REEL 1

Approximately ninety percent of antibiotic use is in the community, rather than hospitals, and employed as life-style rather than life-saving drugs. Their role is to reduce the magnitude and term of morbidity of acute bacterial infections that would normally be cleared by the patient's anti-bacterial defenses. Although the contribution of these defenses to the course of antibiotic therapy is well recognized, the rational (as opposed to purely empirical) approach to the design of antibiotic treatment regimes focuses on the worst case, where these drugs are the sole mechanism responsible for clearing infections. Can the doses of antibiotics and their term of administration be reduced if antibiotic treatment regimes considered the collaboration between these drugs and the host's antibacterial defenses for these normally self-limiting acute infections? To begin to address this question, we use a combination of mathematical models and in vitro experiments with *Staphylococcus aureus* and bactericidal and bacteriostatic antibiotics to explore the joint action of these drugs and phagocytic leucocytes to the course of treatment. In Part I of my talk, I describe this study, the profound and exciting (at least to us) results obtained and discuss their implications.

REEL 2.

In Part II of my talk, I will address and provide an answer to a question you think would have been answered before the majority of this audience was diploid. How do ribosome-targeting bacteriostatic antibiotics prevent the replication of bacteria? I present the hypothesis that by binding to these structures, these drugs reduce the effective number of ribosomes to levels where the cells are no longer capable of replication and die slowly. To test this hypothesis we use *E. coli* constructs with different numbers of ribosomal RNA, *rrn*, operons (*E .coli* has 7 *rrn* operons) and the ribosome targeting bacteriostatic antibiotics, chloramphenicol, tetracycline and azithromycin. The results of these and other experiments are consistent with this "numbers game" hypothesis as a sufficient (and maybe even correct) explanation for the mode of action of this broad class of antibiotics.