cells with lesser degrees of neoplastic change have more complex requirements, mesoinositol being prominent among the required components.

An evaluation of the significance of the present findings regarding the promotion of nodulation by mesoinositol must await further experimentation (7).

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Fibrillation and Potassium Influx

Abstract. Absolute influx and efflux of potassium-42 have been measured in isolated rabbit atria during acetylcholine-induced fibrillation. The efflux of potassium was increased three to four times; influx was not changed. The data are interpreted as indicating that an inhibition of active K uptake is not involved in the initiation of fibrillation, and that the process results from a marked increase in Na permeability.

Fibrillation has been induced by stimulating, at high frequency, isolated rabbit atria suspended in low potassium (K) media (1) in the presence of acetylcholine. Ion-exchange studies revealed that fibrillation began when the rate of net loss of K and gain of sodium (Na) exceeded critical values (2). Isotope investigations showed that with the onset of fibrillation the efflux of K reached a rate three to four times that of the spontaneously beating preparation (3). Net losses occurring under the conditions of the experiment prevented an accurate determination of influx. Therefore, we were unable to ascertain the nature of the permeability change involved in the process.

Recently a method has been devised (4) which permits an estimation of K^{42} influx with the onset of fibrillation. Absolute rates of influx were calculated by methods described by Keynes and Lewis (5). Influx is given by the product of the initial rate of entry of K^{42} to the tissue, the sensitivity of the counter, and the volume–to–surface-area ratio of the atrial fibers (6). The initial rate of entry can be obtained from the following relation:

$$\left(\frac{dy}{dt}\right)_{t=0} = \frac{Y}{T}\left(\frac{kt}{1-e^{-kt}}\right)$$

where Y is counts in the tissue after time T and k is the specific transfer coefficient obtained from efflux. During fibrillation, k was estimated to be of the order of 7.5 to 8.0×10^{-4} sec^{-1} (3).

Table 1 is a summary of our findings. First, it should be noted that acetylcholine increases both efflux and influx of K, whereas during fibrillation only an increase in efflux is obtained. Influx remains essentially unchanged. Thus, the changes induced by acetylcholine result from an increase in membrane permeability to K, while those that occur during fibrillation cannot be so interpreted. Earlier studies on the effects of temperature on efflux during fibrillation and acetylcholine treatment also suggested that different mechanisms were involved (7). A marked increase in Na permeability will explain the findings during fibrillation: Potassium leaves the tissue in exchange for sodium. This is in keeping with an earlier finding that the rate of entry of Na^{24} to atria was markedly increased (15 to 20 times) during the arrhythmia (7). These data suggested that the quantity of Na entering the tissue exceeded that of K which was lost. This would indicate that there was a sudden release of an anion in the tissue or, more probably, that membrane permeability to chloride is increased.

It should be noted that the mechanism proposed for the permeability change accompanying the onset of fibrillation is similar to that postulated for excitation and conduction in nerve (8) but differs in that K permeability is not increased. This is probably one of the factors responsible for the observed differences between the electrical properties of heart muscle and nerve (9).

Finally, it should be pointed out that the normal or slightly increased rate of influx during the early phases of fibrillation indicates that a depression of active transport is not a factor in the initiation of the arrhythmia, as was recently suggested by Goodford (10).

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Table 1. Effects of acetylcholine and fibrillation on the transmembrane flux of potassium. Fibrillation was induced by stimulating at 1200 count/min for 1 min. Atria were suspended in Ringer's solution containing 1.35 mmole of K^+ in the presence of acetylcholine (6.4×10^{-3} mole).

No. of observations	Experiment	Absolute flux (pmole cm^{-2} sec^{-1})	
		Influx	Efflux
8	Control	1.15 ± .08	4.32 ± .14
10	5 min after addition of acetylcholine (6.4×10^{-3} mole)	2.22 ± .13	7.88 ± .62
5	5 min after onset of fibrillation	1.20 ± .11	12.7 ± .48

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Failure of Nicotine to Affect Development of Offspring When Administered to Pregnant Rats

Abstract. Administration of nicotine to rats at any point in pregnancy has no apparent effect upon completion or duration of pregnancy, or upon body development, litter size, weight, or mortality of offspring. These results differ sharply from the effects in mice reported by others. The possible etiologic significance of anoxia in the malformations reported in mice is discussed.

Nishimura and Nakai recently reported (1) the development of a variety of skeletal anomalies, predominantly of the limbs, in the offspring (sacrificed at term, or examined at midpregnancy) of mice injected with a 0.1-percent aqueous solution of nicotine (0.025 mg/g) sometime between the 5th and 15th days of pregnancy. The percentage of congenital malformations, the number of pregnancies undergoing complete resorption, and the lethal effects of the drug upon the embryo were greatest when the drug was administered daily on days 9, 10, and 11 of pregnancy, although any or all of these effects could be produced, though to a considerably lesser