Hyperarousal in Space Flights

SIR,—I was fascinated by your leading articles before and after the Apollo 13 flight (11 April, p.67 and 2 May, p.249). In these you drew attention to physiological matters, but did not refer to the effects of the psychological stresses to which the astronauts were exposed. As symptoms were experienced on this flight, and have occurred on previous flights, and as these symptoms are known to occur in hyperaroused states, it is pertinent to consider the role of arousal in their aetiology.

Staggering of rest periods, unusual sleeping positions, and cold could indeed have produced insomnia; but a contribution from hyperarousal, and perhaps the major one, should not be ignored. It is noteworthy that sleep deprivation was greatest in the flight commander. Sleep deprivation is unlikely to affect life or death decisions made in a short period on a primary task—it is on vigilance tasks that mistakes (and these would be of omission) are more likely, such as in transit flight.

Weight reduction occurs when energy expenditure and water loss exceed food and water intake. You reported that fluid intake was reduced but shortage of drinking water was not emphasized as a serious problem. Anorexia is an early and marked symptom of hyperarousal, and can produce considerable weight loss rapidly. Reduced calorie intake is accompanied by increased water excretion so producing a fall in body weight of several kilogrammes. Sweating, tachypnoea, diarrhoea, and polyuria occur in hyperarousal and also lead to increased water loss. The energy expenditure of these astronauts was likely to be more than on previous similar flights, as muscle activity would have been greater in response to the more prolonged need for high alertness.

Hyperarousal produces hypertension, increased cardiac output, and a considerable shift from skin to muscle blood flow. These changes in haemodynamics will reverse on attaining normal arousal, such as is likely to occur after successful re-entry and splash-down. It is just as relevant to consider such factors in the aetiology of some momentary unsteadiness of gait as it is to consider cardiovascular adaptation to changes in gravitational forces. Hyperarousal may also lead to changes in feelings and behaviour such as irritability, altered threshold to somatic sensations, liability to perceptual abnormality, impairment of concentration, tunnelling of attention, depersonalization, hypocapnia, muscular incoordination, and deterioration of performance. Information has been released that on some previous flights disorders of behaviour occurred which jeopardized their safety; and indeed there were reasons to suspect that at least one cosmonaut was landed prematurely on account of unexpected inefficiency as a control-system operator. From my experience of working with others whose lives are exposed to danger, such symptoms occur more often when the task load is low—and that was rare on the flight of Apollo 13.

When symptoms of hyperarousal occur, they do so quite beyond an individual's control. It is a tribute to the selection and training of these astronauts that on this flight so few symptoms occurred. Only someone inexperienced in the clinical practice of medicine could dismiss the possibility

that the explanations which I have put forward are contributory to the aetiology of symptoms occurring in space flight.—I am, etc.,

R. C. B. AITKEN.

Department of Psychiatry,
University of Edinburgh.

Drugs for Dysentery

SIR,—The otherwise excellent article under the heading of Today's Drugs (4 April, p. 36) unfortunately contains the strong implication that an antibiotic should be used in the treatment of all cases of dysentery. It cannot be too strongly emphasized that the great majority of cases of Sonne dysentery as seen in this country at the present time require only bed rest and an adequate fluid intake. The routine use of antibiotics in such a comparatively mild disease is a disservice both to the patients as well as to the community. It is accepted that in a few patients antibiotic or chemotherapy may be fully justified owing to the severity of the attack or because of pre-existing illness, or for some other good reason, but the majority of cases do not require any specific therapy.—I am, etc.,

JOHN F. WARIN.

Department of Health,
City of Oxford.

Unhopeful Signs in Lung Cancer

SIR,—Professor J. H. Burn (May 9, p. 361) appears to find some encouragement in the recent figures quoted in the Registrar General's Statistical Review of England and Wales for 1968—a view which is apparently endorsed by you in the heading to the letter "Hopeful Signs in Lung Cancer."

I find this extraordinary. May I recast his letter, but with "women" substituted for "men"? I have had to use 1967 figures¹ as the 1968 report has not yet reached Scotland. For women under the age of 50 the peak has not yet been reached. In 1953 the number was 362, in 1961 it was 442, and in 1967 it was 479. For women aged 50-59 the number rose from 524 in 1953 to 783 in 1961, and to 1,080 in 1967. For women aged 60-69 there were 807 in 1953, 1,127 in 1961, 1,519 in 1966, and 1,640 in 1967.

If one considers (a) these figures in combination with the latest report on tobacco consumption, which shows that cigarette smoking in women is still rising, and (b) that young men are smoking more, and beginning at an earlier age I see no cause for rejoicing.

Perhaps, Sir, you would care to compose a title for this letter.—I am, etc.,

EILEEN C. CROFTON.

Department of Respiratory Diseases
City Hospital,
Edinburgh 10.

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Poisoning with PCP

SIR,—I was interested in the leading article "Deadly Diapers" (9 May, p. 314). It may not be generally known that there exists another source of pentachlorophenol in society—namely, certain pesticide mixtures used on roof timbers. Dr. P. Robson and I reported a case under the heading "Pentachlorophenol Poisoning from Bath-water."¹

The initial reason that my case was diagnosed was because my attention was drawn to the possibility of poisoning by wondering if there could be any connexion between my patient's condition and the simultaneous presence of plumbers, wood preserving specialists, insecticide, and old cisterns, in the hallway. At that time I had not heard of PCP.—I am, etc.,

J. B. CHAPMAN.

Sevenoaks, Kent.

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Hypothalamic Dysfunction and Antidepressant Drugs

SIR,—We have shown that some severely depressed patients do not suppress their plasma 11-hydroxycorticosteroids (11-OHCS) after a midnight dose of 2 mg. dexamethasone phosphate.¹ On recovery from the depression, this abnormality disappears. An abnormal response of 11-OHCS to hypoglycaemia has also been shown in some of these patients and correlated with resistance to dexamethasone suppression.² These tests are used in clinical research to study the integrity of hypothalamic mechanisms which control corticotrophin release.³

A relationship between this abnormality and poor short-term response to antidepressant medication has been suggested by the following investigation. Consecutive patients to the professorial psychiatric unit, Melbourne University, with a primary depressive illness were studied. Patients with persistent symptoms but not thought severe enough to merit E.C.T. after ten days of supportive care were treated in a double-blind trial with either a monoamine oxidase inhibitor—tranylcypamine (Parnate 10 mg. t.d.s.) or a tricyclic antidepressant—imipramine (Tofranil 50 mg. t.d.s.). If significant improvement occurred (as judged clinically), identical inert tablets were substituted for the active tablets and progress observed.

The aims were to define specific drug response and relate this to initial ratings of depression, anxiety, and personality measures and also the presence or absence of hypothalamic dysfunction.

Before treatment was started the midnight dexamethasone test was done.¹ Ten patients suppressed 11-OHCS normally while six patients were non-suppressors. The two groups of patients had similar mean scores of depression (Hamilton and Zung Self Rating Inventory); anxiety (Taylor), and neuroticism (Eysenck). They had the same age and sex distribution.

Plasma 11-OHCS and Questionary Results (Means $\pm$ S. D.)

N	A.M. Plasma 11-OHCS (μ g./100 ml.)					N Score Eysenck Personality Inventory
	Basal	Post Dexa- methasone	Zung Self Rating Score	Hamilton Depression Score	Taylor Anxiety Score	
10	21.4 (6.9)	4.4 (1.4)	54.3 (9.0)	21.3 (3.9)	32.6 (7.8)	17.3 (4.0)
6	19.9 (6.8)	19.1 (5.8)	54.6 (13.2)	22.0 (5.3)	27.1 (8.9)	18.4 (2.8)

At the end of one month the ten suppressors were well, all having responded to the particular antidepressant drug and not having relapsed, at that time, with placebo substitution. The six non-suppressors, after one month's antidepressant treatment had not improved and were all then treated with E.C.T. with subsequent improvement.

This small study suggests that poor short-term response to antidepressants is related to hypothalamic dysfunction. This lack of response and the presence of hypothalamic dysfunction could not have been predicted from clinical or questionnaire data. Further studies of specific treatment responses and tests of hypothalamic function are needed in depressed patients. If these findings are

replicated, they may be of clinical value in deciding on appropriate treatment for the particular patient and may help in elucidating the action of antidepressants.—We are, etc.,

W. R. McLEOD.
B. J. CARROLL.
BRIAN DAVIES.

Department of Psychiatry,
University of Melbourne,
Royal Melbourne Hospital,
Victoria, Australia.

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- 1 Carroll, B. J., Martin, F. I. R. and Davies B., *British Medical Journal*, 1968, 3, 285.
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Perioral Dermatitis

SIR,—Drs. J. L. Verbov and E. Abell (6 December, 1969, p. 621) have suggested that the syndrome which has become known as perioral dermatitis is iatrogenic. They base this suggestion on their observation that their patients with this syndrome had been applying a topical corticosteroid.

We join in deploring the current abuse of corticosteroids, which has reached such proportions that few patients referred to dermatological departments with any skin disorder have not been so treated. Drs. Verbov and Abell have not, however, established the nature of the condition from which their patients were suffering before the corticosteroids were prescribed.

In the past eight weeks we have examined 25 patients with perioral dermatitis. Six of the patients had not applied a corticosteroid before their first attendance. Of the remaining 19 patients, 17 gave a clear account of lesions compatible

with perioral dermatitis present for from two weeks to four months before corticosteroids were first prescribed. One patient had used corticosteroids intermittently for acne and one for a rash not reliably identifiable from her description of the lesions. Dr. N. Hjorth from the Finsen Institute, Copenhagen, writes in a personal communication that his experience and conclusions agree with our own.

Topical steroids can provoke pustular episodes in acne and rosacea, and they may aggravate perioral dermatitis, but they cannot be incriminated as the cause of that syndrome. Though a rebound exacerbation may occur when the steroids are discontinued we have found the condition relatively easy to cure with oral tetracyclines.—We are, etc.,

Cambridge

Amersham, Bucks.

A. J. ROOK.

D. S. WILKINSON.

Chemotherapy of Bronchitis

SIR,—The action of clindamycin on *Haemophilus influenzae*, among other micro-organisms, has been brought into focus once more by the recent paper of Dr. I. Phillips and others (11 April, p. 89). Moreover, your leading article on chemotherapy of bronchitis (17 January, p. 125) in its final paragraph assumes that, among other antibacterial drugs, 7-chloro-7-deoxy-lincosamin (clindamycin, Dalcacin) offers little or no advantage in the treatment of bronchitis, similar to erythromycin. It is disturbing to the scientifically minded that this assumption has not been declared as such, but is stated as a safe prediction—almost as a fact—although at present there is inadequate evidence for such prediction.

The usefulness of an antibacterial drug depends on several features. These are absence of serious side-effects, good absorption, maintenance of adequate blood levels

for an adequate length of time, low serum protein binding, adequate concentrations in tissues or body fluids at or near the site of infection, and minimum inhibitory concentrations (M.I.C.) of the drug for pathogenic microorganisms within the range of levels obtainable in body fluids and tissues. Although in the case of clindamycin many of these factors are favourable, so far only serum levels but not lung tissue or sputum levels obtainable with his drug have been reported.

Meyers *et al.*¹ reported M.I.C.s for *H. influenzae* ranging from 1.2 to 3.0 μ g./ml. and Oppenheimer and Turck² from 0.5 to 5.0 μ g./ml.; in other words, well within the range of peak and average serum levels. However, the M.I.C.s recorded in other observations, including those of Dr. Phillips and colleagues, were rather high, ranging from 3.0 to 50.0 μ g./ml.^{3,4} These conflicting

results had created a rather intriguing situation in which we decided to test the sensitivity to clindamycin of 50 freshly isolated and correctly identified *H. influenzae* strains. In our hands the M.I.C.s fell within the limits of 0.12 to 4.0 μ g./ml., and 42 strains (84%) were sensitive to 2 μ g./ml. or less. Our investigations did not explain the discrepancies in the literature, nor were they designed to do so. Nevertheless, as peak serum levels of clindamycin are about 6 μ g./ml. and average levels are about 3 μ g./ml. the possibility exists that this drug may be of use in bronchitis with *H. influenzae* as a pathogen. No certain prediction one way or the other, however, can be made at this stage as any valid statement is dependent on adequate sputum levels still to be determined, perhaps followed by comparative and double-blind clinical trials in bronchitis.

We felt, therefore, that the true situation regarding the new lincomycin derivative should be placed before the readers of the *B.M.J.* None of the considerations outlined above are applicable to the considerable inhibiting action it has on other potential pathogens in bronchitis—i.e., *Staphylococcus aureus*, pneumococci, and beta-haemolytic streptococci.

It is perhaps of some interest that erythromycin, according to our results,⁵ is of considerable in-vitro activity against *H. influenzae*, and may deserve a place in the armamentarium against bronchitis, particularly when combined with a sulphonamide.⁶—We are, etc.,

K. ZINNEMANN.
JOYCE FRAZER.

Bacteriology Department,
School of Medicine,
Leeds, Yorks

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SIR,—After reading the recent article by Dr. I. Phillips and his colleagues (11 April, p. 89) it would seem that any possible role for 7-chloro-lincosamin (clindamycin) in the treatment of bronchitis would depend on its activity against *Haemophilus influenzae*, and its ability to produce inhibitory concentrations in sputum.

I have recently carried out a small series of investigations with clindamycin, the results of which might be of interest at this stage. Of 12 strains of *H. influenzae* tested, five had a minimal inhibitory concentration (M.I.C.) of less than 1.0 μ g./ml., and the most resistant were inhibited by 4.0 μ g./ml. In comparison, the M.I.C. of lincomycin for the 12 strains was 8.0 μ g./ml.

The results of sputum levels have been determined in five patients and are as follows: