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On the transformation of the plasma clot.

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It has previously[1] been shown by the author that in tissue cultures and in wound healing in the frog a fibrous tissue which is apparently identical with normal connective tissue may be formed by a direct transformation of a plasma clot. In an endeavor to analyze this reaction, plasma clots made from centrifuged blood plasma have been subjected to various conditions of tension and pressure. The results obtained show that with the aid of these mechanical factors it is possible to directly transform a typical fibrin net into a fibrous tissue. Judged from its histological structure when stained with Mallory's connective tissue stain, this new fibrous tissue is apparently identical with normal connective tissue of the frog. By varying the conditions it is possible to obtain preparations which will show various stages in the transformation ranging from a typical fibrin net to a fibrous tissue made up of bundles of wavy fibers such as is characteristic of normal connective tissue.

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The effect of moderately high atmospheric temperatures upon the formation of agglutinins.

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In an earlier communication[2] we have pointed out that previous experiments on the effect of atmospheric temperature upon the development of various immunity reactions suggest two general conclusions: (1) That very high atmospheric temperatures, over 35° C., tend to produce a condition of fever and to hasten

[1] (*a*) *Jour. Exp. Med.*, Vol. 21, 1915, pp. 455–479; (*b*) *Jour. Exp. Med.*, Vol. 23, 1916, pp. 439–456.

[2] PROC. SOC. EXP. BIOL. AND MED., 1916, Vol. XIII, p. 93.

the production of antibodies of various sorts, while (2) moderately high atmospheric temperatures (30°–35° C.), apparently tend to decrease the power of producing antibodies, presumably by a lowering of general vital resistance without the stimulus which accompanies the production of fever. We reported certain experiments of our own which were in harmony with the last conclusion, inasmuch as they showed an apparent diminution in hemolysin production in rabbits kept at an atmospheric temperature of 29°–32° C. The present report deals with similar experiments upon the effect of moderately high temperature upon the formation of agglutinins.

This particular immunity reaction has been studied in relation to temperature by several observers. Rolly and Meltzer[1] kept rabbits in an incubator at 34°–38° under which condition their body temperature rose to 40°, they lost weight and showed a decrease in hemoglobin; yet when injected with typhoid bacilli they showed a marked increase both in bactericidal and agglutinating power. On the other hand Graziani[2] studied the agglutinating power of the blood of rabbits kept at lower temperatures and found, as workers on other immunity reactions have done, that moderately high heat was harmful and not helpful. The blood of rabbits kept at 2°–4° C. would agglutinate at a dilution of 1 in 1,541; at 18°, 1 in 854; at 32°, 1 in 727. In another series the blood of rabbits kept at 32° agglutinated at a dilution of 1 in 1,250, while if the animals were occasionally relieved by cold baths the agglutinating power rose to 1 in 2,425.

Studies on the agglutinating power of the blood of human beings after hot baths are conflicting. Leube[3] reports that typhoid convalescents showed a material increase in the agglutinin content of the blood after hot baths (40° for 30 minutes); while Moon[4] could not find any such increase after Turkish baths (30 minutes in a dry room at 82° C. and 20 minutes in a steam room at 54°).

In our own experiments, which were carried out in the bacteriological laboratories of the University and Bellevue Hospital Medical College, five series of rabbits, including 14 animals in all, were

[1] *Deut. Arch. f. klin. Med.*, XCIV, 1908, p. 335.

[2] *Centr. f. Bakt. Orig.*, XLII, 1906, p. 633.

[3] *Verhandl. d. Deutschen Kongresses f. innere Med.*, XXVII, 1910, p. 218.

[4] *Jour. Infect. Dis.*, XIV, 1914, p. 56.

kept (2–4 at a time) in a large incubator (12′ x 2′ x 4′) at a temperature ranging between 29° and 32° C. A similar series of 13 control animals was kept at room temperature (18°–21°). The animals were immunized by giving them intraperitoneally successively increasing doses of a suspension of killed typhoid bacilli. The injections were given twice a week. Bleedings were taken at weekly intervals and serum was drawn off from the clot and diluted with sterile salt solution.

For microscopic agglutination tests, one loopful of diluted serum and one loopful of a twenty-four hour broth culture of the typhoid bacillus were mixed on a cover glass, and a hanging-drop mount made. This was incubated at 37° Centigrade and readings made after one hour. In every case the figures in the table represent the actual dilution of serum found effective; the larger the fraction, the weaker the agglutinating power.

The results of the experiments are given in full in Table I and the averages by series in Table II. No general average can be fairly calculated because the agglutinating power of all the rabbits in Series V was so low that in a general average these Series V figures swamp all the rest and the net result depends simply on the number of Series V results included in a given week.

TABLE I.

EFFECTIVE DILUTION OF SERUM EXPRESSED IN DECIMALS.

Series.	Heated Animals.						Control Animals.					
	Rabbit.	Week.					Rabbit.	Week.				
		1	2	3	4	5		1	2	3	4	5
I...	3	.00500	.00066	——	——	——	101	.02000	.00025	——	——	——
	4	.02000	.00100	——	——	——	102	.00100	.00067	——	——	——
II..	5	.00200	died				15	.00050	.00012	.00003	.00005	——
	9	.00050	——	.00050	——	——	16	.00020	.00012	.00010	died	——
	6	.00200	.00100	.00010	.00010	died	17	.00050	.00010	.00010	.00010	——
	7	.00200	.00012	.00010	.00010	.00012	18	.00050	.00012	.00010	.00010	——
	8	.00500	.00012	.00010	.00010	.00012						
III .	172	.01000	.00025	.00020	.00020	.00050	170	.01000	.00010	.00013	.00017	.00025
	173	.02000	.00025	.00029	.00033	.00050	171	.01000	.00017	.00020	.00025	.00045
IV .	76	.00018	.00017	.00017	.00010	——	93	.00500	.00029	.00200	.00008	.00010
	176	.00050	.00017	.00017	.00011	——	141	.00500	.01000	.05000	died	
V ..	92	.10000	.01000	.01000	.02000	——	44	.10000	.02000	.01000	.01000	——
	143	——	.02000	——	.01000	.02000	54	——	.01000	.01000	.02000	.02000
	145	——	——	.02000	.02000	.02000	72	——	.01000	.01000	.00400	——

TABLE II.

RESULTS AVERAGED BY SERIES. EFFECTIVE DILUTION OF SERUM EXPRESSED IN DECIMALS.

Series.		Week.				
		1	2	3	4	5
I.....	Heated.....	.01250	.00083			
	Control.....	.01050	.00046			
II.....	Heated.....	.00520	.00078	.00020	.00010	.00012
	Control.....	.00380	.00023	.00008	.00008	——
III.....	Heated.....	.01500	.00025	.00024	.00027	.00050
	Control.....	.01000	.00013	.00017	.00021	.00035
IV.....	Heated.....	.00034	.00017	.00017	.00010	——
	Control.....	.00500	.00514	.02600	.00008	.00010
V.....	Heated.....	.10000	.01500	.01500	.01660	.02000
	Control.....	.10000	.01400	.01000	.01100	.02000

In general our results confirm those of Graziani and suggest that a moderately high atmospheric temperature (29°–32° C.) tends slightly to decrease the power of agglutinin formation in the rabbit. In Series IV alone this was not indicated. Here both control rabbits gave abnormal results. No. 93 showed a marked drop in agglutinating power during the third week; while No. 141 never formed any powerful agglutinins and died after the third week. With the exception of this series there are sixteen weekly averages of heated and control rabbits compared in Table II. In these sixteen cases the effective dilution for heated and control animals was on two occasions the same while in the other fourteen instances a consistently larger amount of serum was needed to produce agglutination in the case of the heated animals.

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Improved methods for the quantitative determination of plasma proteins.

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The blood is drawn into a tube containing an amount of potassium oxalate sufficient to make 0.2 or 0.3 per cent. oxalate solution, and is centrifuged twenty minutes.