Population: Covered Dish Dynamics

A recent Associated Press report quoted Jonas Salk as having said, at the annual meeting of the American Institute of Aeronautics and Astronautics, "There is some sort of intuitive response to overpopulation in all living organisms. We don't know what this signalling is, but we see it even in cell cultures, which stop growing once they have covered a laboratory dish with a layer one cell deep." The report was headlined "Population Explosion Will Halt, Salk Says."

Salk is entitled to a private opinion about human population dynamics, but one may wonder whether he appreciates the grave responsibility that he bears when he appears to speak as an expert on a matter of such importance, outside his own area of special competence.

It may be that he did not really say "*We* don't know . . ." (italics added), or that he was misquoted in other ways. However, it seems worthwhile to remind scientists whose names have become household words of the special responsibility that they assume when they make public statements. I have personal knowledge of the misleading effect of Salk's statement on an intelligent nonscientist, who made the common assumption that a scientist justly famous for his work in one field must also be expert in others.

As an ecologist aware of the intractability of the human population problem, and participating in efforts to arouse public concern over it, I am appalled equally by the optimistic statements of some agriculturists concerning the elasticity of the world food supply and by those of some scientists about intrinsic mechanisms that will limit human population growth. Both ignore the fact that the longer we postpone effective action to control human populations, the more overcrowded and degraded will be the environment in which equilibrium is finally approached. I join many biologists (and others) in the conviction that to lull the general public into a false sense of security is the surest way to betray future generations by depriving them of a decent world to live in. Salk perhaps gives us a glimpse of the future in the second sentence quoted above, as we may realize too late when we have covered our dish!

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Upjohn's Position on Panalba

Morton Mintz's discussion of the questions concerning Panalba and the Food and Drug Administration require some comment (29 Aug., p. 875). The Upjohn Company has taken the Panalba matter to court as a last resort because it feels the FDA has not followed an orderly scientific process in its evaluation of this and other antibiotic combinations. The FDA has refused to provide an evidentiary hearing or to allow time for scientific validation of data on antibiotic combinations when their criteria for adequate and well-controlled clinical studies are in a state of change.

The term "ineffective in fixed combination" which is the basis for the FDA's removing the product from the market is a novel term, not used prior to December 1968 and not part of the FDA's regulatory terminology. The concept involves only comparative efficacy of combinations as opposed to individual ingredients. Without an evidentiary hearing there is no basis for determining whether the factual assertion in the FDA commissioner's order and in the NAS–NRC reports are valid and supportable.

The product has been marketed for 12 years and has been used by thousands of physicians for millions of patients. During that time the FDA raised no question of safety or efficacy. Although the product presents no imminent hazard to public health, the FDA now still will not grant a hearing. Two federal judges have concluded that the commissioner's actions on combination antibiotics have not been based on any new evidence but upon reevaluation of previously existing evidence.

Since the FDA required no comparative data prior to December 1968, the company has requested time to do the additional clinical studies now required. That such tests will produce satisfactory results is based on the following knowledge accumulated during the past 12 years. Many clinical papers have appeared attesting to the efficacy of the combination of tetracycline and novobiocin in a variety of commonly encountered infections. Their authors have observed the response of many clinical infections to other antibiotics and their almost uniformly favorable evaluation of the combination certainly contributes to the evidence of its relative value among other antibiotics available. This includes comparison to an untreated group (*1*), a placebo group (*2*), and to the components (*3–7*).

Novobiocin is not usually used as a broad spectrum antibiotic. When combined with tetracycline, however, it adds activity in a portion of the spectrum where tetracycline has lost some efficacy over the years (*8*). By the usually accepted methods of performing sensitivity tests, the spectrum of the combination is definitely broader than that of either of its components (*8–9*). It is known that resistance develops to novobiocin. However, there is good evidence in vitro that the combination of novobiocin and tetracycline retards resistance to each, but primarily to novobiocin, the chief concern (*10*). In addition, the use of novobiocin in combination with antibiotics has been found not to result in an increase in resistant strains of staphylococci in a hospital study (*11*). Finally, no significant increase in clinical strains resistant to novobiocin has occurred over the years of its use (*12*), which has been primarily in combination with tetracycline.

It is said that combinations of antibiotics increase the hazard of toxicity. This may be true in theory, but in actual use no greater incidence of serious toxicity has been reported with the combination of novobiocin and tetracycline than with other commonly used antibiotics. Upjohn's research laboratories are conducting tests of antibacterial activity in blood. So far, blood tests of individuals who have been given doses of Panalba and Albamycin T reveal a broader activity than they do when doses are given for either of the single antibiotics. In addition, Upjohn has arranged for comparative clinical tests of combination products. Such tests require time and the company feels that it should proceed on an orderly basis toward accumulating scientific evidence.

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