
Résumé

THE THERAPEUTIC EFFECT OF
OLEANDOMYCIN ON PYODERMA

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Oleandomycin was administered orally to human beings and rabbits, and its concentration was measured in their blood serum and skin. Patients with pyoderma were treated with oleandomycin, and the clinical efficacy of the drug was evaluated.

1) Blood serum level in man: Four healthy adults were administered 500mg (capsules) of oleandomycin one hour after breakfast. Blood specimens were taken at 1, 2, 4, 6 and 12 hours after administration, and the sera were prepared for measurement of the drug content by TORII's superposing method. Maximum values showed to be 2.6~3.8 cc at 2 or 4 hours, and then decreased rapidly to 0.9~1.8/cc (average 1.45/cc) after 6 hours and 0.22~0.44/cc (average 0.37/cc) after 12 hours.

2) Skin level in rabbits: Three matured rabbits were given oral doses of 70mg oleandomycin per kg of body weight. The skin of about 1g was taken out from normal and artificially inflamed regions with crotonic oil at 2, 4 and 6 hours after administration, and was immediately homogenized. The concentration of oleandomycin was determined by TORII'S method. At the same time, blood samples were taken, of which serum levels were measured and compared with those of the skin. Normal skin levels were generally lower than those of the serum. At 2, 4 and 6 hours after administration, skin levels were 0.88~1.8/cc, 0.34~1.6/cc and 0~1.3/cc, while that of serum were 0.9~6.4/cc, 0.44~2.6/cc and 0~1.3/cc, respectively. Maximum level of the skin of dermatitis with crotonic oil, 1.2~10.8/cc at 2 hours, was higher than those of serum and normal skin, but its decrease was more rapid, which showed 0~2.7/cc and 0~0.82/cc at 4 and 6 hours after administration.

3) Skin level in man: The concentration in the normal human skin was markedly lower than that of the serum. After single oral administration of oleandomycin of 500 mg to one healthy adult, the skin level was 0.67/cc at two and a half hours after administration, while the blood level was 4.5/cc. At 4 hours, one of three volunteers showed very high value in the skin (17.5/cc in the skin and 3.1/cc in the serum), but skin levels in the other two

were lower than those of the serum (0.2/cc, 0.85/cc in skin specimens and 1.3/cc in blood sera).

4) Therapeutic effect: Fourteen patients with pyoderma were administered orally oleandomycin of 0.5~1.0 g a day. The drug seemed to be remarkably effective in 11 patients. It showed no side reaction in every case.

STUDIES ON KANAMYCIN AND
TETRACYCLINE RESISTANCE
OF DYSENTERY BACILLI

Relationships between the Sensitivity to
Sulfa Drugs and the Drug Resistance to
Antibiotics of *Sh. flexneri*

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Using the sensitive, natural resistant and artificial resistant strains of *Sh. flexneri* to sulfa drugs, comparative studies were made, with the following results, on the acquisition of kanamycin or tetracycline resistance *in vitro* and *in vivo*.

1) *Sh. flexneri* has acquired the drug resistance about 27-fold higher against kanamycin, about 3.3-fold higher against tetracycline than that of the original strains by 15 times subculture in serial nutrient broth containing each of the drugs of successive high concentration.

2. *Sh. flexneri* has acquired the drug resistance 7, 15 and 20.5-fold higher with the sensitive strains, the artificial and the natural resistant ones against kanamycin, 25, 14.7 and 4.6-fold higher with the sensitive ones, the artificial and the natural resistant ones against tetracycline than that of the original strains by 12 times subculture in serial ENDO media containing each of the drugs of successive high concentration. On the other hand, *Sh. flexneri* has acquired the drug resistance 2.5, 4 and 4-fold higher with the sensitive strains, the artificial and the natural resistant ones against kanamycin, about 1.7-fold higher with the all strains against tetracycline than that of the original strains by 12 times subculture in ENDO media containing each of the drugs of constant concentration.

3. *Sh. flexneri* has acquired the drug resistance 2.5-fold higher than that of the original strains with 2 out of 4 strains by serial 10 passages in testicle of mice which were injected with kanamycin.

4. *Sh. flexneri* which has acquired high drug

resistance *in vitro* against kanamycin, again reverse to sensitive for the drug by serial 40 passages in ENDO media.

5. We discussed about *Sh. flexneri* from the viewpoint of relationships between the sensitivity to sulfa drugs and the acquisition of drug resistance against kanamycin or tetracycline.

DRUG RESISTANCE OF *SHIGELLA* RECENTLY ISOLATED IN TOKYO

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Investigations were undertaken with 100 strains of *Shigella* isolated in the Institute of Hygiene of Tokyo during the period of January to April, 1959. All the strains showed to be resistant against sulfa drugs and to be sufficiently sensitive to kanamycin, colistin and polymyxin B, except 4 strains having showed to be resistant to streptomycin, 4 strains to chloramphenicol, and 6 strains to tetracycline. In the antibiotic resistant strains, 2 strains showed to be resistant against 2 kinds of antibiotic; 2 strains, against 3 kinds of antibiotic; and 2 strains, against tetracycline alone. The degree of the resistance against streptomycin and chloramphenicol showed to have increased more remarkably in this year than in last year.