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Action of Acetyl Beta Methylcholin on Ventricular Rhythms Induced by Adrenalin.

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Fibrillation of the ventricles is the most frequent cause of sudden cardiac death. It is generally accepted that this is the mechanism of sudden death characteristic of coronary arterial disease in man. Adrenalin tends to raise the rhythmicity of the ventricular foci leading to ectopic ventricular rhythms. There is considerable evidence that accelerator nerve impulses and adrenalin play an important part in the genesis of ventricular fibrillation. Levy and Lewis[1] induced ventricular fibrillation by the injection of adrenalin in cats under light chloroform anesthesia. Otto[2] observed that section of the cardioaccelerator nerve fibers prevented the ventricular fibrillation which follows ligation of branches of the coronary circulation. Nahum and Hoff[3] found that inhalation of benzol regularly produced ventricular fibrillation. This did not occur in animals in which the adrenal glands had been removed. Hoff and Nahum[4] showed that removal of the stellate ganglia and adrenal glands enormously decreased the susceptibility of the heart to ventricular fibrillation following electric shock. They concluded that adrenalin acts synergistically with some other factor to increase ventricular rhythmicity leading to ventricular fibrillation.

Acetyl beta methylcholin, a synthetic choline derivative, produces effects similar to those which follow stimulation of the parasympathetic nerves. Nahum and Hoff[5] demonstrated that the ventricular fibrillation induced by inhalation of benzol can be prevented by adequate amounts of acetyl beta methylcholin. Hoff and Nahum[4] more recently showed that this substance lessened the susceptibility of the ventricles to fibrillation following electric shock. In the present study, ectopic ventricular rhythms were produced in 6 elderly patients by the intravenous injections of 0.1 mg. of adrenalin. Electrocardiographic records were taken before the injection and a

[1] Levy, A. J., and Lewis, T., *Heart*, 1911, **3**, 99.

[2] Otto, H. L., *Arch. f. d. ges. Physiol.*, 1927, **217**, 528.

[3] Nahum, L. H., and Hoff, H. E., *J. Pharm. and Exp. Therap.*, 1934, **50**, 336.

[4] Hoff, H. E., and Nahum, L. H., *Am. J. Physiol.*, 1935, **110**, 675.

[5] Nahum, L. H., and Hoff, H. E., *Am. J. Physiol.*, 1934, **109**, 78.

continuous record following the injection until the reaction had subsided. In each case ectopic ventricular beats from multiple foci appeared within a minute, quickly increasing in number. The height of the reaction took place within the first 2 minutes and at this time practically all the beats were ectopic ventricular in origin. (Fig. 1, C.) The effect of the adrenalin subsided rather quickly so that there was a return to normal rhythm within 5 minutes after the injection. (Fig. 1, F.) Fifteen minutes after this reaction had subsided, acetyl beta methylcholin chloride, 20 mg., was injected subcutaneously. Adrenalin, 0.1 mg., was again injected intravenously and the reaction observed with a continuous electrocardiographic record.

In the first patient the second dose of adrenalin was administered intravenously one and one-half minutes after the subcutaneous injection of acetyl beta methylcholin. At this time the systemic effects such as flushing of the face, sweating and salivation were most intense and there was an increase in pulse rate. In this case, the second dose of adrenalin induced ventricular premature beats sim-

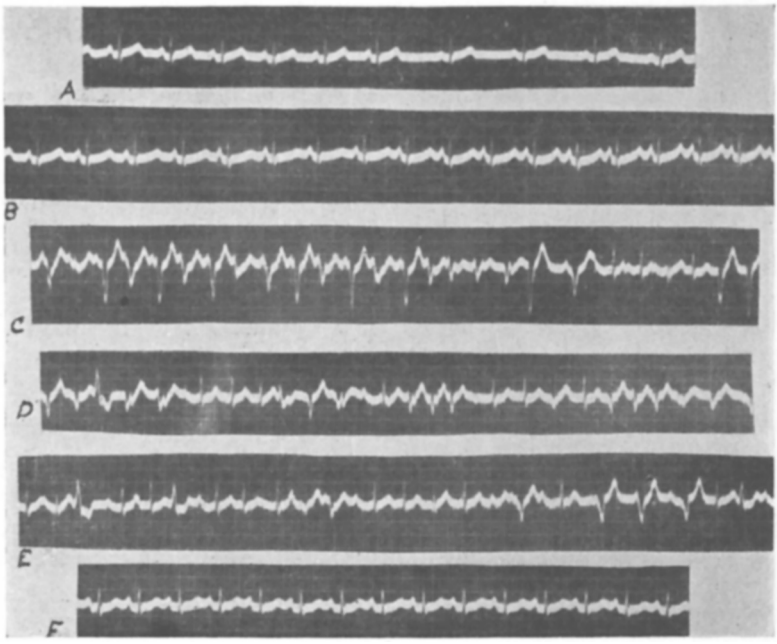

FIG. 1.

(Patient M.D.) A, lead 2, before injection of adrenalin. B, taken 30 seconds after injection of adrenalin. Lower strips taken at one-minute intervals following the injection. Note ectopic ventricular beats from multiple foci in strips C, D, and E.

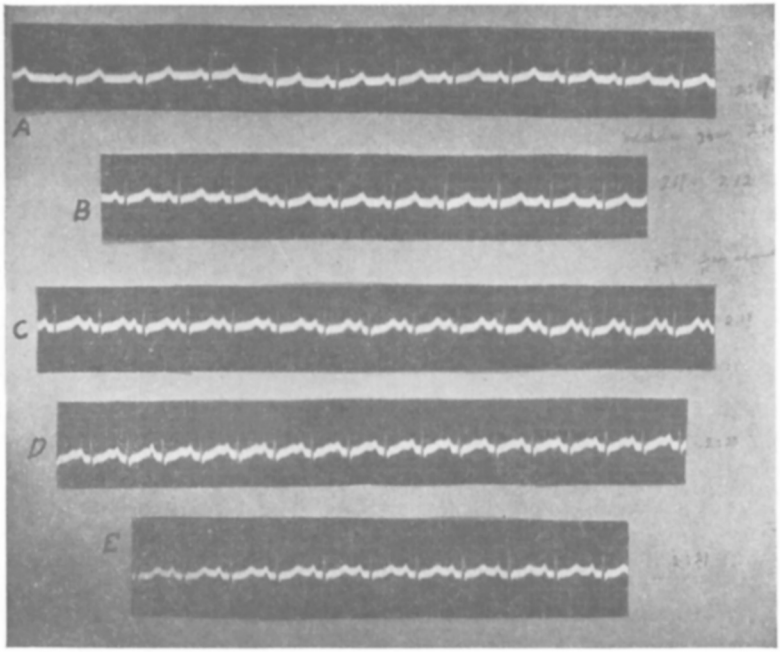

FIG. 2.

(Patient M.D.) A, lead 2, before the administration of acetyl beta methylcholin. B, taken 2 minutes after subcutaneous injection of acetyl beta methylcholin chloride, 20 mg. C, taken 2 minutes after the intravenous injection of 0.1 mg. adrenalin which was administered 6 minutes following the acetyl beta methylcholin. D and E taken 4 and 5 minutes after the adrenalin. Note complete absence of ectopic ventricular beats.

ilar to those observed with the first dose of adrenalin. In the second patient the initial rise in heart rate following the acetyl beta methylcholin changed after an interval of 5 minutes to a rate slower than that of the control period. The second dose of adrenalin was then administered 6 minutes after the acetyl beta methylcholin. There was only a slight reaction so that during the entire period of 10 minutes only 2 ventricular ectopic beats appeared. In the remaining 4 cases the second dose of adrenalin was injected 6 minutes after the acetyl beta methylcholin. In all 4 instances, adrenalin failed to induce a single ectopic ventricular beat (Fig. 2). In one case a short series of ectopic auricular beats appeared 4 minutes after the injection of the adrenalin.

Conclusion. Acetyl beta methylcholin in man tends to counteract the effect of adrenalin on the rhythmic property of the ventricles.