but it would be interesting to know what brand was used in the study by S. J. Cameron and J. Richmond. As usual, the final answer will probably be found in a combination of a toxic and an allergic mechanism.—I am, etc.,

C. HENDRIKSEN

Leyden, Holland


SIR,—Your leading article describing the skin reactions to ampicillin (22 January, p. 195) misleadingly suggests that the aetiology still remains a mystery.

It has been shown that hypersensitivity to penicillins results from the presence of small amounts of protein residues derived from the fermentation process in manufacture and carried through to the final product. 1 The process for manufacture of ampicillin has already been modified to reduce the former content of protein residues and a similar preparation of purified benzylpenicillin is now available.2

In man, benzylpenicillin freed from protein impurity does not react in the skin test in 90% of penicillin-sensitive patients.3 Aqueous solution of penicillins form polymers on standing which may result in an anaphylactoid type of reaction, so they should be used as soon as possible after preparation.—I am, etc.,

ROBERT ALLAN

General Hospital, Birmingham


Huntington’s Chorea and the Adrenal

SIR,—On the basis of the observation that: (1) Disturbances in sexual behaviour and progressive loss of weight are early symptoms in Huntington’s chorea; (2) the urinary excretion of dehydroepiandrosterone is reduced in this disease; (3) inclusion bodies occur in the adrenal cortex in Parkinsonism, the clinical counterpart of Huntington’s chorea; (4) 1-Dopa loading in those sibs from families with Huntington’s chorea who will later develop the disease elicits choreic movements,1, 2 this in vivo connotation buttressing both a prognostic test and indicating deranged catecholamine metabolism to underlie Huntington’s chorea (as already been proven in Parkinson’s disease) a study was made of plasma testosterone, cortisol, dehydroepiandrosterone (DHEA), dehydroepiandrosterone-sulphate (DHEA-S) in 12 patients with Huntington’s chorea. All blood-samples were obtained either at 1500 hrs or at 2100 hrs. The testosterone and DHEA-levels were normal in all patients. In eight of them, the cortisol levels were very low, ranging from 3 to 6 µg/100 ml, which may be explained by the diurnal rhythm of this hormone. In nine patients, DHEA-S (not subject to diurnal variation) was considerably reduced (below 25 µg/100 ml). The discrepancy between normal DHEA and markedly reduced DHEA-S apparently points to a defect of sulphation (sulphokinase-deficiency) in the adrenal reticular zone, which develops during the third year of life and is innervated by the sympathetic nervous system. The focal adrenal zone synthesizes DHEA-S.3

The findings reported above may not essentially constitute more than a parameter in Huntington’s chorea, though a speculative link (DHEA-S—adrenal zone reticulo-sym pathetic nervous system—catecholamine/dopamine/neostriatum) might be considered to relate this finding to the pathogenesis of the disorder.—We are, etc.,

G. W. BRUYN

F. H. DE YONG

J. H. VAN DER MOLEN

Bilthoven, Holland

1 Oepen, H., personal communication.
4 Klauwens, H. C., Paulson, G. W., and Barbeau, A., Lancet, 1185.

Clofazimine in Leprosy

SIR,—The paper by Dr. A. B. A. Karat and others (27 November, p. 514) entitled “Controlled Clinical Trial of Clofazimine in Untreated Lepromatous Leprosy” provides some interesting data on a small number of patients observed for a short period of time. Although statistical analysis may give no very clear results, some of their clinical findings show an interesting trend. For instance, the marked changes observed in body weight may reflect improvement (in the case of clofazimine) or deterioration (in the case of dapson) in the general condition. It is furthermore noted that the only patient showing improvement in motor function was in the group taking clofazimine, and that the

Clinical trials of clofazimine (Commercial name: Leproderm) in the treatment of leprosy have been undertaken in the last few years. The drug has a relatively low toxicity but is, as the authors pointed out, a very expensive one. Clofazimine is a nitrogen-tetrazolium dye and it was previously used for the demonstration of acid-fast organisms on histological sections.

The results of the clinical trial clearly indicate that clofazimine has a significant effect on the disease process, particularly in patient group one. The authors state that their results confirm previous reports from India. The study by Drs. Karat et al. is further evidence of the value of clofazimine in the treatment of leprosy. Further clinical trials and investigations are needed to assess the long-term effects of clofazimine and to determine whether it can be used as a primary treatment for leprosy.
only patient experiencing deterioration in sensory function was in the group given dapsone. Again, clofazimine at a higher dosage did control a necrotizing erythema nodosum leprosum eruption in one patient. These unfounded findings reflect a general trend in the report indicating the advantages of clofazimine in clinical usage. It may be that had clofazimine been given in a higher dose than 100 mg daily to these South Indian patients—notoriously liable to severe exacerbation in the presence of widespread bacillary load—many of the reported advantages of clofazimine in preventing erythema nodosum leprosum might have been demonstrated.

While the summary may accurately represent the results seen in this limited trial, the authors give little indication of the general tenor of the numerous reports in this field which bring out clearly the advantages of clofazimine that appear only as trends in their report; nor do they take cognizance of the arguments that have inclined some cost-conscious physicians to prescribe clofazimine in certain circumstances to reaction-prone patients suffering from lepromatous leprosy.

The authors, the authors cannot of course be gainsaid, but the definite and rather sweeping conclusions they draw are not directly derived from the evidence they adduce from a small number of patients treated for an insufficient period of time, and given a fixed (and probably inadequate) dosage of the drug.—I am, etc.,

S. G. BROWNE
Leprosy Study Centre, London W.1

Mobile Coronary Care Unit

Sir,—The communications of Dr. H. C. Smyllie and others (1 January, pp. 31 and 34) demand comment. Their absence of logic is astounding. They investigate in detail the number of coronary beds required in the Doncaster area but go on to argue that a mobile coronary care unit is unnecessary. They seem to be unaware of the published data on mobile coronary care. Certainly they do not refer to the numerous publications on this subject,1-7 nor to the W.H.O. report on mobile coronary care units published by the latter. Yet it is inconceivable that the addition of a mobile coronary care unit to an existing hospital coronary care unit will treble the impact of the latter on the mortality from acute myocardial infarction.

A mobile coronary care unit or similar prehospital coronary care scheme can influence the mortality in several ways.

(1) The early initiation of intensive care outside hospital may prevent ventricular fibrillation and the authors and his colleagues argue that the application of intensive care some two hours after the onset of symptoms cannot have an impact on mortality because of the risk of death is slight. Their argument is based upon the incorrect assumption that a coroner’s report in clinical usage is a white sheet of coronary deaths. Reference to any of the published statistics, such as those of McNeilly and Pemberton,9 covering the early course of coronary mortality as a whole will show that the risk of death is far from slight during the period between 15 minutes and 4 hours after the onset of infarction. The streamlined admission system employed in Doncaster may do something to improve the situation, but the salvage of life must be slight compared with the potential of a mobile coronary care unit with which it is possible to reach half the patients within 1 hour 40 minutes.8

(2) The correction of ventricular fibrillation outside hospital is a practical proposition. Not all who develop it soon after the onset of symptoms are beyond salvage, as Dr. Smyllie and his colleagues assume.

(3) A properly organized mobile coronary care unit removes the risk of death during transport. It has been estimated that mortality as high as 13% of early deaths from acute myocardial infarction occur in ambulances.7

(4) The early initiation of intensive care and the correction or prevention of dysrythmias and hypotension diminish the incidence of shock and pump failure by preventing the extension of the initial area of infarction.8

It is of interest that among patients under the age of 70 who get intensive care within one hour and before transport to hospital the overall mortality is 8-6%.8 This contrasts with a mortality of 25-6% among the patients in the Bristol study who contacted their general practitioner within one hour but who probably did not get intensive care within the hospital.9

The communications of Dr. Smyllie and his colleagues contrast with that of Dr. B. J. Duffy in the same issue of the B.M.J. (p. 49). The latter rightly casts doubt on the value of coronary care units in community hospitals. It is already clear that a hospital coronary care unit has nothing to offer unless the patients arrive early in the course of their illness at a time when they are likely to benefit from intensive care, too. It is certain that four years ago the Edinburgh physicians8 argued against the value of mobile coronary care. However, a mobile coronary care unit started in Edinburgh last year.—We are, etc.,

J. S. GILDEES
A. A. JENNIFER ADGEY
SAMUEL W. WEBB
Cardiac Department, Royal Victoria Hospital, Belfast


Cost and Speed of Medical Publication

Sir,—With reference to Dr. David Pyke’s “Personal View” (5 February, p. 371), might we, as publishers of conferences, draw your attention to the review by Dr. A. Paton (p. 385) of the Seventh Symposium on Advanced Medicine. “Printing by photolithography may not produce the most elegant books as judged by the present one, but it certainly appears to be speedy. Contributors, editor, and publisher have collaborated so effectively that the finished product was made available within a few months of the seventh conference on advanced medicine at the Royal College of Physicians in February 1971. Like-minded editors please note that there really is no excuse for the usual delay of a year or two. I have to confess, however, such is the weakness of human nature, that it has taken me almost that time to read and review this book.”

This conference ended on 26 February and copies of the book were available on 5 July. For 345 pages, the price was £3.00.

Over the years we have developed a conference reporting service, the aim of which is to achieve speed and to avoid lavish production. This combination has achieved considerable success and popularity.—I am, etc.,

D. K. C. DICKENS
Publishing Manager, Pitman Medical Publishing
London W.C.2

Pharmacologically Active I.U.D.s

Sir,—Dr. D. Wolfers (8 January, p. 112) has raised interesting and, to a certain extent, valid reservations about pharmacologically active I.U.D., particularly those wound with metallic copper wire. There is no dispute that the pharmacologically active ingredient of the I.U.D. must be without general systemic effects. Most of Dr. Wolfers objections to copper are, however, speculative, and the evidence thus far obtained does suggest that the copper has only a local effect and is rapidly eliminated from the genital tract. Furthermore, there is no increase in the incidence of cancer in patients with Wilson’s disease, in which large amounts of copper accumulate in the tissues. He also states that “for inactive devices pregnancy rates appear to be roughly proportioned to surface area and large devices carry compensating disadvantages.” So however much the design and retention rate of the I.U.D. is improved, the price for a negatively charged pregnancy rate is not acceptable. The increased surface area of the I.U.D., is frequently a concomitant heavy and prolonged bleeding problem, which can aggravate the endemic anaemia of many of the populations to which he refers.

There seems to be an interesting relationship between copper and zinc in the genital tract. The concentration of trace amounts of zinc is increased in the secretory phase of the endometrium and there is evidence which suggests that this might be altered in the presence of a copper-releasing I.U.D. It might also be relevant that the more fertile specimens of semen contains a higher concentration of zinc.

We are currently studying sperm penetrability of cervical mucus in the presence or absence of a copper-releasing I.U.D. We have observed that there is a change in the rheological properties of the mucus when it remains in contact with a copper-7 device (Searle). There is a complete loss of spinnbarkeit; the mucus becomes a liquid suggesting a destruction of the orientation of the organic material. The depth of penetration of the sperm into the mucus and the viability of the sperm is also affected.

We therefore suggest that there is room for several different avenues of exploration of intrauterine devices involving improvement of design of inert I.U.D. and also the evaluation of pharmacologically active