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Electrocardiographic Changes Preceding Catecholamine-Induced Arrhythmias.* (28424)

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A lengthening of the QT interval of the electrocardiogram preceding onset of ventricular fibrillation was reported by Chenoweth during a study of epinephrine-hydrocarbon syncope(1). The increase in the QT interval was observed in tracings in which there was a regular unifocal beat before the development of fibrillation. Since epinephrine by itself may increase the QT interval(2), the present study was undertaken to determine the significance of this electrocardiographic change prior to onset of experimental ventricular arrhythmias. In animals treated with hydrocarbons relatively small doses of epinephrine or norepinephrine may precipitate ventricular fibrillation while isoproterenol causes only cardioacceleration(3). The changes in the QT interval produced by these catecholamines were therefore compared in animals predisposed to arrhythmias by administration of petroleum ether.

Methods. Lead II of the electrocardiogram was recorded in 20 cats anesthetized with sodium pentobarbital (30 mg/kg). Control responses to intravenous injection of 5-10 μg/kg epinephrine, norepinephrine or isoproterenol were first observed. Ventricular arrhythmias were induced 15 minutes later using the method of Garb and Chenoweth(3) in which 0.1 ml/kg petroleum ether (B.P. 30-60°C) was injected through an endotracheal tube and the same dose of catecholamine was repeated 30 seconds later. Episodes of epinephrine-induced ventricular arrhythmias are usually transient in cats under pentobarbital anesthesia(4). It was therefore possible to repeat the injections of petroleum ether and catecholamines in most animals.

The PR, QRS, and QT intervals were measured during the various phases of the experiments. Because of the inverse relationship between the duration of the QT interval and the heart rate in various metabolic states (5), the ratios of these intervals to the corresponding cardiac cycle lengths were calculated.

Results. Epinephrine caused a progressive lengthening of the QT interval after injection of petroleum ether and prior to the onset of ventricular tachycardia and fibrillation (Fig. 1). This prolongation of the QT interval was not observed after epinephrine during the initial control period.

Norepinephrine and epinephrine produced similar changes in the electrocardiogram after petroleum ether. In the tracings showing multiple focal ventricular tachycardia or fibrillation after petroleum ether and epinephrine, there was a 28% increase in the QT interval compared to that produced by norepinephrine in the animals in which a regular sinus rhythm was maintained. However, the same dose of isoproterenol injected 30 seconds after petroleum ether did not produce any

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TABLE I. Electrocardiographic Changes in Cats Under Pentobarbital Anesthesia After Petroleum Ether (PE) and Epinephrine (EPI).

	PR interval cycle length	QRS complex cycle length	QT interval cycle length
	$\bar{x} \pm s_x$	$\bar{x} \pm s_x$	$\bar{x} \pm s_x$
Control	.20 ± .01	.09 ± .005	.49 ± .01
PE	.20 ± .01	.08 ± .004	.48 ± .01
EPI	.23 ± .01	.09 ± .007	.52 ± .02
PE and EPI (no multifocal activity)	.25 ± .01	.08 ± .005	.51 ± .01
PE and EPI (multifocal activity)	.21 ± .02	.12 ± .012	.64 ± .02*

* $p < .01$.

significant changes in the length of the QT interval. In 6 animals injected with isoproternol after petroleum ether, there was a 4% decrease in the QT interval. The isoproterenol-hydrocarbon combination also failed to produce ventricular arrhythmias.

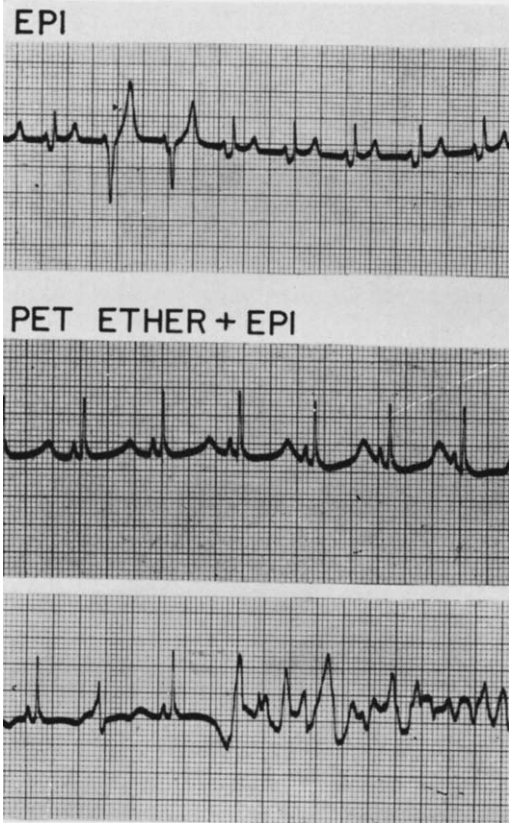

FIG. 1. Electrocardiographic changes caused by 5 μg/kg epinephrine in cats under pentobarbital. Upper record: Epinephrine alone caused only isolated ventricular extrasystoles. Middle and lower records: Epinephrine after petroleum ether caused a progressive increase in QT interval and ventricular fibrillation.

Because of the positive correlation between the duration of the QT interval and the cardiac cycle length previously reported(5), the results obtained after injection of petroleum ether and epinephrine were recorded in terms of the QT/RR ratio (Table I). A slight increase in QT interval in relation to cardiac cycle length was observed after administration of epinephrine and petroleum ether in the animals which failed to develop ventricular arrhythmias. This change was similar to that produced by epinephrine during the control period before the administration of petroleum ether. On the other hand, the mean increase in the QT/RR ratio caused by epinephrine before the onset of multiple focal ventricular tachycardia and fibrillation was significantly greater than that caused by epinephrine in the absence of arrhythmias ($p < 0.01$). Although the duration of the QRS complex was somewhat longer prior to ventricular arrhythmias than in the presence of a regular sinus rhythm, this increase in the length of the QRS did not explain the prolonged QT interval observed in these experiments. The prolonged QT interval before the development of the ventricular arrhythmias was primarily due to a lengthening of the ST segment (Fig. 1).

A small but significant increase in the PR interval was observed after epinephrine and petroleum ether in the animals which maintained a regular sinus rhythm. However, this increase in the duration of PR interval was not significantly different from that produced by epinephrine during the control period.

Discussion. The electrocardiographic changes preceding experimental ventricular arrhythmias have also been studied by Fas-

tier(6) who observed a fusion of the QRS of an ectopic complex with the T wave of the preceding beat at the onset of ventricular fibrillation. In the present study this simultaneous occurrence of a QRS with the preceding T wave has also been identified before experimental ventricular fibrillation. However, in addition there was the accompanying increase in the duration of the QT interval prior to the onset of the ventricular arrhythmias. These electrocardiographic changes gave a picture suggesting a delay in the repolarization processes of the ventricular myocardium after petroleum ether and epinephrine. Thus, the entrance of an impulse initiated by epinephrine from an ectopic focus into the remaining myocardium at a time when the ventricles were vulnerable to fibrillation appeared to be an important factor in the precipitation of ventricular fibrillation by these agents.

Taken together these observations suggested that petroleum ether and epinephrine increase the vulnerability of the ventricles to fibrillation by inhibiting the biochemical processes responsible for the repolarization of the ventricular myocardium. In support of this view was the observation that isoproterenol did not increase the QT interval after petroleum ether, and this catecholamine also failed to precipitate ventricular arrhythmias in these preparations.

Summary. An increase in the QT interval and the QT/RR ratio was observed prior to the onset of multiple focal ventricular tachycardia and fibrillation induced by petroleum ether and epinephrine or norepinephrine in cats under pentobarbital anesthesia. This prolongation of the QT interval before experimental ventricular tachycardia and fibrillation was significantly greater than that produced by these catecholamines in the absence of arrhythmias. Isoproterenol, which did not lead to ventricular tachycardia after petroleum ether, also failed to increase the duration of the QT interval. The appearance of the electrocardiogram preceding these experimental arrhythmias suggested that a delay in the repolarization of the myocardium was a factor in the precipitation of ventricular fibrillation during hydrocarbon-catecholamine syncope.

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Effect of *Salmonella typhosa* Endotoxin on Perfused Dog Spleen.* (28425)

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Changes in calculated vascular resistance following injection of endotoxin in various vascular beds perfused at constant blood flow have been reported(1-7). The forelimb(1), lung(3), stomach(5), and kidney(6) demonstrated increased resistance while the coronary vasculature(4) responded with a decrease. Earlier reports suggested that the immediate systemic hypotension following lethal doses of endotoxin resulted from hepatic and intestinal congestion(2,7). Hepatic venoconstriction and engorgement are of short duration; however, intestinal pooling persists(2, 7). Even though the gastric and intestinal circulations are contiguous, the responses of the veins to endotoxin are apparently dissimilar. The stomach behaves more like the

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