

Example of prefixed combinations

	<i>Number</i>
Penicillin-streptomycin -----	20
Tetracycline-novobiocin -----	3
Tetracycline-oleandomycin -----	5
Tetracycline-nystatin -----	13
Tetracycline-amphotericin -----	4
Penicillin-sulfonamide -----	22
Tetracycline-sulfonamide -----	2
Erythromycin-sulfonamide -----	3
Oleandomycin-sulfonamide -----	1
Sulfonamide-methenamine mandalate -----	2
plus	
Tetracycline-analgesic (aspirin) -----	2
Oleandomycin-analgesic -----	1
Penicillin-analgesic-antihistamine-vasoconstrictor -----	3
Tetracycline-analgesic-antihistamine -----	2
Sulfonamide-pyridium -----	6
Sulfonamide-scopolamine -----	2
Methenamine-pyridium -----	1
Methenamine-scopolamine -----	2
Methenamine-analgesic -----	1

Note.—Each of the above 95 prefixed combinations has a different trade name.

(2) Lack of Therapeutic Indications for Prefixed Combinations of Anti-infective Agents.

In the selection of a therapeutic program for any of the etiologic agents, listed in Table 1, there is no logical indication for use of any prefixed combination when they are viewed in light of indications for therapy with single or multiple anti-infective agents.

(3) Lack of Controlled Clinical Studies.

No adequately controlled clinical studies have been conducted to prove the superiority of prefixed combinations over the use of singly administered antimicrobial agents.

(4) Limitation of Dose of One Ingredient by the Toxicity of Other Ingredients in a Prefixed Combination of Antibiotics.

There are few disease entities which should be treated concurrently by more than one drug. Examples are tuberculosis, bacterial endocarditis caused by *Streptococcus fecalis*, mixed infections caused by two or more different etiologic agents with differing antibiotic susceptibility, and infections caused by gram negative bacilli before antibiotic susceptibility is determined.

There is no question that subacute bacterial endocarditis caused by *Streptococcus fecalis* should be treated with penicillin in a daily dose of 10.0 to 20.0 million units plus streptomycin in a daily dose of 1 to 2 grams. However, only one of the prefixed combinations of penicillin and streptomycin provides a daily dose of 2.4 million units of penicillin without exceeding a toxic dose of 2.0 grams of streptomycin. None of the prefixed combinations of penicillin and streptomycin could be used to provide a daily dose of 20.0 million units of penicillin without giving a toxic dose of over 10 grams of streptomycin.

(5) Lack of Therapeutic Advantage of Prefixed Combinations.

The combinations of tetracycline and novobiocin, tetracycline and oleandomycin, penicillin and sulfonamide, tetracycline and sulfonamide, erythromycin and sulfonamide, oleandomycin and sulfonamide afford no therapeutic advantage over single antibiotics, when there is single antibiotic susceptibility, such as is the case with pneumococci, streptococci, staphylococci, meningococci, gonococci, vibrios, spirochetes, anthrax, clostridial gangrene, and listeria in which the penicillins are more effective, nor in the case of bedsonia, rickettsia and mycoplasma in which single effective antibiotics are indicated. The rest of the bacterial infections such as caused by Mimeo, Horrellea, and the gram negative non-spore forming rods, require *in vitro* susceptibility tests to determine antibiotic susceptibility for specific antimicrobial therapy, if maximal opportunity for cure is to be attained.

None of these combinations have any effect against viruses, which cause most of the infections in the United States, nor against the fungi.

(6) Use of Unnecessary Drugs in Prefixed Combinations.

When a single drug is maximally effective there is no logical reason for the administration of a second drug which adds nothing more to the clinical result.