

U.S. Naval Medical School
Translation
Pittsboro, N.C.

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L.E. Khundanov, E.I. Kuptsevich, E.E. Demidova, & L.A. Smirnova,
& E.D. Shkurko: O kombinirovannoi terapii eksperimental'nogo
meliodosa antibiotikami i sul'fodimezinom. Antitiotiki,
Vol. VI 1013-16, 1961.

Translated from Russian:

COMBINED TREATMENT OF EXPERIMENTAL MELIOIDOSIS WITH
ANTIBIOTICS AND SULFADIMESIN

By

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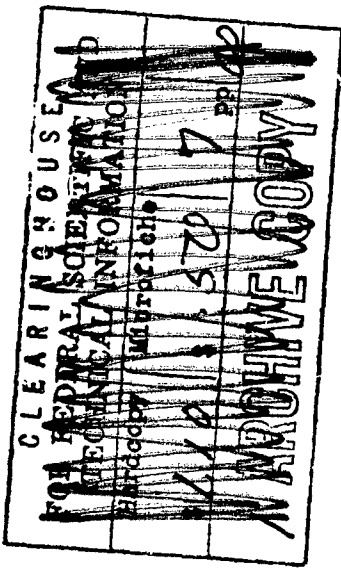
Combined administration of antibiotics with other drugs
was completely justified in many diseases. In particular, in
case of anthrax, tuberculosis, mixed infections and infections,
caused by drug-resistant microbes.

The advantages of the combined therapy consist of the
synergism, lowered toxicity, prevention of the appearance of
drug-resistant forms of microorganisms and, finally, of possible
successful treatment of gravely ill patients without preliminary
bacteriological diagnosis.

The purpose of the present work was the study of possible
use of antibiotics in combination with sulfadimesine (spelling?)
in/ the treatment of experimental melioidosis infection.

As therapeutical agents we used in the experiments the
following antibiotics: monomycin (footnote: monomycin is a new
domestic antibiotic, obtained at the laboratory of Prof. G.F.
Gause at the Institute for the Study of New Antibiotics, Academy
of Medical Sciences, USSR).

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Combined Antibiotics & Sulfa
drugs (for Melioidosis)

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tetracyclin (footnote: in this experiment we used series of tetracyclin, especially prepared for intramuscular injections); oxytetracyclin, chlortetracyclin, bicyllin, streptomycin, mycerin (spelling?) and llevomycetin (spelling?). Of the sulfamide substances, sulfodimoxin was tested.

Experiments were carried out on white mice weight 18-20 Gm. The animals were infected by means of subcutaneous injection of 0.5 ml suspension of one-day agar culture of the B. strain of galcomyces pseudomallei (4). The infecting dose was 5 mln. of microbe cells (1 Dcl).

Therapy was started after 14-15 hours since infection, (phase) i.e. during the stage of generalization of the infection. The substances being tested were dissolved in the physiological solution and administered twice a day (?blur) in the amount of 0.2 ml. Insoluble substances (chlortetracyclin, levomycetin and sulfodimoxin) were given to the animals per os. The course of treatment lasted 10 days. Observations of the animals were continued for 3 weeks.

The criterion of effectivity of the therapy was: survival of the animals, average longevity of those who died (of the dead animals), as well as the data of bacteriological examinations.

Preliminarily, toxicity of all drugs was checked upon and on the same animals tolerated dose of each substance was established. As a result of this check-up it was found that the tolerated daily dose for monomycin was 2.5 mg., and for

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tetracyclin, oxytetracyclin, chlortetracyclin, streptomycin, mycerin, bicyllin - 2 mg (barred text, looks like 2), for levomycetin, 4 mg. and for sulfodiazin, 6 mg.

Results of experiments are represented in Table 1.

As one can see from the Table 1, in spite of somewhat milder conditions of experiment, monomycin, streptomycin, mycerin and bicyllin proved to be poorly effective in the treatment of melioidosis. In the groups of mice which received the mentioned antibiotics, there was observed death of animals in 70% to 90% of cases. At the same time, longevity of the treated dead mice was somewhat greater, than that of the controls which did not receive treatment.

In the groups of mice of this experiment, the therapy of which was carried out with chlortetracyclin, levomycetin, sulfodiazin, there was observed survival of 75% to 90% animals with average longevity of the dead animals from 13.4 - to 16 days, whereas the control mice lived on the average 8 days.

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Table 1 Therapeutical Effect of Antibiotics & Sulfodiazin in Experimental Melioidosis						
Drug	Method of administration	Single dose in mg.	Number of mice in exper.	Dead	Survived	Average longevity of dead mice in days
Monomycin	Intramuscular					
Tetracyclin	"					
Oxytetracyclin						
Bicyllin						
Streptomycin						
Mycerin						
Chlortetracyclin	peroral					
Levomycetin						
Sulfodiazin						
control						

figures not retyped, see. p. 1014

Among the animals treated with tetracyclin and oxytetracyclin, survival was from

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cyclin, survival was from 45 to 55%, with average longevity of the dead animals being from 11.7 to 15.7 days.

In this manner, of the 9 tested substances, the most effective drugs in melioidosis were levomycetin, sulfodiazin and chlortetracyclin. The therapeutical effect of these substances was reflected not alone in the high percentage of survival of the animals, but in considerable postponement of the time of death of the treated mice.

Tetracyclin and oxytetracyclin, had therapeutic effect but it was much weaker than that of lecomycetin, sulfodiazin and chlortetracyclin. Nevertheless, these antibiotics may be recommended, especially in such cases, when we are dealing with antibiotic-resistant forms of pathogenic agent, requiring combined effect of several antibiotics. As for other antibiotics (monomycin, bicyllin, streptomycin, mycerin), these, in contrast to other drugs, possessed equally low therapeutical effect, although among the animals treated there was observed prolonged survival as compared to the controls.

Bacteriological examination of material from animals, dead during the course of treatment, showed melioidose microbes more or less regularly eliminated from the site of infection, lymph nodes and internal organs; in this respect, no difference was noted in separate groups of animals, receiving one or other drug.

The second part of our research studies was dedicated to investigating the possibility of using antibiotics in

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combination with sulfodiazin in the treatment of experimental melioidosis infection.

These experiments were done on white mice infected with the same dose as used in the first series of experiments ~~1/5~~ (5 mln. of microbe cells).

Considering the fact that chemotherapy of melioidosis produces sufficiently marked effect only under conditions of treatment with large doses, which maintain sufficiently high level of concentration of the drug in the organs and the blood, we were forced to confine to the same doses which were used in testing each substance separately.

Of the substances tested, sulfodiazin, chlortetracyclin and levomycetin were used perorally; monomycin, tetracyclin oxytetracyclin, bicyllin, streptomycin and mycerin were used intramuscularly with simultaneous administration of sulfodiazin perorally.

As one can see from Table 2, combination of sulfodiazin with monomycin, tetracyclin, bicyllin, streptomycin, mycerin and levomycetin, in the conditions of our experiment, proved to be ineffective, since the survival of animals, treated with sulfodiazin alone, is much higher (85%) than when treated with the combined method. Moreover, the combined therapy with antibiotics and sulfodiazin gives a better therapeutical effect than the therapy with the antibiotics alone.

Whereas the use of chlortetracyclin, under similar experimental conditions, in combination with ~~up~~ sulfodiazin,

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gave excellent therapeutical effect, reflected not alone in high percentage of survival of animals (90%), but in marked prolongation of life in case of dead mice which had been treated, as compared to the controls (more than twice).

Table 2

Results of treatment of experimental melioidosis with antibiotics in combination with sulfodimexin

Drug	Number of mice in experiment	Dead	Survived	Average life span of dead mice (in days)
Monomycin / sulfodimexin				
Tetracyclin / sulfodimexin				
Oxytetracyclin / sulfodimexin				
Bicyllin / sulfodimexin				
Streptomycin / sulfodimexin				
Mycerin / sulfodimexin				
Chlortetracyclin / sulfodimexin				
Levomycetin / sulfodimexin				
Control				

table not retyped, see p. 1015

Conclusions

1. Of the nine (9) tested drugs, the greatest therapeutical effect in the treatment of melioidosis was obtained with levomycetin, sulfodimexin and chlore chlortetracyclin; 75% to 90% of white mice, treated with these substances, remain alive.

2. Tetracyclin and oxytetracyclin, even though they do have some therapeutical effect, have much weaker effect than levomycetin, sulfodimexin and chlortetracyclin.

3. Monomycin, bicyllin, streptomycin and mycerin, under same experimental conditions, have weak therapeutical effect and in practice their use should be considered unsuitable.

(continued)

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4. ~~Treatment of infected animals with melioidosis-~~
sulfodimazin therapy, combined with monomycetin, tetracyclin, oxytetracyclin, bicyllin, streptomycin, mycerin and levomycetin, in treatment of animals, infected with melioidosis, under the conditions of our experiments, should be considered as irrational.

5. The combined administration of sulfodimazin with chlortetracyclin guarantees a high percentage of survival of animals ~~(94%)~~ (90%) and a considerable increase prolongation of the average life span of the dead mice.

Received for publication 2-28-61

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For Mr. Joseph

Mr. Joseph: please note, some of these new drugs are not listed in dictionaries, and I do not know how to figure out their spelling; the Russians use phonetic transcriptions of what they imagine the English should be. -two

Translated by Tatiana Boldyreff

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