COMMITTEE ON DRUGS

THE TREATMENT OF ACNE WITH ANTIBIOTICS

WHEN broad-spectrum antibiotics were first introduced two decades ago for the treatment of acne, justification for such therapy seemed reasonably straightforward, e.g., the suppression of the suppurative inflammatory lesions commonly encountered in acne. As time went on, however, certain observations raised questions concerning the rationale for this form of treatment. First, it became apparent with cumulative clinical experience that the disease could ordinarily be controlled by doses of antibiotics lower than those required to treat bacterial infections. Second, bacteriologic studies disclosed that the only bacteria regularly recoverable from acne lesions were the anaerobic diphtheroid Corynebacterium acnes and aerobic coagulase-negative cocci, predominantly staphylococcus type II; both of these bacteria are known to be normal resident skin organisms. Thus, as no reports of controlled studies were then available for assessing the true efficacy of antibiotics used in the treatment of acne, the uneasy suspicion arose that such therapy might be inducing a primarily placebo response.

In 1965, Freinkel and her collaborators demonstrated that the oral administration of tetracycline, even in doses as small as 250 mg daily, resulted in a significant reduction of the free fatty acid concentration of the lipid (sebum) secreted to the skin surface by the sebaceous glands. This effect could be observed in normal subjects as well as in patients with acne and was entirely reversible on discontinuance of drug. The inflammatory lesions of acne are known to result from disorganization of the follicular epithelium, with consequent liberation of the intrafollicular contents, containing sebum, into the dermis. Because the free fatty acids were found to be the most irritating components of this lipid material, it was concluded that antibiotic therapy achieved its beneficial effect in the treatment of acne by reducing the concentration of inflammation-producing free fatty acids. It was further postulated that this effect was the indirect result of suppression of the resident bacterial flora, primarily C. acnes, with resultant inhibition of bacterial lipases responsible for the elaboration of free fatty acids. The following evidence was established in support of this hypothesis: (1) C. acnes was sensitive to broad-spectrum antibiotics in vitro; (2) C. acnes was capable of releasing free fatty acids in vitro from sebum triglycerides, and this action was suppressed by the prior incorporation of tetracyclines into the in vitro experimental system; and, (3) the daily oral administration of 250 to 500 mg of tetracycline resulted in a marked decrease of the skin surface bacterial population. At the present time this explanation seems convincing enough; however, in view of the recent demonstration in vitro that tetracyclines inhibit a lipase of nonbacterial origin, bacterial suppression may not be the only mechanism involved.

The indication for the treatment of acne with antibiotics is the presence of inflammatory lesions. Little or no improvement can be expected with the noninflammatory lesions (comedones), and antibiotics should not be used in patients with these lesions. Tetracycline is the antibiotic most frequently prescribed with numerous controlled studies attesting to its effectiveness. The relative inexpensiveness of tetracycline also favors wide usage, especially because the average patient is usually treated for months at a time. Erythromycin and demethylchlortetracycline have been shown to be similarly efficacious and also significantly lower the free fatty acids of sebum. Penicillin and sulfonamides are largely ineffectual.

Treatment dose schedules are empirical, a circumstance not likely to change until

The Committee wishes to acknowledge the generous assistance of Dr. Peter E. Pochi, Associate Professor of Dermatology, Boston University School of Medicine, in the preparation of this statement.
TREATMENT OF ACNE

more exacting data become available about the effect of wide-ranging doses on clinical responsiveness, accompanied by correlative studies of fatty acid and bacterial profile measurements. It is customary to begin tetracycline therapy with 500 to 1,000 mg daily, depending on the severity of the disease, and to eventually adjust the dosage downward (as is usually possible) to the lowest, optimal level. On occasion it can be reduced to as little as 250 mg every other day. Antibiotic treatment of acne does not appear to affect existing lesions but rather to help in preventing the formation or reducing the severity of newly developing lesions. Moreover, the anti-lipolytic action, as determined by free fatty acid analyses of sebum, can be delayed as much as 4 to 6 weeks. For these reasons, clinical improvement may take place slowly, so this therapy should not be abandoned without benefit of an adequate trial period. If the acne responds quickly, the effect is probably the result of coincident natural remission or of a placebo reaction, which can be considerable in acne. Not all patients with acne improve under antibiotic treatment. The reason for this is not clear, nor is it known with certainty why some patients who respond well initially eventually develop resistance with continued drug administration. No information is available at the present time for comparison of such antibiotic-resistant patients with antibiotic-sensitive patients in terms of possible differences in bacteriologic flora, sebaceous lipid patterns, and antibiotic tissue levels.

The treatment of acne with antibiotics is suppressive rather than curative. As the disease is rarely of short duration, the occasional need for long-term therapy raises the inevitable issue of the risk for the development of significant side effects. However, reports of serious toxicity are singularly lacking. This is probably the result of the low doses of antibiotic usually employed and the relative youth and general good health of those afflicted with acne. Minor difficulties are occasionally encountered, such as gastrointestinal symptoms and candidal overgrowth. There is a problem of photosensitivity with all of the tetracyclines, but demethylchlortetracycline is the most potent producer of that side effect. For this reason, caution should be exercised when using this particular tetracycline in the treatment of acne.

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THE TREATMENT OF ACNE WITH ANTIBIOTICS


Pediatrics 1971;48;663

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DEDICATED TO THE HEALTH OF ALL CHILDREN™
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