

In summary:

1. There is lack of indications for prefixed combinations of anti-infective agents.
2. There is lack of controlled clinical studies to prove indications for prefixed combinations of anti-infective agents.
3. When a prefixed combination of anti-infective agents is used here in a limitation of dose of one ingredient because of the toxic concentrations of the other.
4. In most infections there is a lack of therapeutic advantage of prefixed combinations over one specific antibiotic.
5. If one ingredient is unnecessary, there is hazard of increased unnecessary adverse drug reactions including the development of resistant strains of micro-organisms.
6. When a prefixed combination of antibiotics is chosen empirically, there may be interference with further diagnostic techniques. Unless, during the time of that empirical judgment, appropriate tests are in progress.
7. Specific narrow spectrum antibiotics may be more advantageous than a "wide spectrum" combination of antibiotics.

Thank you.

(The complete prepared statement and supplemental information submitted by Dr. Wise follows:)

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SELECTION OF ANTIBIOTICS IN THERAPY OF INFECTIOUS DISEASES

I. Introduction

The modern era of therapy of infectious diseases began in 1935 when Gerhard Damagk introduced protosil, a dye stuff derived from sulfanilamide, which protected mice against fatal doses of hemolytic streptococci. The many antimicrobial agents developed since that time have provided a potentially curative armamentarium against infectious diseases considered incurable only 35 years ago.

II. Factors influencing treatment

Many factors influence the concepts and habits of physicians who treat infectious diseases. Medical students, interns and residents are taught principles in the diagnosis and management of these diseases. Representatives of pharmaceutical manufacturers discuss their companies' antimicrobial products with physicians. Medical journals publish reports of varying degrees of excellence on observations of the use of anti-infective agents; advertisements containing statements that would not be acceptable in a scientific manuscript are printed in the same journals. Exhibits at every major medical convention attempt to influence the physician in his choice and use of antimicrobial products. Patients may suggest and demand the administration of an anti-infective drug. The busy physician is pressed to prescribe.

III. Reasons for the rational use of anti-infective agents

A patient who has indications of infection can be assumed to have a disease caused by one or more of the following: (1) bacteria, (2) viruses, (3) rickettsia, (4) bedsonia, (5) mycoplasma, (6) fungi, (7) other parasites, protozoa, etc. or (8) a host of noninfectious agents. The patient should be treated by methods that will eliminate the etiologic agent as rapidly as possible in order to prevent the progression of disease, the development of complications and death, and to decrease morbidity and expense. If adequate therapy is not begun promptly, the disease or its sequela may become irreversible.

It must be emphasized that any bacterial infection is potentially a serious illness which, if it is inadequately treated, may result in death. If, for example, the disease is caused by *Streptococcus hemolyticus*, the possible complications