

ginning combinations were thought to be rational because they might delay the emergence of resistant mutant strains, the synergistic effect, the amelioration of certain symptoms, and so forth.

It seemed reasonable to put these together. Unfortunately, there is no current support for these reasons. That whole area of development is simply now an anachronism. What we are dealing with now is a holdover. Actually, in the 1950's, very well known authorities, Dr. Finland, Dr. Weinstein, Dr. Jawetz, Dr. Hewitt, and other people, pointed out very clearly that these combinations were bad medicine.

Senator NELSON. This is over 10 years ago?

Dr. KUNIN. Oh, yes. I would just like to read you a very brief paragraph that was prepared by Dr. Finland in 1957. That is 12 years ago. This statement was signed by the leading experts in antimicrobial therapy at that time, and most of them are still around ticking, yet they really had no action on this point. This is a very brief paragraph showing you the state of affairs in 1957. The remarkable thing is that our opinion is exactly the same as pronounced by these individuals.

Senator NELSON. You mean the conclusions of your present panel are the same as the conclusions reached in 1957?

Dr. KUNIN. That is right. In other words, there is very little that we actually have added that was not fully known and fully published more than 12 years ago. In a sense one of the real pleasures, I believe, for myself and my colleagues is to be able to bring to the public through journals, such as the New England Journal, a reiteration and a rejustification of the position held by the experts in 1957.

This is Dr. Finland's statement. He says:

Considerable caution is warranted in accepting the trend to fixed antibiotic combinations as inevitable or in lending support to a trend that may not be desirable. We would be remiss in our duties as physicians, teachers, and investigators were we to encourage, adopt, and recommend the use of new agents that we cannot consider to be as good as, or no better than, those previously shown to be good, even if they are legally certified. It is particularly incumbent on us to be very circumspect about the use of drugs of any sort in fixed combinations that do not offer the physician discretion as to the choice of components, or of the ratios in which they are used. The presence in any combination of a new or unproved components, or of a substance that may be inferior to others that might well be used instead, should make us even more cautious. They should be recommended and adopted, if at all, only after adequate, carefully controlled, and critically evaluated, study shows them definitely to be useful and superior.

And that position was taken prior to the enactment of the Food and Drug Act amendments. It is a position that is as good today as it was before, and it still keeps the door open for any drug that can be shown to be efficacious.

Senator NELSON. Please go on.

Dr. KUNIN. I won't read this in detail.

Senator NELSON. If you wish to summarize it in some places, feel free to do so. We will have a few questions as you go along. We have the time.

Dr. KUNIN. The first area of consideration is the combination of penicillin and sulfonamide. This is where our joint panels pick up first. Our charge was to examine the efficacy of a compound according to the claims made for it, so that the analysis by each of the panel was in relation to claims that appeared on the package insert. One of the indications given for the use of oral sulfonamide-penicillin combina-