Résumé

STUDIES ON STAPHYLOCOCCAL INFECTIONS

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Several biological properties were studied on 1,491 staphylococcal strains which were isolated from any focus in the hospital and non-hospital. In these series, sensitivity of 502 strains to antibiotics and the phage-typing of 288 strains were investigated. Also, a part of these strains were made researches through the animal experiments.

The results obtained were as follows.

1) The pathogenic staphylococci isolated from the foci were less in number than from the others. Significant differences in the staphylococcus distribution between hospital and non-hospital could not be found, but the pathogenic staphylococci were more distributed in the hospital. The strains originated from the foci were resistive to antibiotics than strains from the others. However, there were no significant differences in sensitivity between hospital staphylococcus and non-hospital staphylococci.

2) The sensitivity of pathogenic staphylococci in the foci were different from that of pathogenic staphylococci in the others.

(3) According to the distribution of the pathogenic strains, the incidence of infectious source fell into following order; nasopharyngeal cavity, disgestive tract, feces. Also, it assumed that the air-borne staphylococci were most difficult to be the infectious source. However, pathogenic staphylococci were considerably influenced by the place where many people had come together and moved, although these among the air-borne bacilli were not always many in number.

4) According to the phage-typing, many staphylococci consisted of the phage-type strains belonging to the miscellaneous group, although the accurate infections sources could not be detected.

5) The clear relation between the strains of the nasopharyngeal cavity, the digestive tract and feces could not be found, from the biological properties, sensitivity and phage-typing.

6) Although the percentage of possession of staphylococci was lower in the higher intestinal tract than in lower tract, pathogenic staphylococci were found more frequently in the former than the latter. There were differences between the strains of the upper digestive tract and lower tract from the point of sensitivity.

7) It was found through the biological experiments that the detectable percentage of coagulase-positive strains in the liver and kidney was higher than that of coagulase-negative strains. Also, no evidence of changes concerning the pathogenesis strains caused more frequently the inflammatory forcus in the kidney of the mouse than the non-pathogenic strains, but some of the non-pathogenic strains gave rise to the inflammatory focus of the liver. Therefore, it is assumed the decision of pathogenesis through the only biological properties requires further examination.

8) To prevent the cross-infection by staphylococci, it is important to take care of the disseninated route from the nasopharyngeal cavity and also the aseptic manipulation during the procedure of gastro-intestinal surgery.

In addition, from the point of cross-resistance to antibiotics, the comfined treatment of chloramphenicol and erythromycin appears to be the most effective for the serious infections.

STUDIES ON ANTIFUNGAL AGENTS. III

On Several Mercuric Compounds, especially on Bis-Ethylmercuri-Phosphate

3. On the Clinical Effect of DD-59 Ointment.

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In the previous papers, we reported that bis-ethylmercuri-phosphate (BEMP) had the excellent antifungal activity *in vitro* and showed the marked therapeutic effect for fungous infections of the skin *in vivo*. In this short report, the results obtained by topical use of DD-59 ointment containing BEMP for various superficial fungous infections of the skin are presented.

The ointment examined is a water-soluble ointment containing BEMP in 0.2 %, 2,5-dichloro-4-thiocyanoaniline (DTA) in 0.2 %, Guaj Azulen (1,4-dimethyl-7-isopropylazulen) in 0.01 % and diphenylhydramine in 1.0 %.

The preparation was applied topically once a day and no other therapy, local or systemic, was given during the period of observation.

Twenty six patients suffering from superficial fungous diseases were treated with this agent. Eight of them were cured, fifteen improved, one slightly improved and two showed no improvement.

Of seven patients with trichophytia pompholyciformis, two were cured, three improved and one was not benefitted. Six patients with trichophytia interdigitalis were treated, of whom three were cured and the others improved. Two patients with trichophytia maculovesiculosa were improved. Of nine patients with eczema marginatum, five were improved and the rest failed to be improved. Two patients with pityriasis versicolor showed improvement. No side reaction, such as dermatitis, was seen in these patients initiating therapy with DD-59 ointment.

The clinical effect of this agent was especially excellent in controling itchiness and the most of our patients ceased to complain itchiness within a week.

TREATMENT OF STAPHYLOCOCCAL INFECTIONS AND ANTIBIOTICS RESISTANT STAPHYLOCOCCI

Report of Research Group of National Hospitals concerning to Antibiotics Resistant Bacteria

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848 patients with staphylococal infection, collected from 15 National Hospitals, were observed on the results of clinical and laboratory studies during past twenty-two months.

1) Age-distribution were 279 patients younger than 9 years, 108 patients in the range of 10 to 19 years, 136 patients 20 to 29 years, 72 patients 30 to 39 years and 125 patients older than 40 years. In some king of infections there were seen some speciality to age distribution.

2) The phage-type in 693 strains were classified as follow : type I was 105 strains; type II, 156 strains ; type III. 93 strains ; type IV, only 1 ; mixed group, 63 strains ; unclassified-group, 275 strains. There were no speciality among the kind of disease and phage-type.

3) Due to the resistant of staphylococci to antibiotics we selected the dilution method and determined the sensitivity of the isolated organisms to penicillin, streptomycin, tetracycline, chloram phenicol and erythromycin.

When the antibiotics were clinical effective, the thereshrld resistant concentrations of causative staphylococci to antibiotics were as follow: penicillin was 1 u/ml, streptomycin 1 mcg/ml, chloramphenicol 3 mcg/ml, tetracycline 1 mcg/ml. But these relationship were not constantly by condition of the host and kind of infection. It is, of course, extremly important in surgical treatment of some kinds of infections with antibiotics.

4) If staphylococcal infections were complicated with another infection such as tuberculosis or mycosis prognosis were no good.

THE THERAPEUTIC EFFECT OF A NEW VAGINAL SUPPOSITORY (PENTAMYCIN-ESTROGEN-BAC. VAGINALIS DOEDERLEINI) ON THE TRICHOMONAL AND MYCOTIC VAGINITIS

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We used a new vaginal suppository for 18 women who were diagnosed as trichomonal vaginitis with or without mycotic infection.

This new drug consists of pentamycin, a new antibiotic, ethinylestradiol and freeze-dried bacillus vaginalis Doederlieni.

The result is: trichomonads disappear after from, 7.2 (cytological study) to 9.4 (in culture) days' therapy, the length of time required is longer than by another drugs, for example, trichomycin, aminitrozol *etc.* : but reappear sooner or later in 50% of patients. The effect on the mycotic infection is also not so good.

Although therapeutic results are not so satisfactory, such a vaginal medicament seems very interesting and needs further investigation and improvement.

BACTERIOSTATIC ACTIVITY *IN VITRO* AND THE DISTRIBUTION IN THE INTERNAL ORGANS OF MICE OF SULFAMETHOXYPYRIDAZINE (LEDERKYN), MS-53 (SINOMIN), SULFAPHENAZOLE (ORISUL, MERIAN) AND SULFISOMIDINE (DOMIAN)

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Bacteriostatic activity *in vitro* and the concentrations in the blood and the internal organs of mice of several new sulfa drugs were tested. The drugs tested were sulfamethoxypyridazine (Lederkyn), MS-53 (Sinomin), sulfaphenazole (Orisul, Merian) and sulfisomidine (Domian).

The findings were compared with those of sulfisomidine which has been already in clinical use.

Results :

1) There was no evidence that these new drugs have stronger bacteriostatic activity than sulfisomidine.

2) Sulfamethoxypyridazine, MS-53 and sulfaphenazole, in this order, were found to maintain higher concentrations in the blood and the internal organs for longer periods of time than sulfisomidine.

3) New sulfa drugs showed better transfer from the blood to the internal organs than sulfisomidine.

4) Ratios of the concentration in one organ where it is the lowest and the concentration in the other organs were 1 : 1～3.2 for the new sulfa drugs and 1 : 1～8.1 for sulfisomidine.

No tendency for the new drugs to deposit in any particular organs was found. In other words, they distributed evenly to all the internal organs.

5) Conentrations in the blood and the internal organs, except the brain and the spleen, of MS-53 and sulfisomidine reached their peaks at the same time after their administration, and their transfer from the blood to the internal organs was rapid.

In the instances of sulfamethoxypyridazine and sulfaphenazole, however, the peaks of the concentrations in the organs appeared two hours after those in the blood and transfer of these drugs from the blood to the internal organs seemed slower than with MS-53 and sulfisomidine.

THE CLINICAL APPLICATION OF COSA-SIGMAMYCIN IN UROLOGICAL FIELD

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Last year, we have reported oleandomycin, sigmamycin and cosa-Tetracyn as new antibiotics in order to solve the important problem of resistant bacteria.

That is, sigmamycin has a broad antibiotic spectrum and continuous use causes no considerable side effects. And after oral administration, Cosa-Tetracyn (tetracycline with glucosamine) reaches the peak at two to three hours and effective concentration in blood was maintained up to six to eight hours and continuous use causes no considerable side effects.

Recently we have had a new antibiotic named Cosa-Sigmamycin which is sigmamycin with glucosamine.

The summary of the results of some fundamental experiments and clinical use is described below :

1. After oral administration, Cosa-Sigmamycin reaches the effective concentration in blood more rapidly than sigmamycin.
2. Excretory quantity in urine reaches 74 mg at 8 hours after oral administration.
3. Excretory quantity in stool is uncertain, but comes out in stool at 12 hours after and disappear from stool at 72 hours after oral administration.
4. The continuous use causes no considerable side effects.
5. The application of 12 causes of various urological infections resulted in the efficacy of 91.0%.

SOME OBSERVATIONS ON THE CROSS RESISTANCE IN *MYCOBACTERIUM TUBERCULOSIS* VAR. *HOMINIS*. I

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The cross resistance problems have been discussed

by many investigators. However, the studies reported were conducted without taking an accurate care as to the size of inoculum. The author claimed previously that, in order to express the degree of resistance accurately, utilization of small size of viable numbers is needed for the drug resistance test. The present study was conducted utilizing inocula containing 10 to 150 viable organisms. The results obtained revealed that different resistant mutant strains derived from the same parent strain have similar degrees of resistance as to the resistance (sensitivity) to PAS, 4-acetylaminobenzaldehyde-thiosemicarbazone (tibione) and sulfisoxazole. However, some exceptional cases were found. Highly PAS-resistant strains (both H_{37} Rv and Aoyama-B) were much more resistant to tibione, and however, tibione-resistant strains were as sensitive as the parent strains to PAS. Lowly PAS-resistant strains were as sensitive as the parent strains to tibione. Streptomycin-resistant strain and kanamycin-resistant strain derived from the strain Aayama-B were more sensitive to PAS than the parent strain. This relationship was not observed in the H_{37} Rv strain and, therefore, this finding is considered to be strain-specific.

FUNDAMENTAL STUDY ON CARZINOPHILIN

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1) Carzinophilin (CZP) is an unstable antitumor antibiotic. This compound reacts with the SH group and is easily inactivated by the materials containing SH group (*e.g.* cystein, vitamin B_{12} *etc.*) in human body. In this report, it was proved that blood level of CZP in rats was 287/cc instantly after intravenous injection, it soon became undetectable after 60 minutes of injection.

2) CZP was determined in lung and liver but hardly appeared in tumor tissues of rat.

3) The remarkable properties of CZP is to inhibit very active glycolysis in tumor cells strongly, and when it comes to contacting with the tumor cells, CZP shows most powerful antitumor activity than nitromin, azan, and sarkomycin at the lowest amounts.

4) In this report, another remarkable results was that the activity of liver catalase of rat which was inoculated Yoshida Sarcoma increased by treatment of CZP, which that of none treated Yoshida Sarcoma bearing rat decreased proportional to growing of tumor.

5) We improved the formulation of CZP by means of using surface active agent, there by blood level of CZP was prolonged and leucopany which originate in reaction of CZP was protected considerably.

STUDIES ON CHEMOTHERAPY OF TUBERCULOSIS. XIII

Bateriostatic Action of Isonicotinic Acid Acylhydrazide against *Mycobacterium tuberculosis*

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In order to study the relationship between the antitubercular activity of isonicotinic acid acylhydrazide and its length of acyl, acetyl, butyloyl, capryloyl, lauroyl and palmitoyl derivatives were synthesized and their activities against tubercle bacilli (human type, Frankfurt strain) were tested in Kirchner medium containing 10% goat serum. They all showed remarkable activities and the differences among them are not so great, but it was found that as the acyl becomes longer, the activity increases at first, goes through a maximum at lauroyl, then decreases again.