appearances. The age of the patients and also the absence of the commoner causes of ulceration are also valuable clues. This kind of ulcer may also be seen on the upper extremities.

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ARGININE-INFUSION TEST FOR GROWTH-HORMONE SECRETION

SIR,—The reports by Best et al.[1,2] on "nonspecificity of arginine infusion as a test for growth-hormone secretion" were criticised [3-6] because those subjects who did not show an adequate growth-hormone (H.G.H.) rise with arginine infusion were in a "non-basal state", having been ambulant before the study was commenced. Furthermore, it was suggested that responses seen following saline or no infusion were due to instability of the H.G.H. control system after ambulation. We have repeated these investigations in six male and five female healthy volunteers.

All tests were performed in the fasting state between 6 and 7 A.M., the subjects remaining in bed after at least 6 hours' sleep. Four tests were performed at random on separate days, consisting of one arginine infusion (0·5 g. per kg. L-arginine monochloride as 5% solution in distilled water) over 30 minutes, two 0·9% sodium-chloride infusions equal in volume to the arginine infusion over 30 minutes, and one day when no infusion was given. Three subjects had only one saline infusion. Blood was taken for plasma-H.G.H. estimation at half-hourly intervals for 180 minutes. A positive response was taken to be a rise of 5 ng. per ml. H.G.H. or greater over the initial level in the first 2 hours. Results are shown in the accompanying table.

H.G.H. RESPONSES OF NORMAL SUBJECTS TO ARGININE, SALINE, AND BLOOD-SAMPLING

Subject	Sex	Nil*	Saline 1†	Saline 2†	Arginine ‡
1	M	−	−	+	−
2	M	−	−	−	−
3	M	+	−	−	+
4	M	−	−	−	−
5	M	−	−	..	+
6	M	−	−	..	−
7	F	−	−	−	+
8	F	−	+	+	+
9	F	+	−	−	+
10	F	−	−	−	+
11	F	−	−	..	+

* H.G.H. responses to no infusion (Nil).
† 0·9% sodium-chloride infusion (Saline 1 and 2).
‡ Arginine infusion: + = >5 ng./ml. rise in plasma-H.G.H. over initial level in first 120 minutes; − = no rise in H.G.H. level, or <5 ng./ml.

It can be seen that two males responded to arginine. One of these also had a rise in H.G.H. when no infusion was given, and one other male had a rise during a saline infusion. All the females had a positive response to the arginine infusion, but one of these also had rises with both saline infusions, and in one H.G.H. rose with no infusion. Thus, of the responses to arginine, one male and three females were "specific" and one male and two females were "nonspecific".

This investigation further supports the original contention of Best et al. that arginine may not be a specific stimulus for growth-hormone secretion, and provides evidence against the argument that the lack of response of some subjects was due to a "non-basal state". Penny et al.[7] have lately suggested that arginine infusion is a specific stimulus to H.G.H. secretion; and their investigation was well controlled. The disparity between their findings and our own may in part be due to the fact that in the present study three control experiments were performed, rather than a single saline control infusion.

The question of the specificity of putative stimuli to growth-hormone secretion such as arginine may be resolved by integrated plasma-H.G.H sampling.[8]

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DELAYED PSYCHOSIS DUE TO L.S.D.

SIR,—There are several criticisms of our paper to which we would like to reply.

Dr. Malleson (Oct. 17, p. 831) suggests that an emotional factor, rather than a pharmacological agent, could account for the patients' illnesses. But neither of our patients had any emotional problems; and if they had, we doubt whether emotion alone, in hitherto healthy girls, could account for a psychosis of such severity. Furthermore, it has never been demonstrated, as Dr. Malleson claims, that excellent results have been obtained with L.S.D. treatment.

Since the publication of our paper, one of us (K. D.) has been studying the incidence of L.S.D. psychosis in three mental hospitals. Among twelve probable cases currently under investigation, two patients developed delayed psychoses after L.S.D. treatment for anxiety states. We cannot, therefore, agree with Dr. Thomas (Oct. 24, p. 877) that the proper selection and the adequate supervision of patients will prevent such a reaction developing weeks, and even months, after discharge from hospital.

Dr. Weisbuch (Nov. 7, p. 979) and Dr. Malleson take issue with us for basing our conclusions on only two cases. But we also took into consideration the larger American series which we surveyed in some detail. Our patients, too, were specially selected; they had a *delayed* psychosis; they had stable premorbid personalities with no personal or familial history of nervous or mental illness; they ingested only *one* dose of L.S.D.; and they had never previously taken drugs. There would, undoubtedly, be a higher incidence of L.S.D. psychosis if less strict criteria were adopted, as is clear from Dr. Ryle's experience (Oct. 24, p. 877).

Dr. Weisbuch, apparently ignoring the many published reports, describes the statement that L.S.D. causes psychotic reactions as "hypothetical". The proof he requires is a tightly controlled double-blind experimental study. We agree with him that this experiment will never be done unless human beings are subjected to similar controls as laboratory animals. Until more scientific data are forthcoming we believe that the publication of clinical histories, despite their limitations, will help to widen our awareness of the problem and, in particular, will provide a useful guide to differential diagnosis and treatment.

It is now fashionable to use the word "anecdotal", with its slightly disparaging flavour, when referring to case-reports. All clinical histories are by definition anecdotal, and a number of them with similar characteristics establish a clinical syndrome which may later be confirmed scientifically. Clinical medicine has advanced in this manner since the time of Sydenham.

It is our impression that the problem of delayed L.S.D.

psychosis is greater than has been realised hitherto. We hope to extend our investigations, but until more information is available we believe that we are justified in drawing attention to the fact that the unpredictable actions and the risk of severe psychosis outweighs any therapeutic advantage of L.S.D.

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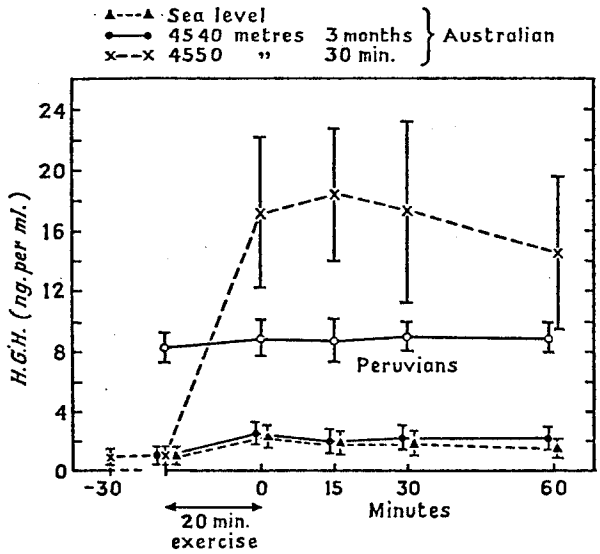
HORMONAL RESPONSE TO ALTITUDE

SIR,—We have carried out a study to determine the role of plasma sugar, insulin, glucagon, growth-hormone (H.G.H.), and cortisol in adaptation to high altitude.

8 healthy Australian males aged 23–28 were studied during submaximal exercise on a bicycle ergometer and treadmill in three different situations—at sea-level; after 30 minutes in a pressure chamber at a simulated altitude of 4550 m. (barometric pressure 444 mm. Hg); and at Morococha, Peru, 4540 m. (barometric pressure 446 mm. Hg), after 3 months' acclimatisation to altitude. The submaximal work-load was 40–50% of W170—i.e., 40–50% of the work-load required to produce a pulse-rate of 170 beats per minute. Similar studies were performed on Peruvians who were born and had lived continuously at Morococha. All estimations were made on venous blood, and the experiments were begun after an overnight fast. Plasma-sugar was measured on an 'AutoAnalyzer'. Insulin, glucagon, and growth-hormone were estimated by radioimmunoassay, and cortisol by competitive protein-binding.

The sea-level studies were identical to those described in a previous study in physically fit young men.[1] During submaximal exercise no significant change was demonstrated in H.G.H. from the basal level of $1{\cdot}1 \pm 0{\cdot}4$ ng. per ml. (see figure). The other parameters did not vary. When the subjects performed identical submaximal exercise at a simulated altitude of 4550 m. a striking and sustained rise in serum-H.G.H. from $1{\cdot}6 \pm 0{\cdot}4$ ng. per ml. to $17{\cdot}3 \pm 5{\cdot}2$ ng. per ml. was found. No change was demonstrated in plasma glucose, insulin, or glucagon, but there was a significant rise in plasma-cortisol. After 3 months' acclimatisation to altitude in the Peruvian Andes between 4000 and 6000 m. these experiments were repeated at Morococha in Peru (4540 m.). During submaximal exercise basal H.G.H. was $1{\cdot}5 \pm 0{\cdot}5$ ng. per ml., and there was no significant elevation with exercise—a pattern identical to the previous studies at sea-level. The other parameters showed no significant change. The acute altitude experiment illustrates the profound effect of hypoxia on H.G.H. secretion and suggests that anaerobic metabolism and its resultant metabolites are a potent stimulus to H.G.H. release. After 3 months at altitude it appears that sufficient adaptation has occurred in cellular metabolism to produce an identical hormonal response to that found previously at sea-level.

When the same study was performed with physically fit Peruvian males of the same age who were born at Morococha, no change occurred in H.G.H. However, the fasting basal H.G.H. was $8{\cdot}5 \pm 1{\cdot}1$ ng. per ml. and $9{\cdot}3 \pm 2{\cdot}2$ ng. per ml. on two separate occasions, and these remained elevated without variance during the exercise. These levels for H.G.H. are significantly higher than those for unstressed, basal, fasting males at sea-level and are interesting for several reasons. These Peruvians, who are physically fit, are shorter than Peruvians who have lived all their lives at sea-level. They have adapted remarkably to high altitude, as evidenced by their work-capacity at altitude,



Plasma-growth-hormone levels during submaximal exercise in Australian men at sea-level, at 4550 m. simulated altitude, and at 4540 m. after 3 months' altitude acclimatisation, and in Peruvian men living at 4540 m.

and they have a larger chest, heart, and red-cell mass and a lower plasma-lactic-acid following exercise [2] than their Peruvian cousins living at sea-level. We postulate that in the Morococha Peruvians an elevated H.G.H. is necessary to produce and maintain acclimatisation, firstly in a somatotropic role in facilitating organ hypertrophy and enhancing the release of erythropoietin, and secondly in a metabolic role to assist lactic-acid utilisation during exercise, or to engage free fatty acids as the prime energy substrate, resulting in less lactic-acid formation.

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PHENOBARBITONE IN RHESUS HÆMOLYTIC DISEASE

SIR,—There are a number of things to be said about Dr. Walker's criticisms (Nov. 21, p. 1088) of our controlled trial.[3]

1. Dr. Walker seems to have had some difficulty in interpreting our tables. It is nowhere stated or implied that 14 infants required "late" exchange transfusions. In fact only 1 infant in the treated group who did not require exchange transfusion at birth by our criteria required exchange transfusion later. In the control group there were 8 infants who did not require exchange transfusion at birth but required it later. Thus in the control group 8 infants required 12 exchange transfusions, while in the treated group 1 infant required 2 exchange transfusions under this heading.

2. As regards the criteria for exchange transfusion we would accept that a serum-bilirubin level of greater than 20 mg. per 100 ml. is not an absolute indication for exchange transfusion. Probably the most important single criterion for exchange

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