# Failure of 17α-Ethyl-19-Nortestosterone to Effect Plasma 17-Hydroxycorticosteroids and ACTH Responsiveness in Man.* (24116)

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17α-ethyl-19-nortestosterone (Nilevar) has been reported to cause suppression of adrenocortical secretion(1,2). Brooks and Prunty administered 50 to 100 mg of 17α-ethyl-19-nortestosterone daily for 7 to 15 days to 4 men and one woman. Four subjects received the medication intramuscularly and one orally. They found significant reduction in the 17-ketosteroid excretion in all patients; the 17-ketogenic steroids were depressed in only 3 of the 4 patients studied. All major 17-ketosteroids were decreased; 11β-hydroxyandrosterone was least affected.

The present study was undertaken to evaluate the effect of Nilevar on adrenocortical function employing as indices levels of plasma 17-hydroxycorticosteroids (17-OHCS) and their response to ACTH.

*Materials and methods.* Five patients, 4 males and one female, were studied. Their ages and diagnoses are presented in the table. All were treated over a prolonged period with 17α-ethyl-19-nortestosterone, 10 mg 3 times a day orally. Plasma 17-hydroxycorticosteroids (17-OHCS) were determined using the method of Silber and Porter as modified by Peterson(3). Normal control levels range from 4 to 30 μg/100 ml of plasma in our laboratory. The adrenocortical response to ACTH was measured by the effect on plasma 17-OHCS levels of 25 USP units of ACTH in 500 ml of 0.9% saline in water given intravenously over 6 hours. Control samples were obtained and the infusions begun between 8 and 9 a. m. The anabolic effectiveness of Nilevar was evaluated by weight gain, increase of appetite, muscle mass and strength as well as loss of bone pain.

*Results.* All patients had a beneficial effect from the Nilevar. E. K. had a 15-lb weight gain. K. L. had marked reduction in bone pain and the other 3 patients showed significant increases in appetite, muscle mass and strength.

The levels of plasma 17-OHCS and their rise after ACTH, prior to and during administration of Nilevar, are shown in the Table. The control plasma 17-OHCS levels were all within normal limits and were unaffected by Nilevar, 30 mg daily, administered for 12 to 80 days. In 4 of the 5 patients, the response

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TABLE I. Effect of 17 α-Ethyl-19-Nortestosterone (Nilevar) on Plasma 17-Hydroxycorticosteroids and on Their Response to ACTH.

| Patient | Sex | Age | Diagnosis | Pre-Nilevar, plasma 17-OHCS, μg/100 ml | | Nilevar, 30 mg/day p.o. (No. of days) | Post-Nilevar, plasma 17-OHCS, μg/100 ml | |
|---|---|---|---|---|---|---|---|---|
| | | | | Pre-ACTH | Post-ACTH | | Pre-ACTH | Post-ACTH |
| A.S. | ♂ | 59 | Diabetes mellitus, hip fracture, osteomyelitis | 17.9<br>30.3 | 56.2 | 14<br>50 | 24.9<br>33.4 | 68.1 |
| H.M. | ♂ | 51 | Hip fracture, osteomyelitis | 28.5<br>13.4 | 41.0 | 14<br>50 | 16.3<br>13.9 | 42.4 |
| F.G. | ♂ | 60 | Osteoporosis, peripheral neuritis | 23.2<br>17.6 | 72.4 | 12<br>80 | 19.2<br>16.6 | 77.6 |
| E.K. | ♂ | 23 | Regional ileitis, cachexia | 23.0 | 50.3 | 40 | 16.2 | 35.2 |
| K.L. | ♀ | 58 | Rheumatoid arthritis, osteoporosis | 17.3 | 21.9 | 40 | 26.6 | 43.8 |

of the plasma 17-OHCS to ACTH was not altered by Nilevar therapy for 40 to 80 days. K.L. had only a slight rise in the plasma 17-OHCS prior to therapy and a normal response after 40 days of Nilevar. In patient F.G., the control levels of plasma 17-OHCS were normal prior to and after therapy; however, the levels of 17-OHCS were elevated after ACTH. This increased response of the plasma 17-OHCS levels was unaltered by Nilevar therapy for 80 days.

It is well known that cortisone and its derivatives will suppress the adrenal cortex and its ability to respond to ACTH, as measured by the plasma 17-OHCS, and will produce adrenal atrophy. On the other hand, testosterone propionate and 17$\alpha$-methyl-19-nortestosterone (unpublished) do not alter control plasma 17-OHCS levels. Similarly, these studies indicate that adrenocortical function, as evaluated by plasma 17-OHCS levels and response to ACTH, was unaltered by Nilevar given orally over a prolonged period of time.

*Conclusions.* In 5 subjects receiving clinically effective oral doses of Nilevar, there was no alteration in adrenocortical function as measured by plasma 17-OHCS levels before and after intravenous ACTH.

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## Studies on Copper Metabolism. XXVI. Plasma Copper in Patients with Tropical Sprue.* (24117)

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Although increased concentration of copper in plasma has been observed in a wide variety of clinical disorders(1), hypocupremia has been observed in relatively few conditions. It has been observed consistently in newborn infants(2); it is the usual finding in hepatolenticular degeneration (Wilson's disease)(3); and it has been observed frequently in the nephrotic syndrome(4). In addition, hypocupremia has been recorded in an occasional patient with hypochromic anemia(5,6, 7), idiopathic hypoproteinemia(8,9), kwashiorkor(6), and celiac disease(6,10). The causes of hypocupremia were discussed recently and a classification presented(7).

Because of the finding of hypocupremia in 2 patients with "non-tropical" sprue and severe microcytic hypochromic anemia(9), a study of plasma copper in patients with tropical sprue and megaloblastic anemia was undertaken. The results of this investigation are here reported. Observations on 6 patients with megaloblastic anemia of pregnancy are also presented.

*Materials and methods.* Blood samples were obtained from 29 Puerto Rican subjects with sprue in relapse. The diagnosis of sprue was based on clinical findings of chronic diarrhea, flatulence, weight loss, weakness and glossitis; macrocytic anemia with typical megaloblastic morphology in bone marrow; and laboratory evidence of intestinal malabsorption. The average hemoglobin value for the group was 5.5 g % (1.2 to 10.9 g %). Malabsorption was demonstrated for at least 2 test substances, usually xylose, Vit. A, or butter(11). In addition, steatorrhea was demonstrated by a modified fat balance technic in all 21 subjects on whom such studies were

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