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Motility of the Stomach of the Mammalian Fœtus.

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Very little is known about the reaction of the stomach of the mammalian fœtus to drugs. According to Tani[1] the stomach of the newborn rabbit is less sensitive to sympatho- and parasympathomimetic drugs than is the stomach of the fœtus. Adrenaline accelerates the spontaneous gastric movements of the rabbit fœtus whilst it has a restraining action on those of the human fœtus. Inada[2] observed that intestinal strips from the human fœtus were excited by parasympathomimetic and inhibited by sympathomimetic drugs. The experiments of Koshtoyantz and Mitropolitanskaya[3] on the effects of adrenaline and pilocarpine on the movements of the gastrointestinal tract of the human fœtus are few and inconclusive.

The results herein recorded were obtained in experiments on the isolated stomach of the fœtal cat, the newborn cat and the newborn dog. The newborn dogs were taken from the mother about 10 hours after birth. Their digestive tract was without visible signs of milk, so it is possible that the puppies had not suckled. Of the 4 newborn kittens, all less than 4 hours old, 2 had suckled and 2 had not.

The fœtal cats were obtained by anæsthetizing the mother with ether and performing a laparotomy. It was found that rapidity was essential when removing the fœtuses, since handling of the uteri initiated gasping reflexes in the fœtuses causing them to swallow amniotic fluid.

A strip of stomach tissue or (where the stomach was very small) the whole stomach was attached to a lever, and suspended in a bath of mammalian Ringer solution at 37°C. The bath was of 500 cc. capacity. Air was bubbled through the solution at a constant rate with a force insufficient to disturb the otherwise sensitive recording lever.

The drugs employed were acetylcholine bromide (Eastman Ko-

1 Tani, K., *Jap. J. Obst. Gynecol.*, 1927, **10**, 2.

2 Inada, H., *Fukuoka Acta Med.*, 1928, **21**, 596 (German summary).

3 Koshtoyantz, C. S., and Mitropolitanskaya, R. L., *Fiziol. Z.*, 1934, **17**, 1309 (Russian).

dak), adrenaline hydrochloride (Parke-Davis), atropine sulphate (Merck), ergotamine metansulphonate (Sandoz), and pilocarpine hydrochloride (Merck).

Body length was measured as the distance from the crown (region of ears) to the base of the tail.

We do not know exactly at what stage in the development of the cat fœtus the stomach begins to show spontaneous movements. According to Tani[1] the stomach of the rabbit fœtus shows spontaneous movements when the body weight has reached 7.5 gm. Koshtoyantz and Mitropolitanskaya[3] claim the fœtal human gastrointestinal tract is without automaticity before the 6th to 7th week. The small size of the stomach made kymographic recording difficult in cat fœtuses less than 70 mm. long. According to Latimer[4] the length of the entire digestive tube in a fœtal cat 70 mm. in body length (tip of nose to anus) is only 120 mm. In a few experiments we observed movements of the stomach of cat fœtuses of about 58 to 60 mm. body length but the influence of drugs on the movements could not be studied. Shaklee, Christensen and Oppenheimer[5] noted that the iris of the fœtal pig did not react to choline esters before the 71st day of gestation.

The stomach of the cat fœtus as well as that of the newborn cat and dog is very sensitive to the slight succussion produced by the air bubbling through the bath. Shutting off of the air supply greatly diminishes the rhythmic contractions and also produces some fall of the tonus. Similar observations on strips of stomach from the adult cat and dog were made by Brown and M'Swiney.[6]

The contractions occurring in the fœtal cat's isolated whole stomach under the conditions of the experiment take the form of either peristaltic or antiperistaltic waves. The normal peristaltic type was observed to be the more frequent. Thus in the stomach of a fœtus 92 mm. body length a wave of constriction originating at or near the gastro-œsophageal junction would reach the pyloric region in 18 to 25 seconds. A second wave might commence when the first was half-way down the stomach, but usually the second wave would originate only when the preceding wave was well within the region of the pyloric antrum. Both the peristaltic and antiperistaltic waves occurred in groups, 3 or 4 constrictions following consecutively with relatively long intervals between the wave-

[4] Latimer, H. B., *Anat. Rec.*, 1934, **60**, 23.

[5] Shaklee, A. O., Christensen, K., and Oppenheimer, H. E., PROC. SOC. EXP. BIOL. AND MED., 1936, **34**, 225.

[6] Brown, G. L., and M'Swiney, B. A., *Quart. J. Exp. Physiol.*, 1926, **16**, 9.

groups. A series of 3 waves of a total duration of about 45 seconds might be followed by a resting phase of about 60 seconds or more before a new series of waves would commence.

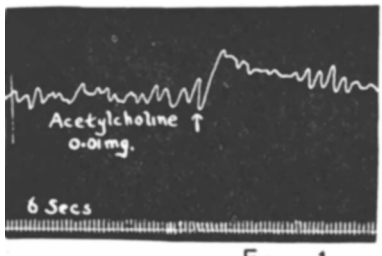

Fig. 1

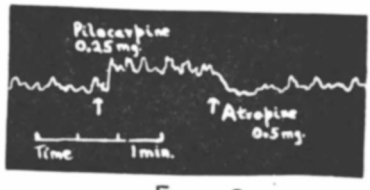

Fig. 2

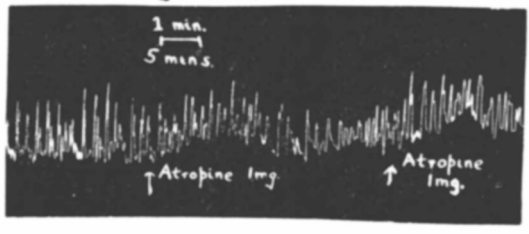

Fig. 3

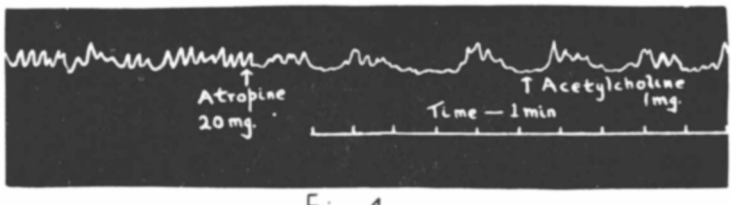

Fig. 4

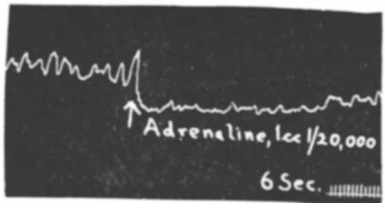

Fig. 5

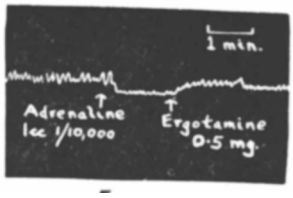

Fig. 6

All records are from the stomach of the foetal cat. In each case the capacity of the bath was 500 cc The body lengths (crown-rump) of the foetuses were:

Fig. 1—162 mm. Effect of acetylcholine (1/50,000,000).

Fig. 2—89 mm. Atropine (1/1,000,000) abolishes the effect of pilocarpine (1/2,000,000).

Fig. 3—110 mm. Temporary rise of tonus induced by small doses of atropine (1/5,000,000).

Fig. 4—98 mm. Periodic changes in tonus and rhythmicity induced by large doses of atropine (1/25,000).

Fig. 5—162 mm. Effect of adrenaline (1/10,000,000).

Fig. 6—116 mm. Ergotamine (1/1,000,000) antagonizes the effect of adrenaline (1/5,000,000).

Parasympathomimetic drugs have a definite stimulatory effect, raising the tonus and in some instances increasing the rate of contractions of the stomach of both the fœtal and newborn cat and dog. (Fig. 1). Acetylcholine initiated rhythmic movements at a higher level of tonus in those cases in which the fœtal stomach did not show spontaneous contractions. The stomach in a cat fœtus 98 mm. long was sensitive to acetylcholine in dilutions even in excess of 1/50,000,000, and to pilocarpine in a dilution of 1/2,500,000. The fœtal stomach is slightly more sensitive to acetylcholine than is the newborn cat's stomach as shown by our experiments and also more sensitive than is the adult cat's stomach.

Atropine when given after either acetylcholine or pilocarpine antagonized these (Fig. 2) and brought about partial to complete cessation of motility. Very small doses of atropine (1/500,000) when not preceded by previous treatment of the stomach by other drugs raised the tonus for a short period of time (Fig. 3). Larger doses of atropine (1/25,000) arrested the motility of the stomach often at a high tonus level or else induced periodic tonic and rhythmic contractions which were not affected by subsequent addition of acetylcholine (Fig. 4). This twofold effect of atropine is in agreement with Magnus' theory[7] of atropine action on the myenteric plexus.

Adrenaline had predominantly an inhibitory effect on both tonus and contractions (Fig. 5) though in low concentrations its effect on gastric tonus was frequently excitatory especially in the case of the large fœtuses and the newborn cat. An initial rise in tonus was sometimes seen in stomachs from the larger fœtuses: this would perhaps indicate that the stomach of the smaller fœtuses were the most sensitive to adrenaline.

When acetylcholine was followed by adrenaline the reaction was sometimes synergistic but most often the result was one of antagonism. The type of response to adrenaline after acetylcholine apparently depended on the concentration of adrenaline. The occasional synergistic effect produced on the fœtal stomach by these 2 drugs in combination is strikingly similar to that observed on strips of stomach of Necturus (Friedman[8]). Apparently no such synergism occurs in the adult cat's stomach.

Ergotamine produced only an occasional rise in tonus. However, this drug had a very marked inhibitory effect on adrenaline.

[7] Magnus, R., *Münch. med. Wochenschr.*, 1925, S. 249.

[8] Friedman, M. H. F., *Trans. Roy. Soc. Canada*, 1935, **29**, Sect. V, 175.

Used after adrenaline, ergotamine restored the tonus level of the muscle which adrenaline had lowered (Fig. 6).

Conclusion. Spontaneous contractions of the stomach of the cat fœtus are already present in fœtuses of 58 mm. body length. Both peristaltic and antiperistaltic movements can be observed. Acetylcholine and pilocarpine raises the tonus and in some instances increases the rate of contractions. The effects of these drugs are abolished by atropine. Atropine by itself has a double —inhibitory and excitatory—effect. Adrenaline in small doses stimulates and in large doses inhibits the motility. Ergotamine paralyzes the effect of adrenaline. The usual effect of adrenaline after acetylcholine is one of antagonism but sometimes the 2 drugs act synergistically.

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Tonsillitis in Dogs Due to Hemolytic Streptococci.

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Recent observations in our laboratories were reported indicating the constant presence of hemolytic streptococci of the beta type in the tonsils of the cow, sheep and hog.[1] As in man these organisms constitute part of the normal flora of the lymphoid tissue of the oropharynx of cattle, differing in certain biologic properties from the human streptococci. The rôle of these bacteria in the production of disease in animals is still undetermined. One of us[2] has observed the occurrence of tonsillitis in dogs with manifestations of enlarged, red tonsils, often with exudate and fever. A study was undertaken to determine the relation of the hemolytic streptococci to this tonsillar infection and the incidence of similar streptococci in normal tonsils of dogs. All of the observations were made during the months of February, March and April, 1936.

Swabs of the tonsils during the acute stage of illness in the dogs and the tonsils removed surgically from the affected dogs were

[1] Pilot, I., Buck, C., and Davis, D. J., PROC. SOC. EXP. BIOL. AND MED., 1936, **34**, 233.

[2] Eastman, D. A., *North Am. Veterinarian*, 1936, **17**, 37.