Fish with bradycardia (4.3/min) paced electrically 12-36/min.

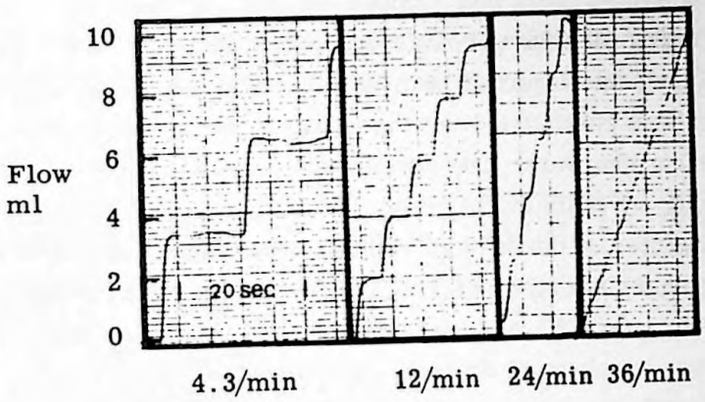
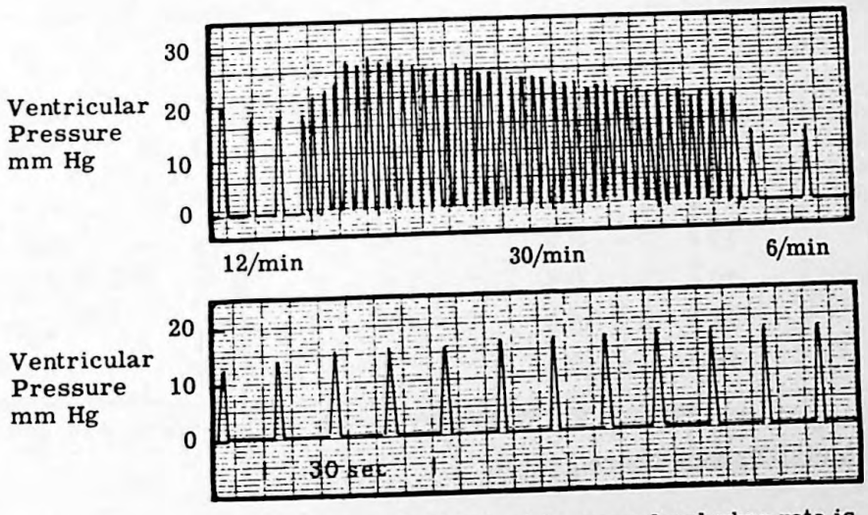


Figure 8



The pressure stabilizes at the same level when rate is changed by pacing.

Figure 9

Most hearts would not pace above 40 per minute. Over a wide range of $\dot{Q}_B$, aortic pressure was relatively constant, suggesting strong neural control mechanisms (Figure 9).

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1967 #30

EFFECTS OF TRICAINE METHANESULPHONATE (MS 222) ON THE CIRCULATION OF *Squalus acanthias*

E. Converse Peirce II, Esther M. Peirce, and Edmund C. Peirce III, Emory University School of Medicine, Atlanta, Ga.

MS 222 (tricaine methanesulphonate, Sandoz) is recommended for the immobilization of cold blooded animals, but has been found to reduce cardiac output ($\dot{Q}_B$) in *Squalus acanthias*, as shown by changes in cardiac green dye curves (Murdaugh, V. and Robin, E. D., oral communication

1967). It was felt that it would be useful to measure $\dot{Q}_B$ directly using the methods described in the last abstract.

Seven experiments using MS 222 were carried out in fish 1.4 to 3.5 kg. In three experiments, 30 mg/kg of the drug was injected into the dorsal aorta while a flow of fresh sea water greater than 1 L/kg/min was continued over the gills. In other experiments MS 222 was added to 20 liters of recirculating sea water, the concentration being either 1:50,000 or 1:20,000 (2 each). Abrupt gill washout, by changing to fresh sea water, was generally started at one hour. In some experiments, samples of dorsal and ventral aortic blood and sea water were analyzed for MS 222 by Vincent Stenger courtesy of Thomas Maren by their usual method. Dorsal aortic pressure (DAP), stroke volume (SV), $\dot{Q}_B$, arterial pH (pH_A), pCO_2, non-carbonic acid level (NCA), and hematocrit were measured directly or calculated.

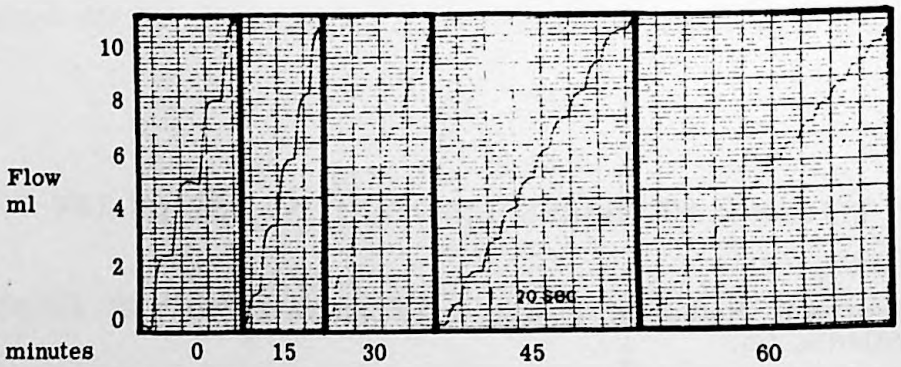
In each instance MS 222 resulted in a drop in SV, $\dot{Q}_B$, and DAP. For the single dorsal aortic injections, this was surprisingly large. Table 1 gives data from one such experiment.

Table 1

Time min	Rate	$\dot{Q}_B$ L/Kg/hr	SV ml	DAP mm Hg	MS 222 A/V μg/ml*
Control	19	0.9	2.6	12/18	
5	19	0.9	2.6	18/16	10.8/30.0
10	20	0.5	1.5	17/14	10.0/31.7
15	21	0.3	0.9	15/13	14.6/41.3
35	20	0.4	1.2	16/14	14.6/33.3

100 mg MS 222 (30 mg/Kg) injected into the dorsal aorta at 0 time.
*Arterial/Venous concentration.

At one hour, exposure to MS 222 1:50,000 in sea water caused moderate hemodynamic changes. In one experiment there was an increase in heart rate (15 to 20), a drop in SV (2.9 to 0.7 ml), and a drop in $\dot{Q}_B$ (1.8 to 0.6 L/kg/hr) (Figure 1). The arterial level of MS 222 was almost twice that of recirculating sea water at 60 min but fell rapidly on washout with fresh sea water was reported by Maren, Embry and Broder (Bull. M.D.I.B.L. 6-24:25-28, 1966).



Time minutes	0	15	30	45	60
Stroke Volume ml	2.9	2.4	1.7	1.2	0.7
$\dot{Q}_B$ L/kg/hr	1.8	1.9	1.7	0.9	0.6

Figure 1

When the sea water concentration of MS 222 was increased to 1:20,000 hemodynamic deterioration was evident in 5 minutes. $\dot{Q}_B$ fell profoundly and progressively (Table 2). There was cessation of opercular motion within a few minutes. Good recovery occurred in one fish held for 20 minutes but was limited in one held for 60 minutes (Figure 2, Table 2).

Table 2

#	Wt. Kg.	Time min	Rate	SV ml	DAP mm Hg	$\dot{Q}_B$ L/Kg/hr
25	1.6	Control	16	2.3	22/17	1.4
		20	15	0.4	9/7	0.3
26	3.0	Control	15	3.5	18/14	1.1
		30	21	0.3	11/9	0.1
		60	16	0.2	7/6	0.06

MS 222 to give a concentration of 1:20,000 added to sea water at 0 time.

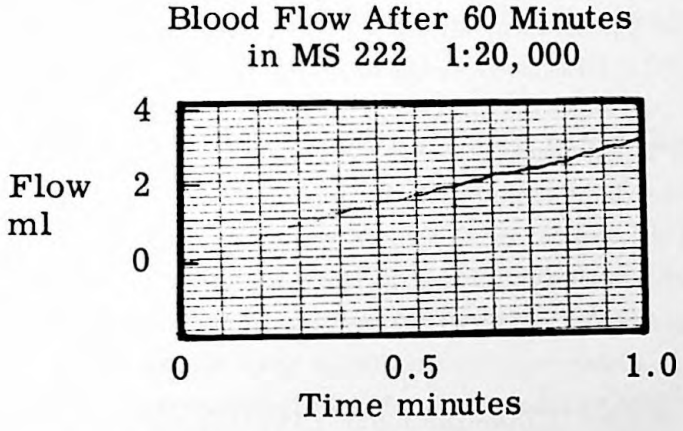


Figure 2

A surprise was a gradual decrease in the level of NCA and a decrease in pCO_2 even while cardiac output was markedly depressed. The data in Table 3 are for the experiment shown in Table 1 and are representative. They suggest that NCA may be eliminated via the gills.

Table 3

Time min	Arterial pH	pCO_2 mm Hg	NCA mEq/L
Control	7.47	5.1	3.5
60	7.60	4.4	1.5
120	7.66	4.2	0.7

MS 222 in usual dosages depresses cardiac function of Squalus acanthias markedly. At such levels it becomes unsuitable as an immobilizing agent in cardiovascular and metabolic research. The arterial levels quickly climb above that of the immersing sea water.

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