Thus, estrogen treatment at the appropriate dose level during the neonatal period acts, as does testosterone, to reduce the sexual responsiveness in females which is normally induced by estrogen and progesterone. Although it seems likely that estrogen treatment acts to alter the responsiveness to hormones of those neural cells which determine sexual behavior, it must be admitted that the actual mode of action of the estrogen administered in infancy is obscure.

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15 May 1963

Respiration of Heart Muscle as Affected by Oxygen Tension

Abstract. *Isolated cat papillary muscles were exposed to gas mixtures containing carbon dioxide and oxygen. In muscles exposed during the second of three periods to 25 percent oxygen, the volume of oxygen consumed* (Q_{O_2}) *was depressed by 50 percent, but returned to the control level during a third period at 98 percent oxygen. The work capacity was not significantly altered if the partial pressure of oxygen was low.*

The close correlation usually found between blood flow and oxygen consumption in various organs and tissues of the body has usually been interpreted to mean that blood flow is adjusted to the demand for oxygen. However, as discussed previously (*1*), evidence has been accumulating that the reverse may also be true, that is, the blood flow may normally impose a limitation on oxygen uptake (*2*). This evidence suggests that some oxidative metabolic reactions may "run-free," simply generating heat, if blood flow exceeds a certain minimum level.

We have attempted to test the hypothesis in vitro by making the assumption that it is the partial pressure of oxygen (pO_2) rather than some other constituent of the blood which is the limiting factor. If the Q_{O_2} (mm^2 O_2 STP/mg [dry wt.] per hour) of the isolated papillary muscle from the cat heart varied directly with the pO_2 in the medium without affecting the capacity to perform mechanical work, the hypothesis would be tenable, although far from proven.

The techniques used have been described previously in detail (*1*, *3*). Briefly, each of two muscles was mounted in a respirometer which allowed the simultaneous measurement of oxygen consumption and mechanical work. A third respirometer served as a control. The respirometers contained bicarbonate-buffered medium held at a constant temperature of 31.4 ± 0.01°C, and at a *p*H of 7.3 ± 0.1. Pardee's solution (*4*) was used in the "absorbed" cups to maintain the pCO_2 at about 2 percent. Since the gas phase consisted of 4 to 5 cm^3, little change in pO_2 with time might be expected. Even so, for technical reasons, the pO_2 in the chambers may have been slightly lower than in the aerating gas.

A day's run, which lasted about 7 hours, consisted of three periods of 2 hours each. Each period was preceded by 15 minutes of gassing with 2 percent CO_2 and either 98 or 25 percent O_2. After the gas was turned off, an hour was allowed for stabilization, after which O_2 readings were taken for three or more 20-minute intervals. The constancy of the 20-minute readings suggested that a steady state had been attained. At the end of the first gassing with 98 percent O_2 and hourly thereafter, the muscles were stimulated to contract 10 to 15 times (stimulation frequency of 30 per minute) while lifting a near maximal load, and the work for each contraction computed. The work capacities reported below are, in order, those measured after the first gassing with 98 percent O_2, and at the end of the second and third periods. At the end of the experiment, the muscles were measured, dried overnight at 100° C, and weighed.

In a series of 13 control muscles (Fig. 1, light stippling) exposed to 98 percent O_2 in the three periods, the Q_{O_2} and work capacity changed little with time.

In the experimental series of 18 muscles (Fig. 1, dark stippling) the Q_{O_2} fell significantly when the muscles were exposed in the second period to 25 per cent O_2. Upon regassing with 98 percent O_2 in the third period the Q_{O_2} returned to the control level, within the limits of error, suggesting that no damage to respiratory enzymes had occurred in 25 percent O_2 (see *5*). On the other hand, the work capacity of the muscles in 25 percent O_2 did not fall significantly, indicating that the contractile mechanism was not impaired.

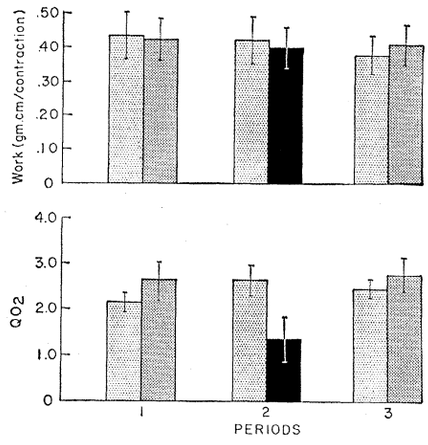

Fig. 1. Mean work capacity (by brief test) and Q_{O_2} (average of three or more 20-minute intervals succeeding stabilization) from 13 muscles (light stippling) exposed to 98 percent O_2 throughout; and 18 muscles (dark stippling) exposed in the middle period to 25 percent O_2 (solid block). Bars indicate the standard error ± 1.

In view of the hypothesis that the pO_2 may limit the Q_{O_2} it might be expected that muscle size would be a critical factor. Indeed, very thick muscles did have a lower Q_{O_2} (Fig. 2, top). On

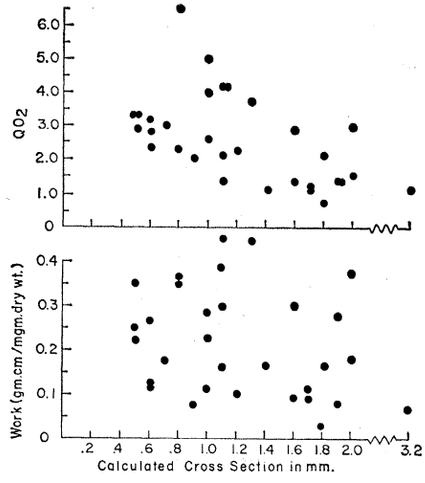

Fig. 2. (Top) Q_{O_2}, average of periods 1 and 3 at 98 percent O_2) plotted against the approximate cross-sectional area, determined from the ratio of the calculated wet weight to the length, where the wet weight to dry weight ratio was assumed to be 4.1 (*14*). (Bottom) Mechanical work and approximate cross-sectional area.

the other hand, very thin muscles did not consistently have higher Q_{O_2}'s (see *6*). There would seem to be an optimum size, but the data are not conclusive in this respect. When muscles which weighed more than 3 mg (dry wt.) were eliminated from consideration, the Q_{O_2} in 98 percent O_2 was higher ($\bar{X} = 3.6$), and the depression in 25 percent O_2 was slightly greater ($\bar{X} = -55$ percent). The Q_{O_2} of 3.6 is similar to that reported by Lee (*7*) for cat papillary muscles, if the difference in temperature is considered. However, Cranefield and Greenspan (*6*) found considerably higher values for thin muscles and, even if allowance is made for the higher temperature they used, there is no obvious explanation for the different results.

We further examined the data to see if the thinnest muscles had the greatest work capacity per unit of weight, but found they did not (Fig. 1, bottom). The number of very thick muscles was too few to warrant comment on this point (see *8*).

The significance of these results lies not in the fact that the Q_{O_2} was depressed by low pO_2, but that the effect was reversible, and the work capacity was not affected during the time when the Q_{O_2} was depressed. Fuhrman *et al.* (*5*) and others cited by them found that in rat heart slices the depression of Q_{O_2} was irreversible.

We have found no comparable studies in which the work capacity was tested, but Furchgott and Shorr (*9*) did find evidence that the rate of synthesis of high energy phosphate in heart-muscle slices was reduced in 20 to 23 percent O_2. However, the assumption that the contractile mechanism would be correspondingly reduced is, as they said, not necessarily true. Our data suggest that it might not be true.

Our results may help to explain the "stretch response" in muscle, that is, the increase in heat liberation and O_2 consumption when a muscle is stretched (*10, 11*). As suggested by Cranefield and Greenspan (*6*), at least part of the response may be due to the smaller cross-sectional area of the stretched muscle.

In the calculations of the "limiting thickness" for O_2 diffusion through tissues (*12*) it is generally assumed that the Q_{O_2} is independent of the pO_2 as long as a finite amount of O_2 is present. In view of the present results it may be appropriate to re-examine this assumption.

There is additional inferential evidence which seems to support the hypothesis that the pO_2 may limit a heat-generating reaction (see *1*), but speculation at this time seems fruitless. A proof of the hypothesis would demand a complete audit of energy liberation and utilization. We have simply shown that one function of muscle, albeit the primary one, is not deprived of an energy source at a time when the resting respiration is markedly reduced (*13*).

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22 May 1963

Littorina littorea: An Indicator of Norse Settlement in North America?

Abstract. *It is suggested that the originally European species* Littorina littorea *was introduced to North America by Norse settlers about* A.D. *1000. Its subfossil distribution might be used in tracing the extent of Norse travel in this region. Recent archeological finds match very well with the historical records of the Norse exploration and settlements. This activity seems to have been concentrated in Nova Scotia and Newfoundland.*

Clarke and Erskine (*1*) have reported specimens of *Littorina littorea* from a cultural site at Halifax, Nova Scotia. The species, which is widely distributed along the coast of western Europe, was earlier thought to have been introduced by ships from Europe about A.D. 1840. The Nova Scotia material gave a radiocarbon age of 700 ± 225 years ago and Clarke and Erskine concluded that the species must have been native to the Halifax area before the advent of European culture.

This is not supported by the radiocarbon dating, which certainly is "pre-Columbian" but not older than the Norse exploration and settlements which started about A.D. 1000. The history of these activities has mainly been known from the literature, but the recent expeditions of Helge Ingstad have shown a Norse settlement on Newfoundland (Lance aux Meadows) (*2*). This find is the first archeological evidence of Norse activities in North America. One of us (K.H.) took part in last year's expedition, which gave evidence of a highly specialized settlement, probably by the Norse population from Greenland. This is supported both by the archeological data, and by 12 radiocarbon ages all indicating an origin at about A.D. 1000.

Littorina littorea is very common along the coasts of Norway and Iceland, and studies indicate that it was equally common in the period A.D. 1000–1400. It is a hardy species, which can survive for a long time in the bottom water of open boats. It might be introduced into the boats either inadvertently through ballast stones, or purposely because it is edible and is used as bait when fishing. It is frequently found in refuse heaps in archeological sites in Norway, with other mollusks which have evidently been used for food. Experience has shown that it is very difficult to keep Viking ships dry when passing the North Atlantic, and *L. littorea* might therefore easily have survived the transatlantic trip. In fact, it is more likely to do so than most other marine mollusks.

It is therefore possible that the fossil specimens found at Halifax are from a population of the mollusks introduced by the Norse settlers. The present populations along the coast from Nova Scotia to New Jersey might be descendants of this one, or they might be due to a later introduction of the species about A.D. 1840.

It seems less probable that the fossil population should represent a stock