

COMPARISON OF THE ACTIVE CONCENTRATIONS OF SOME ANTIBIOTICS IN THE LYMPH OF THE PERIPHERAL VESSELS AND THE THORACIC DUCT

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The concentration of antibacterial preparations in the body is usually judged by their concentration in the blood. However, the active concentration should be considered to be that which is attained by the preparation in the tissue fluids.

Certain workers judge the concentration of chemotherapeutic drugs in the tissue fluids by their content in the cerebrospinal fluid [3, 4], but the results so obtained do not reflect sufficiently accurately the changes in their active concentrations in the tissue fluid over a period of time. This is explained by the fact that diffusion and the dynamics of the circulation of the tissue fluid and cerebrospinal fluid are brought about by different factors.

Work published in recent years on the study of the diffusion of antibacterial drugs from the blood stream into the tissue fluid was carried out by comparing the active concentrations of these substances in the blood and in the lymph obtained from the thoracic duct [1, 2]. These workers started from the assumption that the concentration of the antibiotics in the lymph of the thoracic duct corresponded to their concentration in the tissue fluids.

However, it is well known that the lymph from the peripheral vessels differs considerably in its composition from the lymph of the thoracic duct: it contains a smaller quantity of proteins, and practically no fibrinogen, therefore it does not clot. The lymph of the thoracic duct is profoundly changed by the influence of many substances entering the lymphatic system from the liver. For this reason many chemotherapeutic drugs, which enter the lymph of the thoracic duct through the liver, must be present here in higher concentrations than those found in the lymph of the peripheral vessels.

Since this question is important in principle, we attempted to study concurrently the active concentrations of certain antibiotics in the lymph of the peripheral vessels (jugular lymphatic trunk) and of the thoracic duct in animals.

EXPERIMENTAL METHOD

Experiments were performed on 15 dogs weighing from 10 to 21 kg. The thoracic duct and jugular lymphatic trunk were exposed under morphine anesthesia. Morphine was injected subcutaneously in a dose of 15 mg per 1 kg body weight of the animal. In the exposed and isolated lymphatic vessels glass cannulas were introduced through which periodically samples of lymph were withdrawn. Blood was taken from the jugular vein.

Investigations were made of the concentration of penicillin, biomycin, tetracycline and terramycin. The preparations were injected intravenously in a single dose: penicillin in a dose of 10,000 units/kg, biomycin, tetracycline and terramycin in a dose of 10 mg/kg. Samples of blood and lymph from the thoracic duct and jugular lymphatic trunk were taken 5, 15, and 30 min after the injection of the drug, and then every 1-2 hrs for 24 hrs. As a control, samples were taken from the blood and lymph of all the experimental animals before the injection of antibiotic.

The active concentrations of penicillin in the lymph and serum were determined by the method of serial dilutions in Hiss' medium with glucose and Andrade's reagent. The test microorganism used was Staphylococcus aureus strain No. 209. The concentration of the antibiotics of the tetracycline group in the serum and lymph was determined by the method of diffusion in agar on Petri dishes with cylinders (test microorganism a spore-bearing culture of L_2).

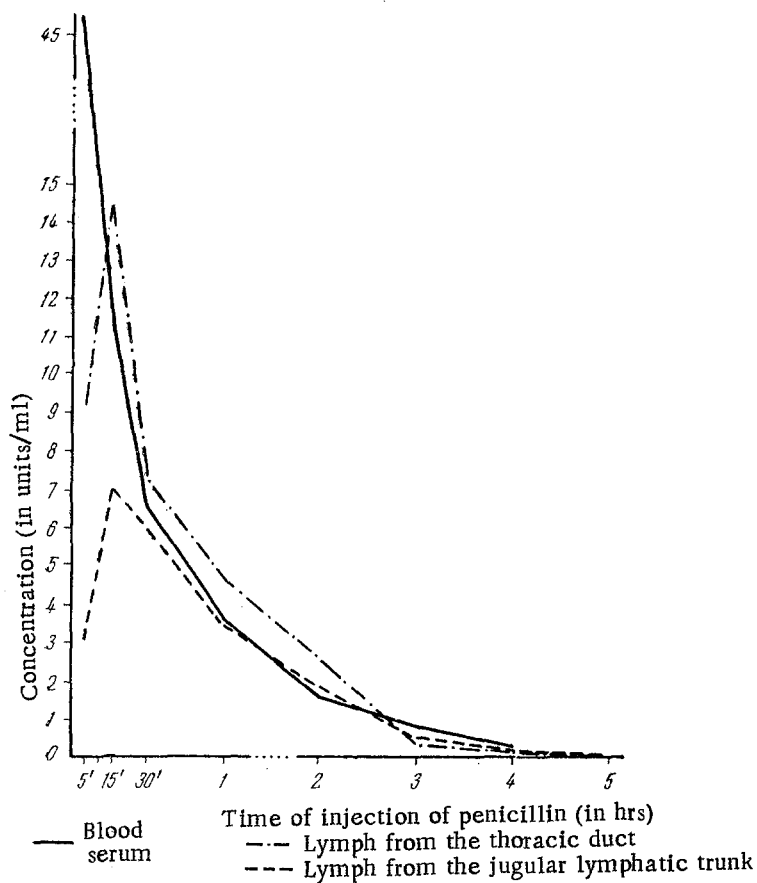


Fig. 1. Concentration of penicillin in the blood serum and lymph from the thoracic duct and jugular lymphatic trunk of dogs after intravenous injection of 10,000 units/kg.

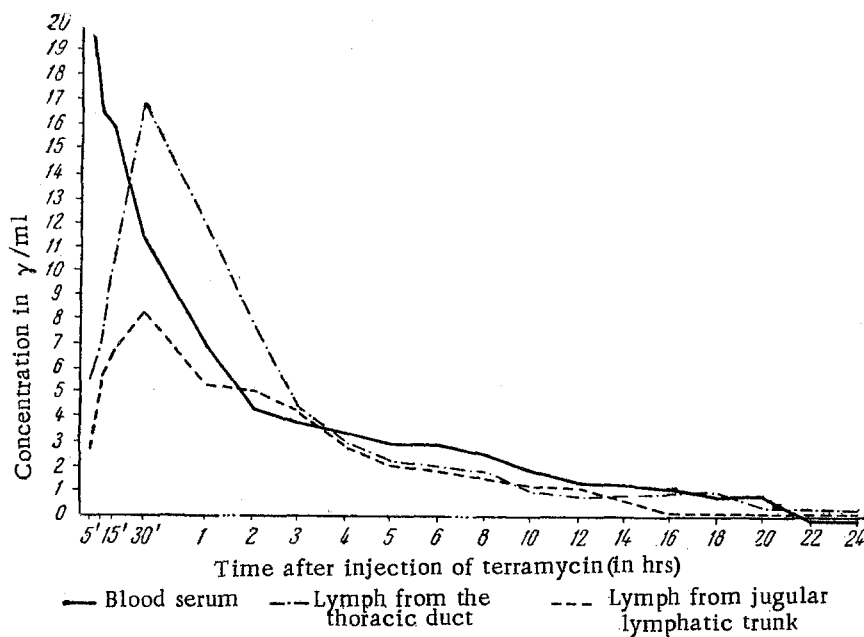


Fig. 2. Concentration of terramycin in the serum and lymph from the thoracic duct and the jugular lymphatic trunk in dogs after intravenous injection of 10 mg/kg.

Summarized Results of a Comparative Study of Active Concentrations of Antibiotics in the Lymph of the Peripheral Vessels and the Thoracic Duct

Time after injection of antibiotic	Penicillin			Biomycin		Tetracycline			Terramycin			
	Concentration, units/ml			Concentration in γ /ml			Concentration in γ /ml			Concentration in γ /ml		
	in blood serum	in lymph of thoracic duct	in lymph of jugular lymphatic trunk	in blood serum	in lymph of thoracic duct	in lymph of jugular lymphatic trunk	in blood serum	in lymph of thoracic duct	in lymph of jugular lymphatic trunk	in blood serum	in lymph of thoracic duct	in lymph of jugular lymphatic trunk
5 min	45.4	9.2	3.2	6.2	2.2	0.6	15.0	2.0	1.1	20.0	5.5	2.6
10 »	—	—	—	5.3	3.7	1.3	9.7	6.0	3.4	16.5	7.0	5.5
15 »	11.3	14.4	7.2	3.3	5.5	1.8	9.4	13.3	5.9	15.8	10.0	6.5
30 »	6.6	7.2	6.1	2.6	5.3	1.5	7.5	13.8	4.6	11.3	17.0	8.3
1 hrs	3.6	4.6	3.6	1.8	2.8	1.1	4.7	9.5	4.1	7.0	12.0	5.3
2 hrs	1.6	2.5	1.8	1.3	2.2	0.9	3.2	4.0	2.3	4.5	8.0	5.1
3 »	0.8	0.4	0.5	1.1	1.5	0.6	2.7	3.4	1.6	3.9	4.5	4.3
4 »	0.2	0.1	0.1	1.0	1.3	0.5	2.2	2.8	1.3	3.4	3.0	3.0
5 days	0.05	0.1	0.05	0.8	1.1	0.4	1.8	2.4	1.0	3.0	2.3	2.3
6 »	0	0.01	0.01	0.7	1.0	0.3	1.5	1.7	0.8	2.9	2.1	2.1
8 »	0	0	0	0.6	0.8	0.2	1.2	1.2	0.8	2.5	1.8	1.8
10 »	0	0	0	0.5	0.7	0.1	1.1	1.0	0.7	1.9	1.2	1.3
12 »	0	0	0	0.5	0.6	0.1	0.8	0.8	0.5	1.3	1.0	1.3
14 »	0	0	0	0.3	0.5	0.1	0.6	0.7	0.4	1.3	1.0	0.8
16 »	0	0	0	0.2	0.4	0.05	0.5	0.6	0.2	1.2	1.0	0
18 »	0	0	0	0	0.2	0	0.4	0.4	0.2	0.9	1.0	0
20 »	0	0	0	0	0	0	0.3	0.1	0.1	0.8	0.5	0
22 days	0	0	0	0	0	0	0.05	0.1	0.05	0	0.4	0
24 »	0	0	0	0	0	0	0.05	0.1	0.05	0	0.3	0

Symbols used: 0 — no activity; — no test.

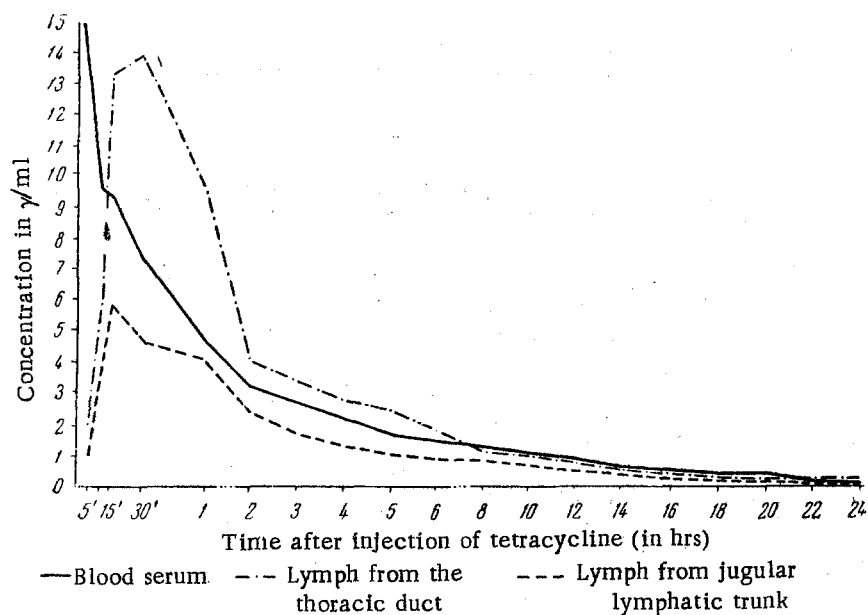


Fig. 3. Concentration of tetracycline in the serum and lymph from the thoracic duct and the jugular lymphatic trunk in dogs after intravenous injection of 10 mg/kg.

The experimental results are shown in the table.

Changes in the active concentrations of penicillin, biomycin, tetracycline and terramycin in the serum, and lymph from the thoracic duct and the jugular lymphatic trunk are shown in Figs. 1, 2, and 3.

It follows from the table and figures that the greatest concentrations in the lymph from both the thoracic duct and the jugular lymphatic trunk are found from 15-30 min after the intravenous injection of the antibiotics. The active concentrations of all the antibiotics tested were as a rule lower in the lymph from the jugular lymphatic trunk than in the lymph from the thoracic duct. Only in rare cases and in later tests were the concentrations of the antibiotics in the lymph from the jugular trunk and thoracic duct equalized.

It follows from these experiments that the study of the concentration of antibiotics in the tissue fluid of the body must be based on estimations of their concentrations in the lymph of the peripheral vessels and not the lymph of the thoracic duct.

SUMMARY

A comparative study was carried out on the active concentrations of certain antibiotics in the lymph of the peripheral vessels and in the lymph of the thoracic duct. Experiments were performed on dogs. Antibiotics under investigation were introduced intravenously in a single dose (10,000 units/kg penicillin, 10 mg/kg biomycin, tetracycline and terramycin). Active concentrations of all of these antibiotics are as a rule lower in the lymph of the duct of the head than in the lymph of the thoracic duct. Conclusion may be drawn that the study of concentration of antibiotics in tissue fluids of the organism must be based on determinations of their concentration in the lymph of peripheral vessels and not in the lymph of the thoracic duct.

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* In Russian.