

Effects of ACTH on Plasma Iron Levels in Normal Human Subjects. (24898)

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The mechanism of hypoferremia of infection has been obscure. It has been suggested that adrenal steroids cause a lowering of serum iron levels in dogs and rats(1). Hypoferremia in man after other stresses has also been attributed to adrenal steroid release (2,3). Reports of the effect of adrenocorticotrophic hormone (ACTH) and adrenal steroids on serum iron levels in man have been at variance, and often been equivocal(4-9). The present study compares changes in plasma iron level in normal human subjects, following administration over 8 hours of a standard test dose of ACTH, with changes occurring during comparable control period.

Procedure. Normal healthy volunteers, on regular diet but enjoined from strenuous activity during 3 days of this study, were the subjects. Diurnal-nocturnal variation of their plasma iron concentrations was observed during 24 hour control period. Forty mg of ACTH (Upjohn) in 1000 cc of 5% glucose in water were then administered intravenously for 8 hours. During and following the infusion, plasma iron levels were determined by the method of Schade *et al.*(10). Duplicate determinations were performed on each specimen.

Results. Fig. 1 depicts results when ACTH was administered from 8 a.m. to 4 p.m. when plasma corticosteroid levels normally fall(11). ACTH did not alter plasma iron level, either during or after infusion, that could not be accounted for by diurnal-nocturnal or random variation, as shown by initial 24 hour control period.

Because plasma corticosteroid levels themselves undergo diurnal-nocturnal variation, the experiment was altered so that ACTH was administered when plasma corticosteroid levels normally rise. In Fig. 2, results are shown of administering 40 mg ACTH between 11

p.m. and 7 a.m. after 24 hour control period. Subject K attained quite elevated plasma iron levels during the first 24 hours compared with her later levels. Subject I, on the other hand, reversed this pattern and had a lower plasma iron level during the first 24 hours than on the second day. One may conclude that ACTH did not significantly affect the diurnal-noc-

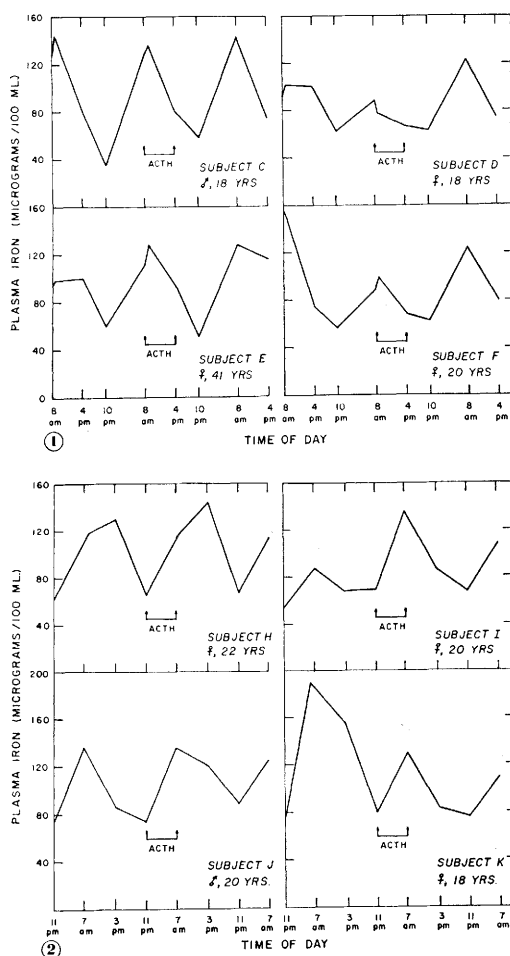


FIG. 1. Changes in plasma iron concentration before and after administration of ACTH. Intrav. infusion, 8 a.m. - 4 p.m.

FIG. 2. Changes in plasma iron concentration before and after administration of ACTH. Intrav. infusion, 11 p.m. - 7 a.m.

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tural variation of plasma iron in these subjects.

Summary. A standard dose of ACTH was administered intravenously for 8 hours to normal volunteers. Plasma iron levels were not affected in any way that could not be accounted for by normal diurnal-nocturnal or day to day variation. Altering normal daily periodicity of corticosteroid concentration by administering ACTH at different phases of the cycle did not affect the curves of plasma iron variation.

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Tryptophan Oxidation by Yellow Mouse Skin. (24899)

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There has been for some time a good deal of evidence that tryptophan is the source of intermediates in production of pigments in insects (See 1, 2, for reviews), but in mammals, tryptophan has been suggested as a possible precursor of pigments only recently(3). An interesting example was discovered by Foster(4), while studying pigment formation by skins of a strain of mice with yellow fur due to dominant gene, A^y/a . Foster found that skin powders from these mice showed very little ability to oxidize tyrosine, the usual precursor of melanin, but vigorously oxidized tryptophan with production of yellow pigment. While in insects, tryptophan appears to lead to pigments by way of kynurenine(1,2), the pathway recently suggested for mammals and possibly other animals(3), is quite different, namely *via* a 5-hydroxyindole compound. No experiments have been reported to determine which, if either, of these

alternative routes may be followed in skins of A^y/a mice. In addition, it is of interest to determine whether or not kynurenine is formed by these skins, since Knox(5) studied a number of tissues from several species, including rat, rabbit, and guinea pig, and reported conversion of tryptophan to kynurenine only in the liver. The experiments reported here indicate that kynurenine is not utilized in pigment formation by skins of A^y/a mice, and that it is probable that a hydroxyindole is an intermediate.

Materials and methods. Mice, obtained from Jackson Memorial Laboratories were A^y/a females, from various matings with pa/pa individuals, and males of a black inbred strain, C57Bl/6. Grüneberg(6) describes the phenotypes. The mice were maintained on stock ration supplemented with occasional fresh vegetables. Only progeny of yellow phenotype were used. Coat color in the A^y/a mice varied from light yellow to deep orange. At 8-11 days after birth, mice were sacrificed by decapitation. Skins from back and head

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