

isolated that are highly resistant to streptomycin. The recommended dosages of procaine penicillin are 2.4 million units for males and 4.8 million units for females. There is so little procaine penicillin in the combination that an adequate dosage of penicillin would be accompanied by seriously toxic doses of streptomycin.

3. *Documentation:* References 41-45.

I. Urinary Tract Infections

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

2. *Comment:* These infections may be caused by a wide variety of bacteria, some of which may be sensitive to one or both of the ingredients of this mixture. Such sensitivity is highly unpredictable.

Infections with enterococci do occur; however, they are unusual and account for fewer than 5 percent of infections. When present, enterococci are frequently associated with resistant gram-negative bacilli which are better treated with agents other than penicillin and streptomycin. Enterococci are the major pathogens that are predictably more sensitive to the combination of penicillin and streptomycin than to either agent alone; however, in those rare cases in which they might be used, the two agents could readily be given in separate dosage forms.

3. *Documentation:* References 16, 47, 48.

J. Middle Ear Infections and Mastoid Infections

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

2. *Comment:* Acute otitis media is most commonly due to pneumococci and streptococci (other than enterococci) and, in infants, to *Haemophilus influenzae*. Penicillin is optimal therapy for pneumococcal and streptococcal infections. Simultaneous administration of streptomycin is of no value. Enterococci are responsible for an exceedingly small proportion of streptococcal middle ear infections, and amounts of penicillin considerably greater than are available in these combinations would be needed for treatment of these entities. The relative effectiveness of procaine penicillin alone or in these combinations in treatment of *H. influenzae* ear infections has not been the subject of critical study, and tetracycline or ampicillin would constitute a better drug choice for treatment of such infections.

Chronic otitis media is usually due to staphylococci or gram-negative bacillary aerobes and anaerobes. These organisms are usually resistant to penicillin and streptomycin or, in the case of gram-negative bacilli, are likely to become so very early in the course of treatment.

3. *Documentation:* Reference 6.

K. Bronchiectasis, Bronchitis, and Other Respiratory Infections

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

2. *Comment:* It is misleading to imply that these antibiotic combinations would be preferable to the penicillin component alone if a specific clinical-microbiologic diagnosis were made. Group D streptococci are more susceptible to the combination but are virtually never implicated in respiratory tract infections. Chronic bronchitis is often associated with a mixed bacterial flora, but a penicillin-streptomycin combination is not the regimen of choice. *H. influenzae* is a very important pathogen in this condition and would be better treated with tetracycline or ampicillin.

3. *Documentation:* References 10, 16, 49, 50.

L. Brain Abscess

1. *Evaluation:* Ineffective.

2. *Comment:* The bacteriology of brain abscess is exceedingly diverse. Microorganisms commonly isolated include anaerobic cocci, gram-negative anaerobic bacilli, staphylococci, Actinomyces, Veillonella, Enterobacteriaceae, and enterococci. Although penicillin is effective against some of the potential pathogens and streptomycin against others, only enterococci (group D streptococci) are more susceptible to the combination, and then only if the penicillin is used in very high doses and in the aqueous form. Large doses of penicillin are required to achieve adequate levels across the blood-brain barrier. The use of this fixed combination would be unwise.

3. *Documentation:* References 51, 52.