

of the physostigmine in inhibiting the choline-esterase was tested by adding known amounts of acetyl choline to the eserinated heart's blood. In 11 of 12 experiments the leech was sensitive to at least 1×10^{-7} of acetyl choline; usually about 2 or 3×10^{-8} caused a vigorous contraction.

In no case did the leech muscle contract following the addition of the shocked rabbit's blood. On the contrary, relaxation of the leech occurred in some instances.

Summary. No direct evidence could be found to support the view that acetyl choline is released into the blood stream in detectable amounts in anaphylactic shock in the rabbit.

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Transmission of Endocarditis Lenta to Rabbits.

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Rosenbach¹ produced experimental bacterial endocarditis in dogs by passing an instrument down the right carotid artery to wound the valves. Most of his experiments on dogs and rabbits produced aseptic lesions but 2 of his dogs developed large vegetations on the aortic valve and numerous septic infarcts and petechial hemorrhages in various organs. Colonies of micrococci, apparently staphylococci, were demonstrated in these lesions. Ever since that pioneer observation there has prevailed the idea that some accessory injury of the endocardium is necessary in addition to the introduction of bacteria into the blood-stream, if one is to succeed in causing experimental endocarditis. Welch, Murdock and Ferguson² punctured the heart and then rotated the needle to produce a preliminary endocardial wound before introducing their bacteria intravenously or into the pulp of a tooth. In addition they resorted to accessory respiratory infection and dietary restriction to lower the resistance of their animals. In this way they succeeded in producing gross endocardial vegetations in 20% of their rabbits inoculated with endocarditis-

¹ Rosenbach, Ottomar, *Arch. f. exp. Path. und Pharm.*, 1878, 9, 1.

² Welch, Henry, Murdock, Thomas P., and Ferguson, John A., *J. Lab. and Clin. Med.*, 1936, 21, 1264.

streptococci. Dietrich³ has introduced various substances parenterally to injure the valves and then has injected staphylococci or colon bacilli to produce the vegetations. British investigators, however, have been successful without the preliminary injury to the endocardium. Apparently the first success of this kind was obtained by Dreschfeld,⁴ who succeeded by the simple intravenous injection of endocarditis-streptococci into rabbits long before *Streptococcus viridans* had been distinguished from other streptococci. More recently Lloyd-Jones⁵ has made a most significant contribution. He was able to produce endocarditis in rabbits with great regularity by repeated daily intravenous injection of hemolytic streptococci and particularly by such injection of serum-broth cultures of viridans types of streptococci obtained from the human intestine and uterine cervix.

For our more successful experiments we have used serum-broth cultures of various strains of *Streptococcus viridans* isolated from the blood of clinical cases of endocarditis lenta. The culture has been injected into the ear vein of a rabbit in doses of 1 to 4 cc daily for six days with a pause for 48 hours. Then a blood culture has been taken and the series of six daily injections repeated. This program has been continued until two or three successive positive blood cultures have been obtained and the animal has shown a definite loss of weight. Then the inoculations have been discontinued and the disease allowed to take its course or, in some instances, various therapeutic procedures have been undertaken, which cannot now be discussed. Weekly or more frequent blood cultures were continued and the body weight has been observed. Careful necropsy has been performed as soon as possible on all the animals that have died. Up to February 12, 1939, the series includes 21 rabbits already dead. Of these there were 12 with definite vegetative endocarditis and a glance at Table I will show that the positive results have been obtained with considerable regularity in the recent series. It should be noted, however, that positive results have been obtained so far with only two bacterial strains and standard results are being obtained with only one. We are undertaking experiments with other bacterial strains at the present time.

The lesions recorded as positive have been large and easily recognizable in the gross examination. In sections of the vegetations un-

³ Dietrich, Wolfgang, *Virchow's Arch.*, 1937, **299**, 285.

⁴ Dreschfeld, *Brit. Med. J.*, 1887, **2**, 887.

⁵ Lloyd-Jones, D. M., *An experimental study of malignant endocarditis*, Appendix to *Bacterial Endocarditis*, pp. 113-137, John Wright and Sons, Ltd., Bristol (Eng.), 1936.

TABLE I.
Rabbits Inoculated Intravenously with *Streptococcus viridans*.

Rabbit	Strain	Initial Inoculation	Death	Significant lesions
12	M	Jan. 19, 37	Mar. 4, 37	Mitral vegetation
11	S	" 19	" 12	Negative
19	M	" 30	Apr. 12	"
466	W	Feb. 8	Feb. 11	"
467	G	" 8	" 15	"
458	P	Dec. 5, 38	Dec. 11, 38	Uncertain
143	P	" 5	" 16	Negative
148	P	" 5	" 19	" (?)
345	P	" 5	" 20	" (?)
469	P	" 5	" 23	Aortic vegetation, splenic infarct
472	P	" 5	" 27	Negative
304	P	" 5	" 30	Mitral vegetations
302	P	" 5	" 30	Tricuspid vegetations, renal infarct
465	P	" 5	Jan. 5, 39	Mitral vegetation
316	P	" 28	" 11	Mitral and mural vegetations, kidney, lung
315	P	" 28	" 16	Mitral vegetation
303	P	" 28	" 25	" "
317	P	" 28	" 28	" "
313	P	" 28	Feb. 1	Tricuspid, aortic, mitral vegetations
307	P	" 28	" 4	Tricuspid, mitral vegetations
309	P	" 28	" 12	Mitral vegetation, lung

der the microscope one can easily recognize the colonies of streptococci in the necrotic substance and the inflammatory reaction in the adjacent living fibroblastic granulation-tissue of the lesions.

We conclude, therefore, that it is possible to transmit endocarditis lenta from man to the rabbit by repeated intravenous injection of pure cultures of the specific bacteria, without accessory injury or other depression of the animal. It is hoped that there may thus be provided suitable material for detailed study of the experimental disease and for the testing of various therapeutic measures.