Resistance to the Newer Penicillins

SIR,—In reply to Dr. G. N. Rolinson (February 23, p. 542) we cannot agree that the methicillin-resistant organisms in our cultures Nos. 4516/62 and 6637/62, as sent to him, were present "only as minority populations." In our laboratory and in the Staphylococcal Reference Laboratory,[1] among others, those cultures when isolated were resistant to 20–50 μg./ml. of methicillin. Our titrations were carried out in liquid and solid media with cells which mostly grew into normal colonies in drug-free media. Since this correspondence started we have rechecked our reference cultures without finding any reason to change the view expressed in our paper. In case further reference is required, cultures are being lodged with the National Collection of Type Cultures.

We have also retested our cultures against three isoxazole penicillins, including cloxacillin; here again there is no departure from the level of resistance which we defined—i.e., 5–10 μg./ml. As we emphasized in an earlier letter (February 16, p. 465) these drugs are inactivated only when tested at about 2 μg./ml., at the threshold of their *therapeutic* concentration. We agree that the *rate* of inactivation of higher concentrations of these drugs is no higher with the Carshalton strain than with some other penicillinase-forming strains: we never said it was.

Dr. Rolinson also calls in question our evidence that these methicillin-resistant strains were invasive and pathogenic. Of their invasiveness, we can only repeat our statement that cross-infection spread to 71 children (now over 100). Of the pathogenicity and "clinical" resistance, we have to reiterate the facts that the organism caused wound infection in a child who was receiving methicillin at the time; septicaemia developed, proved rapidly fatal, and the identical organism was re-isolated freely from several organs at necropsy. The nature of the operation (resection of meningomyelocele with insertion of Spitz–Holter valve) and the presence of congenital abnormality may well have made the child unduly vulnerable to infection, but the fact was that she died of generalized staphylococcal infection which methicillin could neither prevent nor control. Having been so closely concerned with the original evaluation of methicillin,[2 3] we are able to view this breakthrough in perspective. We share Dr. Rolinson's dismay, but we believe that, if action follows awareness, this type of resistance need not spread uncontrollably.—We are, etc.,

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Diabetes Mellitus and Pernicious Anaemia

SIR,—Professor L. J. Witts and his colleagues (January 19, p. 159) refer to the patients with diabetes mellitus and pernicious anaemia in my series of 1937,[1] remarking they are open to criticism being based on a retrospective survey. May I correct this? All the patients had been and were under my own personal supervision from the time of first being referred to me for diagnosis and continued to attend my clinics at monthly or three-monthly intervals thereafter until in subsequent years some died but most are still alive to-day.

From 1929 to 1962 I have had under my care in this way 2,284 patients with pernicious anaemia, of whom 33 subsequently developed diabetes mellitus while attending my follow-up clinics, while 15 were found to have diabetes mellitus at the same time that pernicious anaemia was diagnosed. From a series of 338 patients with diabetes under my care during the same period (1929–62) 11 subsequently developed pernicious anaemia.

1929–1962
From 2,284 Pernicious Anaemias

Initial Diagnosis	Males	Females	Both Sexes	Incidence 10)
Pernicious anaemia	17	16	33	1·4
,, ,, and diabetes mellitus	7	8	15	0·65
Diabetes mellitus	2	9	11	0·48
Total	26	33	59	2·6

As long ago as 1933[2] I referred to the association of these two diseases, since Parkinson[3] first reported his case, and at that time collected from various sources 10,038 patients with diabetes mellitus, of whom 18 were said to have developed pernicious anaemia, while 15 patients developed diabetes mellitus in a collected series of 2,461 patients with pernicious anaemia.

At that time I had already observed that pernicious anaemia and diabetes mellitus occurred frequently in different members of the same families, while Brockbank and I[4] also discussed the high incidence of achlorhydria in at least 24% of all members of many families examined in which pernicious anaemia had been noted by us.

The late T. H. Oliver and I[5 6] referred to the frequent occurrence of achlorhydria observed in patients with diabetes mellitus, noted by many others besides ourselves, to the extent of 29–49% of the cases.

Since 1933 many further similar observations have been made in many quarters, while in my Oliver-Sharpey lectures to the Royal College of Physicians,[7] I referred again in detail to these associations of pernicious anaemia, diabetes mellitus, and achlorhydria.

Dr. A. G. Stewart (February 16, p. 472) reminds us that pernicious anaemia and thyroid disease may be associated—this is so, of course. Thus, in my own personally observed series of 2,284 with pernicious anaemia, 92 of them had thyroid disease:

Pernicious Anaemia with Thyroid Disease

	Males	Females	Total
Hypothyroidism	7	71	78
Hyperthyroidism ..	2	12	14

I think one has to be careful, of course, in associating different diseases with pernicious anaemia, for with the excellent prognosis now for all properly treated patients with pernicious anaemia they live so long that they now have the opportunity of developing other diseases to which we are all prone. Consequently, when you keep under observation for many years a large series of more than 2,000 patients with pernicious anaemia with only an annually mortality of about 1%, you will ultimately find as I have done that some of the patients with pernicious anaemia can be associated with almost any other disease—hence isolated reports of "case of pernicious anaemia with 'such and such' disease." Nevertheless, I think there may be some more definite

aetiological connexion between pernicious anaemia and diabetes mellitus, thyroid disease, and with gastric cancer, but I doubt any others.—I am, etc.,

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The Elderly in Hospital

SIR,—I read with interest the letter by Dr. J. Andrews (January 26, p. 263) concerning the differences in "misplacement" percentages between elderly patients admitted to a geriatric unit and those admitted to a mental hospital shown recently in this journal.[1] He rightly raises the suggestion that the higher number of patients assessed as "misplaced" in the geriatric unit may reflect the greater ease with which a general practitioner may arrange his patient's admission there. Actually at the time of this survey the reverse was true: while emergency admissions are always promptly catered for at both hospitals, under the Mental Treatment Act (N. Ireland), 1948, in force at this time, patients were admitted directly to the mental hospital by one general practitioner without necessarily making prior request for a bed. In contrast, the geriatric unit arranged elective admission from a waiting-list following stringent out-patient and domiciliary assessment.

Dr. J. L. Struthers (February 16, p. 470) finds an interesting similarity between the timing patterns of deaths and discharges shown for these patients and those of the Southampton Geriatric Unit in that they seem to comprise two distinct groups; those who get well quickly or die quickly, and those who become long-stay patients. I have no qualified opinion on this to give in respect of the geriatric unit patients, but I did examine this finding for the mental hospital patients.[2] Most of those who died did so within three months of admission, and similarly most of those who went home did so within three months of admission. The proportion of those still in hospital at the end of three months remained substantially unaltered by the end of one year. This was accounted for by their diagnostic composition; early discharges had been admitted suffering from affective disorders and paraphrenia predominantly, early deaths had predominantly confusional states. Those with arteriosclerotic psychosis or senile dementia tended to become long-stay patients. The social and demographic variables examined related more to the diagnosis than to the feature of their discharge or death.—I am, etc.,

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Detection of Glaucoma

SIR,—I would like to make one more brief suggestion over the question of the early detection of glaucoma. I thought that the letter by Mr. A. H. Briggs (January 26, p. 256), where he stresses the failure of those in the Supplementary Ophthalmic Service to diagnose not only glaucoma but cataract, detachment, and diabetes, is an indictment not of the ophthalmic opticians but of the general practitioner. It is the job of the latter to use an ophthalmoscope and to diagnose such diseases, not only of the ophthalmic opticians. I would prefer to see ophthalmic opticians concentrate on refraction and its relationship to muscle balance rather than on the ophthalmoscope. Screening, as I suggested in my earlier letter, is a most comfortable and simple technique which the ophthalmic optician could well carry out, and, in my opinion, should, as glaucoma poses a specially tragic problem. I would like to see all newly qualified opticians directed to work under a consultant eye surgeon in a hospital eye department for one year after qualifying before he is allowed to go out and work in public. I know he is forced to do a year in the refraction hospital and in some selected hospitals, but I feel it is the peripheral eye departments which should absorb these people. There the surgeon could supervise his training in perimetry and screening and some sort of human relationship might better be established.

These suggestions of mine are based on the premise that the Supplementary Ophthalmic Service and the ophthalmic optician are here to stay. This country has an astronomical national debt and harder times seem to lie ahead. The Utopian eye service envisaged by Messrs. P. Richard Day (February 9, p. 396) and Briggs, I believe, is a pipe dream. If I am correct, then clearly the only sensible thing to do is to raise the standard of the ophthalmic optician and for that matter the ophthalmic medical practitioner as well.

One final point bears reference. If there was a steady supply of qualified trainees attending the hospitals, men already fairly competent in refraction, this would give us the chance of running a good ophthalmic service for schoolchildren within the Hospital Service. We might even be able to make it illegal to have children under 18 tested outside the Hospital Service. This I consider almost as important as detecting early glaucoma.—I am, etc.,

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Treatment of Osteomyelitis

SIR,—I read, with interest, your excellent summary on the treatment of osteomyelitis in the leading article (February 23, p. 488).

You rightly state that in the infant "septic arthritis is quite a common consequence." As often as not the disease presents in this way. It should be emphasized that this may occur with few constitutional symptoms and is easily overlooked. Early diagnosis and treatment are essential if crippling complications such as permanent dislocation of the hip, or damage to the growing-end of a long bone, with consequent shortening, are to be prevented. It is fortunate that sinuses and recurrent or chronic osteomyelitis are infrequent in neonates. Again you say, "No one disputes that the most important factor in treatment is early diagnosis." With this everyone will agree, but I cannot agree with your later statement, "Radiological appearances are normal at this time, and will remain so for two to three weeks." This may be true of the older child, but is certainly not true of the infant. The earliest diagnosis of septic arthritis associated with osteomyelitis may be made by radiology—the appearance of soft-tissue swelling, capsular distension, and subluxation are almost pathognomonic of this condition in an infant with a raised temperature and who refuses to move a limb: in some cases slivers of bone may flake off from the