ly eradicated by the tetracyclines and probably also by the erythromycins. And this just about covers all of the acute upper respiratory infections that are amenable to any specific therapy; in none would a combination of two antibiotics, or antibiotics with sulfa drugs, be indicated.

The tetracyclines are marketed in combination with analgesics such as asprin and phenacetin. Here, the superfluous drugs are usually the antibiotics. The discomfort or pain that occurs in the common cold is usually relieved by drugs such as aspirin, but it has been shown that the antibiotics have no usefulness in the common cold. In the sinusitis that sometimes follows a common cold, antibiotics may occasionally be helpful (although other antibiotics are more likely to be effective than the tetracyclines), but the doses should be given at regular intervals and for a definite period of time until the infection is cleared and is not likely to recur, whereas the pain-relieving drugs should be given for the symptoms of pain, which sometimes would require doses at more frequent intervals than the antibiotics are given, and at other times no analgesics at all. Also, therapy is usually needed only for a day or two in contrast to the longer period of time required for the tetracyclines.

Possible synergistic effects cannot be used as a reason for giving any of the fixed combinations of antibiotics that are on the market. The cases where combinations of antibiotics can be given for a synergistic effect before sensitivity tests are done on the infecting microorganism, are limited to the use of penicillin and streptomycin in endocarditis, and even here it is wise to check the effect of the combination in the laboratory. The dose of the two antibiotics needed in the treatment of endocarditis would prevent the use of the fixed combinations of penicillin and streptomycin that are on the market. Sometimes, other antibiotics are given concomitantly in serious infections until sensitivity tests can be done, but never in the doses or combinations that are marketed.

The use of antibiotics concomitantly has also been shown to be effective in delaying the appearance of resistant bacteria in the treatment of tuberculosis, but the doses and routes of administration used prevent the use of fixed combinations. My colleagues and I showed that spiramycin given concomitantly with novobiocin would delay the appearance of resistant staphylococci, as compared with novobiocin given alone; but this delay was not very great, and other drugs are now available which are so much more effective that this study is of no practical value.

The only one of these fixed combinations that has any rationale is the combination of a tetracycline and nystatin. The latter has been shown to lower the number of candida in the intestinal tract of patients receiving tetracyclines, as compared with those receiving a tetracycline alone. Although it has not been proved that candida infections are less frequent following the use of these infections, it seems reasonable that this combination might be used in high-risk patients.

One might ask, even if a combination is effective only once in 10,000 times when the most active drug in the combination is not effective alone, why should the combination not be used. The answer is that the increased number of adverse reactions that occur as a result of using two or more drugs instead of one does not justify the possibility that in a very rare instance the combination may have an added advantage. In addition, as has been mentioned, the optimal doses and dosage-intervals for any two drugs are usually not the same.

Antagonism, the diminution of the effect of the one antibiotic when a second antibiotic is used concomitantly, although infrequent, is a real possibility when two antibiotics are used at the same time. Although some general rules have been devised for predicting whether synergism or antagonism will occur, there are enough exceptions to these rules to make it advisable in most cases to determine what a combination of two antibiotics will accomplish in the test tube before it is used clinically.

One frequently hears the statement that it is all very well for someone in an academic position to recommend the use of laboratory tests before therapeutic procedures, but that such procedures are not practical for the practicing physician. Yet, as one who was in the private practice of medicine for sixteen years and who has been in a full-time academic position for nineteen years, I am confident that the good physician in either locality approaches diagnosis and treatment in the same way. Neither in the academic community nor in the private