than after 8 weeks, indicating an apparent biphasic effect of the estrogens. In the present study the orchiectomized rats treated with estrogens showed a lower retention of administered radioactive cholesterol in the aorta, even though the plasma radioactive cholesterol concentration was similar to that of the other groups (Table). Estrogen treatment in the intact group did not result in a lower aortic concentration of cholesterol, which may be the result of an antagonistic action of the circulating androgens. Both estrogen treated groups, however, showed an increased hepatic concentration of radioactive cholesterol, and an increased degradation and excretion of cholesterol, as indicated by the higher fecal content of both the digitonin-precipitable sterols and the non-digitonin-precipitable metabolites of cholesterol in these groups. Orchiectomy also seemed to increase the rate of degradation and excretion of the administered cholesterol. These results are consistent with the observations in other investigations that the oxidation of cholesterol by hepatic mitochondria in vitro is enhanced by prior estrogen treatment or castration of male rats[13]. It appears from the present studies that estradiol may effect a redistribution of cholesterol, possibly mobilizing it from the arteries and other tissues, and preferentially concentrating it in the hepatic pool, where it is metabolized in both the parenchymal and Kupfer cells and excreted in increased amounts into the intestine[15].

Zusammenfassung. Vorbehandlung mit Östradiolbenzoat führte bei kastrierten männlichen Ratten zu einer verminderten Aufnahme von oral zugeführtem Cholesterin-4-C^{14} in die Aorta. Bei kastrierten wie auch bei intakten Tieren war nach Östrogenbehandlung die Aufnahme von markiertem Cholesterin in die Leber erhöht. Durch Analyse der Faeces liess sich nachweisen, dass Östrogenbehandlung sowie Kastration die Sterolausscheidung beschleunigt.

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Succinic Dehydrogenase and Isocitric Dehydrogenase Activities in Vitamin E-Sufficient and -Deficient Fetal Rats

Our recent study of the E-sufficient and -deficient rat fetuses[1] indicated increase of the acid phosphatase positive granules in the latter indicating liberation of lysosomes in the pathological condition caused by E-avitaminosis. Since lysosomal enzymes are known to affect the mitochondrial membranes[2], it was decided to study the activity of succinic dehydrogenase (SDH) which is a mitochondrial marker. The activity of isocitric dehydrogenase (IDH), another oxidative enzyme, was undertaken for comparison. Sections 45 μ in thickness from fresh frozen embryos of both types[3], 15-, 17-, 19- and 21-day-old (three of each age group) were cut. For SDH activity the method of BARKA and ANDERSON[4] with the addition of 1 ml of 0.5% NaCN, and for IDH activity that of DICULESCO et al.[5] were followed.

The results indicate the presence of SDH in the liver, the heart and the CNS in 15-day-old E-sufficient as well as E-deficient embryos. By the 17th day the enzyme was demonstrable in many other structures, viz. lung, skin, intestine, stomach, kidney, skeletal muscle, cardiac muscle, cartilage and mesentery (Figure 2). From the

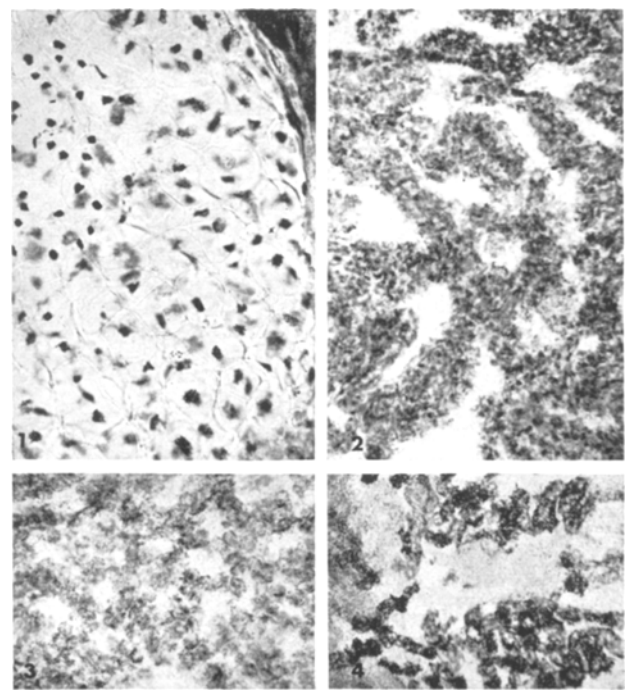

Fig. 1. Section of bone of a 21-day-old E-deficient fetus showing isocitric dehydrogenase activity in the different bone cell types. × 250.

Fig. 2. Section of the heart of a 17-day-old E-deficient fetus showing succinic dehydrogenase activity. × 240.

Fig. 3. Section of the liver of a 21-day-old E-deficient fetus showing succinic dehydrogenase activity. × 250.

Fig. 4. Section of the kidney of a 21-day-old E-deficient fetus showing succinic dehydrogenase activity. × 125.

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beginning the liver and the heart were conspicuous by the higher concentration of the enzyme. In 19- and 21-day-old fetuses skeletal muscle, adipose tissue, hair follicles, intestinal villi, gastric mucosa, choroid plexus, proximal convoluted tubules and intervertebral discs showed intense reaction besides the liver and the heart (Figures 3 and 4). In the 21-day-old fetuses osteoblasts, osteocytes and osteoclasts clearly showed enzyme positive reaction (Figure 1). The quantity of the enzyme was found to increase progressively from day 15 onward. No appreciable difference between the E-sufficient and -deficient embryos could be detected. The demonstration of IDH activity was more or less similar to that of SDH. The findings of this experiment are in accord with FULLMER[6] and disagree with WALKER[7] who denied the presence of these enzymes in all the bone cells of young rats except slight IDH activity in the osteoblasts[8].

Zusammenfassung. Die vergleichende Untersuchung der Aktivität der Bernsteinsäure- und Isozitronensäuredehydrogenase bei 15–21 Tage alten Rattenföten mit Vitamin-E-Mangel und normalem Gehalt ergab keine bedeutenden Unterschiede zwischen den verschiedenen Organen. Die Gegenwart dieser Enzyme in Osteoblasten, Osteoclasten und Osteocyten ist auffallend.

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The Origin of the Action Potential in Frog Stomach Muscle and Heart

Frog stomach muscle, when frequently washed with deionized half-isotonic (0.112 *M*) solution of sucrose, and frog heart perfused with similar solution, lose all sodium in 1 h[1,2] but exhibit spontaneous contractions[3–6] with conducted action potentials for several hours[7–14]. The spontaneous contractions and the action potentials therefore could not be due to the influx of sodium or any other ion into the muscle fibres. Two possibilities therefore remain for the origin of the action potential. Either it is due to efflux of anions[14] or it is not due to ionic fluxes at all.

The efflux of anions does not appear to be the cause of the action potential. With sodium, all the chloride is washed away from the frog stomach muscle and heart by a half-isotonic solution of sucrose, so that the efflux of chloride ions as the cause of action potential is ruled out. When immersed in Ringer solution the spontaneous contractions with the accompanying action potentials continue to occur if sodium phosphate at pH 7–7.4, or lactate or bicarbonate, is added to the solution to abolish the ionic gradients of these anions across the muscle membrane, or are added in such excess so that there could be no efflux, but rather an influx of these ions if any movement occurs at all. Frog stomach muscle remains excitable to chemical and electrical stimulation if the sodium chloride of the Ringer solution is replaced with an isoosmotic (0.08 *M*) quantity of sodium phosphate at pH 6.6; if perfused with this phosphate solution the frog heart beats vigorously with the accompanying electrical changes. With such high concentration of phosphate in the external solution, efflux of phosphate from the muscle fibres is ruled out. Frog stomach muscle, whether treated with Ringer solution or half-isotonic solution of sucrose, contains phosphates and lactate in the following concentrations (m*M*/kg wet muscle; water content about 80%): adenosine triphosphate 1.7, creatine phosphate 2.2, adenosine diphosphate 1.1, adenosine monophosphate negligible, inorganic phosphate 5.5, total acid soluble phosphate 17, and lactate 1.1[15]. The presence of any other diffusable anion in significant quantity is not known.

The conclusion, therefore, is that the actionpotential is not due to ionic fluxes at all. But how actually it is produced is difficult to explain. It is suggested that the action potential is due to change in the electronic configuration of the molecules of the membrane. There is some support for this suggestion. It is known that muscle can be excited by light[14]. Photons most likely change the electronic configuration of the cell membrane. They may knock out electrons, which thus freed will make the outer surface of the cell membrane negative.

Zusammenfassung. Das Aktionspotential von Herz- und Magenmuskulatur des Frosches scheint nicht vom Ein- und Ausstoss der Ionen, sondern vom elektronischen Aufbau der Zellmembran abhängig zu sein.

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