Correspondence

Letters to the Editor should not exceed 500 words.

Death from Exposure

SIR,—Many mountaineering deaths are put down as being due to "exposure," either alone or in conjunction with injuries. These unfortunate people are often diagnosed as being dead by lay people on the hill, and treated accordingly—that is, head covered, often by plastic or similar impervious material. Perhaps, therefore, it would be wise to emphasize the difficulties of diagnosing death in a patient suffering from hypothermia.

Mountain Rescue Figures in 1961-5 *for Great Britain*

	Accidents	Deaths	Reported Cases of Exposure
1961	106	23	Number not given: "several deaths"
1962	132	41	—
1963	159	19	16
1964	153	27	10
1965	187	35	23

In the body temperature range 75–90° F. (24–33° C.) shivering ceases, and muscular rigidity sets in; this can easily be confused with rigor mortis. Also the skin is pale and cold and subcutaneous oedema develops—again as in death. The pupils react poorly, if at all, to light, and the pulse and blood pressure are often unrecordable.[1] Respiration may be so shallow and slow as to be unnoticeable, especially on the hill, where one is not stripping the body to look for chest movement. One clue is that often, but *not* always, the pupils are constricted, whereas in death they are dilated. Thus if the pupils are constricted then the patient is alive; if dilated he may be either alive or dead. Therefore, unless the injuries are such that the victim cannot possibly be alive, in my opinion rescue teams should not abandon hope and should carry these people down with their mouth and nose uncovered.

One or two other points arise. It is well known that cold is often an added stress on the adrenals in a patient already subjected to other stresses, as in the case of mountaineering mishaps, such as fright, unaccustomed exercise, and injuries.[2] It has been noted that in hypothermia there is evidence of adrenal damage and depletion of cardiac and hepatic glycogen, which may lead to heart failure even at relatively high temperatures. Cortisone, glucose, and digitalis were recommended as treatment.[3] Attempts are now being made to measure plasma cortisols in people suffering from exposure. There is evidence to show that corticosteroids produce a rise in body temperature when used in resuscitation.[4] Glucose is already advised for exposure cases, and I can see no contraindications for cortisone—preferably a quick-acting form such as Betnesol—either orally in a conscious victim or by injection. Lay people can do no harm with this and it would be well worth a try in the apparently hopeless case. Patients should be suitably labelled, as is already done with morphine.

A working party on exposure[5] recently stated categorically that when a patient has been suffering from exposure but has apparently recovered and insists that he is quite fit he must still be treated as a stretcher case. It is very difficult to maintain body temperature of a victim under conditions where exposure is likely to have arisen, and once completely immobilized on a stretcher the victim would almost certainly tend to lose heat. I quote from Cranston[6]: "For purposes of thermal regulation heat production may be increased rapidly by increased muscular activity, or shivering, in man; this appears to be the only mechanism whereby heat production can be increased rapidly . . ." I cannot therefore understand the rationale of denying a patient who feels fit and wishes to walk down the chance of getting himself back to normal by carefully supervised muscular activity. This would also constitute less of a danger to other members of the party, who themselves are liable to become exposure cases while awaiting a rescue team. —I am, etc.,

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REFERENCES

1 Duguid, H., Simpson, R. G., and Stowers, J. M., *Lancet*, 1961, 2, 1213.
2 Selye H., *Physiology and Pathology of Exposure to Stress*, 1950. Montreal.
3 Rees, J. R., *Lancet*, 1958, 1, 556.
4 Kolpakov, M. G., *The Adrenals and Resuscitation*, 1965. New York.
5 Exposure, *The Climber*, October 1963.
6 Cranston, W. I., *Brit. med. J.*, 1966, 2, 69.

Multiple Sclerosis

SIR,—The clinical observations recorded by Professor Henry Miller and his colleagues (22 April, p. 210) and your leading article (p. 192) draw attention to some factors which may influence localization of the pathological process in multiple sclerosis, at least in the first instance. Since both clinical and experimental observations[1–3] have raised the possibility that the disease may represent an infection with prolonged incubation or latent period, some recent results on the way in which scrapie (a paradigm of "slow" virus infections) reaches the nervous system may be of interest.

When scrapie material is inoculated intraperitoneally into mice pathological changes are first found in the spinal cord; when inoculated into a forelimb the first lesions occur in the cervical cord at a time when the brain and lower cord are immune; when injected into the leg the first lesions are found in the lumbar cord, while the rest of the nervous system is yet clear. Moreover, if the animal is examined at the right moment, then lesions after inoculation into a limb may be limited to the ipsilateral side of the cord in the corresponding segments. It would seem that the disease agent reaches the nervous system by the blood, and that its initial localization is conditioned, to some extent at least, by the site of inoculation. Presumably the stimulation associated with inoculation or peripheral trauma in some way facilitates access to the corresponding segments of the neuraxis. In a much neglected paper W. J. German and J. D. Trask[4] clearly showed the influence which trauma might have in localizing blood-borne poliomyelitis virus to particular regions of the spinal cord.—I am, etc.,

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REFERENCES

1 Schapira, K., Poskanzer, D. C., and Miller, Henry, *Brain*, 1963, 86, 315.
2 Pálsson, P. A., Pattison, I. H., and Field, E. J., in *Slow, Latent, and Temperate Virus Infections*, 1966, edited by D. C. Gajdusek, C. J. Gibbs, jun., and M. Alpers. U.S. Department of Health, Education and Welfare. NINDB Bethesda, Monograph No. 2, p. 49.
3 Field, E. J., *Brit. med. J.*, 1966, 2, 564.
4 German, W. J., and Trask, J. D., *J. exp. Med.*, 1938, 68, 125.

Propranolol-induced Depression

SIR,—We have noted with interest Dr. H. J. Waal's letter (1 April, p. 50) suggesting that the high incidence of depression among her hypertensive patients was associated with propranolol administration. This, however, does not agree with the experience of other workers. Published reports,[1–5] excluding Dr. Waal's paper,[6] describing experience with propranolol in 154 patients with hypertension include only one case of transient depression.[5]

We have attempted to determine the incidence of depression in patients receiving propranolol. At present there are follow-up studies with propranolol in hypertension in progress both here and in other parts of the world in collaboration with this department. The trials involve some 167 patients, and so far only one case of overt depression during treatment with propranolol has been reported. This patient was known to be a depressive prior to propranolol treatment. No patients have had to stop their treatment because of depression. Thus the published and unpublished reports concern 321 patients who have been receiving doses of propranolol ranging from 70 to 1,000 mg. or more per day over a period of 6 to 39 months. Therefore there is at present no evidence from these studies to support Dr. Waal's suggestion that the depression she associates with propranolol is either time or dose dependent. With regard to general clinical experience, we estimate that approximately 60,000 patients are currently receiving propranolol in various indications. All reports of side-effects associated with propranolol administration are recorded and followed up by our adverse reactions section. Examination of these records to determine the incidence of depression shows that a

total of 11 cases have been reported, 5 in publications and 6 privately. This gives an incidence of depression of 0.1% or less.

There may be several explanations for this variance in clinical experience, in particular the recognized pitfalls of retrospective surveys, direct questioning to seek a predetermined clinical complex, concomitant drug administration (which Dr. Waal herself mentions), and the natural incidence of depression in hypertension. Space will not permit us to discuss these points here. Present evidence does not indicate that there is an important incidence of depression associated with propranolol administration. We will continue to keep a careful watch on the incidence of any side-effects due to propranolol and hope that investigators using this drug will assist us in this respect.—I am, etc.,

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REFERENCES
1 Paterson, J. W., and Dollery, C. T., *Lancet*, 1966, **2**, 1148.
2 Prichard, B. N. C., *Angiologica*, 1966, **3**, 318.
3 —— *Amer. Heart J.*, 1965, **69**, 716.
4 Richards, F. A., *Amer. J. Cardiol.*, 1966, **18**, 384.
5 Prichard, B. N. C., and Gillam, P. M. S., *Brit. med. J.*, 1964, **2**, 725.
6 Waal, H. J., *Clin. Pharmacol. Ther.*, 1966, **7**, 588.

Cephaloridine and Staphylococcal Endocarditis

SIR,—The experience of Dr. H. A. Burgess and Dr. R. J. Evans (19 November 1966, p. 1244) in the failure of cephaloridine to influence the course of the illness of a patient with staphylococcal endocarditis, and the subsequent letters (31 December 1966, p. 1656; 4 March, p. 566) and discussion (4 March, p. 515) prompt us to report a similar experience.

The patient was a man aged 51 who on 26 August 1965 had a Starr-Edwards valve inserted as a replacement for a calcified aortic valve, and whose immediate postoperative course was uneventful. He was discharged from hospital on 1 October, although on the two days before discharge he had had two small spikes of temperature to 99.4° F. (37.5° C.). He was readmitted on 6 October in congestive cardiac failure and with pyrexia to 102° F. (39° C.). Two blood cultures taken immediately after admission both grew *Staphylococcus aureus*, phage type 84, which was resistant to penicillin, streptomycin, and tetracycline, but sensitive to methicillin, chloramphenicol, and erythromycin. Since the patient was known to be hypersensitive to penicillin, it was decided to treat him with cephaloridine, which had recently become available, and on 7 October treatment was begun with 3 g. daily, given intravenously in 1-g. doses at eight-hourly intervals. On 8 October 12 mg. of dexamethasone a day was added to his therapy.

The staphylococcus was tested for sensitivity to cephaloridine by a tube dilution method using a large inoculum of approximately 2×10^6 actively growing cocci per 1 ml. of medium; the minimum inhibitory concentration was 5 μg./ml., and subculture showed that the minimum bactericidal concentration was 20 μg./ml. When these results were known, on 9 October, the dosage of cephaloridine was increased to 6 g. a day. Cephaloridine blood levels were determined on three different days. Two hours after a dose of 2 g. the blood level was between 40 and 80 μg./ml., and the dilution of serum of 1 in 8 inhibited the patient's staphylococcus; four hours after a 2-g. dose the blood level was between 20 and 40 μg./ml. and at seven hours it was 10 μg./ml.

On 8 October the patient was found to have a sternal abscess at the site of the operation wound; pus aspirated from this grew the same staphylococcus as the blood cultures. By 9 October the patient was afebrile and continued to be so until 16 October. On 15 October the dose of cephaloridine was reduced to 4 g. a day. On 16 and 17 October the patient's temperature rose in spikes to 101° F. (38.5° C.). On 18 October he became hypotensive and died that evening.

At necropsy he was found to have a large abscess tracking from above the plastic valve through the myocardium; as the pericardium was being stripped from the heart this abscess ruptured to the exterior of the heart. From this abscess and from the substernal abscess the infecting staphylococcus was grown in profuse numbers. Eleven colonies were phage typed and tested for cephaloridine sensitivity; all were identical with the original isolates and showed no decrease in sensitivity.

The concomitant administration of a steroid with the antibiotic makes it difficult to determine whether the antibiotic or the steroid or both were the cause of the abatement of this patient's pyrexia. The apparent clinical response to therapy masked the progress of the underlying suppurative process.

While it is true that staphylococcal endocarditis is notoriously difficult to treat successfully and that this seems to be especially so in the presence of plastic prostheses, nevertheless from this patient, who received 55 g. of cephaloridine in 10 days, the staphylococci were recovered in large numbers from a sternal and a myocardial abscess, which were situated in areas with a plentiful blood supply. It should also be noted that in the patient of Drs. Burgess and Evans the infecting staphylococcus was found in large numbers in the spleen.

Nowadays "hospital" staphylococci showing multiple resistance to the commonly used antibiotics are also sometimes resistant to either kanamycin or methicillin. Tests in our laboratory (to be reported in detail later) indicate that "hospital" strains show a marked inoculum effect when tested for cephaloridine sensitivity. Although we think cephaloridine has a place in the treatment of certain infections, we would not regard this antibiotic, used alone, as suitable therapy for infection with "hospital" strains of staphylococci.—We are, etc.,

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Anxiety and the Pulse

SIR,—We were most interested to read Dr. K. L. Granville-Grossman and Dr. P. Turner's letter (7 January, p. 49) commenting on your leading article (10 December 1966, p. 1407).

With regard to the recent observations that propranolol has a calming influence on the mental state of anxious subjects,[1-3] they suggest that this drug may relieve anxiety by direct sedation of the central nervous system and not by a mechanism secondary to peripheral beta-adrenergic blockade, and that this problem might be solved if beta-adrenergic blocking agents devoid of central action became available. It may therefore be of interest to report some preliminary results obtained with 1-(4-nitrophenyl)-2-isopropylamino-ethanol (I.N.P.E.A.), a beta-adrenergic blocking agent devoid of C.N.S.-depressant properties.[4]

We have investigated the effects of I.N.P.E.A. on anxiety neurosis in a series of 13 outpatients treated orally (50 mg. q.i.d.) and then in four inpatients treated intravenously (50 mg. q.i.d.). Our object was simply to find out whether a full-scale trial was worth while. The results in the orally treated patients were encouraging (11 good, 2 fair). The most troublesome somatic manifestations (sweating, tachycardia) decreased and patients stated that they felt better in themselves. With intravenous I.N.P.E.A. the results were even more marked. In three of the four patients it was found that I.N.P.E.A. relieved anxiety markedly, especially the symptoms mediated through the autonomic nervous system. No noteworthy side-effects were observed in the majority of cases; only two patients (treated orally) showed mild transient dyspnoea.

While this finding does not disprove the existence of some association between the C.N.S. effects of propranolol and its effectiveness in relieving anxiety states, it does seem to indicate that beta-adrenergic blocking mechanisms are also operative.

To find out definitely whether this is so we have now started a controlled sequential study with the pure optical isomers D(−)-I.N.P.E.A. and L(+)-I.N.P.E.A. of which only the former has beta-adrenergic receptor blocking activity.[5]—We are, etc.,

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REFERENCES
1 Turner, P., Granville-Grossman, K. L., and Smart, J. V., *Lancet*, 1965, **2**, 1316.
2 Nordenfelt, O., *Acta med. scand.*, 1965, **178**, 393.
3 Granville-Grossman, K. L., and Turner, P., *Lancet* 1966, **1**, 788.
4 Murmann, W., Almirante, L., and Saccani-Guelfi, M., *J. Pharm. Pharmacol.*, 1966, **18**, 317.
5 Almirante, L., and Murmann, W., *J. med. Chem.*, 1966, **9**, 650.

The Scabies Epidemic

SIR,—In your leading article on this subject (22 April, p. 193) you advocate confirmation of the diagnosis "by scraping a run with a scalpel moistened with a little liquor potassae and examining the debris under a low-power microscope." This method can only be a poor second-best. The diagnosis of scabies, particularly in a patient who has had any sort of treatment, depends upon finding a *live* acarus, and this can be done more easily, quickly, and reliably than searching for mangled remains. The acarus in her burrow is readily visible with a low-power hand-lens or a watchmaker's glass, and her appearance is quite distinctive. The grey or buff dome at the forward end of the burrow, with a conspicuous brown crescent at the leading end formed by the head and forelimbs, is unmistakable; and once it is seen the creature is readily removed *alive* with a needle-point. Placed on the skin she moves actively and provides a convincing demonstration to any doubting patient. A word of