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Influence of Progesterone on Experimental Tuberculosis in Male Guinea Pigs.

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As the condition of tuberculous patients appears to improve during the early months of pregnancy, we were interested in noting what influence the hormone, progesterone, might have on experimental tuberculosis.

Steinbach and Klein[1] found that pregnant mare serum, Antuitrin-S and Follutein to a less degree, retarded tuberculosis in rabbits and guinea pigs. Since the latter two agents stimulate the ovaries to luteinization, it seemed not unlikely that the effect on tuberculosis might be due to a hormone from the corpus luteum, which develops and persists during pregnancy.

Male guinea pigs were used to eliminate fluctuations in secretion of hormones from the ovaries that would occur in the female. Animals used had an initial range of weights from 370-470 g and were negative to tuberculin. Twenty were inoculated subcutaneously with 1 mg of the C3 strain of bovine tubercle bacilli. On the same day, ½ unit of progesterone* was given to each of 10 of these animals and to a non-infected one by the subcutaneous route. The dose was administered 3 times weekly for 6 weeks. One non-infected animal which was not given progesterone was included in the series. The hormone preparation was an oil solution and contained one rabbit unit per cc as defined by Parke, Davis & Co. The original culture of tubercle bacilli was obtained from the laboratories of the New York City Department of Health. The culture used had been grown for 3 weeks on Petroff's medium and the suspension was made in saline. At autopsy, the animals were scored for tuberculosis by the method of Petroff and Steenken.[2] Tissues from 8 infected animals, of which 4 had received progesterone, and tissues from the 2 non-infected animals were fixed in Zenker's solution. Alternate paraffin sections were stained by the hematoxylin and eosin and Ziehl-Neelsen methods.

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1 Steinbach, M. M., and Klein, S. J., *J. Exp. Med.*, 1937, **65**, 205.

* We appreciate the courtesy of Parke, Davis & Co. in supplying us with Lipo-Lutin.

2 Petroff, S. A., and Steenken, W., *J. Immunol.*, 1930, **19**, 79.

TABLE I.
Macroscopic Tuberculosis in Animals Given Progesterone and Control Animals.

Animal No.	Lung	Liver	Spleen	Kidney	Lymph nodes					TB score	Duration of experiment
					Inguinal	Retroperitoneal	Tracheobronchial	Hepatic	Mesenteric		
Experimental											
2-1*	3+	2+	2+	0	M‡	0	3	2	0	3+	47
2-2	2+	3+	2+	0	M‡	1†	2†	1†	1†	3+	46
2-3*	2+	4§	4+	0	M†	2†	2†	1†	0	4+	47
3-1	1+	2+	4+	0	M‡	2†	3†	1	0	3+	46
3-2	3+	2+	2+	0	M‡	2†	4†	2	1†	3+	46
3-3	2+	3+	3+	0	M‡	3†	3	1	1	3+	38
4-1*	1+	1+	3+	0	M†	3†	4	3	1	3+	45
4-2	1+	1+	1+	0	M‡	3†	2	0	0	2+	24
4-3*	3+	3+	2+	0	M‡	3†	3†	1	2	3+	45
5-1	2+	4§	1+	1+	M‡	3†	3	3	0	4+	46
Control											
5-2	1+	3+	2+	1+	M†	4†	3†	4	0	3+	46
6-1*	4+	2+	1+	0	M‡	5†	2†	1†	0	3+	47
6-2*	1+	4§	3+	0	M‡	2†	2†	1†	0	4+	47
6-3	1+	3+	2+	0	M‡	2†	2†	3†	0	3+	46
7-1	2+	3+	2+	0	M‡	1†	2	0	0	3+	38
7-2	2+	3+	2+	1+	M‡	2†	5†	2†	0	3+	46
7-3	1+	4§	2§	1+	M‡	2†	3†	1	0	4+	46
8-1	1+	1+	1+	0	M†	2†	3	0	0	2+	24
8-2*	2+	3+	3+	0	M†	2†	2†	1	0	3+	45
8-3*	3+	3+	2+	0	M†	3†	5†	1	1	3+	45

*Sections taken.
†Caseous.
M‡ Much enlarged, caseous, and ulcerated.
§Infarct.

Four weeks after inoculation, the animals receiving hormone weighed, on an average, 80 g less than the controls. At 2 weeks, tuberculin reactions were 3+ in both groups. All animals had inguinal lymph nodes which were much enlarged. At 4 weeks, the reactions were less intense and several animals did not respond to tuberculin. The variations were common to both groups. Most animals had ulcerations at the site of inoculation in the inguinal region. Non-infected guinea pigs were negative to tuberculin.

One animal from each group was killed on the 24th day and on the 38th day and the remaining guinea pigs were sacrificed 45-48 days after inoculation. Each of the latter animals receiving hormone had been given a total of 9 units.

Individual scores for macroscopic tuberculosis ranged from 2+ to 4+ (Table I). The average score for the tuberculous animals which received progesterone was 3.1. That for animals not given hormone was also 3.1. Variations in type and extent of lesions in various organs were common to both groups.

Sections were prepared from the lung, liver, spleen and some of the lymph nodes. These showed the presence of tubercle bacilli. Involved areas consisted of single and confluent miliary tubercles made up of epithelioid and giant cells with a peripheral zone of lymphocytes. Central necrosis was not common. Extensive caseation was rare except in the lymph nodes. Sections from the kidney and testis revealed no involvement with tuberculosis.

The dose of tubercle bacilli was large but the degree and extent of involvement was not maximum in control animals. A decided retardation of the tuberculous process by progesterone would probably have manifested itself. However, it might be that the hormone would show some effect in female animals.

Development of a tuberculous infection in male guinea pigs was not retarded by small doses of progesterone nor was there an altered skin sensitivity to tuberculin.