THE APPEARANCE OF THE PRESSOR SUBSTANCE IN THE FETAL HYPOPHYSIS.

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PLATES 96 AND 97.

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It has been demonstrated (Lewis, Miller, and Matthews1) that the pressor substance of the posterior lobe of the hypophysis is secreted by the pars intermedia, a derivative of the pharyngeal pouch. The present study was undertaken with the hope of determining at what period in fetal life the pressor substance appears and of correlating the cytological changes in the pars intermedia with the establishment of secretory function, using the appearance of the pressor substance as an index. The cytological studies are now in progress.

I have used extracts from the entire gland. The hypophyses of pigs just before birth are large enough to permit of separation of the two lobes, but in the earlier stages this is impossible. In order to secure uniform material for injection the extracts were made from the entire gland in all instances. The glands were obtained fresh and extracted in absolute alcohol to remove the depressor substances. After extraction was completed, the alcohol was filtered off and the residue dried in a desiccator. The dried residue was kept in small bottles until desired for use, when a salt solution extract was made for intravenous injection.

Fetal pigs just before birth measure from 275 to 285 mm.; the measurement being taken from the crown of the head to the tip of the coccyx. Fig. 1 indicates the effect upon blood pressure of an intravenous injection of 0.1294 gm. of dried hypophyses removed from pigs just before birth, extracted in 5 cc. of normal salt solution.

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This extract must be carefully filtered before injection, for much of the dried glands is insoluble. Intravenous injection of 5 cc. of this extract caused a prompt and marked rise in blood pressure which was followed by a fall and a second rise to almost the same level as the first, accompanied by marked slowing of the pulse and an increase in the length of the pulse wave. This type of tracing is often obtained after intravenous injections of extracts made from adult glands, but it is not the most common type of tracing obtained after such injections. It has been suggested that the fall following the primary rise, which is of short duration, is probably due to coronary artery contraction. This type of tracing seems to occur more frequently when extracts of the entire posterior lobe are used than when those of the pars intermedia alone are employed. It has been suggested that the variations from the common type which will be noted later may be due to the action of substances extracted from the nervous part of the posterior lobe.

Intravenous injection of 0.05 gm. of dried hypophyses from fetal pigs measuring 175 mm. extracted in 5 cc. of normal salt solution gave a decided pressor effect such as is usually obtained by the intravenous injection of extracts made from adult glands. The pressor reaction followed the injection rapidly and was long continued, being unassociated with any marked change in the tracing (Fig. 2).

Intravenous injections of saline extracts of hypophyses from fetal pigs measuring 125 mm. gave different results. In some cases a slight pressor effect following a primary fall was noted, while in other instances no change in the tracing was noted. Fig. 3 is a tracing obtained after intravenous injection of an extract of 0.08 gm. of dried hypophyses in 5 cc. of normal salt solution. The injection of this extract caused a fall in pressure which was followed by a rise slightly above the level existing before the injection was made. This reaction was of short duration, the pressure soon sinking to the level which existed before the injection was made. Another tracing was made after the injection of an extract of 0.06 gm. of dried hypophyses from pigs measuring 125 mm. extracted in 3 cc. of salt solution. The amount of extract injected was therefore practically the same as in the preceding experiment. The injection of this extract caused a fall in pressure followed by a rapid return to the
level existing before the injection was made (Fig. 4). An injection of the residue left after filtration of the preceding solution extracted in 5 cc. of normal salt solution caused another fall with a rapid return to the level existing before the injection. The fall in pressure observed in the last experiments occurs frequently after injections of glands, even after attempts to remove completely the depressor substance which exists in all parts of the gland have been made by thorough extraction with absolute alcohol.

Fig. 3 indicates that in some instances a slight but unmistakable pressor effect of short duration may follow the intravenous injection of extracts made from the hypophyses of pigs measuring 125 mm. This reaction does not follow the injection of all extracts made from the glands of pigs of this measurement. It is possible that in attempts to obtain fresh material a few pigs measuring slightly more than 125 mm. have been occasionally used, but if this is the case, they have exceeded this measurement only by a few mm.

I believe that I am justified in stating that the active principle of the pars intermedia, using the pressor substance as an index, begins to appear in fetal pigs measuring 125 mm. or slightly more.

It is somewhat difficult to determine the age of fetal pigs as estimated by measurements. Koch says that great difficulty is experienced in finding any statement concerning the age of pig fetuses. The statements of different authors do not always agree, but the two which come closest to an agreement are those of Bradley and Coe. Bradley compared the length of the embryos with the time of coition. Coe estimated the age from the rate of development of other mammals. While considerable uncertainty is attached to these figures, it may be assumed that the 50 mm. pig fetus is about 40 days old from conception; the 100 mm. fetus is 55 to 62 days old; and the 200 mm. pig is 88 to 90 days old from conception.

As determined by the pressor reaction the secretion of the pars intermedia seems to be established in pigs measuring 125 mm. The reaction is not obtained after the injection of all extracts of glands removed at this period and even when present is not marked. There are, however, often definite indications of a pressor effect as indicated in Fig. 3. As far as can be estimated, a pig measuring 125 mm. is about 9½ or 10 weeks old from conception. During the period rep-
presented by the differences between 125 and 175 mm., the secretion of the pars intermedia becomes as active as that of the adult gland.

McCord has recently attempted to determine the time of appearance of the active principle of the pars intermedia. Its presence was determined by the oxytocic activity of extracts of glands by means of the method of Dale and Laidlaw, using histamine as a standard. The tests for pituitrin were begun with embryos at or near full term. These tests and others as far back as 9 weeks were quantitative tests. Pituitrin was found in the extracts of glands as early as 9 weeks, and the quantity for unit of weight was larger than in the adult. In the 7th and 8th weeks of fetal life the pituitary could no longer be recognized, although the sella turcica was plainly visible. The experiments, therefore, could not be made earlier than the 9th week of fetal life.

McCord worked with bovine fetuses and it is difficult to determine the relative ages of calf and pig fetuses by the lengths. McCord found that the first indication of an active pars intermedia occurs in a bovine fetus measuring 165 mm., while evidences of an active pars intermedia are found in a pig fetus measuring 125 mm.

Fenger has shown that both the thyroid and suprarenal glands of the beef, hog, and sheep contain their active principles not only at birth, but also in the fetus. He believes that both the thyroid and suprarenals of the fetus take a distinct and active part in its growth.

SUMMARY.

The pressor substance of the hypophysis is so marked in the pig fetus measuring 175 mm. that it seems probable that a fetus of this length is independent of the secretion of the mother's hypophysis.


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EXPLANATION OF PLATES.

PLATE 96.

Fig. 1. Effect upon blood pressure of the intravenous injection of 0.1249 gm. of dried hypophyses removed from pigs just before birth, dissolved in 5 cc. of normal salt solution. This type of tracing is often produced by injection of extracts of the adult gland, but is not the most common form.

Fig. 2. Effect upon blood pressure of the intravenous injection of 0.05 gm. of dried hypophyses removed from pigs measuring 175 mm., dissolved in 5 cc. of normal salt solution. A prompt and long continued pressor effect is noted.

PLATE 97.

Fig. 3. Effect upon blood pressure of the intravenous injection of 0.08 gm. of dried hypophyses removed from pigs measuring 125 mm., dissolved in 5 cc. of normal salt solution. The fall in pressure is followed by a distinct but temporary rise.

Fig. 4. Effect upon blood pressure of the intravenous injection of 0.06 gm. of dried hypophyses removed from pigs measuring 125 mm., dissolved in 3 cc. of normal salt solution. A fall in pressure is noted with a rise to the level existing before the injection.
(Lewis: Pressor Substance in Fetal Hypophysis.)
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