.A.S. is to fulfil these vitally important functions it must be adequately staffed, trained, and equipped. At present it is often regarded by many as a second-class service for second-class citizens—starved of resources and relatively impotent. There should be an occupational medical service for adolescents corresponding to the University Health Service and linked to the C.A.S. as the Student Health Service is to the academic staff. The Bill¹ makes impossible demands on an inadequate service, and thus performs a confidence trick on those who are led to believe that young people are to be benefited by the proposed Bill.

A potentially invaluable set of statutory duties is to be abolished and, due to lack of experiment and information, a speculative muddle is introduced.—I am, etc.,

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Bucks.

REFERENCE

- 1 Employed Persons (Health and Safety) Bill, 1970.

Medical Management

SIR,—May I be permitted to congratulate Dr. P. Sleight and others (14 March, p. 682) on their report "Oxford and McKinsey: Cogwheel and Beyond." They have exposed at ground level the inadequacies of the cogwheel report¹ and the half-hearted approach by the Department of Health to medical management. The cogwheel report failed to recognize that:

(1) The formation of a small executive in which the management committee, nursing officer, and administrator would be equal partners with the medical members was even more important than medical reorganization.

(2) Local medical management is impossible without local medical financial control.

(3) Financial control is impossible without restriction of clinical freedom.

(4) A clinician will not "waste his time" in administration without an adequate incentive.

The Oxford report has brilliantly solved (1) and (2). Their solution to (3) has been the only acceptable one of retaining savings in medical expenditure for the use of the savers. One wonders how acceptable this would be in a non-teaching hospital; the regional board might very easily insist that any savings could more profitably be used elsewhere.

The Oxford report is weakest in dealing with (4). I suspect that when the early en-

thusiasm dies down the clinicians involved in this heavy extra burden will reasonably ask "what is in it for us?" Satisfaction in a job well done will hardly compensate for the loss of clinical opportunities. I suggest such executive work should automatically be entitled to extra reward equivalent at least to a C merit award (it is well worth it), and until such recognition is given the response by the majority of consultants to "medical management" will continue to be lukewarm at best.—I am, etc.,

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REFERENCE

- 1 Cogwheel Report. *Organization of Medical Work in Hospitals*. London, H.M.S.O., 1967.

Vocational Registration

SIR,—Recent proposals for early legislation to implement the principles of vocational registration as outlined by Sir George Godber in a letter to the Secretary of the British Medical Association (*Supplement*, 11 October, 1969, p. 5) have aroused considerable misgivings among the medical staff of this hospital. The matter has been widely discussed at a series of meetings of the group medical staff, senior and junior, and the following paragraphs represent the