emergence of resistant strains to penicillin and particularly resistant strains to streptomycin, making streptomycin almost worthless today for many gram negative infections. This has led to the emergence of resistant organisms to penicillin, one of our most valuable and least toxic drugs.

Senator NELSON. And this has come about in your opinion because of its indiscriminate use in combinations?

Dr. KUNIN. Yes, the streptomycin-penicillin combination I think is more to blame for the irrational use of antibiotics and the evolution of the resistance problem than any other mode. I would be most interested to hear my colleagues on my right support this contention. But I think this is the thing that really upsets us more than anything else, the blind use of these drugs in large doses indiscriminately for a wide variety of problems.

This is the major reason for doing away with this particular combination.

A physician can always prescribe these two drugs singly, if he wishes. There are instances in which they are valuable drugs when used individually or together in a nonfixed fashion. But as a fixed combination the temptation has always been too easily to use both.

Senator NELSON. Do I understand you to be saying that this fixed combination has been widely used for nonindicated cases; in other words, whatever the affecting agent was, neither of them would be indicated for it anyway?

Dr. KUNIN. Yes. The best example of this would be what we call the prophylactic use of penicillin and streptomycin in either the unconscious patient or the patient undergoing clean surgery. This is an area where I really believe that the surgeons have clearly demonstrated to their own colleagues very, very nicely—most of these studies have been done by surgeons—indicating that the prophylactic use, that is, the arbitrary use of this drug in an individual that is undergoing surgery which is not necessarily complicated by infection—this was a widespread practice at one time—has no effect, and not only does it have no effect, but it always runs the danger of superinfection now with a resistant organism. Because of its change or its impact on the flora, of the ecology of the entire body, it probably is one of our important factors in the resistant variety of staphylococcus infections. This is well demonstrated by the surgeons and should not be part of the practice.

There are many, many papers that clearly indicate this to be true.

This probably would be the area of greatest misuse of this agent.

On page 9 we provide general comments and a review of the indications for penicillin and streptomycin. These fixed combinations would usually not provide optimum therapy for the complex clinical problems encountered with these 15 conditions. In each case, the characteristics of the invading organisms and the results of in vitro bacterial sensitivities must be known. Many of these infections could be treated with penicillin alone, with penicillin and streptomycin in a different ratio, or with other antimicrobial agents.

In the judgment of Antiinfective Panels II and IV, the availability of fixed combinations of streptomycin and penicillin has:

1. Led to inappropriate use of these drugs for treatment of disease states in which the combination is no more effective than one of the