but it would be interesting to know what brand was used in the study by S. J. Cameron and J. Richmond.² 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

¹ Knudsen, E. T., *British Medical Journal*, 1969, **1**, 846.

² Cameron, S. J., and Richmond, J., *Scottish Medical Journal*, 1971, **16**, 425.

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 penicillin 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 anaphylactic type of reaction, so they should be used as soon as possible after preparation.—I am, etc.,

ROBERT ALLAN

General Hospital,
Birmingham

¹ Batchelor, F. R., Dewdney, J. M., Feinberg, J. G., and Weston, R. D., *Lancet*, 1967, **1**, 1175.

² Williams, J. D., *Prescribers' Journal*, 1971, **11**, 126.

³ Chain, E., *Journal of the Royal College of Physicians*, London, 1972, **6**, 103.

⁴ Dewdney, J. M., Smith, H., and Wheeler, A. W., *Journal of Immunology*, 1971, in press.

Trial of Clofibrate

SIR,—Dr. R. J. Jarrett (8 January, p. 109) asks whether in the Newcastle and Scottish trials the reduction in the group taking clofibrate of deaths due to ischaemic heart disease was matched by an increase in the number of deaths due to non-cardiac causes. While this happened in the Los Angeles diet-trial¹ the diet and clofibrate trials were not comparable in one important respect: the mean age of the males in the diet trial was 65 years and in the clofibrate trial was 52 years, so that mortality from all causes including non-cardiac was greater in the former. Nevertheless, the point has importance. Unfortunately, in the Newcastle trial patients who withdrew because of intercurrent illness were not followed to the termination of the trial, so that the full figures of non-cardiac deaths are not accurately known. In the Scottish trial these figures are known and are declared in one of the reserve tables. The position can be summarized as follows:

	Newcastle		Scottish	
	Clofibrate	Placebo	Clofibrate	Placebo
Non-cardiac deaths ..	4	3	8	10
Cerebrovascular ..	1	—	3	2
Cancer of bronchus ..	1	1	2	4
Other cancer ..	1	—	1	1
Accident ..	—	—	1	1
Other non-coronary cause ..	1	2	1	2

Thus, there is no indication in either trial that the reduction in death due to ischaemic heart disease was balanced by an increase in number of non-cardiac deaths.—We are, etc.,

H. A. DEWAR

Newcastle

M. F. OLIVER

Edinburgh

¹ Pearce, M. L., and Dayton, S., *Lancet*, 1971, **1**, 464.

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;¹ (3) inclusion bodies occur in the adrenal cortex in Parkinsonism, the clinical counterpart of Huntington's chorea;² (4) L-Dopa loading in those sibs from families with Huntington's chorea who will later develop the disease elicits choreic movements,^{3,4} in this way constituting 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), and 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 fetal adrenal zone synthesizes DHEA-S.⁵

The findings reported above may not essentially constitute more than a parameter in Huntington's chorea, though a speculative link (DHEA-S—adrenal zone reticulosa—sympathetic 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.

² den Hartog Jager, W. A., *Archives of Neurology*, 1970, **23**, 528.

³ Barbeau, A., *Lancet*, 1969, **2**, 1066.

⁴ Klawans, H. C., Paulson, G. W., and Barbeau, A., *Lancet*, 1970, **2**, 1185.

⁵ Cooke, B. A., and Taylor, P. O., *Journal of Endocrinology*, 1971, **51**, 547.

Generalized Pustular Psoriasis

SIR,—Your recent leading article "Generalized Pustular Psoriasis" (29 January, p. 262) managed to be remarkably misleading in so short a space. It stated, misquoting Ryan and myself, that "the disease is often caused by therapy, since generalized pustular psoriasis is often associated with systemic corticosteroid and methotrexate treatment." It should be made absolutely clear that there is not a shred of evidence that the use of methotrexate for any phase of psoriasis can precipitate generalized pustular disease, although the evidence implicating corticosteroids is substantial.

Apropos of the findings of McFayden and Lyell, while stating that these authors "found a coagulase-positive staphylococcus in the blood of seven consecutive patients with generalized pustular psoriasis," the leader did not mention that of 93 blood cultures made from these seven patients only 15 were positive. One patient had four out of seven cultures positive so that in the other 6 patients only 11 of 86 cultures were positive. Since the incidence of transient bacteraemia in other extensive dermatoses is unknown, the significance of these findings must remain in doubt until and unless further confirmatory evidence, suitably controlled, is available. Furthermore, McFayden's and Lyell's suggestion that deaths previously attributed to corticosteroids were more likely due to concealed bacteraemia shock is purely speculation unsupported by any evidence.

The leading article's "important practical conclusion" that "bacteraemia should be looked for and treated appropriately" has been practised by physicians looking after these patients for at least 60 years from Von Zumbusch onwards, generally with negative results. It would be hard to do otherwise in a febrile toxic patient with massive cutaneous pustulosis and (usually) a polymorphonuclear leucocytosis. However, it is not in dispute that either methotrexate or systemic corticosteroids can control this syndrome, if necessary for months. In view of the fulminating course which may be taken by infections in patients on high doses of methotrexate or steroids, it is difficult to accept that those who do well on such treatment are harbouring a virulent staphylococcus in the blood. If McFayden and Lyell are right, they have uncovered a very curious story indeed.—I am, etc.,

HARVEY BAKER

London Hospital,
London E.1

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 dapsone) 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