

### Résumé

## EFFECT OF ANTIBIOTICS ON THE INTESTINAL FLORA OF GUINEA PIGS

Penicillin Toxicity in Guinea Pigs

MIKIO KIMURA and TAKURO ADACHI

Department of Pediatrics, School of Medicine  
Keio University

When guinea pigs received a certain dose or more of penicillin intramuscularly or orally, they died in several days. In the bowel of healthy guinea pigs, there are usually found gram-positive, anaerobic *Loctobacillus difidus*-like rods, but no *E. coli*.

After administration of penicillin, however, gram-positive rods markedly decreased and *E. coli* groups have been become predominant in the bowel.

Guinea pigs that died or were killed after penicillin administration have shown a decrease of gram-positive rods and a marked increase of *E. coli* groups in the bowel and, at the same time, pathological findings of enteritis and pulmonary hyperaemia or hemorrhage.

Though the intracerebral injection of penicillin have presumably given some effect on the intestinal flora, it has been less marked than by the intramuscular or oral administration.

Further studies will be needed to see whether the effects of penicillin are only by the its direction to the intestinal flora or also indirection via nervous system.

## THE QUANTITATIVE ANALYSIS OF THE DRUG RESISTANCE OF *MYCOBACTERIUM TUBERCULOSIS* IN SPUTUM. IV

The Pattern of Isoniazid Resistance During  
Isoniazid-PAS Therapy and Its Relation to  
the Therapeutic Effect

MICHIO TSUKAMURA

The Obuso National Sanatorium  
(Director : Dr. ROKURO KATSUNUMA)

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The quantitative analysis of bacterial population occurring in sputum was made in 15 patients with far advanced pulmonary tuberculosis with chronic cavities. The percentage of organisms resistant to various concentrations of streptomycin, PAS and isoniazid was bi-monthly determined during isoniazid-PAS therapy (6 to 16 months). In the present paper, the results on the isoniazid resis-

tance was reported.

(1) The percentage of organisms resistant to isoniazid per total viable units remained in low rates throughout the observation period. Among 15 patients, it was found only one case, whose population contained above 10% of organisms resistant to 1 mcg, and there were 4 cases, whose bacterial population contained consistently above 10% of organisms resistant to 1 mcg, while there were three cases, whose population contained always no organisms resistant to 1 mcg.

(2) Even during isoniazid-PAS therapy, the reduction of the percentage of organisms resistant to 1 mcg until 0% (the remission of isoniazid resistance) occurred in several cases, but an increase of the percentage could be found by the prolonged quantitative analysis.

(3) A close relationship could be not found between the average percentage of resistant organisms and the therapeutic effect of isoniazid-PAS therapy, but between the pattern of change of the bacterial population and the effect. The patients, whose bacterial population had consistently 0% of the percentage of organisms resistant to 1 mcg or whose bacterial population had remission of resistance, even if it sometimes contained several percent of resistant organisms, were beneficially influenced by the isoniazid-PAS therapy, while the patients, whose population contained consistently resistant organisms, were poorly influenced by the therapy. There was a significant difference between these two groups of the patients.

(4) It appeared that one can not practically expect attenuated virulence of isoniazid-resistant organisms, even if the bacterial population contained a high percentage of resistant organisms. However, there was one case that was improved by the therapy in spite of high percentages of isoniazid-resistant organisms.

## A PATHO-HISTOLOGICAL STUDY OF EXPERIMENTAL CANDIDIASIS, WITH SPECIAL EMPHASIS ON THE EFFECT OF ANTIBIOTICS

TAKASHI TANAKA

The Third Internal Department, the Medical  
College Osaka University

(Director : Prof. Dr. IMASATO DONOMAE)

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After searching for the patho-histological change and the early cell reaction in the case of experimental candidiasis, a further study was made as

to the effect of the antibiotics, — especially the materials of the tetracycline system, on the said disease, and another experimentation was made regarding the mechanism of causing the candidiasis due to the use of antibiotics.

The results of the studies may briefly described as follows :

1. According to the patho-histologic impressions obtained by directly injecting *C. albicans* into the pulmonary parenchyma of a rabbit, the corpulence of the alveolar wall, nodules, necrosis, abscess, etc. were recognized. Generally speaking, however, the cell reaction was negligible, in view of the amount of *C. albicans* in the tissue.

2. In order to examine the cell reaction in the early period after the infection of *C. albicans*, an experimentation was carried out by using the expansion specimen of the subcutaneous connective tissue of the rabbit to which *C. albicans* was inoculated. As the result, the effusion of polynuclear leucocyte was witnessed, succeeded by the monocyte reaction. Moreover, the multiplication

of fibrocyte cells was recognized. In general, however, no special difference from the ordinary inflammation was seen.

3. The effect of the materials of tetracycline system on the candidiasis was observed, and it was discovered that the animal in which tetracycline was inoculated, fell badly ill.

4. In reference to the mechanism of causing the ill of experimental candidiasis by the use of antibiotics, that may be had on the protective ability of the rabbit, was observed by using the expansion specimen of the subcutaneous connective tissue of the rabbit to which *C. albicans* was inoculated. As the result, it became apparent that the use of materials of tetracycline system tends to weaken the cell reaction of the animal, while it markedly lowers the phagocyte rate of *C. albicans*. It became clear, furthermore, that as the result of executing the examination of the function of the reticuloendothelial system, the similar decrease of the function was seen.

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