(7) Increased Risk of Adverse Drug Reactions When Combinations of Drugs are Used.

The use of any drug may result in an adverse reaction in the patient. An unnecessary antibiotic in a prefixed combination can result in hazards varying from mild reactions to fatal results. Superinfection resulting during treatment with combinations of antibiotic may reach considerable magnitude. The hazard of neutralization of the effects of one antibiotic by another antibiotic may result in decreased efficacy of therapy.

(8) Increased Resistance of Micro-organisms to Antibiotics.

The acquisition of microbial resistance to antibiotics is related to the use of an antibiotic in an environment. The unnecessary use of an antibiotic as occurs with the use of prefixed antibiotics results in the appearance of resistant strains of bacteria with increased number of superinfections.

(9) The Erroneous Implication of "Wide Spectrum" of Antimicrobial Effect.

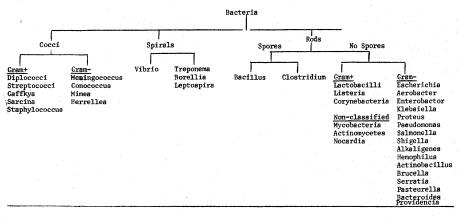
Selection of a fixed combination of antibiotics, because there is a wide spectrum of antibacterial activity against a larger group of micro-organisms, indicates a lack of specificity in choosing the most effective antibiotic with a more direct specific effect against the micro-organism causing the disease. This philosophy of therapeutics may result in failure to establish an etiologic diagnosis and failure of cure until more appropriate therapy is selected.

## VII. 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 there is 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 mero-organisms.
- (6) When a prefixed combination of antibiotics is chosen empirically, there
- may be interference with further diagnostic techniques.
- (7) Specific narrow spectrum antibiotics may be more advantageous than a "wide spectrum" combination of antibiotics.

T A B L E 1

ETIOLOGIC ACENTS OF INFECTIOUS DISEASES



Rickettsia

Fungi

Mycoplasma

Protozoa

Bedsonia