

Senator NELSON. And this is an article which summarizes the findings of all 30 panels, is that correct?

Dr. EICHENWALD. No. This deals only with the findings on fixed combinations of antibiotics by five panels.

Senator NELSON. And this—who is the author of the article?

Dr. EICHENWALD. It is a number of people. It was basically authored by Dr. Calvin Kunin and Dr. Bill Hewitt, who were chairmen of the two of the antibiotic panels. It was also commented on and modified by the other panel chairmen.

Senator NELSON. And did all of the panel chairmen approve of the article?

Dr. EICHENWALD. Yes, sir; unanimously.

The reasons why combinations are not useful and why they are potentially dangerous are summarized in this article in the *New England Journal of Medicine*; in my statement, I would like to comment on some of the factors which led to these conclusions.

One might ask if expert medical opinion is so unanimously opposed to fixed combinations of antibiotics, why were these preparations ever marketed? The pharmaceutical houses have provided several justifications which, to them, provide a basis for the commercial preparation of these mixtures:

(1) They are useful in the treatment of mixed bacterial infections.
(2) There is enhancement of antibacterial activity from the use of combinations.

(3) Because combinations "widen the spectrum of activity," they provide for satisfactory treatment of infections before etiology is known or in cases when it is impossible to determine the etiology.

(4) Antibiotic combinations were used extemporaneously by physicians prior to the introduction of the fixed dosage commercially available drugs.

(5) Combinations are cheaper than the sum of the price of the individual ingredients.

(6) Combinations are easier to administer and thus more convenient.

(7) Physicians demanded combinations and the pharmaceutical houses simply followed the demand.

(8) Following their introduction, combinations were used widely, some of them in fact becoming "best sellers". Thus, the acceptance by physicians indicates that these preparations must be useful and have filled a so-called therapeutic gap.

Allow me to comment on each of these reasons.

First, the problem of mixed bacterial infections. The sort of situation, where several microbial organism work together to cause disease is relatively uncommon but may occur in such illnesses as bronchiectasis, peritonitis, urinary tract infections, chronic otitis media, and occasionally in burns. Many different species of bacteria are associated with these conditions and patterns of antimicrobial sensitivity are very variable. Thus, it is unlikely that any given fixed combination would contain either the proper drugs or the proper amounts of each drug to be effective in even a relatively modest proportion of cases. Additionally, it has been demonstrated that while under some rather prescribed circumstances a "broad spectrum" effect may be produced by the com-