

## 7682 C

Normal Variations in the Susceptibility of Human Fibrin to *Streptococcus Fibrinolysin*.\*

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There are marked differences in the susceptibilities of different samples of presumably normal human plasma-clot to the thrombolytin formed or secreted by certain strains of *S. hemolyticus*. While one clot may be completely liquefied within 30 minutes after admixture with a given lytic culture, the clot from a second, presumably normal individual may show no sign of softening even after 24-hours incubation with this culture.<sup>1</sup>

To test the possibility that this difference may be due to quantitative differences in fibrin-content, parallel fibrinolytic titrations were made with different concentrations of the same isolated fibrin. Typical data thus obtained are recorded in Table I.

TABLE I.  
Quantitative Variations in Fibrin-Content.

Human fibrinogen and thrombin isolated by the Tillett-Garner technic<sup>2</sup> and redissolved in such concentrations as to produce serum-free clots having 1-fold, 2-fold and 4-fold the fibrin-content of the average normal plasma, quantities and dilutions being otherwise the same as that adopted by Tillett and Garner. Fibrinolytic titration made throughout with the same lytic filtrate.

+, complete liquefaction of the serum-free fibrin-clot at the time of observation; ±, partial liquefaction; 0, no demonstrable softening.

Dilution of fibrinolytic filtrate	The same fibrinogen-thrombin complex tested in:											
	1-fold concentration				2-fold concentration				4-fold concentration			
	10 min.	30 min.	1 hr.	2 hr.	10 min.	30 min.	1 hr.	2 hr.	10 min.	30 min.	1 hr.	2 hr.
1:5	+	+	+	+	0	+	+	+	0	+	+	+
1:10	+	+	+	+	0	+	+	+	0	+	+	+
1:50	0	+	+	+	0	±	+	+	0	0	+	+
1:100	0	0	+	+	0	0	0	+	0	0	0	±
1:200	0	0	±	+	0	0	0	0	0	0	0	0
Control (auto- lytic test)	0	0	0	±	0	0	0	0	0	0	0	0

From this table it is seen that the rate and completeness of fibrinolysis with a given lytic filtrate varies inversely with the fibrin-content. Complete insusceptibility to lysis, however, does not re-

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<sup>1</sup> Van Deventer, J. K., *Proc. Soc. Exp. Biol. and Med.*, 1934, **32**, 50.

<sup>2</sup> Tillett, W. S., and Garner, R. L., *J. Exp. Med.*, 1933, **58**, 485.

sult from an increase in fibrin-content even to 4 times that of the average normal human plasma-clot. This result is in line with the statistical evidence reported by Hadfield, Magee and Perry.<sup>3</sup> These investigators found no correlation between fibrin-content and fibrinolytic susceptibility in different blood samples.

To test the possibility that the observed differences in susceptibility may be due to qualitative differences between "normal" and "immune" fibrins, parallel fibrinolytic titrations were made with fibrins isolated from susceptible and resistant plasma-clots. A typical comparison of this type is recorded in Table II.

TABLE II.  
Qualitative Variations in Fibrin-Content.

Serum-free fibrins from susceptible and resistant plasmas titrated against the same fibrinolytic filtrate.

Dilution of fibrinolytic filtrate	Fibrin from susceptible plasma				Fibrin from resistant plasma				Susceptible fibrinogen reisolated from resistant serum			
	10 min.	30 min.	1 hr.	2 hr.	10 min.	30 min.	1 hr.	2 hr.	10 min.	30 min.	1 hr.	2 hr.
1:1	+	+	+	+	±	+	+	+	+	+	+	+
1:2	+	+	+	+	0	+	+	+	0	+	+	+
1:4	+	+	+	+	0	+	+	+	0	+	+	+
1:8	+	+	+	+	0	+	+	+	0	+	+	+
1:16	+	±	+	+	0	0	+	+	0	0	+	+
1:32	0	0	±	+	0	0	0	±	0	0	0	±
Control (autolytic test)	0	0	0	0	0	0	0	0	0	0	0	0

From this table it is seen that serum-free fibrins isolated from resistant and susceptible plasmas are very nearly identical in their fibrinolytic susceptibilities. The slightly delayed softening of the "immune" fibrin is presumably due to adsorbed antibodies. This is confirmed by the fact that susceptible fibrinogen redissolved in and afterwards reisolated from resistant serum, has approximately this same slight degree of insusceptibility. This conclusion is in line with data reported by Fuchs<sup>4</sup> in his study of "normal" and "immune" fibrins by other technical methods.

Variations in plasma-clot susceptibility, therefore, are apparently due solely to qualitative or quantitative variations in anti-fibrinolytic serum factors. To test this conclusion, parallel antifibrinolytic titrations were made with serums isolated from susceptible and resistant plasma-clots. A typical titration of this type is recorded in Table III.

From this table it is seen that the serum from the most susceptible normal human plasma thus far tested by us contains an "antibody"

<sup>3</sup> Hadfield, G., Magee, V., and Perry, C. B., *Lancet*, 1934, **226**, 834.

<sup>4</sup> Fuchs, H. J., *Z. f. Immunitätsforschung*, 1928, **57**, 320.

TABLE III.  
Antifibrinolytic Titer of Susceptible and Resistant Serums.

An arbitrary fibrinolytic unit was adopted, equal to approximately three times the minimum 30-minute lytic unit for serum-free fibrin. This arbitrary lytic unit was mixed with serial dilutions of susceptible and resistant serum, the mixtures incubated 30 minutes, then tested against the same serum-free fibrinogen-thrombin complex.

Dilution of neutralizing serum	Serum from susceptible plasma-clot				Serum from resistant plasma-clot			
	10 min.	30 min.	1 hr.	2 hr.	10 min.	30 min.	1 hr.	2 hr.
1:3	0	0	0	0	0	0	0	0
1:9	0	0	0	0	0	0	0	0
1:27	0	+	+	+	0	0	0	0
1:81	+	+	+	+	0	0	0	±
1:243	+	+	+	+	0	0	+	+
Control (no antiserum)	+	+	+	+	+	+	+	+

capable of neutralizing our arbitrary fibrinolytic unit in dilutions as high as 1:9. Serum from our most resistant plasma neutralizes the same lytic unit in dilutions as high as 1:81.

## 7683 C

### Dorsal Roots of Spinal Nerves and Regulation of Skin Temperature.\*

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Stricker<sup>1</sup> first showed that stimulation of the dorsal roots of spinal nerves produced a vasodilatation in peripheral blood vessels. This observation has been confirmed by Bayliss,<sup>2</sup> Ranson and Wightman<sup>3</sup> and others. Hinsey and Gasser<sup>4</sup> showed that the fibers mediating vasodilatation on stimulation of the dorsal roots were ones whose potentials were found in the C-spike of the action potential. Vasodilator reflexes over the dorsal roots were demonstrated in positive experiments by Bayliss<sup>5</sup> and Fofanov and Tschalussow.<sup>6</sup> Recently

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<sup>1</sup> Stricker, M., *Sitzber. d. k. Akad. d. Wiss., Wien Math. nat. Kl.*, 1876, **74**, 173.

<sup>2</sup> Bayliss, W. M., *J. Physiol.*, 1901, **26**, 173.

<sup>3</sup> Ranson, S. W., and Wightman, W. D., *Am. J. Physiol.*, 1922, **62**, 392.

<sup>4</sup> Hinsey, J. C., and Gasser, H. S., *Am. J. Physiol.*, 1930, **92**, 679.

<sup>5</sup> Bayliss, W. M., *J. Physiol.*, 1902, **28**, 276.

<sup>6</sup> Fofanov, L. L., and Tschalussow, M. A., *Pfloger's Arch.*, 1913, **151**, 543.