days may be useful. If the flap necroses it must be removed early as described, but in favourable cases the flap will survive and grafting will be avoided. Spontaneous healing will occur under a Viscopaste bandage with the patient ambulant. I cannot understand why Mr. David uses the medial aspect of the thigh as a donor site. The postero-lateral aspect is much safer to use, but in the elderly the deltoid region is even better as it allows early ambulation.—I am, etc.,

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Abnormal Cells and Hodgkin's Disease

SIR,—Dr. M. R. Halie and colleagues (10 June, pp. 609 and 611) re-emphasize the importance of abnormal cells found in the circulation as evidence of haematogenous dissemination in Hodgkin's disease and involvement of the spleen.

Vascular invasion of lymph nodes, capillaries, and small arteries in the lungs have been described and illustrated earlier.¹ The lumina contained Reed-Sternberg cells and "bizarre polymorphous cells" (that is, large histiocytic cells). The spleen was not enlarged, and pathological elements were found in a spleen weighing as little as 100 g. In my opinion the involvement of this organ is more likely to be a sign of haematogenous dissemination than the cause of it.

In view of the therapeutic implications, Dr. Halie and colleagues' findings of "moderately basophilic cells" in the peripheral white cell concentrates in 14 out of 25 patients require urgent confirmation. While the morphology of Reed-Sternberg cells as they appear in bone marrow aspiration material,^{2,3} and much less frequently in the peripheral blood,¹ is well known, the specificity of the "moderately basophilic blast-like cells" remains to be established. Morphologically these latter cells sound not unlike the "large histiocytic cells" described by me¹ or some of the "atypical" or "neoplastic" cells of Bouroncle.—I am, etc.,

S. VARADI

Staines, Middx

¹ Varadi, S., *British Medical Journal*, 1960, 1, 1239.
² Varadi, S., *Sang*, 1938, 12, 106.
³ Varadi, S., *British Journal of Haematology*, 1955, 1, 184.

Chemotherapy and Leukaemia

SIR,—Dr. J. Stuart (15 April, p. 152) draws our attention to the fact that the generation of leukaemic blast cells in acute leukaemia is not a rapid proliferating process. He discusses the profound implications in respect to the effectiveness of antimitotic chemotherapy in the treatment of acute leukaemia which arise therefrom. I believe he puts his finger on a point of considerable significance in discussing chemotherapy when he states that it is surprising that these agents are able to show their marginal selectivity for leukaemia cells since the more frequently dividing haemopoietic cells might be expected to provide the major target organ.

There is an accumulating body of evidence which may suggest that the blast cell in acute leukaemia is a secondary phenomenon,

and indeed may be an integral part of a specific immune response.

Both in natural and experimental situations leukaemic cells have been known to pass from the involved subject to another recipient. Secondary disease, however, has not been recorded, though leukaemia in an infant born of a mother with leukaemia is noted nine months after delivery.¹ This is the only incident of this type recorded in the total world literature and may even be related to other factors.

On the other hand leukaemic transformation of engrafted marrow cells in vivo in a leukaemic patient has been documented.² There is evidence that the frequency of abnormal karyotypes in leukaemic cells in adults with acute leukaemia increases with increasing leukocytosis, and that chromosomal aberrations occur with increasing frequency as patients approach death.³ This suggests that the genetic changes in leukaemic cells may themselves be secondary to continuing disease.

The demonstration of specific antigens on the surface of the blast cell,⁴ the mitogenic effect of leukaemic blast cells on autologous lymphocytes in vitro,⁵ and the indirect immunofluorescence of sera from two children with acute leukaemia demonstrating positive membrane fluorescence with their own blasts⁶ lend some credence to the suggestion that if "non-self" antigen is present on the blast cell that the blast may itself be part of the total immune response.

Perhaps the chemotherapeutic agents used in leukaemia should be considered as immunosuppressants rather than as simple antimitotics—that is, their effectiveness results from the suppression of an immune reaction in which blast cells play an integral part. The wisdom of the philosophy of "total kill" of blast cells, however, may be open to some question if those factors responsible for blast formation remain operative.—I am, etc.,

JAMES E. PARKER

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¹ Cramblett, H. G., Friedman, J. L., and Najjar, S., *New England Journal of Medicine*, 1958, 259, 727.

² Fialkow, P. J., Thomas, E. D., Brvant, J. T., and Neiman, P. E., *Lancet*, 1971, 1, 251.

³ Hart, J. S., Trujillo, J. M., Freireich, E. J., George, S. L., and Frei, E., *Annals of Internal Medicine*, 1971, 75, 353.

⁴ Mann, D. L., Rogentine, G. N., Halterman, R., and Leventhal, B., *Science*, 1971, 174, 1136.

⁵ Viza, D. C., Bernard-Desani, O., Bernard, C., and Harris, R., *Lancet*, 1969, 2, 493.

⁶ Zintl, F., Aurich, G., and Plenert, W., *Folia Haematologica*, 1971, 95(4), 337.

Teaching Nutrition

SIR,—Your leading article "Teaching Nutrition" (29 January, p. 262) is thought-provoking. You have rightly emphasized that a department of nutrition should be established in each medical school. This you speak of the United Kingdom. What about its need for a developing country like India?

There are over 100 medical colleges in the country and in none, so far as I know, is there even a section of nutrition, leave aside a department. There is one Nutritional Research Laboratory at Hyderabad, where good work is being done under the guidance of some able scientists, but its message has not reached medical schools. "A basic doctor" coming out of our medical colleges is

completely ignorant of the nutritional needs of his patients and the community he is supposed to serve. This is so because there is hardly any emphasis on the teaching of nutrition and whatever is attempted is stereotyped.

Out of a population of about 560 million, it is estimated that at least 220 million subsist on submarginal nutrition. Even in a government-run charity hospital (at least 90% are such hospitals), it is a common sight to see 30 to 50% of patients having some stigmata of malnutrition due to poverty, food-fadism, religious bias, and poor dietary guidance by practitioners of indigenous or modern medicine.

Because of financial stringency it may not be possible to open a department of nutrition all at once in every medical school, but to begin with there should at least be a nucleus in important medical colleges in the capitals of large states. Other medical colleges can train an associate or assistant professor of medicine in clinical nutrition, and there should be close co-ordination between the departments of social and preventive medicine or community medicine with the clinical departments including paediatrics.

In the therapeutics of a patient nutrition plays as important a role as drugs. There is a Chinese saying that medicine is given only when nutrition has failed. The French believe that it is better to pay the cook than the doctor.

So far in our clinical teaching we have copied verbatim books like *Clinical Methods* by Hutchinson and Hunter. It is high time we also incorporate the full dietary history of a patient, giving full calories and quality of the diet. Apart from this, we should also include family planning advice. Let such a system be practised in a medical school, whether in a developed or in a developing society.—I am, etc.,

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Screening for Glaucoma

SIR,—There is much controversy over the value of screening whole populations for chronic simple glaucoma. The subject has been reviewed by P. A. Graham.¹ He pointed out the enormous practical difficulties of using tonometry on large populations in view of the number of false positives and false negatives, and the difficulties of persuading patients with no apparent loss of function to put up with the side effects of treatment. He also calculated that for every year a patient spends with any measurable degree of visual field loss, 17 years are spent with an abnormal ocular tension. In general, other studies in Britain² have confirmed the unsatisfactory nature of tonometry as a screening test. In the U.S.A., however, 10 out of 12 major screening clinics practise routine tonometry and the test is generally, though perhaps uncritically, accepted.

As the first functional disability in chronic simple glaucoma is loss of visual field, it seems logical to detect this by screening procedures. In the early stages, this can often be detected before the patient has noticed anything wrong. Progression normally is slow, so that little is lost by treating at this stage rather than earlier. However, other studies³ have suggested that visual

field testing also gives an unacceptably high number of false positives. Examination of the fundus by a skilled ophthalmologist seems to be the most reliable single test for glaucoma, but this is impractical as a screening procedure.

At the BUPA Medical Centre we have in the last year carried out just over 1,000 routine analyses of visual fields in middle aged men, using a Friedmann visual field analyser.⁴ Three patients were found to have significant defects: one due to myopia, one due to hypertensive exudates, and one due to a local vascular lesion (these diagnoses were made by our consultant ophthalmologist). In addition, nine isolated peripheral lesions were found, which are almost certainly of no significance.

We found the instrument easy to use and acceptable to staff and patients. However, as no case of glaucoma was found, the test is clearly not worth using routinely for screening purposes. We intend continuing the survey, restricting the test to patients aged 65 or over, or those with a positive family history of glaucoma.

Other studies using this or similar instruments have found yields of 0.7%¹ and 0.6%⁵ and of 0.7%² using tonometry. The total absence of chronic simple glaucoma in our population is most surprising. It is possible that they have been missed owing to technical error; however, as three cases of non-glaucomatous field defects were subsequently confirmed this seems unlikely. As the condition is asymptomatic at this stage any form of conscious selection is unlikely. The possibility remains that glaucoma may be less common in our social class 1 and 2 population than in the country as a whole.—I am, etc.,

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The Medical Centre,
London N.1

¹ Graham, P. A., *Proceedings of the Royal Society of Medicine*, 1966, 59, 1215.

² Banks, J. L. K., Perkins, E. S., Tsolakis, S., and Wright, J. E., *British Medical Journal*, 1968 1, 791.

³ Graham, P. A., and Holows, F. C., in *Glaucoma*, Ed. L. B. Hunt, P. 103, Edinburgh, Livingstone, 1966.

⁴ Bedwell, C. H., *Ophthalmic Optician*, 1967, 7, 566 and 616.

⁵ Linfield, P. B., *Ophthalmic Optician*, 1970, 10, 1044.

Sleep and a Bedtime Beverage

SIR,—The critical letter from Miss Aviva Petrie (10 June, p. 652) following the paper by Dr. Vlasta Březinová and myself (20 May, p. 431) raises principles of research strategy. We had used electrophysiological techniques to compare sleep after 250 ml of hot milk, containing 32 g of Horlicks powder, with sleep after an inert capsule. An indistinguishable control was not feasible, and people today are attuned to pills as sleep improvers. There is, actually, no evidence that suggestion will improve sleep when measured electrophysiologically. The sleep of poor sleepers has been reported not altered by blank sleeping pills.¹ Miss Petrie says we should have used hot water and milk as additional variables, evidently thinking nutrient control less important.

It would indeed be nice to use the additional controls she suggests, as well as other proprietary food drinks, bread and cheese, fish and chips, black pudding, and other bedtime snacks, with varying doses of each. In high-virgin territory, however, demands

must be simple. Too complex an initial design merely wastes resources. We asked whether we could find any evidence to support a report that a concentrated, palatable, liquid food before sleep could make sleep less restless. We used two conditions. Had we used four, that would have meant not 18 experimenter-months and 60 miles (96 km) of recordings, but 3 years and 120 miles (200 km).

Miss Petrie, a statistician, would probably say she could have offered us a neat design embodying four conditions and no additional nights, but at the cost of reduced nights per condition. Then the study would have drawn a blank. We found again, as we have often found before, that sleep under a first laboratory condition is not the same as when the individual has had the same condition repeatedly.

No, only when one has got a simple first answer, and learned from practical experience and inevitable discussion and rumination, can one justifiably commit expensive resources to answer the new questions that present themselves.—I am, etc.,

IAN OSWALD

Department of Psychiatry,
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¹ Kales, J., Kales, A., Bixler, E. O., and Slye, E. S., *Clinical Pharmacology and Therapeutics*, 1971, 12, 691.

Febrile Convulsions in Early Childhood

SIR,—I would like to take up two points from your leading article "Febrile Convulsions in Early Childhood" (10 June, p. 608).

The statement that "continuous prophylactic antiepileptic treatment should not be given: it is unnecessary and unhelpful" is too dogmatic. No satisfactory trial has yet been described. Millichap and others¹ compared continuous prophylactic phenobarbitone given only during febrile episodes and found no difference, but their sample was small and there was no control group. One would not recommend continuous prophylaxis after one or two febrile convulsions, but for the child who is having frequent convulsions, often occurring before anticonvulsants can be administered, continuous prophylaxis may be effective.

The desire to exclude the possibility of pyogenic meningitis should not require resort to lumbar puncture in every case. If one raises the age limit for "febrile convulsions" from 6 months to 10 months, then there should be no difficulty in differentiating pyogenic meningitis clinically. Convulsions in meningitis are usually due to cerebral oedema and one would not expect such a child to recover from a convulsion in the way that a child with a simple "febrile convulsion" does. In fact, a careful search of the memories of two senior consultant paediatricians revealed no instance of pyogenic meningitis presenting as a "febrile convulsion." It is mandatory, however, to perform a lumbar puncture if there is the slightest doubt.—I am, etc.,

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¹ Millichap, J. G., Aledort, L. M., and Madsen, J. A., *Journal of Paediatrics*, 1960, 56, 364.

SIR,—The leading article (10 June, p. 608) describing febrile convulsions in early child-

hood was informative, but the advice on treatment was a little inconsistent with the facts given earlier.

If a child is unwell before the convulsion, the fit does not last more than 10 minutes, and is not followed by postepileptic hemiplegia then it fits the diagnosis of a febrile convulsion. If the cause of the pyrexia is obvious—for example, otitis media, and clinical signs of meningitis are absent why should the child be sent immediately to hospital? Tepid sponging and antibiotics are available at home. It would be interesting to know how many paediatricians would perform a lumbar puncture in such a case as the one described above.

As febrile convulsions almost always occur only once in each febrile episode even the "traditional" paraldehyde may be a case of "shutting the stable door."—I am, etc.,

DONALD MORTON

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Teesside

SIR,—Your recent leading article on febrile convulsions (10 June, p. 608) though excellent should not pass without comment.

In the final paragraph are two statements which I would question. Surely there are occasions, for instance where attacks are frequent, when it is undoubtedly best both for the child itself and the family, if the parents, with of course medical help, learn to deal with the problem at home. Secondly, is paraldehyde, unpleasant stuff even in the old days, really still the drug of choice for acute convulsions? I have not seen a glass syringe in years and I cannot believe that many doctors in Britain carry them these days.

No drug is completely without danger, but the popular and very effective treatment in Denmark seems to be intramuscular or intravenous diazepam with which many would combine intramuscular phenobarbitone to avoid the danger of the sometimes rather short therapeutic action of the former drug given alone.—I am, etc.,

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Mode of Action of Verapamil

SIR,—I have read with interest the correspondence concerning verapamil and the heart. Dr. L. Schamroth and others (11 March, p. 660) discussed the possible modes of action of this drug and concluded its action to be uncertain. They were criticized in this by Drs. B. Livesley and S. Oram (1 April, p. 50), who felt that verapamil could act by augmenting vagal tone on the atrioventricular specialized tissue of the heart.

However, in making this suggestion they give no indication as to their source of reference regarding the vagal innervation of ventricular specialized tissue. To the best of my knowledge, morphologic evidence of direct efferent vagal supply to the atrioventricular bundle and its ramifications in the human heart is lacking. This was certainly the conclusion drawn by Vassalle,¹ who stated that while vagal stimulation produced ventricular standstill there was no evidence that this was due to vagal inhibition