

fast bacillus isolated from the human leprous nodule, a disease comparable to human leprosy. The other object was to determine any difference in the pathogenicity of the 2 variants designated "R" and "S". The data indicate that the smooth form of this chromogenic acid-fast bacillus is the more pathogenic for rabbits.

9047 P

Action of Acetylcholine on Heart and Skeletal Muscle.*

M. BODANSKY AND PAUL BRINDLEY. (With the technical assistance of C. L. Herrmann and Katherine R. Campbell.)

From the Laboratories of the John Sealy Hospital and the Departments of Pathology and Pathological Chemistry, University of Texas Medical School, Galveston.

Hall, Ettinger and Banting¹ found that long-continued administration of acetylcholine produced myocardial and coronary artery damage, the effects being more severe and extensive in old than in young animals. In pursuing our interests in the problem of myocardial and skeletal muscle disease in relation to the creatine reserve, we attempted to study the effects in the rat. As in the experiments reported from the Banting Institute, acetylcholine bromide (Eastman-Kodak) and acetylcholine iodide (Hoffmann-La Roche) were used. The dose was 10 mg. of acetylcholine daily, administered in a single dose or in 2 divided doses. The rats were 5-6 months old at the beginning of the experiments and the average weight exceeded 300 gm. Fourteen of the 17 rats on which the present report is based received the drug for a period of 85-90 days, at which time they were sacrificed.

Within a few seconds after each injection, the characteristic effects of the drug referable to autonomic activity, *i. e.*, profuse salivation and lacrimation, accelerated respiration and heart rate, were manifested. These symptoms gradually subsided during the succeeding 10 minutes.

Heart. The changes in the heart were somewhat variable, but in most animals there was present some degree of myocardial degeneration, hyaline change and beginning fibrosis. A striking feature

* Aided by a grant from the National Research Council.

¹ Hall, G. E., Ettinger, G. H., and Banting, F. G., *Canad. Med. Assn. J.*, 1936, **34**, 9.

was the patchy distribution of the small areas of degeneration, often verging on necrosis. Infiltration of these areas with inflammatory cells, vacuolization, hydropic change, thickening of the vessel walls due mainly to endothelial proliferation, and scattered small hemorrhages into the myocardium were likewise in evidence. Despite these changes it was remarkable to discover that the creatine concentration was essentially unaffected (159-237 mg., average 206 mg.) in all the animals that survived the period of experimentation (15 out of 17). In one rat which died in heart failure, the auricles were greatly dilated and there was present generalized edema with ascites. The creatine concentration of the myocardium was only 106 mg. In this animal there was thickening of the walls of the blood vessels due to fibrous tissue production. A nerve ganglion on the wall of the heart showed marked fibrosis. A low value for creatine (113 mg.) was observed in a second animal in which death was associated with considerable accumulation of bloody fluid in the pericardial sac. It, therefore, appears that although the creatine reserve of the myocardium was lowered in the 2 cases just cited, nevertheless severe myocardial damage existed in the greater proportion of animals without any significant change in creatine concentration. This observation confirms our experience in clinical heart disease as disclosed by the results of an extensive series of analyses of human hearts (Bodansky, Pilcher and Duff, unpublished data).

Skeletal Muscle. Rarely, focal areas of myositis with degeneration were noted and somewhat more frequently hyaline change and fibrosis were present, but for the most part the muscles appeared essentially normal, except for hyperplasia of the endothelium of the blood vessels which was a relatively constant finding. Without exception the creatine concentration remained essentially within normal limits.

Muscle Metabolism. A proportion of the rats were kept in suitable metabolism cages for periods of 30 days, or longer, and the urine, collected at intervals of 48 hours, was analyzed for nitrogen, creatine, creatinine, and guanidoacetic acid. Considering the physiological properties of acetylcholine in the dosage administered, it was of interest to find that there was no significant change from the normal in the excretion of these constituents.