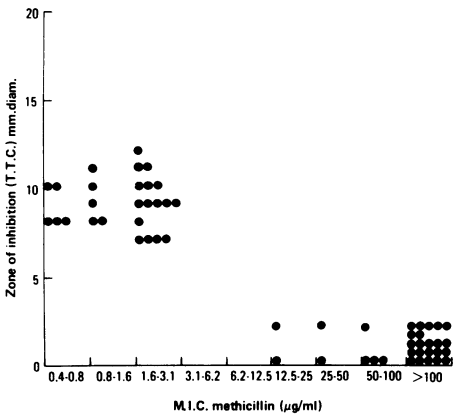

FIG. 2—Correlation of zone size (less diameter of disc) with M.I.C. methicillin determined after 18 hours incubation at 30°C.

are usually regarded as sensitive. The rapid sensitivity test reliably distinguishes between these and methicillin-resistant staphylococci. —We are, etc.,

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Chlorprothixene and Obstructive Jaundice

SIR,—Cholestatic jaundice, which can complicate treatment with phenothiazines and to a lesser extent with butyrophenones, is reported to occur only rarely with chlorprothixene.[1] We therefore report the following case of severe obstructive jaundice occurring during treatment with this drug.

A 59-year-old man was admitted to hospital on 15 June 1972 with acute mania. His past history included mild diabetes mellitus, acute myocardial infarction in 1967, and a cerebrovascular accident in 1970 from which he had fully recovered. During a previous maniac phase in 1971 he had been treated briefly with chlorprothixene (Tarasan) with no ill effects. On admission he was started on Tarasan 100 mg daily intramuscularly and 50 mg orally four times a day as well as digoxin, aldactazide, and chlorpropamide for his various medical conditions. Over the next three to four days he became more co-operative and amiable. On 23 June his skin was slightly yellow, but was thought to be its normal hue. On 27 June Tarasan injections were discontinued and the oral dose increased to 50 mg four times a day. Next day the patient developed a spiking fever and was deeply jaundiced. His liver function tests, previously normal, became quite abnormal. Blood cultures showed a pneumococcal septicemia and a chest *x*-ray confirmed bronchopneumonia. All medication was stopped. Antibiotics brought his infection under control, but he remained deeply jaundiced. On 7 July his bilirubin dropped dramatically and he was eventually discharged with normal liver function. Subsequent investigations showed no evidence of gallstones and the uninterrupted recovery from the jaundice eliminated the possibility of carcinoma, leaving Tarasan as the most likely cause of the jaundice, though chlorpropamide could not be excluded.

Stefko and Zbinden[2] measured bile flow and interbiliary pressure in anaesthetized, cholecystectomized dogs during administration of several different drugs. Whereas chlorpromazine within the range of therapeutic dosage produced a decrease in bile flow and a marked increase in intraductal pressure, chlorprothixene had no effect on these functions. On the other hand, Tesarovâ *et al.*[3] showed that while chlorprothixene had no apparent hepatotoxic effects in most cases it might cause slight changes in liver function within normal limits in up to 29% of cases and even give pathological results in some. These were reversible in all cases.

How neuroleptic and other drugs produce cholestatic jaundice is uncertain. Increased bile viscosity,[4] disordered mobility of the ducts,[5] and damage to the walls of the ductules causing leakage, inspissation, and regurgitation of bile[6] have all been held responsible, though there the direct effect on the ductules may be contributary rather than the sole cause of the jaundice.[2] All three would result in slowing of bile flow or increase in pressure, and it has been suggested that these should be assessed routinely during the screening of new drugs.[2] Nevertheless, the present case would suggest that these tests even when negative, as indeed they were for chlorprothixene, do not totally eliminate the danger of cholestatic jaundice. —We are, etc.,

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Hodgkin's Disease: a Clue or a Fluke?

SIR,—It was with considerable interest that I read the leading article on Hodkin's disease (9 December, p. 564). There is a histological subtype (often called Hodgkin's) which occurs in dogs and cats. We own bullmastiffs, and in this breed the incidence of this type of "leukaemia" is, to quote one veterinary surgeon, ludicrously high. It is virtually unknown in some other breeds. There is a marked family connexion in many cases and there are at least three well-known sires (unaffected themselves) whose second and third generation progeny show a high incidence "showing clustering." In our own case we lost a dog about three years ago with this condition. We now have another which exhibits lymphosarcoma. The granddam of this dog was full litter sister to our last dog. He also has a sire whose grandsire was full litter brother to another dog which died from this condition.

It is easy to check the family relationship in these animals, as pedigrees are always obtainable. This is a numerically small breed, and at the present the breed is losing an average of six animals a year from this disease with a sex ratio of rather more than two males to one female. There would seem to be two distinct "incubation periods"—young (at about 2-2½ years) and mature (at about 6-7½ years). It will be appreciated that until an animal has reached 8 years it cannot be considered "free," and that some dogs will die from other causes before they are old enough to develop the condition. This creates statistical problems. There is no clinical evidence to show which puppy will develop the disease. We know one instance of two animals from the same litter which succumbed to the disease within a few months of each other but in different countries (one had been exported), and therefore environment was excluded.

Many breeders can remember dogs dying from this disease many years ago and the family relationship can be traced through pedigree for several generations. It is also interesting that fellow breeders in the U.S.A. have this condition in their stock. These animals are from the same bloodlines and ancestors as those in Britain—again in a different environment.

A virus was found in cats. It is passed by direct transmission, but the method of infection is as yet unknown.[1] I suspect that when further evidence has been collated we may find this to be so in the bullmastiff. A similar "leukaemic" condition is known in poultry and mice. I hope that scientific research into serious medical problems in our companion animals will improve their health and help further understanding in man.—I am, etc.,

JEAN CLARK

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1 *Animal Health*, 1969, No. 11, p. 14.

Thiocyanate Metabolism in Human Vitamin B_{12} Deficiency

SIR,—Dr. D. G. Wells and others (9 December, p. 588) have focused attention on the role of chronic cyanide intoxication in the aetiology of subacute combined degeneration of the cord. The association between smoking and subacute combined degeneration is confirmed in this study but remains unexplained and, as stated by the authors, their results "provide no support for the hypothesis that chronic cyanide intoxication is responsible for the occurrence of neurological disease in a minority of patients with vitamin B_{12} deficiency, although they do not conclusively exclude this possibility."

I would like to comment on the differing sex incidence in the authors' patients with uncomplicated pernicious anaemia and subacute combined degeneration and in patients with retrobulbar neuritis whom Dr. J. M. Heaton and I reviewed in 1961.[1] Although there were more men (and more smokers) among their patients with subacute combined degeneration than in those presenting with anaemia, the overall preponderance of females in patients with subacute combined degeneration noted in this and in earlier studies[2] is in marked contrast to our findings in retrobulbar neuritis. Our original thesis that retrobulbar neuritis in pernicious anaemia could not be satisfactorily explained on the basis of vitamin B_{12} deficiency alone was based on a critical analysis of 31 cases. Firstly, we noted that there was an overwhelming male preponderance, in that 28 were men. Secondly, it was evident that the development of retrobulbar neuritis in patients with pernicious anaemia was not related to the duration of the disease, to the presence or degree of anaemia, or to diffuse neurological involvement. Unfortunately, we found a lack of precise information about the smoking habits in 31 case reports of

patients with retrobulbar neuritis in association with pernicious anaemia, but in no instance was it stated that the patient was a non-smoker.

These findings suggested to us that there was, in addition to the deficiency factor, a factor which was almost solely confined to men and was responsible for the development of retrobulbar neuritis in patients with pernicious anaemia. We presented evidence that this factor was to be found in tobacco smoke and that tobacco amblyopia and retrobulbar neuritis in pernicious anaemia were similar neuropathological states. As we had previously shown, other clinical manifestations of vitamin B_{12} deficiency may be absent because in pipe-smokers, and occasionally in heavy cigarette-smokers, amblyopia may precede the onset of anaemia, a megaloblastic bone marrow, or diffuse neurological involvement by months or even years.[3]

It is now known that retrobulbar neuritis does occasionally occur in patients with pernicious anaemia[4] and other vitamin B_{12} deficiency states[5] who are lifelong non-smokers. In this connexion, it is important to remind ourselves that besides being present in tobacco smoke and alcohol, cyanide is widely distributed in the plant kingdom, and if the indiscriminate dumping of industrial cyanide waste continues unchecked, there may well come a time when more widespread chronic cyanide neurotoxicity occurs from a dietary source in persons with a genetic or acquired error of cyanide or vitamin B_{12} metabolism.

Further advances in our present knowledge of cyanide and vitamin B_{12} metabolism can be expected with the development and application of the chromatobioautographic method of estimating individual plasma cobalamins in neuro-ophthalmological disorders. Moreover, as stated by Dr. Wells and his colleagues, present methods of measuring free cyanide levels in plasma are inadequate to cope with the small amounts normally circulating. However, in my view enough clinical and laboratory evidence now exists to support the original hypotheses that tobacco amblyopia, retrobulbar neuritis in pernicious anaemia, and Leber's hereditary optic atrophy[6] are clinical manifestations of chronic cyanide intoxication in persons with an acquired or genetic error of cyanide or vitamin B_{12} metabolism.

Hydroxocobalamin, but not cyanocobalamin, is a powerful cyanide antagonist and we have accordingly submitted a case for the withdrawal of cyanocobalamin, with its possible adverse effects in neuro-ophthalmological disorders, in favour of hydroxocobalamin for therapeutic use.[7] It is possible that other cyanide antagonists may soon become available for therapeutic use with the obvious advantage of oral administration. In such circumstances I would again strongly urge that all patients with proved tobacco amblyopia and patients with optic atrophy, myelopathy, or neuropathy of obscure origin should be very carefully screened for evidence of vitamin B_{12} deficiency before any therapy other than hydroxocobalamin is embarked upon.[8]—I am, etc.,

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Special Risks in the N.H.S.

SIR,—Dr. C. E. Astley's letter in the *Daily Telegraph*[1] about the failure of the Department of Health and Social Security to come to terms to provide adequate insurance for workers in dialysis units or on motorways should not be allowed to pass unnoticed. The fact that negotiations on this very important point have come to a halt means that medical staff, especially junior staff or their survivors, can rely only on the charity of the National Health Service in the event of serious accident, illness, or death. This is morally and practically intolerable. I hope all members will join in supporting Dr. Astley's efforts on our behalf.—I am, etc.,

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1 Astley, C. E., *Daily Telegraph*, 5 January, 1973, p. 16.

Fatal Injuries after Car/Lorry Collisions

Sir,—As a constant motorway user I read with great interest the paper Mr. William Gissane and Dr. John Bull (13 January, p. 67).

Examining their figures for fatal collisions occurring when cars and lorries are travelling in the same direction, I am surprised that the death rate is so low. That only 48 car occupant deaths out of a total of 224 occurred in Motorway collisions of this type is, I feel, a great credit to the car-driving public in view of the frequency with which heavy lorries pull out into faster lanes with either no or inadequate warning. This irresponsible behaviour is particularly difficult for the car driver to combat and, I would suggest, is a contributory factor causing cars to occupy the third lane of the motorway whenever possible in an endeavour to avoid either an end-on or a side-on collision.

In view of our large and inadequately used rail system may I support the authors' suggestion that goods be transported by rail rather than road. May I further suggest that a majority of the public would support the use of a rail subsidy to narrow if not reverse the economic advantage of transporting goods by road.—I am, etc.,

C. J. WICKS,

Bushey, Herts.

SIR,—Mr. William Gissane and Dr. John Bull (13 January, p. 67) came to the conclusion that "Some reduction in deaths may be expected from making lorries more conspicuous and eliminating the rear overhang. More fundamental measures are segregation of lorries from cars and return of traffic to railways." Most users of the road would agree with these observations and recommendations, but they are incomplete because they take only the roads and the vehicles into account, while they disregard the mental attitude of the drivers.

The authors suggest that there is "a 95% or more risk of serious injury to car occupants with virtually no risk to the lorry occupants" because of the "mass-ratio" of at least 5. Unfortunately, not only the weight but also the law protects the driver of the lorry. I have repeatedly heard magistrates expressing in private conversation the view that "the police are reluctant to prosecute professional drivers because they know that we do not like to convict them as it would interfere with their livelihood." Lorry drivers know this only too well, and if we are supposed to draw the conclusion from Mr. Kenneth Allsop's article on the subject[1] that an "us-and-they" relationship is developing between drivers of cars and lorries, then some of the "accidents" in the future will be in fact deliberate acts of revenge.—I am, etc.,

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1 Allsop, K., *Sunday Times*, 14 Jauary 1973, p. 15.

Making Hospital Geriatrics Work

SIR,—The letter by Dr. P. W. Hutton (23 December, p. 730) goes to the heart of the problem. His list of the difficulties in turning an old-style geriatric unit into something more dynamic—"staff shortages, medical, nursing, and ancillary, and the rigid mental attitudes of the establishment, lay and professional"—is absolutely correct. Of all, the most important is the rigidity.

The geriatric unit in Sunderland is not new. Our accumulation of severely disabled patients has not interfered with the active part of the unit. The level of medical staffing is acceptable but the provision of ancillary services is low. The provision of hospital beds for geriatrics is 1 per 1,000 of the total population served, but the unit has an active outpatient department and a day hospital. The number of places in local authority accommodation at present is below the level recommended by the Department of Health and Social Security.

A change of heart as advocated by Dr. Hutton is necessary now if the health services are not to be overwhelmed by a rising tide of disabled old people.—I am, etc.,

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SIR,—We too tried much the same technical system as Drs. H. M. Hodkinson and P. M. Jefferys (2 December, p. 536), with acute assessment, intensive rehabilitation, and long stay, but foundered after several years. The "turnover" increased, the "churning around" within the unit increased, the return rate increased with shorter time intervals, the unease between staff, patients, and relatives increased, and long stay, which is scarcely progressive, became even more of a problem. It was the suitable patient to fit the concept of the acute bed who was in short supply, and still is.

The progressive patient-care system involving frequent and considerable changes fits the disabled elderly person badly and is really a compromise between the "tinkering trades service model"[1] and the very unsatisfactory facilities elderly people are expected to accept.[2] Disabled people, moreover, are less able to cope with the demoralized, dead, and isolated conditions that exist in many