treatment of wounds. Dr. Richardson has, however, fallen into the error of regarding débridement as carried out by Larrey with the procedure as now practised. Thus he describes (p. 13) Larrey's practice in gunshot wounds as "... excising all dead and dying tissue and removing all foreign bodies from a wound—a procedure known as débridement." A reference to Larrey's *Clinique Chirurgicale Exercée Particulièrement dans les Camps et les Hôpitaux Militaires depuis 1792 jusqu'à 1829* reveals that this statement, inaccurately describes his practice. His primary treatment for wounds not requiring amputation was *pansement*, a technique of careful bandaging which kept the dressings in place until they spontaneously separated many days, and sometimes weeks, later, and an anticipation of Trueta's practice in the Spanish Civil War.

Larrey's primary use of the verb *débrider* is with the meaning of "to incise." Thus in volume 1 page 54 he writes: "*Si les plaies d'armes à feu sont accompagnées d'hémorragie, il faut nécessairement les débrider pour mettre les artères à découvert et en faire la ligature. . .*" Later he uses it as an extension of its literal sense of "to unbridle" (Fr. *bride* bridle) to refer to the division of actual or potential constricting bands. Thus for deeper wounds which extend to "*les parties charnues et aponévrotiques*" one must divide "*des brides propres à produire l'étranglement*" (p. 55). He goes on to say that wounds in regions where there are neither muscles nor aponeuroses "*ne doivent pas être débridées*" except to ligate arteries. It is true that he says (p. 57) that in deep wounds with fragmentation of bone one should remove separated fragments "*dont on ne peut espérer la soudure avec le reste de l'os*," but this is clearly because they are useless in the healing process.

Larrey did establish the importance of one aspect of débridement, the division of constricting aponeurotic tissues. The other, the removal of tissue debris serving as a culture medium for micro-organisms, had to await the surgical application of modern bacteriology and pathology.—I am, etc.,

DAVID PATEY

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Infections in Asplenic Adults

SIR,—Dr. L. E. Ramsey (27 July, p. 254) writes of the susceptibility of asplenic adults to infection. I must say that in some 40 years' experience I have not found, with one possible exception, an increased susceptibility to infection among asplenic adults. In 1935 I reported¹ a follow-up for an average of eight years of 100 adults in whom the spleen had been removed for rupture (the spleen otherwise being normal) and no increased rate of infectious disease could be found. It has later been suggested that splenectomized persons may be more liable to contract babesiosis of the brain. Of this I have no experience. My original studies in this matter had to do with the incidence of cancer in splenectomized persons, but I could not find any evidence of an association.²—I am, etc.,

E. ASK-UPMARK

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¹ Ask-Upmark, E., *Svenska Läkaresällskapets Förhandlingar*, 1935, 61, 197.

² Ask-Upmark, E., *Medical Masqueraders*, Stockholm, Scandinavian University Books, 1969.

Amitriptyline Poisoning in Childhood

SIR,—Goel and Shanks¹ have called attention to the increasing incidence in children of poisoning by tricyclic antidepressants. Meadow and Leeson² described the problems in managing poisoning from delayed-release tablets (Debendox). We report here a case of accidental poisoning due to a sustained-release form of amitriptyline.

A 5-year-old boy was admitted to hospital at 2.30 p.m. Three and a half hours before then his mother had noticed his gait to be reeling and had discovered that he had ingested four 50-mg tablets of orphenadrine hydrochloride (Disipal) and an unknown number of 50-mg capsules of Lentizol (amitriptyline), which contains a pellet of the drug in a form which delays liberation of the active constituent. On arrival he was disorientated, agitated, and incoherent. His pupils were fixed and dilated and his tendon jerks very brisk. He was subject to episodes of purposeless screaming and thrashing about of his body, which hindered assessment. His temperature was 37°C, blood pressure 120/80 mm Hg, and pulse rate 120/min (before therapy). He was sweating profusely. There was no cyanosis or other evidence of respiratory depression. Intramuscular paraldehyde 4 ml was given to facilitate gastric lavage. No identifiable capsules or pellets were retrieved. His bladder was catheterized in anticipation of urinary retention. We treated him as we do children poisoned with delayed-release tablets—that is, oral purging and colonic lavage. Magnesium sulphate 5 g was left in the stomach after gastric lavage and was subsequently given orally two-hourly. Enemata of soap and water and magnesium sulphate 65 g were given alternately half-hourly for six hours. Further sedation was required at 11 p.m. and thereafter his clinical condition slowly improved. Continuous cardiac monitoring showed only a persistent sinus tachycardia. Recognizable pellet fragments were recovered in the rectal effluent 14 hours after the start of treatment. The boy had completely recovered 36 hours after admission.

This is the first case we have seen of a child poisoned with this amitriptyline preparation. The manufacturers have had no other reports to date. This may be partly because it is not prescribed as often as shorter-acting formulations. In particular, we have not known of it being given for enuresis. The dose of amitriptyline associated with severe symptoms is said to be 20 mg/kg.¹ This child would have had to have taken only six capsules to receive that dose. His mother did not know the exact number taken but thought that the bottle had been "almost full." Our treatment was aggressive because of previous experience in this unit.² We thought it justified in this case because of the difficulty of treating amitriptyline poisoning once the drug has been absorbed, and it seemed imperative to try to remove as much unabsorbed material from the gut as rapidly as possible.—We are, etc.,

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Leeds

¹ Goel, K. M., and Shanks, R. A., *British Medical Journal*, 1974, 1, 261.

² Meadow, S. R., and Leeson, G. A., *Archives of Disease in Childhood*, 1974, 49, 310.

Lawn Mower Injuries

SIR,—May we add to the interesting letter from Dr. J. R. Hulme and Mr. A. R. Askew (13 July, p. 113) by relating the following case, which occurred last year. It illustrates a further complication resulting from such injuries.

The patient, a gardener aged 35 years, injured the four medial toes of his right foot

when a rotary mower he was using struck his boot. He was admitted to hospital where debridement of the wounds, appropriate wiring of his toes, and suturing of tissues were carried out. A first dose of tetanus toxoid and courses of cloxacillin and ampicillin were given. After three days he was discharged home and sutures were removed two weeks later when the wounds appeared healthy. At follow-up three weeks later the vascular condition of his second right toe was poor and its amputation was planned in 10 days' time. During this interval his general practitioner intended giving him a second dose of tetanus toxoid, but at the time of his appointment he felt unwell, his neck and jaw were stiff, and he did not attend the surgery. Two days later he was much worse and he then visited his doctor, who diagnosed tetanus and arranged his immediate readmission to hospital. The second dose of tetanus toxoid was not given.

In hospital the purulent and gangrenous toe was amputated and sheep antitetanus serum and penicillin in high dosage were given. Next day severe spasms of tetanus started which rapidly increased in frequency and severity; he was transferred to the intensive therapy unit where tracheostomy was performed, curarization undertaken, and full supportive therapy initiated. He was kept paralysed for 3½ weeks. *Clostridium tetani* was not isolated from wound swabs taken at the time of amputation, but was recovered from a section of the gangrenous toe placed in a previously boiled Robertson's meat broth. He was discharged from hospital six weeks after admission, at which time the second tetanus toxoid dose was given. At no time previously had he been actively immunized against tetanus; he had received one dose of A.T.S. in 1962.

Dr. A. T. Willis made the comment that this case illustrates that a first dose of toxoid given at the time of wounding is not protective.

We thank Dr. P. A. Thorn, consultant physician, for clinical details and Dr. A. T. Willis, director of Luton Public Health Laboratory, for confirming the identity of the organism.

—We are, etc.,

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Alliterative Anxiety about Arsenic

SIR,—Pleased at the prospect of palates partaking poison-free porcine pâté (24 August, p. 487) the cosmopolitan clientele of your columns craves clarification of the concentration of cacodylic acid in kosher cuisine.—I am, etc.,

S. K. GOOLAMALI

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Pontomedullary Listeriosis in Renal Allograft Recipient

SIR,—We were most interested to read the report by Dr. J. F. Mahony and others (29 June, p. 705) of a case of *Listeria monocytogenes* septicaemia with non-meningitic pontobulbar involvement after renal transplantation. We have seen a similar case.¹ In their case the initial presumptive diagnosis was of fungal meningitis, in ours that of herpes simplex encephalitis—both not un-

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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- 1 Samuel-Gibbon, A. G., et al., *Guy's Hospital Reports*. In press.
- 2 Macnair, D. R., White, J. E., and Graham, J. M., *Lancet*, 1968, 1, 16.
- 3 Lavetter, M. D., et al., *New England Journal of Medicine*, 1971, 285, 598.

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.,

G. ANTONY

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Kensington, N.S.W.

- 1 Asboe-Hansen, G., *American Journal of Medicine*, 1959, 26, 470.
- 2 Asboe-Hansen, G., *Archives of Dermatology*, 1960, 82, 32.
- 3 Bland, J. H., and Frymoyer, J. W., *New England Journal of Medicine*, 1970, 282, 1171.
- 4 Kastin, A. J., et al., *Lancet*, 1972, 2, 740.
- 5 Prange, A. J., jun., et al., *Lancet*, 1972, 2, 999.
- 6 Mountjoy, C. Q., et al., *Lancet*, 1974, 1, 958.

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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GEORGE JENKINS

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London E.1

- 1 Chievitz, E., and Thiede, T., *Acta Medica Scandinavica*, 1962, 172, 513.
- 2 Szur, L., Lewis, S. M., and Path, M. O. *British Journal of Radiology*, 1966, 39, 122.

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)