

ABSORPTIVE FUNCTION OF THE RETICULO-ENDOTHELIAL SYSTEM DURING TETRACYCLINE TREATMENT OF EXPERIMENTAL INFECTION

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It has previously been shown [4] that a single injection of antibiotics of the tetracycline group into albino mice leads, in certain cases, depending on the dose, to stimulation of the absorptive function of the reticulo-endothelial system (RES). Subsequent experiments [3] showed that this effect is not observed during repeated injections of tetracyclines; the state of the absorptive function of the RES either was unchanged or depressed. The object of the present investigation was to study the action of the tetracyclines on the RES in experimental pneumococcal infection.

METHODS

Experiments were conducted on albino mice weighing 18-20 g, inoculated intraperitoneally with 0.2 ml of a 24-h broth culture of *Pneumococcus* type I, diluted to a concentration of 10^{-5} - 10^{-7} . The animals were sacrificed on the 2nd-3rd day. Seedings of the blood and internal organs yielded an abundant growth of the culture on blood agar.

Chlortetracycline, tetracycline, and oxytetracycline were administered by mouth as a single dose of 2 and 4 mg per animal, or repeatedly in a daily dose of 2 mg for 5 days. In the first case the preparations were given 24-48 h after inoculation, depending on the clinical picture. In the second cases treatment began 15-30 min after inoculation. Control animals were either inoculated mice not receiving tetracyclines or healthy mice receiving repeated doses of the antibiotics.

The state of the absorptive function of the RES was determined by the microbiological method described previously [2]. Since in the present investigation the state of the RES was studied in infected animals, it was essential to find out whether the quantitative indices of positive seeding of staphylococci are affected by the presence of pneumococci in the seeding material. Corresponding experiments showed that if seeded on agar without blood, a mixed culture of staphylococci and pneumococci yields the same number of colonies of staphylococci as if a pure culture is used.

The numerical results were analyzed statistically. The arithmetical mean and the confidence limits were determined.

RESULTS

Inoculation of albino mice with pneumococci led to significant depression of the absorptive function of the RES. If the incidence of successful seeding of staphylococci in the experimental group is taken as 100%, its value in the control animals amounted to about 60%. On the basis of previous investigations [1] it may be assumed that in this case the RES was very strongly inhibited.

The repeated administration of tetracycline and oxytetracycline to mice with pneumococcal infection did not change the state of the absorptive function of the RES in these animals from that found in the inoculated animals not receiving antibiotics. Administration of chlortetracycline to mice gave results indicating a tendency towards stimulation of the RES by the preparation in a dose of 2 mg, and depression of the RES in a dose of 4 mg. In these

Effect of Single and Repeated Administration of Tetracyclines on Absorptive Function of RES of Mice with Pneumococcal Infection

Group of animals	Dose (in mg/18-20 g)	Chlortetracycline	Tetracycline	Single administration
		Number of colonies of staphylococci seed from 0.01 ml		

Single Administration				
Experimental	2	309 (272.5 - 445.5)	174 (98.9 - 249.1)	336 (168.6 - 503.4)
Control 1st	—	376 (204.8 - 547.2)	187 (92.8 - 281.2)	342 (182.1 - 501.9)
Experimental	4	191 (90.8 - 291.2)	111 (73.4 - 148.6)	133 (76.7 - 189.3)
Control 2nd	—		117 (63.7-170.3)	
Repeated Administration				
Experimental	2	90 (61.6 - 118.4)	181 (98.6 - 263.4)	176 (115.5 - 236.5)
Control 3rd	—	60 (46.3 - 73.7)	160 (129.2 - 190.7)	186 (124.7 - 247.3)

cases, too, however, the difference between the seedings of the test microorganism in the experimental and control series was not statistically significant (see table). The controls in these series of experiments were animals not receiving antibiotics (1st and 2nd control groups).

Repeated administration of tetracyclines to mice with pneumococcal infection resulted in a high incidence of positive seeding from the infected animals. On the fifth day of treatment with chlortetracycline, tetracycline, and oxytetracycline, 100, 70, and 70% of mice respectively survived, compared with 100% mortality among the controls.

The state of the absorptive function of the RES in the mice receiving tetracycline and oxytetracycline improved very considerably, and reached the values observed in the healthy animals receiving these antibiotics in the same doses (3rd control). Notwithstanding the marked therapeutic effect observed when chlortetracycline was used, the absorptive function of the RES of the treated animals remained depressed (see table). These results corresponded to our previous findings in experiments on healthy mice [3].

Hence, the therapeutic action of the tetracyclines, as demonstrated by the survival rate of the animals and the incidence of successful seeding of the causal agent from the blood and organs, may not be accompanied by normalization of the absorptive function of the RES. In these cases it seems certain that the direct action of the antibiotics on the RES is the responsible factor.

LITERATURE CITED

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