Meanwhile we endorse your analysis of the situation and would regret a too hasty withdrawal of saccharin from the market before all such factors have been properly evaluated.—We are, etc.,

R. M. HICKS
J. CHOWANIEC
J. ST. J. WAKEFIELD

School of Pathology,
Middlesex Hospital Medical School,
London, W.1

1 Hicks, R. M., Wakefield, J. St. J., and Chowaniec, J., *Nature*, 1973, **243**, 347.
2 Hicks, R. M., Wakefield, J. St. J., and Chowaniec, J., *Nature*, 1973, **243**, 424.

SIR,—The comparative passivity with which the profession stood by and watched the banning of cyclamates in Great Britain makes your leading article (28 July, p. 185) both timely and important. It would appear (as many of us suspected) that there are now as good—or one should rather say as inadequate—grounds for banning saccharin as there was for banning cyclamates. Your article reminds us that so far neither ban is justified.

If there be those in Britain who wish to force the unwarranted requirements of the United States Delaney Clause on us they would do well to consider that on the evidence at present available it would undoubtedly be preferable for us to use saccharin and indeed cyclamates rather than sugar whenever that is possible. Since no one else has bothered to do so I hereby take it upon myself to call for the repeal of the entirely unnecessary ban on cyclamates.—I am, etc.,

A. LEWIS

London, W.9

Pneumococci with Increased Resistance to Penicillin

SIR,—A recent article by Dr. J. E. M. Whitehead (28 April, p. 224) describes the changing pattern of sensitivity to antibiotics in pathogenic bacteria. Unlike staphylococci, haemolytic streptococci and pneumococci are mentioned as retaining susceptibility to penicillin despite more than a quarter of a century of use. However, Dr. Whitehead refers to our report describing pneumococci relatively insensitive to penicillin.[1] Such penicillin-insensitive pneumococci (P.R. strains), which were first detected in 1967, have been encountered frequently in New Guinea, occasionally in Australia, and very rarely in other countries. In New Guinea the incidence of P.R. strains has varied from one region to another but was 12% among 530 isolates examined during a preliminary survey in 1968-70. Such strains have been isolated from both carriers and patients with pneumococcal infections, including pneumonia and meningitis. Some patients have suffered a fatal infection.

The degree of penicillin resistance varies from slight to moderate. Whereas pneumococci are normally inhibited by 0·02 μg benzylpenicillin per ml or less, P.R. strains require 0·1-2·0 μg benzylpenicillin per ml for inhibition (resistance ratio 5:100). Resistance has been encountered in 10 different serotypes to date, including types 4, 6, 14, and 19. These are among the pneumococcal types which commonly cause bacteraemic infections,[2] and pneumococci of serotype 4 are also capable of causing epidemic pneumonia.[3] Pneumococci insensitive to benzylpenicillin are in addition, relatively insensitive to phenoxymethylpenicillin, penicillinase-resistant penicillins (methicillin and cloxacillin), and the cephalosporins (cephaloridine and cephalothin); however, such strains are usually either fully sensitive to ampicillin or show only slightly increased resistance. The nature of resistance is not known but is not associated with the production of penicillinase.

It is of some interest to speculate why P.R. pneumococci have been found so rarely outside New Guinea. This may be because such strains are extremely rare or non-existent in most countries or because the laboratory techniques used to test the sensitivity of pneumococci are not always suitable for the detection of penicillin-insensitive strains. If the disc diffusion method is used, it is important to use a suitably low concentration of penicillin (for example, 1 unit = 0·6 μg benzylpenicillin per disc) and not high-strength discs, such as are used in the Kirby-Bauer method. However, it is desirable to use a quantitative technique, such as the plate dilution method, when P.R. pneumococci are sought.

The development of penicillin resistance in pneumococci is likely to have important therapeutic implications, particularly in centres where either procaine penicillin or phenoxymethylpenicillin is used for the treatment of pneumonia, as these preparations produce low blood levels, of the order of 1 μg penicillin per ml. In areas where infection with penicillin-insensitive pneumococci cannot be excluded, we recommend that the initial therapy of a seriously ill (adult) patient with pneumonia should be with ampicillin by intramuscular injection in a dose of 0·5 g 4- or 6-hourly. Where the higher cost of ampicillin precludes its use, benzylpenicillin in large doses, such as 0·6 g (1 million units) 4-hourly by intramuscular injection, is a suitable alternative.—We are, etc.,

DAVID HANSMAN

Bacteriology Department,
Adelaide Children's Hospital,
North Adelaide, South Australia

LORRAINE DEVITT

Garvan Institute of Medical Research,
St. Vincent's Hospital,
Sydney, New South Wales

IAN RILEY

Pneumonia Research Unit,
Public Health Department,
Tari, New Guinea

1 Hansman, D., Glasgow, H. N., Sturt, J., Devitt, L., and Douglas, R. M., *Nature*, 1971, **230**, 407.
2 Austrian, R., *Journal of Clinical Pathology*, 1968, **21**, Suppl. no. 2, p. 93.
3 Hodges, R. G., and MacLeod, C. M., *American Journal of Hygiene*, 1946, **44**, 183.

Is the Xylose Test Worthwhile?

SIR,—As a result of their survey Drs. G. E. Sladen and P. J. Kumar (28 July, p. 223) suggested that "when a jejunal biopsy can readily be performed the xylose test serves little useful purpose in routine practice." I think this statement and their interesting paper merit further consideration.

The technique of giving D-xylose and then collecting a five-hour urine sample is not the best. A considerable amount of this large dose is not absorbed and often produces abdominal distension and diarrhoea, which may itself impair absorption. Santini and colleagues[1] in 1961 showed that a 5-g dose is preferable, and it has since been confirmed that the lower dose is quite satisfactory for the demonstration of absorption.[2 3] Care over the urine collection is vital. Leaving it to nurses in a busy ward brings the test into disrepute, for patients require close supervision or they will not produce an accurately-timed specimen. The duration of the collection is also important since Sammons and colleagues[2] showed quite clearly that a two-hour collection is far better than a five-hour collection. We have since confirmed that the five-hour values produce an inadequate separation of patients with malabsorption from controls, whereas the two-hour values do not overlap[3] provided that age and renal function are taken into consideration. This can be achieved by performing an intravenous xylose test[4] and then presenting the results as an oral/intravenous fraction.[3]

A simple procedure like the xylose test is unlikely to be infallible. Nevertheless, perhaps some of the anomalous results obtained in this survey can be explained. Firstly, the finding of low urinary excretion rates and high serum values in some of the "normal" group raises the possibility of mild renal impairment, and one wonders if some of these were elderly. Secondly, the four patients with low values in the group with gastrointestinal disease but normal histology included three who might have malabsorption due to a motility disturbance and the fourth had an ischaemic intestine. The results of the patients with Crohn's disease are very interesting: 19 out of 52 had a low urinary xylose excretion of whom 14 had a normal or raised serum value. In our survey 15 of 23 patients with Crohn's disease had a low xylose excretion after an oral dose, but five of these also gave low results after intravenous xylose. These results suggest that impaired renal function might be quite common in Crohn's disease.

In conclusion, I would agree that the 25-g D-xylose test using a five-hour urinary collection is not a very good screening test for coeliac disease. However, a 5-g test with a two-hour urinary collection, if performed carefully with attention paid to age, renal function, drugs, and other causes of malabsorption, is a useful guide to small bowel function and is extremely simple to perform.—I am, etc.,

M. J. KENDALL

Queen Elizabeth Hospital,
Birmingham B15 2TH

1 Santini, R., Sheehy, T. A., and Martinez-de-Jesus, J., *Gastroenterology*, 1961, **40**, 772.
2 Sammons, H. G., *et al.*, *Gut*, 1967, **8**, 348.
3 Kendall, M. J., and Nutter, S., **Gut**, 1970, **11**, 1020.
4 Kendall, M. J., *Gut*, 1970, **11**, 498.

Confidentiality

SIR,—Professor M. R. Alderson (28 July, p. 232) has described very clearly the value of centralized systems of medical information for the treatment of the individual