the panel recommendations with respect to the combination antibiotic drugs will not only eliminate some unnecessary risks in therapy, but will help to return antibiotic treatment to the realm of rational therapeutics.

Specific treatment for bacterial infections was not available to the physicians until the late 1930's, when the sulfonamides were first introduced. Before that, only bed rest, cold compresses, and similar palliatives were available to deal with even infectious diseases.

The sulfonamide drugs of the 1930's were the first effective chemotherapeutic agents employed systematically for the prevention and cure of a variety of bacterial infections in man.

Numerous derivatives of sulfonamides were synthesized and tested for their clinical value in various bacterial, protozoal, and viral diseases. Sulfapyridine produced dramatic results in pneumococcal pneumonia and, for a brief period, it was the agent of choice in this disease. In 1938, sulfathiazole replaced sulfapyridine as the preferred sulfonamide because of its higher therapeutic index. Sulfadiazine soon replaced sulfathiazole and has retained a prominent position among the sulfonamides ever since. Two methylated derivatives of sulfadiazine were soon introduced into therapy.

In 1941, English scientists discovered that penicillin was effective against staphylococcus and streptococcal infections. A vast research program was initiated in the United States to produce this antibiotic and, by the spring of 1943, penicillin was available for the Armed Forces of this country.

Although numerous antibiotic agents have been produced since penicillin was discovered, this drug it still the most widely used for the treatment of infections. In the years since the first crude product was obtained from fermentation vats, chemical manipulation of the penicillin molecule has produced a large number of natural and semisynthetic congeners, and several new penicillins have become important therapeutic agents.

Penicillin itself, however, is generally ineffective in the treatment of infections due to gram-negative organisms. And I think it might be appropriate to mention that in the infectious disease field agents are broken down into groups on the basis of staining principles. The gram-negative organisms are those organisms that are usually associated in gastrointestinal infections and things of that type. The gram-positive, of which the pneumococcus is a good example, are involved in respiratory infections to a very high degree, and in skin infections. This fact stimulated the research for antimicrobial agents effective against such bacteria. In 1947, streptomycin became available after it was shown to inhibit the growth of the tubercule bacillus and a number of gram-positive and gram-negative organisms in vitro—that is, in laboratory tests—and in vivo, in animals and in man.

Dihydrostreptomycin was produced the same year. It had about the same degree of antibacterial activity as streptomycin, but its use is fraught with a high risk of producing irreversible deafness.

The development of the tetracyclines followed penicillin and streptomycin. The discovery of these agents was the result of a system screening for antibiotic-producing organisms of soil specimens collected from many parts of the world. The first of these compounds, chlortetracycline, was introduced in 1948. Two years later, oxytetra-