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Enteral Absorption of Insulin.

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Previous studies dealing with the enteral absorption of insulin have demonstrated the marked impermeability of the intestinal mucosa to this hormone.[1] It was considered of practical and theoretical interest to attempt to increase this degree of permeability by means of concomitantly administered drugs.

Normal dogs were prepared with Thierry loops about 12 cm. in length taken from about 50-60 cm. above the terminal ileum. Balloon and catheter arrangements similar to those described by Johnston[2] were used to insure retention of the introduced insulin mixture. This mixture was made up of Insulin-Lilly U-40 or U-80 and diluted with saline to 2½ or 3½ cc. before introduction. Blood samples were taken from the ear and sugar determined by the micro-method of Folin and Malmros.[3] (This method in our hands gives high absolute figures in the hypoglycemic range.) The dogs were ordinarily starved for 40 hours previous to the experiment. For purposes of brevity, the following hypoglycemic reaction, taken from the protocols is referred to as "typical hypoglycemia". Normal blood sugar 102 mg. %; 1½ hr. later 106. Insulin introduced. After 15 min., 94; 50 min., 65; 1½ hr., 65; 2 hr., 58; 2⅓ hr., 62; 3 hr., 79 mg. %.

With insulin in saline alone, about 35 units per kg. body weight represents the minimal dosage producing typical hypoglycemia.

One trial with an addition of hexyl resorcinol and toluene failed to show favorable influence on absorption. One trial with 0.3% saponin and 5% lactic acid produced typical hypoglycemia with ½ the usual amount of insulin.*

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[1] See references by Bollmann, J. L., and Mann, F. C., *Am. J. Med. Sci.*, 1932, **183**, 23, and Harned, B. K., and Nash, Jr., T. P., *J. Biol. Chem.*, 1932, **97**, 443.

[2] Johnston, C. G., PROC. SOC. EXP. BIOL. AND MED., 1932, **30**, 193.

[3] Folin, O., *J. Biol. Chem.*, 1928, **77**, 421. Folin, O., and Malmros, H., *ibid.*, 1929, **83**, 115.

* The use of surface active agents, such as saponin, has been claimed by Lasch and Brugel[4] to produce hypoglycemia when administered orally with insulin. In 4 trials with rabbits we were unable to obtain such effects and are, accordingly, in agreement with the critical observations of Elzas,[5] Samek,[6] and Dingemanse and Laqueur.[7]

Several trials of insulin in a 20% alcohol solution produced typical hypoglycemia with dosages ½ to ⅓ those producing the same effect in saline alone. Typical hypoglycemia was produced with dosages as low as 10 units per kg., but the usual requirement is higher. The systemic effect of similar amounts of alcohol alone was demonstrated to be without influence.

The addition of lactic acid (1½ to 5%) to these mixtures does not decrease absorption and occasionally increases the effect.

Alcohol-lactic acid mixtures with insulin were introduced by catheter into one dog with a fistula anastomosed to communicate with the small gut about 50 cm. above the terminal ileum. Profound hypoglycemia leading to coma was produced with dosages of 32 and 40 units per kg. This dog, however, was in relatively poor shape and died 3 weeks after the last of these trials with partial obstruction from operatively produced adhesions.

Throughout the 35 trials in 6 dogs, the absorption effects were reasonably consistent with each individual dog although there was substantial variation between the different dogs.

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Roentgenologic Visualization of Lymph Nodes and Vessels by Intrapericardial Injection of Thorium Dioxide.*

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During previous experimental work on laboratory animals[1] it was noted that in the intracardiac injection of thorotrast, some of the material being injected also into the pericardium, roentgenograms

[4] Lasch and Brugel, *Arch. Exp. Path. Pharm.*, 1926, **120**, 144.

[5] Elzas, *Nederland. Tijdschr. Geneeskunde*, 1926, **70**, II, 1650.

[6] Samek, *Z. ges. Exp. Med.*, 1928, **62**, 707.

[7] Dingemanse and Laqueur, *Arch. Exp. Path. Pharm.*, 1927, **126**, 31.

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[1] Ané, J. N., and Menville, L. J., *Am. J. Roentgenol. and Rad. Ther.*, 1932, **28**, 784.