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Relation Between Cardiac Size and Cardiac Output Per Minute Following Administration of Digitalis.

A. E. COHN AND H. J. STEWART.

From the Hospital of the Rockefeller Institute, New York City.

Recently Harrison and Leonard[1] have studied the effect of injecting digitalis upon the cardiac output in normal dogs, and found that it diminished. From these experiments they drew the inference that digitalis decreased cardiac output also in patients suffering from heart failure and that its beneficial effect in them was due to this action. It seemed to us that this inference was not justified unless the effect of digitalis upon the size of the heart was also studied.

In making our experiments in dogs the cardiac output was estimated according to the Fick[2] principle. Samples of arterial blood were taken from a femoral artery and those of mixed venous blood from the right ventricle by means of a special cannula inserted into that chamber through the right external jugular vein.[3] The oxygen consumption was measured with a Benedict spirometer equipped with a graphic recording drum. All the dogs were trained in order to accustom them to these procedures.

Tincture of digitalis (Upsher Smith) was injected intravenously. We injected 25 to 30% of the calculated lethal dose for cats which has been regarded as equivalent to the therapeutic dose in man.[4] This dose is multiplied by 1.16 to arrive at a comparable quantity for dogs.[5] Roentgenograms were taken whenever the cardiac output was measured.

TABLE 1.

Effect of injection of digitalis in dogs in respect to cardiac output and cardiac size.

Dog Wgt.	Time with reference to digitalis injection	Cardiac output	Cardiac output, % of initial	Heart area	Heart area % of initial	Digitalis
Kg.		cc. per minute	%	sq. cm.	%	cc.
12.5	Before	4285	100	43.6	100	3.0
	2 hrs. after	2344	55	35.7	82	
	1 day after	2627	61	38.6	89	
	5 days after	4823	112	42.3	99	
14.8	Before	4066	100	44.7	100	3.3
	2 hrs. after	2193	54	35.7	80	
	1 day after	2592	64	37.2	83	
	5 days after	3267	80	41.8	94	

In Table I are shown data from experiments in 2 dogs. These are typical of all our results. There was a decrease in cardiac output after the administration of digitalis with a return toward normal in 5 days. There were also decreases in the size of the heart. These changes in the size of the heart paralleled the changes in cardiac output, that is to say, with decrease in output there was decrease in size. This result is the same as that found by Harrison and Leonard so far as cardiac output is concerned. We injected digifolin in one of our experiments in order to make our results comparable with theirs. The decrease in cardiac output and size of heart was always present 2 hours after the administration of digitalis and occurred irrespective of the heart rate which was sometimes increased and sometimes decreased.

The per cent decreases in cardiac output are greater than the per cent decreases in heart area. This is, of course, expected for the output is a cubic while the area is a square measurement.

We conclude that there is close correlation between volume output and cardiac size in the same dog. When the output decreases this results from the effect of digitalis on the dimensions of the heart, in this case the dimension in the frontal plane. In patients with heart failure a similar comparison between size and output should be instituted; but in this case the relation of length of cardiac muscle fiber to optimum length must no doubt be taken into consideration.

[1] Harrison, T. R., and Leonard, B. W., *J. Clin. Invest.*, 1926, iii, 1.

[2] Fick, A., *Verhandl. physik.-med. Ges. Würzburg.* 1870.

[3] Stewart, H. J., *J. Biol. Chem.*, 1925, lxii, 641.

[4] Robinson, G. C., and Wilson, F. N., *J. Pharmacol. and Exp. Therap.*, 1918, x, 491.

[5] Cohn, A. E., unpublished experiments.

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Physiological Action of Cyanide on Protoplasm.

FLOYD J. BRINLEY.* (Introduced by J. H. Bodine.)

From the Zoological Laboratory, University of Pennsylvania.

Since it is known that hydrogen cyanide passes through living membranes very rapidly,[1] it was thought desirable to ascertain whether the toxicity of cyanide is due to its action on the internal

* National Research Fellow in Biological Sciences.