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Study of bacterial toxins by means of the isolated mammalian heart.

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The excised rabbit heart is a delicate reacting index of toxic action. It is well suited to the study of bacterial products giving little or no recognizable reaction with intact animals. The technique we have used is the simplified technique proposed by Gunn[1]. The preferable perfusion fluid is Locke's solution containing 1 per cent. carefully filtered defibrinated rabbit blood. Control hearts perfused with this mixture beat regularly and strongly for over three hours. With hemolytic or hemagglutinating bacterial products this blood mixture, of course, can not be used. With such products, Locke's solution alone may be used, or Locke's solution containing 0.1 per cent. carefully filtered laked blood. Perfused with these solutions, the isolated rabbit heart beats regularly and strongly for over an hour. Illustrative cardiac reactions are given below:

1. *Endotheliotoxin of S. cholerae.* Filtrates from broth cultures of *S. choleræ* are almost non-toxic for the contractile and conducting tissues of the isolated rabbit heart. Minor changes in tone, and in rate and strength of contraction are produced, but the hearts beat regularly and strongly for over ninety minutes.

Very marked reactions on the capillary endothelium, however, are produced. Within fifteen minutes, the myocardium becomes markedly edematous and markedly hemorrhagic. Histological sections show the tissue spaces widely dilated, and containing numerous extravasated red blood corpuscles. It is believed that this reaction furnishes a valuable method for the study of the immunological adaptations of the capillary endothelium.

2. *Hemagglutinin of Streptococcus hemolyticus*: The streptococcus was grown in a 10 per cent. dilution of defibrinated rabbit blood in Locke's solution[2]. On testing these filtrates with

[1] J. A. Gunn, *Jour. Physiol.*, 1913, xlvi, 506.

[2] A. H. Clark and L. D. Felton, *J. A. M. A.*, 1918, lxxi, 1048.

1 per cent. blood-Locke-mixtures, a very rapid decrease in the rate of perfusion flow was noted. The coronary perfusion almost ceased by the end of five minutes.

Histological sections of hearts thus perfused show an almost total occlusion of the cardiac arterioles with agglutinated red blood corpuscles. In most of our parallel test tube experiments, recognizable hemagglutination did not take place. It is believed that cardiac perfusion furnishes a more delicate index of hemagglutination than the ordinary test tube reaction[3], and throws important light on the mechanism of streptococcus pathogenicity.

3 *Cardiotoxin of Streptococcus hemolyticus*: In corpuscle-free perfusions, streptococcus filtrates are markedly toxic for the contractile and conducting tissues of the isolated rabbit heart. The filtrates uniformly produce: (i) a marked loss of myocardial tone, usually reaching a maximum within three minutes, (ii) a temporary complete auricular-ventricular dissociation (heart-block) usually lasting about five minutes, and (iii) a progressively decreasing strength of the myocardial contractions, usually leading to complete cessation of recordable movements in from twelve to fifteen minutes.

It is believed that these reactions throw light on the mechanism of streptococcus toxicity, and give a valuable method for the study of the immunological adaptations of cardian tissues.

[3] K. M. Howell, *Jour. Infect. Dis.*, 1920, xxvii, 565.