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Effect of Epinephrine on Experimental Ectopic Ventricular Tachycardias.* (25998)

DAVID SCHERF, DOGAN TANER AND MUHTAR YILDIZ
Dept. of Medicine, N. Y. Medical College

One is occasionally faced with the problem of a patient requiring administration of catecholamines while at the same time exhibiting ectopic cardiac rhythms. The most striking example is seen in shock accompanying acute myocardial infarction and not infrequently associated with ventricular extrasystoles or tachycardia. The investigations on action of epinephrine during chloroform anesthesia(1) as well as later reports on epinephrine-induced ventricular fibrillation while heart was under the influence of benzol, cyclopropane or halogenated hydrocarbons have warned the clinician not to use catecholamines in the course of certain ventricular arrhythmias, the danger being appearance of ventricular fibrillation. At symposium on action of catecholamines on the heart, held in Burlington, Vt., we mentioned the effects of intravenous injections of epinephrine in dogs during ventricular tachycardias(2). This is the report on these experiments.

Method. Twenty-nine dogs were anesthetized with intraperitoneal injections of Nembutal (18 mg/kg) and morphine (8 mg/kg). Morphine was given to increase vagal tonus thus preventing a sinus tachycardia interfering with ectopic rhythms. For the same reasons the vagi were left intact. Artificial respiration was instituted and the heart was exposed. The electrocardiogram was registered in lead 2. Ventricular arrhythmias were provoked by sub-epicardial injection of either 0.05 cc of a 20% solution of sodium chloride, a 3.8% solution of sodium oxalate or application of a few crystals of delphinine to the surface of one of the ventricles. Epinephrine hydrochloride was injected into the superior caval vein in the amount of 0.01 cc/kg as soon as a ventricular tachycardia with a constant rate appeared.

Results. The data from these experiments are shown in Table I. In none of these experiments did ventricular fibrillation occur after intravenous injection of epinephrine nor did epinephrine produce any of the dangerous prefibrillatory arrhythmias. In the tachycardias provoked by sodium chloride in the right ventricle the rate increased after epinephrine in 13 of 25 experiments; it remained unchanged 6 times and decreased in 6 experiments. Data from the left ventricle are similar. In 14 experiments the rate increased 10 times, it was unchanged in 2 experiments and became slower twice after intravenous injection of epinephrine. When sodium oxalate was used to create ventricular tachycardia, the rate increased after epinephrine injection 4 times, decreased once and remained unchanged 3 times. In 5 experiments epinephrine was injected during a ventricular tachycardia elicited by topical application of

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TABLE I. Ventricular Rates before and after Injection of Epinephrine.

Date	NaCl on right ventricle		NaCl on left ventricle		Delphinine on right ventricle		Sod. oxalate on right ventricle	
	Before	After	Before	After	Before	After	Before	After
9/29/59	272	300	250	275				
10/ 6			214	214				
13	230	250	220	250	187	272		
	240	250						
20					193	187		
27	214	230	206	214				
11/10	230	230	222	228			156	171
							214	214
17	214	214					187	214
24	250	250						
12/ 1	187	230						
8	187	200	250	250				
15	214	187					206	187
22	138	251						
1/ 5/60	272	276						
12	214	214					200	200
19	230	214						
26	206	214						
2/ 9	200	187	230	206				
16	200	150	214	275				
30	200	225	206	275				
3/22			175	214			138	230
29			206	250				
4/ 5	214	200						
12	187	230	230	222				
19	150	214	214	240			136	200
5/ 3	160	230						
10	230	250			200	136		
17	240	214	230	250	206	275		
24	214	214					214	214
6/14	230	230	300	300	250	300		

delphinine. The rate increased in 3 experiments and diminished in 2.

The increase of rate amounted often to a few beats per minute and only exceptionally was it remarkable (Table I). In only 4 experiments did new extrasystoles appear at the peak of epinephrine action each time originating in the ventricle opposite the one from which the tachycardia originated. In all experiments varying types of A-V heart block appeared at end of the tachycardia due to reflex vagal effects secondary to the rise of blood pressure. Tachycardias never lasted more than 2 minutes and 20 seconds and were not definitely prolonged by epinephrine. When ventricular tachycardia was suppressed by a sinus tachycardia it was possible to reestablish it temporarily by faradic vagus stimulation and inhibition of the atria.

The disappearance of experimental ectopic rhythms under the influence of epinephrine or faradic stimulation of cardiac sympathetic nerves has been reported with aconitine extrasystoles(3), in ventricular arrhythmias provoked by acetyl strophantidine(4) and it was found that in 9 out of 16 experiments epinephrine protected the heart from fibrillation provoked by electrical stimulation in presence of acetylcholine(5). A longer duration of atrial action potential because of a slower repolarisation rate under epinephrine(6) may be responsible. The dual effect of epinephrine in the present experiments, the increase and decrease of rate of tachycardia is certainly related to the complex action of the drug; vulnerability of the heart was briefly enhanced, then depressed when epinephrine or norepinephrine was given(7).

These experiments do not demonstrate the safety of use of catecholamines in presence of ventricular ectopic rhythms. While epinephrine abolishes an existing ventricular tachy-

cardia it may provoke other ectopic rhythms. It may, however, be concluded, that when catecholamines are clinically indicated, the presence of a ventricular ectopic rhythm should not be a deterrent.

Summary. Intravenous injection in the dog of epinephrine in the amount of 0.01 cc kg in presence of a ventricular ectopic tachycardia, did not elicit ventricular fibrillation in 54 attempts. The tachycardia was moderately increased in most experiments or slowed down. Only in 4 experiments did the rate rise for more than 50 beats/minute.

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Glucuronic Conjugation of Steroids in the Avian Adrenal Gland.* (25999)

W. S. NEWCOMER AND R. W. HENINGER
Department of Physiology and Pharmacology, Oklahoma State University, Stillwater

It is well established that adrenal steroids are conjugated with glucuronic acid as one phase of their inactivation prior to excretion in mammals. Furthermore, the liver is generally regarded as being the primary site of this conjugation, enzymatic control of which has been ascribed to 2 enzymatic systems: UDPG dehydrogenase (in particle-free fraction) (1, 2) and a glucuronosyl transferase (in microsomes) (3,4,5).

During another study, evidence was obtained indicating that a considerable portion of total steroid content of the avian adrenal tissue was in a bound form—conjugated with both glucuronide and sulfate (6). This report presents data which support the previous finding by demonstrating that the avian adrenal gland possesses the enzymatic systems responsible for both conjugation of adrenal steroids with glucuronide and hydrolysis of glucuronide-bound steroids.

Methods. The adrenal glands used to measure glucuronide formation were obtained by dissection from 3-4 month old White Leghorn cockerels immediately after decapitation, weighed and homogenized in ice-cold Krebs-Ringer-PO_4 buffer (pH 7.4) with a Potter-Elvehjem homogenizer.

Replicate fractions of the homogenate were incubated in Warburg flasks at 37°C for 2.5 hours with one of the following steroids† as a substrate: 11-dehydro-17-hydroxycorticosterone (E, cortisone), 17-hydroxycorticosterone (F, cortisol), pregnane-3α,17α,21-triol-11,20-dione (H_4E, tetrahydrocortisone), or pregnane-3α,11β,17α,21-tetrol-20-one (H_4F, tetrahydrocortisol). Each flask contained: 0.5 ml uridine diphospho-glucuronic acid (UDPGA) (100 γ ml); 2.0 ml homogenate (equivalent to 80-100 mg wet tissue); 1.0 ml steroid (100 γ ml $\cong$ .27 μmoles; and 4.5 ml Krebs-Ringer-PO_4 buffer containing 90 mg glucose/ml, making a total volume of 8 ml.

Prior to incubation of the homogenate with substrate, 4 ml was removed from each flask and boiled to inactivate enzymes. These 4 ml portions were left at room temperature to function as unincubated controls.

After incubation, the flasks were placed in boiling water to inactivate enzymes. Both incubated and nonincubated control samples were then extracted 3 times with methylene

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