dogfish heart is highly sensitive to $[Ca]_o$ and to the duration of the action potential. There appeared to be no internal releasable stores of Ca^{2+} as demonstrated by the lack of post-extrasystolic potentiation, post-clamp potentiation, and the lack of a phasic component of tension during long voltage clamp steps. These findings are consistent with the ultrastructural findings that peripheral couplings and the SR are poorly developed and the t-tubular system is absent. The relation between structure and function in the shark heart is similar to that of the frog heart supporting the hypothesis of Morad & Goldman (Prog. Biophys. & Molec. Biol., 27:257-313, 1973), that in the absence of peripheral couplings and t-tubular system the heart cells rely primarily on the electrical activity of the surface membrane to transport the activator Ca^{2+} from an external source and thus to directly control contraction.

INOTROPIC EFFECTS OF ADRENALINE IN DOGFISH HEART (SQUALUS ACANTHIAS)

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In amphibian and mammalian hearts epinephrine markedly potentiates tension and suppresses contracture tension (Kavaler & Morad, Circ. Res. 18:492-501, 1966; Morad & Rolett, J. Physiol. 224:537-558, 1972). In the dogfish heart catecholamines are thought to have little or no positive inotropic effect. In the experiments to be described below the positive and the relaxant effects of adrenaline on the isolated ventricular trabeculae were studied. Adrenaline was found to have both a positive inotropic and a relaxant effect on the ventricular trabeculae in a manner quite similar to mammalian and amphibian hearts.

Positive inotropic effect at various $[Ca]_o$. Figure 1 shows the effect of adrenaline on a ventricular strip bathed in solutions containing three different Ca^{2+} concentrations. The upper left panel of Figure 1 shows that adrenaline markedly potentiates tension and prolongs the duration of developed tension when added to a strip bathed in 1 mM Ca^{2+} containing shark Ringers in mMole/l (NaCl 280, Kcl 6, $MgCl_2$ 3, Na_2So_4 0.5, NaH_2PO_4 1, urea 350, $NaHCO_3$ 8, glucose 5, at pH 7.4). As the rate of rise of tension increases the peak tension is potentiated and prolonged. Addition

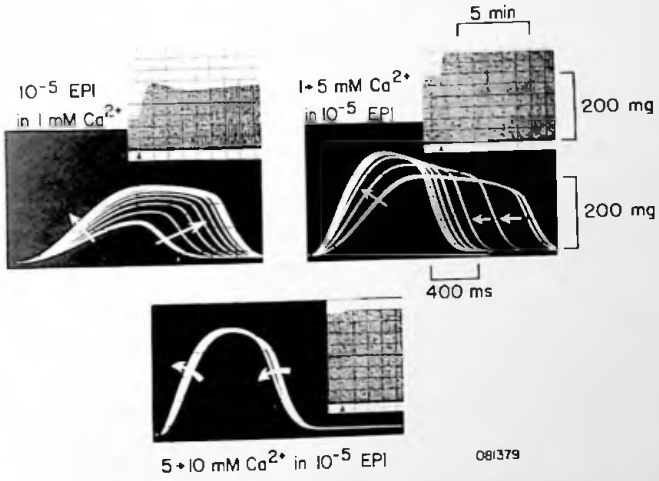

Figure 1. Effect of 10^{-5} g/L of epinephrine on contractility. Each panel shows continuous recording of tension at a fast sweep speed to observe the change in dP/dt (rate of tension development) and the duration of developed tension as indicated by the direction of the arrows. The inset in each panel shows the time course of action on peak tension at a slow chart speed. Addition of epinephrine in 1 mM Ca^{2+} Ringers produced a marked potentiation of twitch tension (left panel) by increasing dP/dt and duration of developed tension. Increasing the Ca^{2+} from 1 mM to 5 mM (right panel) and 5 mM to 10 mM (lower panel) in the presence of epinephrine further potentiated twitch tension by increased dP/dt but the duration of developed tension decreased. This effect was most dramatic when the Ca^{2+} was changed from 1 mM to 5 mM.

of Ca^{2+} shortens the action potential which in turn terminates the development of tension. Thus the positive inotropic effect of adrenaline seems to be related to the $[Ca]_o$. If developed tension is potentiated by high concentrations of Ca^{2+}, ephinephrine will have little or no effect on contraction. Since shark Ringers contains at least 5 mM Ca^{2+}, it is not surprising that epinephrine will demonstrate little or no positive inotropic effect on the heart.

Relaxant effect of epinephrine. KCl-induced contractures have been used as a measure of the ability of the ability of the ventricular muscle to handle states of Ca^{2+} overload. To induce rapid depolarization 350 mM of urea was isotonically replaced with KCl. Tension development in response to KCl-depolarization was often 50-100% of twitch tension (upper and lower left panels, Fig. 2). Addition of adrenaline markedly inhibits the development of contracture

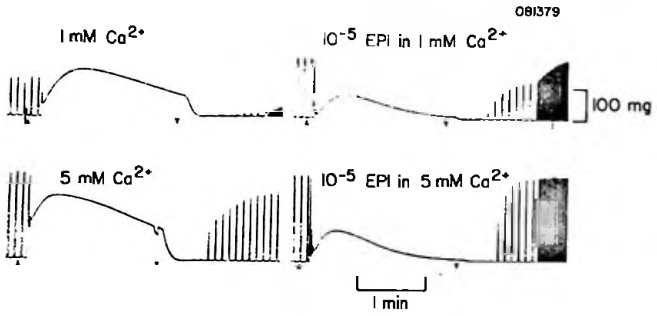

Figure 2. Epinephrine-dependent suppression of KCl-induced contractures in two $[Ca]_o$. The two left panels show that the magnitude of KCl-induced contractures were higher in 5 mM than in 1 mM Ca^{2+}. Addition of 10^{-5} g/L of epinephrine potentiated twitch tension as described in text but suppressed the KCl-induced contractures as demonstrated in the two right panels.

tension independent of $[Ca]_o$ (right panels, Fig. 2). Epinephrine while potentiating twitch tension in 1 mM Ca^{2+} (upper panels, Fig. 2; see also Fig. 1) failed to alter twitch tension significantly in 5 mM Ca^{2+} -containing solutions. Teh relaxant effect of epinephrine seems to be independent of $[Ca]_o$.

The relaxant and inotropic effect of theophylline. It has been suggested that epinephrine produces its relaxant effect through the activation of adenylate-cyclase system. Theophylline (a phosphodiestrase inhibitor) is known to potentiate, twitch tension, and suppress contracture tension in mammalian and frog ventricular muscle (Tsien, Adv. Cycl. Nucleot. Res. 8:363-420, 1977). In the dogfish ventricular trabaculae, on the other hand, theophylline, although it potentiates twitch tension and enhances the magnitude and duration of the action potential, fails to relax tension significantly (upper middle panel, Fig. 3). In fact, at larger concentrations (1-10 mM) theophylline often

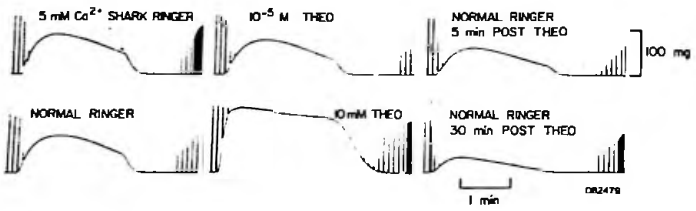

Figure 3. Action of theophylline on KCl-induced contractures. The top three panels show that 10^{-5} M theophylline produced little if any change in twitch tension yet slightly suppressed the KCl-induced contractures (middle record). Removal of theophylline appeared to unmask its full relaxant action and the KCl contracture in theophylline free solutions were further suppressed. The lower three panels demonstrate that addition of 10 mM theophylline in the middle record potentiated twitch tension by 13% and greatly enhanced the KCl-induced contractures. The right panels shows that the magnitude of suppression of KCl contracture in theophylline free solutions was greater following the washout of 10 mM theophylline than 10^{-5} M theophylline.

potentiated contracture tension (lower middle panel). Washout of theophylline for long periods (30 min or longer), however, results in suppression of contracture tension. Often 1-2 hours of continuous perfusion were required to counteract this suppressant effect of theophylline.

The experiments seem to suggest that epinephrine produces its positive inotropic action by altering the membrane permeability to Ca^{2+}. The relaxant effect, on the other hand, may be mediated by stimulation of the relaxing system. The paradoxical effects of theophylline at high and low concentrations of the drug may be in part due to the independent sites of the action of the drug on the membrane and the sarcoplasmic reticulum.

SOME ASPECTS OF CONTRACTILITY IN THE SEA POTATO HEART

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The experiments to be described below were directed primarily towards gaining an understanding of the functioning of the entire heart of the sea potato (Boltenia ovifera).

Experiments with a short segment of the sea potato heart. A new setup was used in order to increase viability and reduce the complexity of the experimental procedures. A segment of the tubular heart (about 5 mm in length) was mounted around two horizontal rods (0.6 mm in diameter) in a shallow rectangular channel (1.6 mm x 8 mm) as shown in Figure 1A. The two rods passed through the lumen of the heart. One of the rods was attached to a tension transducer.

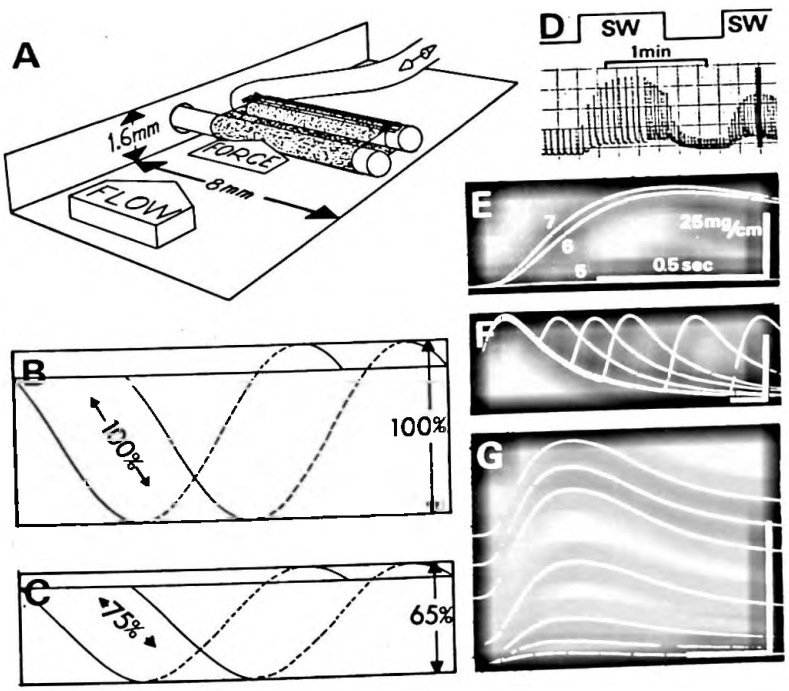

Figure 1. Results obtained with the new setup in panel A are shown in panels D, E, F, and G. Panels B and C show the orientation of the fibers in a short tubular section of the heart and demonstrate that the relative constriction of the heart may be larger than the relative shortening of the fibers. Panel D shows the response to a change of solution. Threshold is demonstrated in panel E. Panel F shows measurement of restitution and panel G shows measurement of length-tension relations. Vertical bars are 25 mg/cm and horizontal bars are 0.5 sec.

The other rod was attached to a motor which made it possible to stretch the preparation. Rapid exchange of the perfusate was accomplished by turning a valve which directs fluid through the channel. The response to a change of perfusate from sea water (SW) to artificial sea water is shown in Figure 1D. The response was complete in 10-20 sec. Myocardial preparations placed in this chamber had a well defined electrical threshold (5-6 volts, Fig. 1E). The