TABLE III.
Effect of Eserine on Pulse Rate of Rats.*

No.	Wt in g	Pulse rate/min. Before	Pulse rate/min. 30' after es.
1	250	324	321
2	210	345	336
3	230	372	388
4	280	480	479

* Eserine sulfate (1 mg/kg) was injected subcutaneously and the effect on the pulse was determined by recording the EKG with an Offner oscillograph.

that eserine directly sensitizes the brain substance to electroshock, quite apart from changes in reactivity resulting from circulatory effects.

There seems to be no good evidence to relate the age dependent susceptibility of rats to convulsions to the water content of the brain (Yannet and Darrow[12]). Donaldson[13] notes that the water content of the brain of the albino rat although declining from the 1st to the 50th day remains constant from there on to the age of 300 days and that no variation occurs in Norway rats varying in weight between 195 and 460 g. However our experiments show clearly that within these ranges of age and weight convulsive reactivity changes greatly.

Finally attention is called to the fact that the excitability of the sympathetic centers declines with increasing age (Safford and Gellhorn[14]). The relation of this fact to the topic of the present paper remains to be determined.

Summary. Experiments on rats varying in age between 4 weeks and more than 1½ years show that the incidence and severity of convulsions induced by application of an electrical current to the head declines with increasing age. This decline is not confined to the period preceding sexual maturity. Comparison of adult rats of different age but similar weight shows that the susceptibility to convulsions is related to age and not solely to weight. Furthermore it is shown that eserine administered subcutaneously increases the susceptibility to electrically induced convulsions without altering the circulation.

12 Yannet, H., and Darrow, D. C., *J. Biol. Chem.*, 1938, **123**, 295.

13 Donaldson, H. H., *The rat, Memoirs of the Wistar Inst. of Anat. and Biol., No. 6, Philadelphia*, 1924.

14 Safford, H., and Gellhorn, E., PROC. SOC. EXP. BIOL. AND MED., 1945, **60**, 98.

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A Comparison of Cardiac Outputs, Determined by Direct Fick and Pressure Pulse Methods.

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A method of determining cardiac output that is more rapid than the standard procedures, and with less dependence on skilled technical help has long been needed. With the publication by Hamilton and Remington[1] of a method for determining stroke volume from a pressure pulse this need has been met if their results are reproducible by others. In addition, their method has the added advantage, for the pharmacologist, of being able to follow the actions of a drug on the output from stroke to stroke.

Using the dye method as their basis of comparison, they found a correlation of $r = +0.994$ with an average variation between the two measurements of $\pm 8.2\%$

1 Hamilton, W. F., and Remington, J. W., *Am. J. Physiol.*, 1947, **148**, 14.

TABLE I.
Comparison of Cardiac Output by Direct Fick and Pressure Pulse Methods.

Dog	Procedure	Direct Fick*	Pressure pulses*	% difference
D.F. 2	Aranthol, 5 mg/kg	2,500	3,000	+20
D.F. 3	Priscol, 1 mg/kg	1,550	1,524	— 1.6
	Oenethyl, 5 mg/kg	3,120	3,400	+ 8.1
D.F. 4	Priscol, 1 mg/kg	2,300	2,567	+11.6
D.F. 5	Normal	5,350	4,520	—15.5
	Hemorrhage	3,950	3,400	—13.9
D.F. 6	Normal	2,910	2,477	—14.8
	Hemorrhage	1,210	1,489	+23.0
D.F. 7	Hemorrhage	2,300	1,950	—15.2
	"	1,350	1,145	—15.1
D.F. 8	Normal	1,350	1,306	— 3.2
	Aranthol, 10 mg/kg	4,810	4,262	—11.3
	½ hr after	1,620	1,661	+ 2.5
D.F. 9	Normal	2,160	1,944	—10.0
	Priscol, 1 mg/kg	2,300	2,700	+17.4

* cc/min.

with a range of +35 to —13%. While the dye method has been shown to give comparable to the Fick method[2] within ± 10%, it seemed essential that a comparison be made between the Fick and the pressure pulse method not only to compare the accuracy of the pressure pulse method but to check our own calculations of cardiac output by that method.

Methods. A total of 8 dogs were used and 15 outputs were determined under a variety of conditions. The dogs were anesthetized with sodium barbital 300 mg/kg administered orally or intraperitoneally. Pressure pulses were obtained by means of a Hamilton manometer[3] of adequate frequency. A No. 9 ureteral catheter was passed down the right jugular to the right ventricle and the position verified by fluoroscopy. A slow, heparinized saline drip was maintained through the catheter. Oxygen consumption was measured by connecting the dog to a McKesson Recording Metabolor, with a tracheal cannula. Blood samples were taken under oil simultaneously from the right ventricle and a femoral artery and promptly iced. Oxygen was determined by the method of Van Slyke and Neill.[4] Pressure pulses were recorded simultaneously with the blood samples. Under certain circumstances marked arrhythmia and a variety of pulse forms occurred. Depending on the frequency, some of each type were calculated and an average figure was obtained.

It was thought desirable to have as wide a range of outputs as possible. This was accomplished by hemorrhaging and the use of the following drugs: 2-methylamino heptane (Oenethyl), 2-methylamino-6-hydroxy-6-methyl heptane (Aranthol), and benzyl-imidazoline hydrochloride (Priscol).* By these means heart rates from 80-260 per minute, systolic pressures from 95-352 and diastolic from 65-220 mm Hg were obtained. The data given by Hamilton and Remington for diastolic pressures does not extend to 220 mm Hg; in this case we extrapolated

[2] Moore, J. W., Kinsman, J. M., Hamilton, W. F., and Spurling, R. G., *Am. J. Physiol.*, 1929, **89**, 331.

[3] Hamilton, W. F., Brewer, G., and Brotman, I., *Am. J. Physiol.*, 1934, **107**, 427.

[4] Van Slyke, D. D., and Neill, J. M., *J. Biol. Chem.*, 1941, **138**, 535.

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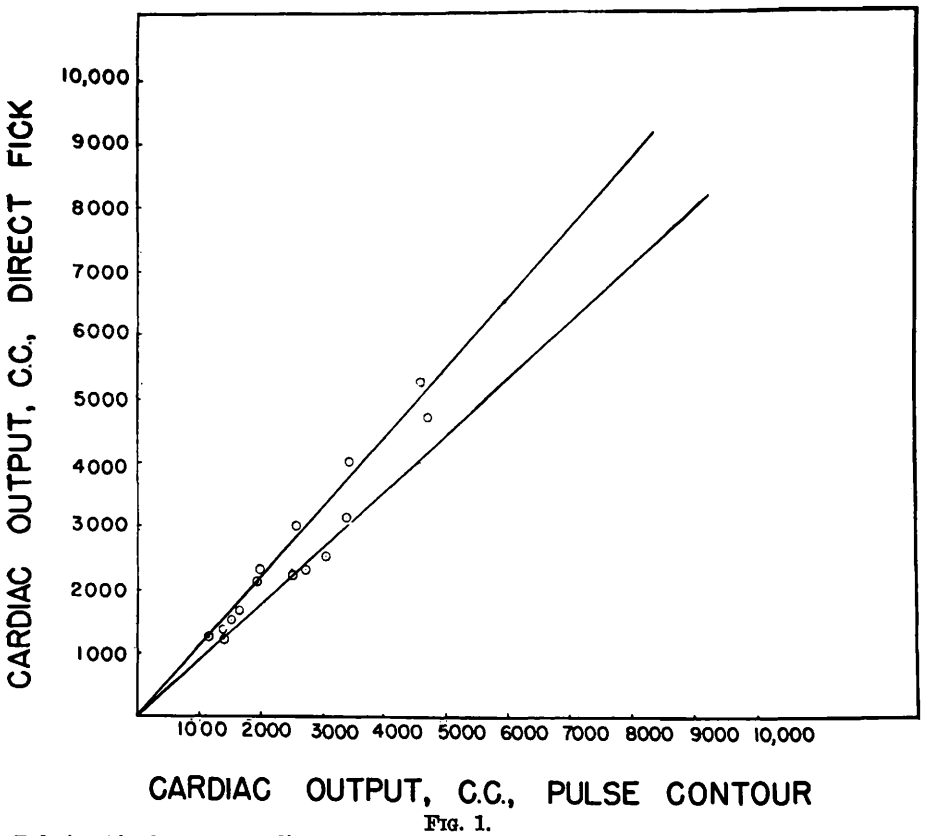

FIG. 1.

Relationship between cardiac output determined simultaneously by the direct Fick and pressure pulse methods. The lines represent a deviation of ±10% from a perfect correlation.

with satisfactory results.

Results and Conclusions. The determination of cardiac output by the pressure pulse method agrees well with the direct Fick method. The average variation between the 2 measurements is ±12.2% with a range from ±23% to —15.5%. The coefficient of correlation, corrected for small samples, is r = + 0.936. Directional changes in cardiac output can be conveniently followed by the pressure pulse method.