component to a desired level, and consequently to give an insufficient dose of the other. This subject is well treated by Weinstein (1):

The most important problem in the field of combined chemotherapy is the use of "fixed-dose" mixtures. On the basis of the presently available knowledge, it appears patently clear that these mixtures have no place in the treatment of infection. The attitude that physicians should adopt toward such preparations has been outlined in an editorial by Finland (1957), written as a joint expression of the views of investigators and teachers in the field of infectious diseases, as follows (7):

> Considerable caution is warranted in accepting the trend to fixed antibiotic combinations as inevitable or in lending support to a trend that may not be desirable. We would be remiss in our duties as physicians, teachers, and investigators were we to encourage, adopt, and recommend the use of new agents that we cannot cosider to be as good as, or no better than, those previously shown to be good, even if they are legally certified. It is particularly incumbent on us to be very circumspect about the use of drugs of any sort in fixed combinations that do not offer the physician discretion as to the choice of components, or of the ratios in which they are used. The presence in any combination of a new or unproved component, or of a substance that may be inferior to others that might well be used instead, should make us even more cautious. They should be recommended and adopted, if at all, only after adequate, carefully controlled, and critically evaluated study shows them definitely to be useful and superior.

Encouragement of the use of such "fixed-dose" antibiotic mixtures and the manner in which they are being exploited represent a major backward step in the management of infections.

Recommendations

In the foregoing discussion, the anti-infective panels of the Drug Efficacy Study state that the contraindications for the use of any sulfonamide-penicillin combination by the oral route far outweigh any indications for such use. Citations from the more recent literature in support of this view are amply supplemented by editorial comment from the early 1950's. (8, 9) On these bases, it is strongly urged that use of these fixed combinations no longer be recommended.

PENICILLIN-STREPTOMYCIN COMBINATION FOR PARENTERAL USE

The reports prepared for the Drug Efficacy Study by the anti-infective panels offer a convenient format for discussion of the penicillin-streptomycin combination for parenteral use. This report format, appropriately edited for economy of presentation, is as follows (each claim cited as an indication in the package insert for this combination is reviewed):

Indications

A. *Bacterial Endocarditis in Patients with:*

1. Pencillin-susceptible streptococcal endocarditis (0.1 mcg/ml or 0.1 unit/ml or less).

a. *Evaluation:* Ineffective as a fixed dose combination.

b. *Comment:* Treatment of this specific form of bacterial endocarditis with injections of a fixed combination providing a maxium of 2.0g of streptomycin and at least 2.4 million units of penicillin per day would probably be effective, but only one of the 17 preparations submitted will provide ths dosage. In most instances, this form of endocarditis can be treated with penicillin alone. If streptomycin were added, it could readily be given in a separate dosage form.

c. *Documentation:* References 10–17.

2. Endocarditis due to enterococci or other streptococci not sensitive to 0.1 mcg/ml or less.

a. *Evaluation:* Ineffective.

b. *Comment:* These more resistant types of bacterial endocarditis would not be optimally treated with any of these fixed combinations. There is so little procaine penicillin in the combinations that adequate dosage of penicillin would be accompanied by doses of streptomycin that would be seriously toxic.

c. *Documentation:* References 10–17.