

The fact that in the present study no change in thyroid metabolism occurred may indicate that a much more prolonged change in the metabolic needs of the body is required in order to alter thyroid function. Previous studies on cold exposure have demonstrated increased rate of removal of circulating thyroid hormone. However, maintenance of body temperature is a major function of thyroxine. Need for the calorogenic action of the hormone on exposure to cold may prove to be the most consistent means of increasing the utilization of thyroxine. In the rat experiment of Bondy and Hagewood(4) the temperature of the water (27°C), rather than the muscular exercise, may have been enough to account for the fall in protein bound iodine. Tan *et al.* have shown that the survival time of rats swimming in water which is below body temperature is limited by the ability of the rat to maintain body temperature at its normal level(9). Muscular exercise itself increases heat production and this may militate against increasing the rate of utilization of thyroid hormone in the present experiments by increasing the body temperature. Whether or not stimuli other than cold do affect the rate of the peripheral metabolism of thyroid hormone remains to be determined. Previous studies of the effect of injurious agents have dealt mainly with the thyroidal uptake of I^{131}

rather than with the rate of disappearance of circulating hormone. The uptake of I^{131} may be influenced by many factors other than the rate of utilization of thyroxine, such as previous diet, adrenal cortical, pituitary and renal function.

Summary. Muscular exercise in human subjects produced no alteration in peripheral utilization of thyroid hormone as measured by concentration of circulating hormone and by rate of disappearance of injected radio-thyroxine.

1. Bogoroch, R., and Timiras, P., *Endocrinol.*, 1951, v49, 548.
2. Dempsey, E. W., and Astwood, E. B., *ibid.*, 1943, v32, 509.
3. Rand, C. G., Riggs, D. S., and Talbot, N. B., *ibid.*, 1952, v51, 562.
4. Bondy, P. K., and Hagewood, M. A., *Proc. Soc. Exp. Biol. and Med.*, 1952, v81, 328.
5. Ingbar, S., and Kleeman, C. R., unpublished data.
6. Man, E. B., Kydd, D. M., and Peters, J. P., *J. Clin. Invest.*, 1951, v30, 531.
7. Sterling, K., Lashof, J. C., and Man, E. B., *ibid.*, in press.
8. Barker, S. B., Humphrey, M. J., and Soley, M. H., *ibid.*, 1951, v30, 55.
9. Tan, E. M., Hamson, M. E., and Richter, C. P., *Fed. Proc.*, 1954, v13, 150.

Received April 27, 1954. P.S.E.B.M., 1954, v86.

Effect of ACTH on Strength of Intestinal Anastomoses in Dogs. (21060)

THOMAS GEOGHEGAN AND BROCK E. BRUSH. (Introduced by C. R. Lam.)

From the Division of General Surgery, Henry Ford Hospital, Detroit, Mich.

Since the original observations by Ragan (1) concerning the retardation of wound healing in patients by ACTH, several studies have been done dealing with this phenomenon. The investigations of Ragan(2), Spain(3), and others in rabbits and mice indicate that ACTH retards the healing of wounds. Recent experiments on skin wounds in guinea pigs(4) and rats(5), and on skin wounds and cardiovascular suture lines in dogs(6,7) failed to demonstrate significant differences in the healing of wounds of control animals and

those treated with ACTH or cortisone. The conflict in these experimental results may be attributable to differences in the species of experimental animal, the particular tissue studied, or to the dosage of the hormone used.

The effect of ACTH and cortisone on anastomoses in the gastrointestinal tract is important for obvious reasons. Great caution has been advocated in the use of these agents in the presence of healing anastomoses(8). In one clinical series unspecified as to detail 4 of 10 cases with intestinal anastomoses

treated with ACTH developed suture line leakage(9). Ragan has stated that the depression of wound healing by ACTH is a function of the dosage, the larger doses inducing depression where lower doses do not (10). The purpose of this study was to determine the effect of varying doses of ACTH on end to end anastomoses of the colon performed with minimal soiling of the peritoneal cavity at the time of operation.

Method. The experimental animals were healthy male mongrel dogs fed on ordinary kennel rations prior to surgery. Ten test animals and 10 control animals weighing from 6.4 to 18.9 kg were subjected to identical procedures following a 24-hour fast. Under ether-oxygen anesthesia the abdomen was entered through a left paramedian incision. The transverse colon was transected between the right colic and middle colic arteries without disturbing the marginal artery. The clamped cut ends of the colon were closed with Parker-Kerr basting stitches. Using fine silk on straight intestinal needles, the anastomosis was performed with a single row of Halsted stitches approximately 3 mm apart. After removal of the basting stitches the abdomen was closed in 3 layers. Postoperatively all animals were fed milk *ad lib.* immediately and for 7 days before sacrifice. After closure of the abdomen each animal in the test series was given an injection of 160 units of reposi-

tory ACTH (Parke-Davis x5964) subcutaneously. A similar injection was given daily for 7 days. As the weight of the animals varied, the amount represented dosages of from about 8 to 23 units of ACTH per kilo per day. No antibiotics were used. Samples of blood were drawn at intervals and examined for total protein, hemoglobin, and eosinophiles. The animals were observed daily for signs indicative of peritonitis from suture line leakage. On the 7th postoperative day each animal was killed with ether. After examination of the contents of the abdomen a 10 cm loop of colon containing the anastomosis was removed and tested for bursting strength by the Harvey method. With the ends of the loop closed the intraluminal pressure was increased at a rate of 10 mm of Hg/second by compressed air until the first bubbles of gas were seen escaping from the submerged specimen. The pressure at this instant and the site of the leak were noted.

Results. The total protein and hemoglobin determinations revealed slight drops from preoperative values within a range of 1 g/100 cc in both treated and control animals. The eosinophile counts of the animals given ACTH fell an average of 99% on the first postoperative day and remained at this low level for the duration of the experiment. The eosinophile counts of the control animals showed a variable change from preoperative values, fall-

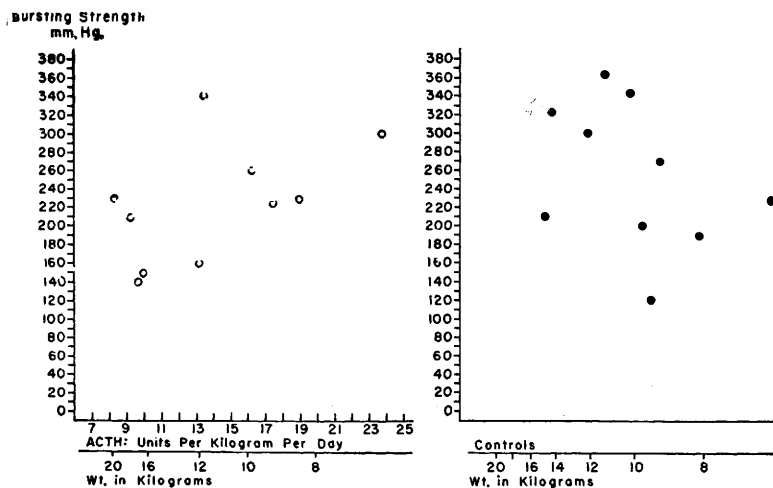


FIG. 1. Seventh day bursting strengths of end to end anastomoses of the colon. Comparison of values from animals given ACTH with those of control series.

ing from 10 to 50%, as has been noted in patients undergoing surgery(11).

No difference was noted in the postoperative course of the animals in either group. Suture line leakage was not induced with doses of ACTH as high as 23.4 units/kg/day. The bursting strength of the anastomoses in the control series ranged from 120 to 365 mm Hg with an average of 257 mm Hg and a mean value of 242 mm Hg. The bursting strength of the anastomoses in the ACTH series ranged from 140 to 340 mm Hg with an average of 224 mm Hg and a mean value of 240 mm Hg. The site of the first leak under pressure was always at the suture line. No correlation was evident between the dosage of ACTH and the anastomotic bursting strength. For example an animal receiving 23.4 units of ACTH/kg had an anastomotic bursting strength of 300 mm Hg, while an animal receiving 10.6 units/kg/day had an anastomotic bursting strength of 150 mm Hg (Fig. 1).

Discussion. The healing curves of intestinal anastomoses tested with and without suture support intersect at the 7th day as shown by Fellows *et al.*(12). It would seem, therefore, that the presence of the sutures in the anastomoses did not alter the experimental results of this study. The bursting strengths found in these experiments correspond to those found in previous studies of anastomoses of the colon(13). Doses of ACTH such as used in this investigation are far in excess of those used clinically, the highest being equivalent to over 1600 units per day in an adult patient.

Summary. Suture line leakage was not observed in a series of 10 dogs given large daily

doses of ACTH following end to end anastomosis of the colon. The strength of the suture lines was not significantly altered by ACTH administration as compared with non-treated controls. No correlation was evident between the amount of ACTH given and the strength or gross appearance of the anastomoses.

The ACTH used in this study was supplied through the generosity of the Parke Davis Co.

1. Ragan, Charles, Grokoest, A. W., and Boots, R. H., *Am. J. Med.*, 1949, v7, 741.
2. Howes, E. L., Plotz, C. M., Blunt, J. W., and Ragan, Charles, *Surgery*, 1950, v28, 177.
3. Spain, D. M., *Science*, 1950, v112, 335.
4. Schilling, J. A., Radakovich, M., Favata, B. V., Filer, L. J., and Jespersen, H. W., *Surg. Gynec. and Obst.*, 1953, v97, 434.
5. Taylor, F. W., Dittmer, T. L., and Porter, D. O., *Surgery*, 1952, v31, 683.
6. Cole, J. W., Orbison, J. L., Holden, W. D., Hancock, T. J., and Lindsay, J. F., *Surg. Gynec. and Obst.*, 1951, v93, 321.
7. Muller, W. H., Spencer, F. C., and Lewis, A. E., *Surgery*, 1953, v33, 399.
8. Hume, D. M., and Moore, F. D., *Proc. 2nd Annual ACTH Conf.*, Blakiston Co., Phila., 1951, 302.
9. Zimmerman, Bernard, Armour Laboratories Clinical ACTH Conf., 1952, 359.
10. Ragan, Charles, Discussion of reference 8.
11. Coppinger, W. R., and Godner, M. G., *Surgery*, 1950, v28, 75.
12. Fellows, N. M., Burge, Joe, Hatch, C. S., and Price, P. B., *Surgical Forum, Am. Coll. Surg.*, W. B. Saunders Co., Phila., 1952, 111.
13. Sako, Yoshio, and Wangenstein, O. H., *ibid.*, 1951, 117.

Received April 30, 1954. P.S.E.B.M., 1954, v86.