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Experimental Coronary Occlusion and Myocardial Fibrosis.

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Colloidal solution of aluminum hydroxide was observed by Beland, Moe, and Visscher[1] to produce rapid stoppage of the heart when the aluminum was perfused into the coronary arteries in a heart-lung preparation. They believed that coronary insufficiency resulted from multiple capillary emboli due to the injection of the aluminum hydroxide. A 2% aluminum hydroxide solution was also injected into the right side of the heart in a similar preparation. In this instance the lungs apparently filtered out sufficient aluminum so that no deleterious effect was noted on the coronary circulation. Irwin[2] studied the effect of aluminum solutions injected intravenously in experimental animals. He found that if sufficient quantities of the metal were injected the animal died due to pulmonary emboli. Nodular fibrotic areas were noted in the lungs of rabbits following experimental inhalation of aluminum dust;[3] the tissue response was that of a foreign body reaction.

In the present study the sternums of 4 control rabbits were removed so that aluminum hydroxide could be injected directly into the cavity of the beating left ventricle. Large doses of the material were injected until the animals died. No gross changes were apparent in the heart or other organs. Microscopic study of various sections of the heart muscle with the hematoxylin and eosin stain reveals numerous small arterioles to be filled with bluish-purple masses which partially or completely occluded the smaller arterioles. In those vessels only partially occluded with the colloidal material the aluminum was found to adhere to the wall of the vessel.

In order to prove that the suspected masses were aluminum the sections were stained for aluminum using a specific stain. The aluminum particles were noted to be cherry-red in color by this method. In some instances the very small aggregates of the material seen in small capillaries with the hematoxylin and eosin stain failed to take the red color with a specific stain (Aurine). This

1 Beland, I. J., Moe, G., and Visscher, M. D., PROC. SOC. EXP. BIO. AND MED., 1938, **39**, 145.

2 Personal communication.

3 Denny, J. J., Robson, M. B., and Irwin, D. A., *Canad. Med. Assn. J.*, 1937, **37**, 1.

may be due to the small quantities of the aluminum present. After some experience the small aluminum thrombi can be detected with little difficulty, using hematoxylin and eosin stain following formalin fixation.

Thirty rabbits were given repeated intraventricular injections of aluminum hydroxide in non-fatal amounts. In animals weighing from 1800 to 2500 g, 1 cc of the 2% solution could be safely given. Twenty-two of the rabbits lived and were sacrificed from one to 6 weeks following repeated injections of the aluminum into the left ventricle while others died immediately following such injections.

Gross examination of the hearts of the 22 animals which survived revealed fibrotic patches in some. A few yellowish areas measuring one millimeter in diameter could be observed in others. Microscopic examination of the heart muscle of these animals revealed numerous small fibrotic patches scattered particularly throughout the left ventricle. These scarred areas are similar to those seen in human cases that are associated with coronary sclerosis. In a few of the sections a chronic inflammatory reaction was the most pronounced change present.

A number of the hearts showed small areas of infarction, particularly in the lower third of the septum and near the tip of the left ventricle. Some of the small arterioles seen in the adjacent myocardium were partially or completely occluded by aluminum thrombi. The cardiac muscle adjacent to the infarcts was partially replaced by actively proliferating fibroblasts and numerous inflammatory cells. The latter consisted of lymphocytes, eosinophils and numerous macrophages.

A more chronic proliferative lesion was noted in some areas of the heart in which large amounts of aluminum were present. In addition to the partial occlusion of the vessels some of the material apparently incited a foreign body reaction. The macrophages in those sections contained numerous particles of aluminum. A few giant cells of the foreign body type were also seen in the nearby tissue. The marked proliferative response of the fibroblasts in some instances produced a picture similar to true Aschoff nodules. Changes in the vessels were not especially frequent; the change most commonly observed was some intimal proliferation and an increased thickness of the vessel wall.

Summary. It is possible to produce coronary occlusion and myocardial fibrosis experimentally in the rabbit by means of injection of colloidal aluminum hydroxide into the left ventricle. This method may be useful in the experimental study of cardiac hypertrophy and coronary disease.