be synthesized during early embryogenesis in the absence of both new messenger RNA synthesis and aerobic metabolism. (These investigations were supported by Grants HD-00519 and DE-02047 from the U.S.P.H.S.)

1966 #9

THE DISASSOCIATION OF BRADYCARDIA AND ARTERIAL CONSTRICTION IN THE DIVING SEAL, Phoca vitulina

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The ability of the seal to remain submerged in water without access to external oxygen source for periods of 20 minutes is accomplished by circulatory adaptive changes that are referred to as the "dive response." These adaptive changes are bradycardia with pronounced decrease in cardiac output (Amer. J. Physiol. 210:176-80, 1966), and arterial constriction that prevents blood perfusion to peripheral tissues (Amer. J. Physiol. 135:557-66, 1942).

In order to evaluate the relative roles of these two circulatory responses in the adaptation to diving it is important to disassociate them during diving. Attempts in the past to individually block one or the other response using a pharmacologic approach have not been successful. Atropine will prevent the dive response, but does not allow individual evaluation of the bradycardia or of the arterial constriction in response to diving.

In this study, the technique of electrical cardiac pacing was used to regulate the heart rate of the seal while out of water and during diving to disassociate arterial constriction from bradycardia. Four harbor seals were trained to dive under laboratory conditions using a teeter board to control the time of submersion (J. Cell. & Comp. Physiol. 58:261-66, 1961). Using procaine for local anesthesia, an intracardiac pacing electrode (Elecath pacing stylet, #550, size 0.034", length 39 cm) was inserted through the chest wall, via a thin wall 18 gauge needle, and positioned in a cardiac chamber. The intracardiac pacing electrode was connected using insulated leads to a battery operated pacemaker (Medtronics, model 5800) with rate and amperage adjustable from 50-180/minute and 1.1 to 22 milliamps respectively. A polyethylene catheter (PE 90) was inserted into a femoral artery and advanced into the aorta. Arterial pressure was monitored using a Statham strain gauge and a polygraph recorder.

Three types of studies were performed. Control dives without cardiac pacing were conducted to ascertain that bradycardia occurred normally. In the second type of study the seal was dived and pacing instituted after the onset of bradycardia to demonstrate that bradycardia could be stopped during diving. In the third type of study, pacing was instituted prior to the dive and bradycardia was prevented for dives of over six minutes in duration. In one seal, arteriograms were performed using a technique previously described (Science 152:540-43, 1966). The arteriograms were performed during normal diving and during diving when bradycardia was prevented by cardiac pacing.

It was found that the heart rate could readily be controlled by the pacemaker during diving. The arteriograms revealed striking arterial constriction during diving with and without bradycardia. The ability of the seal to dive for six minutes without occurrence of bradycardia demonstrated that the onset of the arterial constriction is not dependent upon bradycardia and that ar-

terial constriction was capable of sustaining diving for periods longer than compatible with life when atropine has prevented normal response to diving.

The blood pressure during cardiac pacing was of interest. During diving the blood pressure remained normal or slightly elevated if the rate approximated non-diving rates, 130-150/minute. If the rate was increased to 180/minute, blood pressure and pulse pressure decreased progressively. The blood pressure could be increased or decreased at will by varying the heart rate with the pacer. During rapid pacing an occasional pacer induced stimulus failed to cause a ventricular response. When this occurred, blood pressure and pulse pressure were increased with the next ventricular contraction. These findings can be explained by a limited return of blood to the right side of the heart during diving.

With this restricted return of blood to the right heart, there would occur a decrease in diastolic ventricular filling if the heart rate remained fast. Bradycardia, however, would maintain diastolic ventricular filling by increasing the diastolic period, presumably sustaining ventricular stroke volume and ejection force.

The arterial constrictor response limits oxygen consumption by non-critical areas thus conserving the available oxygen stores for oxidative dependent cerebral metabolism during diving. The decrease in cardiac output serves to prevent an unduly high cerebral blood flow during the period of a restricted arterial perfusion bed. The bradycardia sustains an effective ventricular ejection force and aortic perfusion pressure during the period of limited return of blood to the heart.

1966 #10

PSEUDOCHOLINESTERASE ACTIVITY IN THE DOGFISH, Squalus acanthias

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Pharmacogenetics is a relatively new area in biology which involves the study of genetic processes revealed by the use of newly synthesized pharmacologic agents. An important disorder which falls into this area is the heritable disorder, pseudocholinesterase deficiency. Patients with this disease manifest prolonged apnea when exposed to the pharmacological agent, succinyl choline. This contrasts with the brief duration of apnea found in normal subjects. The prolongation of paralysis is caused by a deficiency of the enzyme pseudocholinesterase which hydrolyzes succinyl choline. With enzyme deficiency, succinyl choline persists at neuromuscular junctions and paralysis persists.

This study was prompted by the known absence of serum albumin in Squalus acanthias, knowledge that mammalian pseudocholinesterase migrates with the albumin fraction in electrophoresis, and an oral communication suggesting absence of psuedocholinesterase activity in dogfish serum.

Dogfish were artificially ventilated with flowing sea water by means of cannulae inserted into the spiracles. Succinyl choline was administered intravascularly by a single dose using the same quantity per kilo body weight effective in man. The duration of paralysis was measured as the length of time the opercular reflex was lost (Nature 211:1187, 1966). Serum pseudocholinesterase activity was measured in dogfish serum by a modification of the technique of McArdle