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Reduced Estrogen Excretion Due to Clofazimine?

TO THE EDITOR:

Biochemical monitoring of complicated pregnancies may be disturbed by the effects of medication taken by the mother. For example, urinary estrogen excretion, which provides a valuable index of feto-placental function and an accurate indicator of the risk of impending fetal death from placental insufficiency⁽⁹⁾, is diminished by high-dose corticosteroid therapy⁽⁸⁾ or by ampicillin⁽¹⁰⁾. In a recent study of estrogen excretion in pregnant Ethiopian women with leprosy⁽³⁾, we have been able to examine the impact of dapsone and clofazimine therapy on urinary estrogen values.

Dapsone treatment had little effect on estrogen excretion since there was no significant difference between the mean estrogen excretion in 13 women with "cured" tuberculoid leprosy and in seven women with active tuberculoid leprosy who received dapsone (50 mg-100 mg daily) (The Figure). Nevertheless, in women with lepromatous leprosy receiving dapsone alone, 52% of estrogen assays were subnormal.

Estrogen levels were further reduced in patients receiving clofazimine. The effect of immunosuppressive doses of clofazimine (300 mg daily) was studied in one patient

who was already receiving prednisolone but whose initial estrogen excretion was within the normal range. Introduction of clofazimine therapy was associated with diminished estrogen excretion, although a live surviving infant (2.8 kg) was delivered at 39+ weeks of gestation. In three other women, who were already established on clofazimine (300 mg per week) for dapsone-resistant leprosy before estrogen assays were commenced, five out of six values (85%) were subnormal (relative to the lower limit of excretion in normal European women for the same period of gestation)⁽⁷⁾.

In considering the possible risks of clofazimine to pregnancy, it should be borne in mind that most patients receiving clofazimine have lepromatous leprosy in reaction. Even in hitherto uncomplicated lepromatous leprosy, the risks of pregnancy are considerable; namely relapse^(2,6), emergence of dapsone resistance⁽⁵⁾, reaction⁽⁶⁾, and new nerve damage⁽⁴⁾. Furthermore, with the increasing emergence of dapsone-resistant leprosy urgently requiring for its control introduction of dual- and triple-drug regimens^(1,11), it is likely that more women of childbearing age will receive clofazimine.

These findings suggest that there is a need

for further studies of the effect of clofazimine on estrogen synthesis in the foeto-placental unit and on pregnancy outcome in humans.

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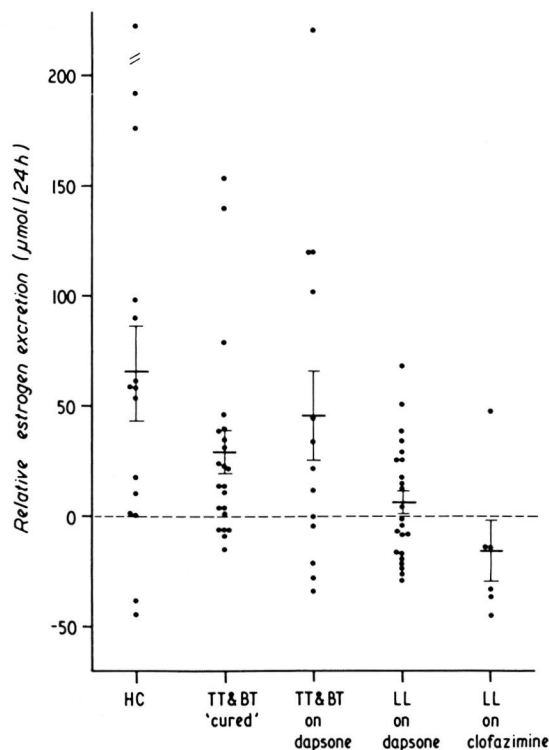
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THE FIGURE. Estrogen excretion according to the clinical classification and treatment of the mother. Values are plotted (in $\mu\text{mol}/24\text{ hr}$) relative to the lower limit of excretion of estriol in European women for the same period of gestation. (Results from patients receiving prednisolone in addition to dapsone or clofazimine are excluded.)

HC = healthy controls

TT and BT = tuberculoid and borderline tuberculoid leprosy

LL = lepromatous leprosy