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Immunologic Studies on Patients Suffering from Bacterial Endocarditis.

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That specific antibodies are present in the circulating blood of patients with *Streptococcus viridans* endocarditis has been accepted very generally[1, 2, 3] and Keefer[4] has recently reviewed the studies supporting this view. Unfortunately varying technics have been used by previous workers, and it is difficult to correlate their results. We present here a study of the antibody responses in bacterial endocarditis, using a uniform technic, and a correlation of these serological findings with the variations of the colony count of successive blood cultures.

The opsonocytophagic power of the blood,[5] agglutination,[5] and bacteriolysin tests* were done on 7 patients with classical, and one patient (Case 2) with suspected bacterial endocarditis. In addition complement fixation tests were performed on Case 7. Three to 7 positive blood cultures were obtained on each patient before the immunologic status was determined. The results before treatment are shown in Table I.

After the completion of preliminary tests for antibodies, the patients were treated by means of a high vitamin diet, with specific

1 Blumer, G., *Medicine*, 1923, **2**, 105.

2 Cecil, R. L., *Textbook of Medicine*, 4th edition, W. B. Saunders, Philadelphia, Pa., 1937, 1105.

3 White, P. D., *Heart Disease*, 2nd edition, The Macmillan Co., New York, N. Y., 1938, 263.

4 Keefer, C. S., *Ann. Int. Med.*, 1937, **11**, 714.

5 Menefee, E. E., Jr., and Poston, M. A., *Am. J. Med. Sc.*, in press.

* Felsen's[6] method for measuring bacteriolysins was modified as follows: After preliminary titration to establish the presence of complement, a series of test tubes containing 0.5 cc of different dilutions of the patient's serum (from 1-10 to 1-1000) was incubated in a 37°C water bath for 4 hours with an equal amount of suspension of organisms. Ten cc of beef infusion broth pH 7.4 (blood broth for *H. para-influenzæ*) was added to each tube and the amount of growth in 18 hours was determined by readings on a calibrated Photronreflectometer (Libby). One cc of the serum organism mixture was used for pouring plates with North's gelatin blood agar for *N. gonorrhoeæ*.

6 Felsen, J., and others, *J. A. M. A.*, 1937, **108**, 1783.

TABLE I.

Case No.	Etiological agent	Before Treatment: No. of colonies per cc of blood*	Before Treatment: Opsonocytophagic power of the blood†‡	Before Treatment: Agglutination†	Before Treatment: Bacteriolysins†	After Treatment: No. of colonies per cc of blood	After Treatment: Opsonocytophagic power of the blood‡	After Treatment: Agglutination	After Treatment: Bacteriolysins	Duration before entry mos	Followed mos	Results
1	*S. viridans*	6	17	Negative	None	Not done; treatment refused				3		Died
2	" "	1	0	"	"	0	50	1-640	1-500 dil. of serum; no growth	1.5	8	Well
3	" "	3	0	"	"	0	21	1-640	1-1000 dil. of serum; no growth	6	6.5	Died
4	" "	23	5	"	"	1	1	1-640	None	2	2.5	"
5	Enterococcus	3	0.5	"	"	0	19	1-80	"	11	1	Died of pulmonary embolus
6	*H. parainfluenzæ*	1	0.4	1-80	"	0	0.5	1-80	"	4	1.5	Died
7	*S. viridans*	6	0	1-40	"	21	4	1-80	"	3	1	Died 7 wks after discharge against advice
	H. parainfluenzæ (hemolytic)	5	0.2	1-20	"	1	11	1-160	1-50 dil. of serum; no growth			
8	Anerobic streptococcus (non-hemolytic)	1	0.5	Negative	"	0	93	1-1280	1-200 dil. of serum; no growth	4	3	Well
	N. gonorrheæ	1	1	1-80	"	0	97	1-1280	1-200 dil. of serum; no growth			

* Average of 3-7 blood cultures. † Average of 2-3 tests. ‡ Average number of organisms per cell.

vitamin supplements, iron, liver, multiple blood transfusions, and sulfanilamide, or one of its related compounds. Serial studies were done on each case over periods varying from 1 to 8 months. The maximal immunologic response after treatment is shown in Table I.

Initial studies in each instance revealed uniformly little evidence of antibodies either in the *Streptococcus viridans* or the other etiological types of endocarditis. In Case 2, the blood, after 3 consecutive positive cultures, became sterile, and immune antibodies previously absent appeared in high titer. In Case 3, immune antibodies appeared when the blood became sterile, but decreased sharply following injections of a formalinized autogenous vaccine. When the colony count in Case 4 decreased from 26 to 1 per cc, the agglutination titer rose to 1-640, but no increase in phagocytosis or bacteriolysins was noted. These agglutinins disappeared when the colony count increased to 45 per cc. In Case 5, after the disappearance of the bacteremia, phagocytosis and the agglutination titer rose before the patient's premature death from pulmonary embolism. Case 7 developed immune antibodies in low titer in the presence of a persistent bacteremia. Case 8 revealed a progressive rise in antibodies after the blood cultures became negative. Gonococcal complement fixation tests, initially 4 plus, later became negative, indicating possibly an inverse relationship to other antibodies. Kinsella[7] in one instance of *Streptococcus viridans* endocarditis, demonstrated an inverse relationship of agglutinins to complement fixing antibodies, but did not comment further upon this finding.

Conclusions. Patients in the active bacteremic stage of bacterial endocarditis exhibit no significant serologic evidence of immunity by the methods used in this study. Immune antibodies developed coincidentally with the disappearance of bacteremia.

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[7] Kinsella, R. A., *Arch. Int. Med.*, 1917, **19**, 367.