

M. *Osteomyelitis*

1. *Evaluation*: Ineffective.
2. *Comment*: Primary non-tuberculous osteomyelitis is most commonly caused by staphylococci. Many of the strains are non-susceptible to penicillin G and streptomycin. If the infecting strain is susceptible to penicillin, adequate dosage of penicillin would be accompanied by doses of streptomycin that would be likely to be seriously toxic. In addition, the duration of treatment usually considered desirable poses a serious risk of streptomycin toxicity. Osteomyelitis following surgical procedures may be caused by gram-negative bacilli; however, such hospital-acquired infections are usually resistant to both agents.
3. *Documentation*: Reference 46.

N. *Secondary Infections in Patients Being Treated for Tuberculosis.*

1. *Evaluation*: Ineffective as a fixed combination.
2. *Comment*: Patients with tuberculosis may develop staphylococcal, pneumococcal, streptococcal, Klebsiella, or Hemophilus pneumonia. The promulgation of these fixed combinations to avoid such infections is undocumented, unnecessary, and unrealistic.
3. *Documentation*: None applicable.

O. *Other Infections in Which the Causative Agent Cannot be Identified without Operative Procedures*

1. *Evaluation*: Ineffective.
2. *Comment*: This claim is too broad to permit its proper evaluation.
3. *Documentation*: None applicable.

GENERAL COMMENT ON REVIEW OF INDICATIONS

These fixed combinations will rarely provide optimal therapy for the complex clinical problems that are encountered with these conditions. In each case, the characteristics of the invading organism and the results of in vitro bacterial sensitivity tests must be known. Many of these infections could be treated with penicillin alone, with penicillin and streptomycin in a different ratio or with other antimicrobial agents.

JUDGMENT OF ANTI-INFECTIVE PANELS II AND IV

Anti-infective panels II and IV wish to record their judgment that the availability of fixed combinations of streptomycin and penicillin has had the following results:

It has led to inappropriate use of these drugs for treatment of diseases in which the combination is no more effective than one of the components or in which the fixed combination is not the treatment of choice.

Patients have been exposed to the increased toxicity that is inherent in a combination without increasing the benefit.

Flexibility in dosage of the individual components of these combinations has been denied.

The marked changes that have occurred in the pattern of bacterial susceptibility in recent years and the development of new and better antimicrobial agents have been ignored.

The availability of penicillin and streptomycin individually for combined use at the discretion of the physician has also been ignored.

These considerations, and the limited indications for the use of these combinations, have rendered fixed dosage forms of penicillin and streptomycin obsolete. Accordingly, it is the judgment of the panels that these combinations no longer belong in the therapeutic armamentarium.

REFERENCES

1. Weinstein, L. Antibiotics. I. General considerations. In *The Pharmacological Basis of Therapeutics*. Edited by L. S. Goodman and A. Gilman. Third edition. New York: Macmillan, 1965. Pp. 1171-1192. Chemotherapy of microbial diseases: sulfonamides. *Ibid.* Pp. 1144-1170. Antibiotics (continued): II. Penicillin. *Ibid.* Pp. 1193-1229.
2. Weinstein, L., Samet, C. A., and Chew, W. H. Studies of effects of penicillin-sulfonamide combinations in man. *Am. J. M. Sc.* 248: 408-414, 1964.
3. Weinstein, L., Madoff, M. A., and Samet, C. M. Sulfonamides. *New Eng. J. Med.* 263: 952-957, 1960.