

REFERENCES

- ¹ Stevens, A. R., Jr., Agranulocytosis induced by sulfaguanidine: danger of antibacterial drug in symptomatic remedy. *Arch. Int. Med.* 123: 428, 1969.
- ² Washington briefing on FDA's drug efficacy review. *FDA Papers* 2(2): 7-31, March 1969.
- ³ Ban on 78 more antibiotic mixes proposed by FDA: firms to fight. *Wall Street Journal*, April 2, 1969, pp. A1 and A3.

APPENDIX VII

COLLEGE OF MEDICINE, DEPARTMENT OF MEDICINE,
UNIVERSITY OF ILLINOIS AT THE MEDICAL CENTER, CHICAGO,
Chicago, Illinois, June 17, 1969.

SENATOR GAYLORD NELSON,
U.S. Senate,
Washington, D.C.

DEAR SENATOR NELSON: I am happy to respond to your request for a statement of my views on the uses of fixed combinations of antibiotics. I have been interested in this problem for some time through teaching, research, and the care of patients, and as a result of membership in the Revision Committee of the United States Pharmacopeia, the Council on Drugs of the American Medical Association, the Medical Advisory Board of the Food and Drug Administration and a number of ad hoc committees relating to the regulation of drugs. (A full curriculum vitae is attached.)

The reasons that can be brought forward for the use of fixed combinations of antibiotics and other drugs used in infections are:

1. Two or more anti-infective drugs may be effective against a larger number of infections than one alone,
2. One drug may delay the appearance of micro-organisms resistant to another drug in the combination,
3. Synergism may result, i.e., a better result than could be obtained with maximal doses of either antibiotic alone.

In addition, certain reasons may be given for the use of combinations of drugs in general:

4. Greater convenience to the patient, and
5. Greater convenience for the physician.

How do the combinations of antibiotics that are marketed today fulfill these criteria? Combinations of penicillin and streptomycin are recommended for fixed infections. If by this is meant peritonitis following a ruptured appendix, for instance, the dose of penicillin which would be effective should be from 16 to 25 times the quantity contained in a single dose. It would be impossible to give this intramuscularly, and, if it could be given, such a dose would contain 8 to 12 times the highest recommended dose of streptomycin and thus would be in the toxic range for that drug. If the combination is intended for use in mixed infections of the urinary tract, it is doubtful whether either antibiotic in the doses used would be effective against the great majority of bacteria which infect the urinary tract, and certainly several other antibiotics are much more effective than this combination. If it is intended to treat chronic bronchitis with this combination, there is no evidence that this combination is more effective than penicillin alone, nor is it anywhere nearly as effective as the tetracyclines.

The sulfa drugs have been combined with several antibiotics, especially the erythromycins, tetracyclines and penicillin. If it is intended that they be used in acute upper respiratory tract infections, there is no evidence that the sulfonamides add anything. All three antibiotics are so much more effective in pneumococcal infections than the sulfa drugs that if one of them fails to cure or improve a pneumococcal infection, the addition of sulfonamides will surely not be of any help. Penicillin and erythromycin are very effective in infections caused by the hemolytic streptococci (such as scarlet fever); sulfonamides only slightly effective if at all. Penicillin or one of its newer analogues, such as oxacillin, are effective against practically every staphylococcus. Erythromycin and the tetracyclines are effective against some; the sulfonamides have a very weak effect against a few staphylococci and no effect against many. Infections caused by mycoplasmas, microorganisms intermediate in some respects between viruses and bacteria, are not affected by the sulfa drugs but are rapid-