common pathogens in an immunosuppressive environment.

The choice of antibiotics in our case was governed by the sensitivity pattern of the initially unidentified Gram-positive bacillus. It was felt necessary to continue antibiotics until the brain-scan and E.E.G. had reverted to normal. In view of possible toxicity with long-term gentamicin the patient was discharged on ampicillin—thought by some authorities to be the antibiotic of choice in listeria infections.^{2,3} Both in initial diagnosis and in assessing improvement the brain-scan proved invaluable as a non-invasive technique.—We are, etc.,

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T.S.H. Level and Thyroid Function

SIR,—I should like to raise some points about the patients described by Dr. W. M. G. Tunbridge and others (13 July, p. 89) as showing a persistently elevated thyroid-stimulating hormone (TSH) level but not found to be hypothyroid on clinical examination and by most "routine" thyroid function tests during the period of observation reported in their paper. The reference to these patients in table I of their article as "euthyroid (all criteria except TSH level)" reflects the authors' feeling, also expressed in the discussion of their observations, that the significance of the elevated TSH level is as yet not sufficiently clear.

May I suggest that if, on describing the thyroid state of these patients, one referred to the physiology of the entire thyroid axis these patients could be assigned a definite and clinically more helpful diagnosis—the elevated TSH, the pattern of the thyroid-releasing hormone (TRH) response (in the patients so tested), and the return of the TSH to normal on thyroid substitution are all consistent with the diagnosis of hypothyroidism. Because the choice of a particular diagnostic term tends to determine one's further approach to a given problem, I feel that the use of the term "euthyroid" in relation to these patients, with whatever qualifications, is undesirable.

With a more complete understanding of the regulation of thyroid function and with the availability of better ways of separating the, at present, clinically not discernible forms of hypothyroidism from euthyroidism, it would seem timely to use diagnostic terms reflecting the progress in this field. The normal ranges for all the presently measurable criteria for characterizing thyroid status are adequately defined. In my view once any one of these measurements falls outside the normal range the use of the term "euthyroid" is no longer acceptable. Thus the term "subclinical hypothyroidism," mentioned in the discussion of the article in question, would seem a physiologically more correct way of referring to such patients. I find "compensated hypothyroidism" actually preferable; it expresses

both the thyroid pathology and the mechanism whereby it is corrected, quite possibly only temporarily. By emphasizing the presence of a thyroid abnormality rather than that the effects of this abnormality are, for the present, clinically not recognized (quite possibly for lack of obtaining the relevant information) both the interest of the patient and progress towards an understanding of their condition would be better served.

In a subsequent article by Dr. A. D. Toft and others (20 July, p. 152) evidence is presented that the elevated TSH in ¹³¹I-treated patients may be a useful guide in selecting those who can be expected to develop clinically manifest hypothyroidism. Thus it would appear that the biological and clinical significance of the persistently elevated TSH may be established, at least in this respect.

There is little firm clinical evidence and considerable controversy about the extra-thyroidal effects of TSH^{1,3} and TRH^{4,6} in man. It would seem certainly appropriate and desirable to look for ways of detecting effects of this kind in patients who are exposed to supraphysiological concentrations of these substances over prolonged periods of time.—I am, etc.,

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Myeloblastic Transformation

SIR,—In their paper on acute transformation of chronic granulocytic leukaemia (C.G.L.) (13 July, p. 77) Dr. A. D. S. Spiers and his colleagues discuss the rapidly progressive form of metamorphosis. They also emphasize the difficulties of definition and classification in this field.

Acute transformation is also seen in polycythaemia rubra vera (P.R.V.) and in myelofibrosis. Of the 18 patients seen at the London Hospital with acute transformation since 1968, six had a diagnosis of C.G.L., five a diagnosis of P.R.V., and seven a diagnosis of myelofibrosis. In the myelofibrotic group two patients originally had C.G.L. and three originally had P.R.V.

In the C.G.L. group the mean survival after transformation was 6.6 months with a range of 4 to 10 months. Two patients were treated with mercaptopurine only; one of these achieved a complete remission and was maintained for six months with mercaptopurine and intermittent methotrexate. During the remission the patient was well and required no transfusions, his peripheral blood having the appearance of C.G.L. When he relapsed two courses of triple drug therapy (thioguanine, cytosine arabinoside, and prednisone) failed to produce another remission and by this time he had developed a rectal carcinoma. In the other patient the white cell count and blast count were reduced, but there was little real benefit. Four patients received three drugs or more as soon as the diagnosis of acute transformation was made, and various combinations of daunorubicin, thioguanine, cytosine arabinoside, hydroxyurea, asparaginase, vincristine, adriamycin, and prednisone were used. One of these patients is currently in full remission 13 weeks after diagnosis, the remission having been achieved with three courses of thioguanine, cytosine arabinoside, and prednisone. The other three patients have died; none achieved a full remission but all had partial remissions. In each case the patient improved symptomatically, required no blood transfusions for at least two

months, and was able to return home. One patient was able to return to work. Most patients received not more than three drugs at a time, but one patient received a five-drug combination at the end of his illness. Thus we have had one surprisingly good response to mercaptopurine alone and some limited success with multiple drug therapy less "aggressive" than TRAMPCO(L).

In the myelofibrotic group the mean survival was nine months with a range of 3-19 months; one patient is still alive. The illness seemed to run a more chronic course, one patient surviving 13 months after developing a peripheral blood blast cell count of 40%. Three patients received no specific drug therapy at this stage of their illness and four were given mercaptopurine, which was combined with intermittent methotrexate in one case. The quality of life in this group was significantly affected by the continuing need for blood transfusions during the later phase of their illness.

In contrast, the P.R.V. group had a mean survival of only 31 days with a range of three days to six weeks, one patient dying with leukaemic deposits in the dura. There was hardly time to institute effective chemotherapy in two of these patients, and the other three had a rapid course despite multiple drug therapy with the same drugs used in the C.G.L. group. One patient in the treated group died with only 25% blast cells in the peripheral blood, but the other two patients had more than 60% blast cells at death. All the patients had received ³²P, the total dosage range being 7-73 mCi. Other workers have also noted the rapid course of this illness. Chievitz and Thiede¹ mention three such cases and Szur and Lewis² record survivals of one month, three months, and one week in their three patients with P.R.V. who transformed to acute leukaemia.

Our experience emphasizes the very wide clinical variation to be found within the spectrum of acute transformation of myeloproliferative disease. Aggressive treatment of transformation in C.G.L. carries clear benefits and TRAMPCO(L) may be superior to other multiple regimens, though we have had some success with less aggressive therapy. In myelofibrosis this type of approach would seem inappropriate as these patients have limited amounts of haemopoietic tissue and are often in poor general condition, sometimes with cardiac and hepatic dysfunction. Our experience with acute transformation in P.R.V. is small, but if the prognosis is significantly worse than that of the C.G.L. group then these patients present a greater therapeutic challenge as they are usually in good general condition at the time of transformation. It would be worth while to try Dr. Spiers's TRAMPCO(L) regimen in this situation in an attempt to improve the particularly poor prognosis for these patients.—We are, etc.,

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Screening for Rickets

SIR,—Nutritional rickets is not uncommon in British paediatric practice, especially in the industrial areas with concentrations of Asian immigrants. It is not intended here to discuss the role of sunlight and skin pigmentation, socioeconomic factors, and low vitamin D intake or food faddism and the high phytate content of chupattis.

On two occasions after a Pakistani child (one aged 14 and the other four) had been found to have rickets the whole family was screened radiologically. Two more cases of rickets (in a girl of 17 and a child of one)