EFFECT OF ANTIBACTERIAL THERAPY ON CHANGES IN THYROID FUNCTION IN EXPERIMENTAL TUBERCULOSIS

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Determination of the basal metabolism and the use of radioiodine and morphological investigations revealed stimulation of the thyroid in the early stages of development of experimental tuberculosis, followed by a gradual subsequent exhaustion.

Of the tuberculostatic drugs investigated, PAS has a thyrostatic action, ethionamide and isoniazid stimulate thyroid activity, while pyrazinamide produces no substantial changes in thyroid function.

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Tuberculosis is a chronic infectious and allergic disease accompanied by disturbances of thyroid function [8, 10, 11, 13, 14, 17]. As a rule these disturbances have been discovered on the basis of morphological investigations and determinations of the basal metabolism [7, 13, 18].

Investigation of the iodine-absorptive power of the thyroid by means of I^{131} in pulmonary tuberculosis [1, 9, 16] revealed stimulation of the thyroid at the beginning of the disease, during its early manifestations, and during recovery. Severe and disseminated forms, as well as exacerbation of the disease in the lungs, mainly cause inhibition of the thyroid [4, 6, 12].

By means of spectrophotometric and biochemical investigations, the hormone-forming function of the thyroid and the supply of thyroid hormones to the body can be studied experimentally [5, 15].

In the present investigation, changes in the hormone-forming function of the thyroid were studied during the development of experimental tuberculosis and, at the same time, the effect of tuberculostatic preparations on the response of the thyroid during this disease was examined.

EXPERIMENTAL METHOD

Experimental tuberculosis was produced in guinea pigs of both sexes weighing 300-500 g and aged 3-6 months by injecting a suspension of 0.1 mg of tubercle bacilli (Mycobacterium tuberculosis, human type, laboratory strain No. 1503) in 0.3 ml physiological saline, intramuscularly in the inguinal region [2, 13]. Altogether 5 series of experiments were carried out, with two groups of animals in each series (Table 1).

Thyroid function was investigated by determining the basal metabolic rate (BMR) [3], and the concentration of protein-bound iodine (PBI) in the blood serum by a spectrophotometric method [5, 15].

The severity of the tuberculosis was assessed by the Mantoux reaction, the postmortem findings, and the results of histological investigations, using a 20-point scale.

EXPERIMENTAL RESULTS

The development of tuberculosis in the guinea pigs was accompanied by changes in basal metabolism and the hormone-forming function of the thyroid (Table 2).

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TABLE 1. Distribution of Animals in Experiments

Series of experiments	Group of animals	Number of animals	Condition	Drug studied	Dose of drug (in mg/kg body weight)
I	1	13	Infected with tuberculosis	PAS	400
	1a	12	Healthy		400
II	2	12	Infected with tuberculosis	Ethionamine	25
	2a	12	Healthy		25
III	3	15	Infected with tuberculosis	Pyrazinamide	250
	3a	15	Healthy		250
IV	4	12	Infected with tuberculosis	Isoniazid	5
	4a	12	Healthy		5
V	5	25	Infected with tuberculosis		
	5a	25	Healthy	–	–

TABLE 2. Basal Metabolism and PBI Concentration in Blood at Various Times of Development of Tuberculosis (series V)

Time of experiment (in days)	Number of tests	Oxygen absorption (in ml/100 g/h)	P	PBI (in μg%)	P
Intact animals					
5-7	30	135.4 ± 12.6	–	16.8 ± 2.2	–
14-15	11	154.8 ± 13.0	0.3	24.2 ± 8.7	0.5
30	11	142.5 ± 16.5	0.8	3.6 ± 0.8	0.001
45	57	99.7 ± 17.6	0.4	5.8 ± 0.8	0.001
60	6	188.2 ± 20.4	0.05	25.2 ± 9.4	0.4
	7	177.7 ± 27.7	0.2	5.3 ± 1.9	0.001

Note. P calculated relative to indices for intact animals.

In the early period of the disease, a tendency was observed (Table 2) for the BMR to increase, and a significant increase was observed in the blood PBI concentration, indicating stimulation of thyroid function. With further development of the tuberculosis, both these indices fell, presumably as a result of depression of thyroid function. Consequently, tuberculosis was accompanied by alternate stimulation and inhibition of thyroid function.

The results of a study of the effect of tuberculostatic drugs on the BMR and hormone-forming function of the thyroid are shown in Table 3. Analysis of these results shows that PAS lowered the BMR and the PBI concentration in the blood. The severity of the disease in guinea pigs receiving this drug was 19-20 points.

Ethionamide stimulated thyroid function. Some discrepancy appeared between the indices of the BMR and blood PBI concentration possibly because these indices do not reflect thyroid function adequately. Its therapeutic effect is greater than that of PAS, and the severity of the disease in animals of this group was 10-12 points.

Pyrazinamide inhibited thyroid function in healthy and sick animals. The severity of the tuberculosis in animals treated with pyrazinamide ranged from 14-16 to 20 points.

Isoniazid does not prevent the lowering of thyroid function in healthy guinea pigs due to age [9]. In sick animals treated with isoniazid, the blood PBI concentration rose. A high therapeutic effect was observed, and the severity of the disease was 3-5 points.

Histological investigation showed depression of thyroid function in infected guinea pigs not receiving the drugs, and in most healthy animals and animals treated with PAS. Administration of isoniazid to animals previously treated with ethionamide revealed stimulation of the thyroid. When pyrazinamide was given to healthy guinea pigs, no changes in thyroid activity were observed, but in sick animals the thyroid was inhibited.

TABLE 3. Indices of Change in Thyroid Function in Guinea Pigs during Treatment with Tuberculostatic Drug

Drug	Time of observation (in months)	Absorption of oxygen	M ± m (in ml/100 g/h)		PBI concentration in serum (in μg%)				
		healthy	P	infected	P	healthy	P	infected	P
PAS	Initial data	92,8±3,2		113,2±12,7		41,4±11,4	0,6	10,8±2,6	
	1	94,3±5,4	0,9	79,6±5,2	0,05	49,3±4,4	0,01	17,6±4,7	0,3
	2	111,7±4,4	0,01	75,2±2,9	0,01	3,5±1,8	0,01	5,8±0,9	0,1
	3	84,8±1,9	0,05	—	—	3,1±0,4	—	—	—
Ethionamide	Initial data	119,2±35,2		97,7±6,1		20,5±5,8		14,6±4,5	
	1	105,8±11,3	0,8	73,9±11,7	0,1	34,6±6,4	0,2	17,6±5,7	0,7
	2	—	—	83,1±3,2	0,05	—	—	26,2±7,8	0,3
	3	83,7±7,0	0,4	108,3±12,1	0,5	30,4±8,2	0,4	21,0±4,4	0,4
Pyrazinamide	Initial data	92,6±10,8		88,6±4,7		33,7±6,9		8,7±2,2	
	1	83,0±9,8	0,6	79,5±3,0	0,2	21,2±6,0	0,2	25,9±5,1	0,01
	2	88,8±7,9	0,8	109,0±18,4	0,3	21,1±5,7	0,5	26,6±12,9	0,2
	3	99,0±13,6	0,8	104,9±4,9	0,05	7,3±4,7	0,01	8,7±1,3	1,0
Isoniazid	Initial data	219,0±24,0		95,2±11,5		20,1±8,7		14,6±4,5	
	1	106,6±11,9	0,001	119,8±16,4	0,5	17,3±3,5	0,8	8,7±2,4	0,3
	2	122,2±11,9	0,1	86,2±4,0	0,5	—	—	38,3±1,0	0,001
	3	110,5±7,4	0,001	—	—	15,0±4,0	0,7	55,6±15,3	0,02

Note. P calculated relative to initial data.

These experiments thus confirmed alternate stimulation and depression of thyroid function observed under clinical conditions [1, 9, 14]. This can be regarded as indicating participation of the thyroid in stress responses evoked by tuberculosis.

The thyrostatic action of PAS was confirmed [2], and the thyroid-stimulating action of isoniazid and ethionamide was discovered, pyrazinamide producing no significant changes in thyroid function.

In the successful treatment of tuberculosis, it is therefore essential to study thyroid function. Bearing in mind the many-sided effects of antibacterial drugs on thyroid function, one method of restoring it to normal must be by the choice of proper tuberculostatic drugs, without, at the same time, lowering their therapeutic action on the specific process.

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