

The aim of this paper is to gain an essential insight which concern with the inhibitory effects in vitro toward the development of resistance in the course of serial passage and for multiplication of the *M. tuberculosis* under the conditions of combined application of the three antituberculous agents, streptomycin, PAS and isoniazid. These drugs were used concomitantly in equal quantities dissolved in Kirchner's synthetic liquid media. Besides this series of liquid media, Ogawa's media, solid egg media, were regularly used between the stages of submerged culture in order to get sufficient amount of organism.

Attempts were made to make the upper limits of growth gradually shift to the higher concentrations of the drugs in the course of serial subcultivation. This, however, was not gained within seven to fourteen generations of the four strains used. In each generation of the four strains, H<sub>37</sub> Rv, H<sub>2</sub>, BCG and H<sub>37</sub> RvR, their growth was found inhibited at lower concentrations of the three drugs used in combination. But, when examining the sensitivity of these seemingly sensitive strains to each drug respectively, the results were different. In general, the bacterial resistance had actually developed against at least two kinds of these three drugs, and they remained at the normal level of sensitivity against one of the three kinds of drug. It was also found that the sensitive phenotype appearing under the environmental conditions of the combined application was the manifestation of this persistent sensitivity to that one drug. Some clinical significance may be attached to this phenomenon of the persistence of sensitivity toward at least one of the drugs, if similar phenomenon would occur in vivo. The kinds of drugs to which bacterial resistance developed and to which bacterial sensitivity could persist were found to be different in each strain. In the case of strain H<sub>37</sub>Rv and BCG, the sensitivity to streptomycin, and in the case of strain H<sub>2</sub>, the sensitivity to PAS were persistent over several generations, but resistance to the remaining two drugs has developed.

Some diagrammatic demonstration of the population size and of the distribution of the phenotypes representing drug susceptibility or resistance in each single or triple environmental conditions was designed. Thus, the foregoing informations on the complicated characteristics of the different populations themselves or of the relations between them were clearly illustrated.

Although the strain H<sub>37</sub> Rv subcultured in these environments showed resistance to isoniazid, it manifested virulence to guinea pigs and positive results in the catalase reactions. These facts suggested that the populations of this strain were composed of two types of organisms isoniazid resistant and isoniazid sensitive.

誤 植 訂 正

本誌，第 30 巻 9 月号に誤植がありますので下記に訂正致します。

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