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As part of a study of the mechanism of metronidazole's efficacy in the treatment of acne and rosacea, its effects on the endocrine milieu and sebum excretion rate were assessed. Thirteen healthy males received oral metronidazole treatment (500 mg/day) for 4 weeks. Serum sex hormone levels were determined in all 13 subjects and the sebum excretion rate was determined in seven of them, before and after treatment. We measured serum levels of estrone (E1), estradiol (E2), total testosterone (T), free testosterone (FT), dihydrotestosterone (DHT), dehydroepiandrosterone sulfate (DHEA-S), and sex hormone-binding globulin (SHBG). There were no significant changes in E1, T, FT, DHT, or SHBG levels, but E2 and DHEA-S levels decreased significantly after treatment. In all seven subjects in whom the sebum excretion rates were determined, the amount of facial skin surface lipids decreased significantly after treatment. These results suggest that metronidazole exerts its clinical effects through suppressing the sebum excretion by a mechanism other than anti-androgenic action.