peak concentration in plasma, when rate of release of the hormone presumably reached equilibrium with its rate of removal or inactivation. In view of reported instances of dissociation between the 2 phenomena, the observed temporal relationship should be interpreted with caution.

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Actual Length of Diastasis for Regurgitation through Normal Mitral Valve; Cinefluorographic Demonstration. (25925)

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Regurgitation of blood can occur through a normal mitral valve. This has been demonstrated by: Hayden, *et al.*(1) utilizing isotope dilution; Friedman *et al.*(2) recording blood impedance changes after injecting sodium chloride; Wiggers(3) and Little(4), in measuring changes in pressure curves; and by Daley, *et al.*(5), using Evans blue in hearts with auricular fibrillation. Paul(6) has recorded this phenomenon by cinefluorography using opaque contrast in dogs with a slowed heart rate. The present study was undertaken as a further elaboration of Paul's work to determine the minimum length of diastasis to permit minimal regurgitation.

Method. Mongrel dogs, weighing 6.8-20.4 kg were anesthetized with sodium pentobarbital (35 mg/kg, *i.v.*). A No. 6 French whistle-tipped catheter was introduced *via* a thoracotomy incision into the left atrium through the auricular appendage and brought out through a stab wound in the chest. Pericardium and chest wall were closed, lung was fully expanded, and spontaneous respiration permitted to reappear. Two catheters (Nos. 6 F and 10 F) were then introduced into the left ventricle *via* the 2 common carotid arteries. The No. 6 F catheters in the left atrium and ventricle were attached to previously balanced strain gauges and pressures recorded simultaneously on a multichannel recorder. These pressures were subsequently used to measure period of diastasis (Fig. 1). After the heart was slowed by stimulation of the left vagus (tied off proximally) contrast material was rapidly injected into the left ventricle *via* the No. 10 F catheter. The opaque medium was visualized by means of a Philips fluoroscopic image intensifier(7,8) and

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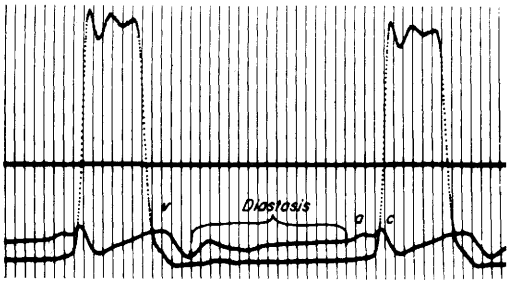

FIG. 1. Pressures from left ventricle and left atrium were recorded simultaneously to measure duration of diastasis. Time interval equals 0.04 sec.

recorded on 16 mm film with a Bell and Howell camera at 64 frames per sec. All dogs were in the supine position and a horizontal X-ray beam was used. Contrast material utilized was 60, 70, or 90% sodium methylglucamine diatrizoate, 70% sodium diprotrizoate or 70% sodium acetrizoate. The dose varied from 1 to 2 ml/kg. Location of the mitral valve was determined by its known relationship to the fat pad in the left atrio-ventricular sulcus and to the opacified left circumflex coronary artery. Contrast material posterior to these structures indicated presence of mitral regurgitation.

Results. A total of 270 injections were made in 18 dogs and diastolic regurgitation

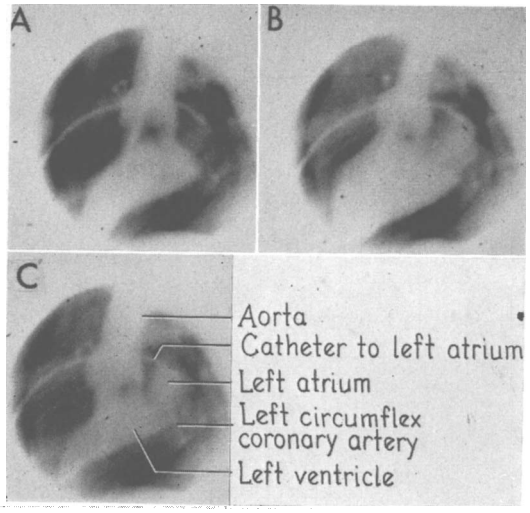

FIG. 2. Selected frames from cinefluorographic study show diastolic regurgitation with slowed heart rate: (A) control, no regurgitation; (B) mitral regurgitation with prolonged diastasis due to slowed heart; (C) subsequent ventricular systole.

was observed in all animals in which there was sufficient prolongation of diastasis (Fig. 2). There is a critical duration of diastasis for regurgitation to occur. No regurgitation occurred when duration of diastasis was shorter than this period, but was always present when diastasis was longer than this critical interval (Table I). Amount of regurgitation increased directly with prolongation of this diastolic period. The average length of diastasis for minimal regurgitation was found to be 0.39 sec. (Table II). This value varied from 0.22-0.60 sec. but a fairly constant time was found for each animal.

TABLE I. Examples of Successive Recordings during the Production of Minimal Diastolic Regurgitation.

Dog #18		Dog #12	
Diastasis (sec.)	Regurgitation	Diastasis (sec.)	Regurgitation
.01	None	.01	None
.44	"	.16	"
.18	"	.32	"
.44	1+	.78	2+
.66	"	.70	1+
.42	None	.68	"
.50	1+	.60	"
.70	"	.48	"
.52	None	.38	None
.50	"	.40	1+
		.38	None
		.38	1+
		.32	None
		.34	"
		.28	"
		.88	2+

1+ = Barely perceptible with motion.
2+ = Definite regurgitation in single frame.

When the No. 10 F catheter was coiled in the left ventricle, or pushed as far as possible against the apex, or deliberately placed through the mitral valve into the left atrium no regurgitation appeared until heart rate was slowed. Similar results were obtained in 10 different dogs after both catheters were removed from the left ventricle and injection was made directly through a needle in the left ventricle.

Systolic regurgitation was seen in 4 out of 18 dogs. This occurred throughout the study and was independent of heart rate. With a slow heart rate and consequent prolongation of the diastasis, diastolic regurgitation also occurred. These dogs were subsequently

TABLE II. Total Series in Production of Minimal Regurgitation through Normal Mitral Valve by Prolonging Diastasis in 11 Dogs.

No. of inj.	Length of diastasis in sec. at which min regurgitation appeared	No. of inj.	Length of diastasis in sec. at which min regurgitation appeared
14	.34	*22	.22
*21	.46	18	.38
19	.28	18	.32
19	.48	17	.32
9	.60	15	.44
16	.42		
		Avg	.39

* Had minimal regurgitation with diastasis of 0.1 sec. with several inj., but could not be reproduced.

found at autopsy to have hemorrhagic mitral valves.

Discussion. The mechanism of mitral regurgitation through a normal valve has been discussed(6,9,10). This phenomenon of regurgitation can readily be recorded with the cinefluorographic technic by slowing heart rate and thus prolonging diastasis beyond a critical point.

Actual determination of this critical time interval was subject to certain limitations. Vagal stimulation often produced an irregular slowing of the heart, making it difficult to reproduce the same rate. Injections of contrast material were made by hand. These varied in speed and force, and were performed during different phases of the cardiac cycle. These factors resulted in considerable variation of amount of contrast material within the left ventricle at any one time. One dog had an irregular auricular rhythm making measurement of the periods of diastasis uncertain. There is a definite subjective element present in interpretation of "minimal" regurgitation.

Thus the average duration of diastasis for minimal regurgitation was found to be 0.39 sec., but because of the above noted limitations, considerable variations from 0.22-0.60 sec. were obtained.

Summary. Diastolic regurgitation of opaque contrast material can occur through normal mitral valve when the period of diastasis exceeds a specific time interval. This period of diastasis in dogs varies from 0.22 to 0.60 second, average of 0.39 second. When diastasis is shorter than this interval no regurgitation occurs, but it always occurs when prolonged beyond the critical period.

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