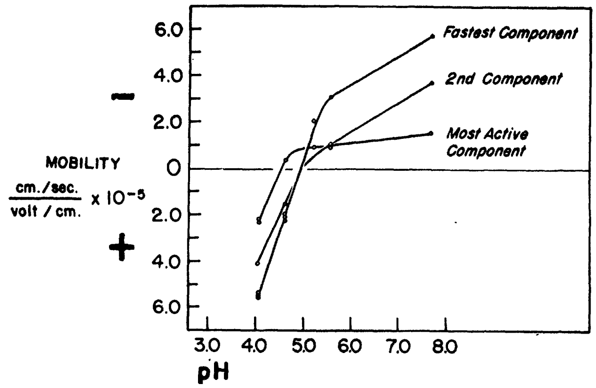

FIG. 2. Variation of electrophoretic mobility (descending limb) with pH of the major components of partially purified prostatic extracts at ionic strength 0.05.

moved toward the anode while the other two components have migrated toward the cathode.

Because of the limited supply of adenocarcinoma of the prostate only one partially purified preparation was analyzed. At pH 5.2 the pattern appeared to be similar to those of preparations from noncancerous prostates.

Figure 2 is a plot of mobility (descending limb) versus pH for the three major components. By interpolation the isoelectric points are as follows: fastest component, between pH 4.9 and pH 5.0; second component, between pH 4.9 and pH 5.0; most active component (acid phosphatase), pH 4.5.

It is of interest that our estimation of pH 4.5 for the isoelectric point of prostatic acid phosphatase is consistent with the value of Kutscher and Pany (*3*), who by the Theorell method of cataphoresis calculated the isoelectric point of purified ejaculate phosphatase to be pH 4.4.

It is apparent that the three proteins share many of the properties usually attributed to albumins. They are soluble in salt-free water and are not salted out by half saturation with $(NH_4)_2SO_4$. In addition two of the proteins remained in solution at their isoelectric points, as evidenced by the fact that they were not precipitated when the pH was adjusted to 4.9.

The electrophoretic mobilities, however, differ sufficiently to permit complete resolution of the components at pH 4.0, a point within 1 pH unit of the isoelectric point of each protein. Since Cohn *et al.* (*4*) emphasize the danger in completely characterizing proteins in terms either of their solubilities in concentrated salt solutions or of their mobilities, without regard to their other properties, no conclusion regarding the chemical nature of the three components is warranted as yet.

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Adrenal Gland Response to Circulatory Distress in Fetal Lambs

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The fetal heart rate is generally stated to be under the control of the autonomic system (*1*). The present report shows that humoral factors are also operating. During a study of reflex control of heart rate in fetal lambs (110–149 days gestation age), marked cardiac acceleration occurred following asphyxial slowing in 11 instances in which the heart was completely denervated. Experiments were carried out to ascertain the physiological basis of such acceleration.

Grade ewes, made available from the flock of C. W. Williams, Stadacona Farms, Glyndon, Md., were anesthetized with Dial urethane, 0.5 cc/kg given intravenously. The fetus was delivered by Caesarean section. Breathing was prevented by drawing a rubber bag containing amniotic fluid over the nose at the moment of delivery. The placental circulation was maintained intact. The fetus was dried and kept warm by an electric pad. Loose ligatures were placed around the 2 umbilical arteries and veins, to permit occlusion of the vessels at will by applying traction upon the ligatures. Carotid blood pressure was recorded oscillographically by means of a strain gage transducer.

After initial observations on the state of the circulation, the 2 vagi were sectioned in the midcervical region, and the 2 stellate ganglia exposed, dissected free, their branches cut, and the ganglia removed. In addition, the postganglionic fibers from T_3 and T_4 were cut.

Upon occlusion of either the umbilical arteries or veins, bradycardia developed, rapidly when the vagus nerves were intact, and slowly after those nerves were cut. Since about two-thirds of the blood passing down the aorta goes to the placenta (*2*), substantial embarrassment of the fetal heart can be induced by occlusion of the umbilical blood vessels. In 10 of 11 instances in which the heart has been denervated, as described above, restoration of blood flow in the umbilical vessel was associated with a marked tachycardia. In these 10 cases the heart rate increased to 240–276 beats/min. Such high heart rates often were sustained for some minutes.

In order to establish the physiological basis of the cardio-acceleration occurring after circulatory distress in fetuses having denervated hearts, 3 fetuses were subjected to bilateral adrenalectomy. Two experiments were unsuccessful, due to excessive hemorrhage. One was completely successful. Repeated observations were made in this fetus. Some of the data as obtained are summarized in Figs. 1 and 2.

In Fig. 1, occlusion, first of the 2 umbilical arteries and then of the 2 veins, was maintained for 44 and 36 sec respectively (see arrows). Within 12 sec after release of the arteries and 20 sec after release of the veins, the heart rate started to increase. The rate gained rapidly to 250 and 270 beats/min. The high heart rate persisted in each instance in excess of 230 beats/min for several minutes. The fetus was then bilaterally adrenalectomized, with the results shown in Fig. 2.

After adrenalectomy, occlusion for 44 sec of the umbilical vessels, arteries first, veins next, resulted in a 20-sec delay in onset of recovery after venous occlusion with return to a rate only 9 beats/min in excess of the pre-occlusion rate (204 vs. 195). After arterial occlusion, there was a delay of 66 sec before a rapid recovery set in. The rate then rose to 220 beats/min. This was maintained for a period of about 10 sec. In both cases, the heart rate returned in 3 min to about 200 beats/min. The curve of heart rate decay with complete cord occlusion and no release is indicated by the circles in Fig. 2. The fetus struggled in each instance just prior to the onset of recovery of the heart rate.

This experiment shows that the latent period for onset of recovery of the denervated heart slowed by circulatory distress is prolonged and that the rate of the heart on recovery is less after adrenalectomy than it is before. The conclusion is clear that, in the case of the lamb fetus near term, a supporting physiological mechanism that helps to overcome the effects of acute circulatory distress is the release of a cardiac stimulating agent from the adrenal gland. This could be only epinephrine or a related substance.

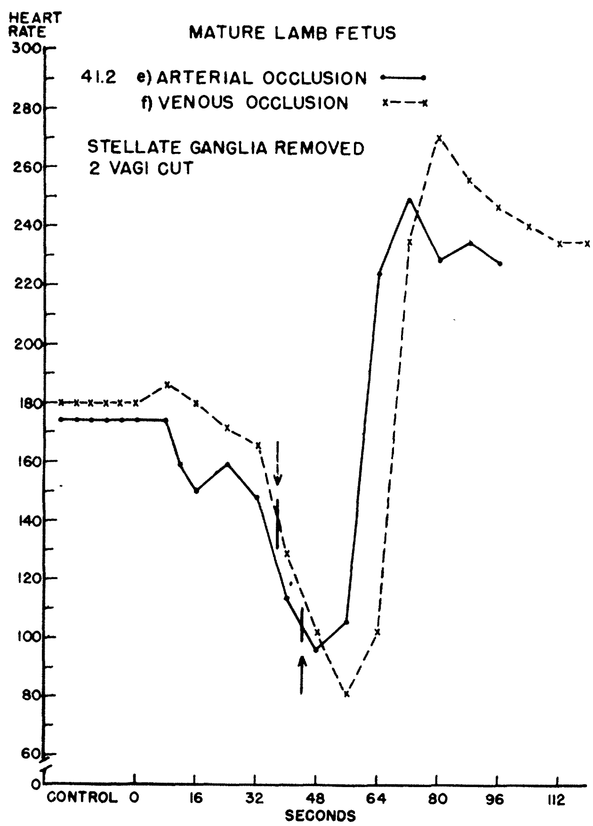

FIG. 1. Curves of heart rate recovery after temporary umbilical artery (——) and vein (x—x) occlusion. Release indicated at arrows. See text for description of prompt and extreme acceleration of heart rate. Mature fetal lamb at term, fetal condition, with 2 vagus nerves and stellate ganglia excised.

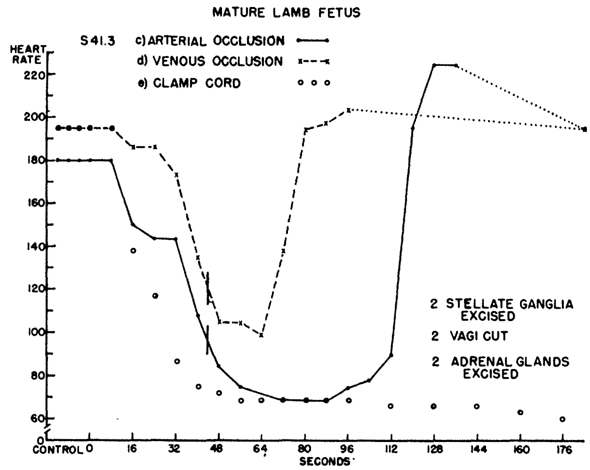

FIG. 2. Same as Fig. 1 except that both adrenal glands were likewise removed. Note long delay in recovery, especially after arterial occlusion, and small increase above pre-occlusion heart rate.

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Resolution of Isopropyl Nor-Adrenaline into Optical Isomers and Their Pharmacological Potency Ratio

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The resolution into optical isomers of sympathomimetic amines of the type

$$(OH)_2—C_6H_3—CHOH—CH_2—NH—R$$

has been performed for several terms of the series. Among these are epinephrine (*1*) and arterenol (*2*), but it is still an open problem for isopropyl noradrenaline. Since this drug differs markedly from the compounds involved in the sympathetic transmission of nerve impulse (*3, 4*), especially as far as its hemodynamic properties are concerned, it seemed worth while to resolve the racemate into its optical active components and to see if the L isomer would be more potent than the D form, akin to epinephrine and arterenol, or if another condition occurs.

By proper management of solvents and temperatures, the separation succeeded in the following manner: 22.1 g of the racemic base were treated with a solution of 15.5 g D-tartaric acid in 50 ml absolute