

develops concealed hostility and difficulty in demonstrating feelings of aggression to people around. Is this true and do you think that this is responsible for their depression?

DR. ZAPHIROPOULOS It is true that patients with chronic disability are likely to exhibit 'conflicts in the expression of hostility', but I do not know whether the anxiety and depression is a result of this; they are all part of the general disturbance seen in rheumatoid patients (Robinson, Kirk, Frye, and Robertson, 1972).

#### References

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**Effect of Corticotrophin and Oral Corticosteroids on nocturnally released Growth Hormone.** By R. MOTSON, D. N. GLASS, J. I. EVANS, P. HILL, J. R. DALY, and N. RUDOLF (*Clinical Research Division, Kennedy Institute of Rheumatology, West London Hospital, and Department of Psychiatry, Edinburgh University*)

Corticosteroid therapy in children is associated with dwarfism, although there is uncertainty about the mechanism of this. Chronically administered steroids can inhibit the growth hormone response to insulin-induced hypoglycaemia, but generally only after some years of therapy and without uniformity. It has not hitherto been possible to find an index of growth hormone function which was inhibited by a dose of steroids unless given for more than 2 to 3 days. It is necessary to find a more physiological index for growth hormone before one could relate levels to dose of steroids, rates of growth, or any other metabolic function.

Growth hormone release is now well documented in association with Stages 3 and 4 of slow-wave sleep (Takahashi, Kipnis, and Daughaday, 1968). This sleep-associated growth hormone release appears to be a physiological situation in which one can study growth hormone satisfactorily, and avoids the necessity for artificial stimuli such as insulin hypoglycaemia or arginine infusions which have been used for previous studies of the effect of corticosteroid therapy on growth hormone secretion. We have undertaken a systematic examination of the effects of corticosteroids on nocturnal growth hormone release, and have previously reported the suppressive effect on growth hormone release of a single injection of Depot Tetracosactrin given to normal subjects 16 hours before the onset of sleep (Glass, Evans, and Daly, 1972). Further experience now shows that this effect is not obtained if a single 80 unit injection of ACTH (Acthar gel) is given at a similar time. This dose, whilst containing at least 1 mg. of the porcine ACTH preparation, gives adrenal stimulation for a much shorter period than 1 mg. Depot Tetracosactrin. The mean peak of growth hormone was  $37.9 \pm 12.3$  S.D. in five subjects compared with  $27.4 \pm 16.0$  S.D. in the same subjects during nights when the hormone was not given; the equivalent corticosteroid values being  $7.7 \pm 1.5$  and  $6.7 \pm 2.6$  respectively. In order to investigate whether the effect of Tetracosactrin on growth hormone release was a direct one, or mediated *via* the action of the raised corticosteroid level it produced, we next examined the

effect of oral corticosteroids on nocturnal growth hormone release in a group of normal individuals: a single orally administered dose of long-acting steroid (Flucortolone) significantly suppressed the sleep associated growth hormone peaks.

#### Discussion

DR. B. M. ANSELL (*Taplow*) The team should be congratulated on this difficult work. It is now time to re-think what type of steroid to give to children and when. At this moment it is still difficult to decide and I wondered if there was an urinary method of assessing growth hormone over a 24 hour period, which would be much more practicable for a childhood study.

DR. MOTSON We have done one or two estimations on urine growth hormone but have not been able to find a satisfactory method.

DR. A. ST. J. DIXON (*Bath*) Can I ask a question for information. Is this type seen in growing children?

DR. MOTSON Yes, sleep associated growth hormone release occurs in children from 12 weeks onwards (Vigneri and D'Agata, 1971).

DR. A. ST. J. DIXON (*Bath*) And another question for elucidation. Do you feel that this is applicable to the minimizing of prednisolone damage to the collagen tissues of the body such as the bruising and the thinning of the skin and osteoporosis. Do you feel that the suppression of growth hormone is partly to blame for this?

DR. MOTSON I do not think I should go so far as to say that, since other anabolic hormones may also be suppressed by corticosteroid therapy.

DR. J. N. GLICK (*London*) Have you done any measurements on people who have had intermittent steroids?

DR. MOTSON No, but two subjects whose growth hormone was suppressed by corticosteroids had a good growth hormone rise the following night.

DR. A. ST. J. DIXON (*Bath*) What do you feel about long-acting depot preparations of steroids? I have the clinical impression that some of the worst cases of steroid damage to the tissues occur with this type of preparation.

DR. MOTSON There does appear to be a correlation between continuity of elevation of corticosteroids and suppression of growth hormone. If growth hormone suppression is associated with tissue damage, then very long-acting steroids may not be advantageous.

#### References

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**A Re-examination of the Hypoglycaemia-induced 'Stress' Response of the Hypothalamo-pituitary-adrenal Axis in Patients with Rheumatoid Arthritis on Long-term Adrenocorticotrophin (ACTH) Therapy.** By M. R. FLEISHER, D. N. GLASS, and J. R. DALY (*Clinical Research Division, Kennedy Institute of Rheumatology, and Department of Chemical Pathology, Charing Cross Hospital Medical School*)

There is considerable evidence that treatment with