
 Résumé

BLOOD LEVELS AND TISSUE
CONCENTRATIONS OF LEU-
COMYCIN BY ORAL
ADMINISTRATION
(I & II)

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For the clinical application of Leucomycin (LM), four chemical-forms of LM were administered orally to rabbits, dogs and men under various conditions. The serum-levels and organ distributions of LM were determined by the method devised by the author. The results are as follows:

1) Different serum-levels were obtained by the different forms of LM. In dogs, serum-levels obtained by LM tartrate and free base were much higher than that obtained by acetyl LM. In rabbits, serum-levels obtained by LM tartrate and LM free base were similar to that of acetyl LM.

2) The peak concentration of LM in dogs obtained with a half dose was higher than that in rabbits, which received full doses of LM.

3) The serum concentrations of LM attained their peaks in 30 minutes to 2 hours, declining thereafter and disappearing in 4 to 6 hours after administration. The peak concentrations were not too high, and in some cases there was no evidence of activity in serum, but LM was distributed widely throughout the organs, with the highest concentration in the bile. Some LM were also detected in brain and cerebrospinal fluid.

4) For the oral administration of LM, the influence of gastric fluid must be considered, because LM is slightly unstable in acid reaction below pH 4.0.

5) The *in vitro* activity of LM-B was only 43% of LM-A, but that of *in vivo* identical with that of LM-A.

6) LM was proved in good amount in organs, even in the case no detectable amount of LM was found in blood. Moreover a lot of LM accumulated in bile and the activity of LM is stronger than that of erythromycin in acid solution. Considering these facts, the therapeutic effect of LM might not be evaluated only by the blood-level.

MUTAGENIC EFFECT OF STRE-
PTOMYCIN ON *MYCOBACTE-
RIUM AVIUM* AND ITS RE-
VERSAL BY SULFATHIAZOLE

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The appearance rate of streptomycin (10 mcg)-resistant mutants per viable units was determined in SAUTON medium cultures of *Mycobacterium avium*, strain Jucho, and the effect of streptomycin into media in a nonselective concentration (0.02 mcg/ml), the effect of addition of sulfathiazole into media in a slight amount (1 mcg/ml) and the effect of addition of both drugs in the same concentrations were observed. The following results were obtained.

(1) The addition of streptomycin increased the appearance rate of streptomycin-resistant mutants. In this case, the multiplication of cells was necessary in the presence of streptomycin. However, since the concentration of streptomycin was nonselective, it was considered that streptomycin had a mutagenic effect under the conditions used here.

(2) The appearance rate of streptomycin-resistant mutants often increased in the presence of sulfathiazole added during the multiplication of cells. Since the drug was nonselective for streptomycin-resistant mutants, it was considered that sulfathiazole also had a mutagenic effect on the organism.

(3) The appearance rate of streptomycin-resistant mutants was smaller in the presence of both two drugs than in the presence of streptomycin alone, and, therefore, it was considered that the mutagenic effect of streptomycin was antagonized by sulfathiazole and that of sulfathiazole was antagonized by streptomycin.

THE SUSCEPTIBILITY OF ANTI-
BIOTIC RESISTANT STRAINS
OF *STAPHYLOCOCCI* AND
SHIGELLA DYSENTERIAE
TO OTHER ANTIBIOTICS

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A study is made of strains of *Staphylococci* and of *Shigella dysenteriae* which have become resistant to one kind of antibiotic, as to their susceptibility to other antibiotics.

The following results obtained seem to afford a standard for selective use of therapeutic agents in treating antibiotic resistant *staphylococci* and *Shigella dysenteriae* infections which are frequently encountered :

1) *Staphylococci*

Penicillin resistant strains show an intensive susceptibility to chloramphenicol. An increased susceptibility is observed in streptomycin resistant strains to penicillin, in chloramphenicol resistant strains to penicillin, in tetracycline resistant strains to streptomycin, and in erythromycin resistant strains to chloramphenicol.

2) *Shigella dysenteriae*

Sulfa drug resistant strains show an intensive susceptibility to tetracycline. An increased susceptibility is observed in streptomycin resistant strains to tetracycline, in chloramphenicol resistant strains to streptomycin, and in tetracycline resistant strains to streptomycin.

THE QUANTITATIVE ANALYSIS OF THE DRUG RESISTANCE IN *MYCOBACTERIUM TUBERCULOSIS* OCCURRING IN SPUTUM

The Pattern of Resistance

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The analysis of bacterial population (the determination of percentage of resistant organisms per total viable cell units) was made on 109 specimens from 28 patients with far advanced pulmonary tuberculosis with chronic cavities. The ratio of resistant organisms resistant to 1, 10, 100 mcg of streptomycin, PAS and isoniazid, respectively, was compared in streptomycin resistance, PAS resistance and isoniazid resistance. The difference of ratios was smaller in streptomycin resistance than in PAS and isoniazid resistance. It appeared that the difference of ratios was the largest in isoniazid resistance. It has been therefore concluded that the *in vivo* bacterial population is most homogeneous with respect to streptomycin resistance, consider-

ably heterogeneous in PAS resistance and most heterogeneous in isoniazid resistance.

When one makes determination of drug resistance by routine nonquantitative methods, care should be taken to consider that the results of the determination with respect to isoniazid resistance and PAS resistance may be considerably influenced by the size of inoculum.

PENICILLIN TREATMENT FOR THE OSTEOMYELITIS OF LUETIC RABBIT ; EXPERIMENTAL STUDIES

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Penicillin was given systemically in the experimentally produced pyogenic osteomyelitis of luetic rabbit and general condition, blood picture, X-ray finding and histopathology were studied.

1) Experimentally produced osteomyelitis of luetic rabbit in general showed more severe inflammatory process and less response to penicillin treatment, compared with that of nonluetic rabbit. Therefore it is important to give much more adequate doses of penicillin in the very early stage (within two days) to the osteomyelitis of luetic rabbit.

2) In the experimentally produced osteomyelitis, X-rays taken in the first and second months showed almost the same degree of inflammatory changes, and their histopathologic finding were also nearly the same.

Blood sedimentation rate closely reflected the inflammatory process of osteomyelitis in the acute stage, the haemogram also represented fairly the pathologic changes.

3) There is no marked difference in the concentrations of penicillin in the plasma and bone marrow of luetic and nonluetic rabbits. However, when the experimental osteomyelitis was induced in these cases, the concentration of penicillin in the bone marrow of luetic rabbit became lower than that of the non-luetic rabbit.

4) In the group of luetic rabbits to which was administered 6,000 u/kg of penicillin daily for these weeks no improvement of serum Wasserman reaction was obtained. Whereas, in the other group to which 10,000 u/kg penicillin was given the Wasserman reaction was improved.