2-4969 in the treatment of human tuberculosis must await prolonged clinical trial. It is significant, however, that no toxic reactions to Ro 2-4969 were observed.

Summary. 1. Ro 2-4969, a compound of low solubility, related to isoniazid, has been administered experimentally to human subjects to determine the rate and extent of absorption from the gastrointestinal tract. 2. The compound or its derivatives appeared in the plasma and, probably because of slow absorption, detectable and clinically significant amounts remained for a longer period than when the highly soluble isoniazid was administered. 3. The drug administered in a single daily dose of 10 mg/kg/day was found to maintain drug concentrations of one μg/ml of plasma without dangerous cumulative effect. 4. No toxic reactions have been observed in 26 patients treated for 2 months or more.

1. Grunberg, E., and Schnitzer, R. J., *Quart. Bull. Sea View Hosp.,* 1952, v13, 3.

2. Schnitzer, R. J., and Grunberg, E., personal communication.

3. Benson, W. M., Roe, M. D., and Mermod, C., personal communication.

4. Rubin, S. H., Drekter, L., Scheiner, J., and De Ritter, E., *Diseases of the Chest,* 1952, v21, 75.

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The Effect of Adrenalectomy on Propulsive Motility of the Small Intestine in Rats. (20625)

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Digestive disturbances occur in Addison's disease and in adrenal insufficiency in animals (1,2), but relatively few direct studies of gastro-intestinal behavior after adrenalectomy have been reported. Anorexia, nausea, vomiting, either constipation or diarrhea, and abdominal pain are symptoms in Addison's disease; congestion, diffuse hemorrhage of the intestine and bloody diarrhea are common in adrenalectomized animals. Vogt(3) found that the circular muscle coat of the isolated intestine of the adrenalectomized rabbit frequently developed powerful, spasmotic, rhythmic contractions, while Auerbach's plexus often failed to respond to normally effective stimuli. Since adrenal extract did not restore normal activity, it was concluded that the abnormal intestinal behavior was due to secondary effects of adrenal removal.

Methods. Propulsive motility of the small intestine was studied by the method of Van Liere *et al.*(4) in 82 young male, albino Wistar rats, weighing from 90 to 150 g. Thirty adrenalectomized rats were tested 4 to 7 days after operation. Since two types of control animals (intact and sham-operated) are necessary, 15 intact and 19 sham-operated were tested. Purina Laboratory Chow and tap water was supplied *ad libitum,* and daily food intake was measured. Since adrenalectomized rats lose their appetite, controls for the effect of relative starvation were performed by feeding an additional 6 intact and 12 sham-operated rats a daily amount of food equal to the average amount eaten by adrenalectomized rats and testing them after periods of reduced food intake equal to that after adrenalectomy. In all groups, the rats were starved for 24 hours prior to testing for intestinal propulsion.

Results. The results are presented in Table I as percent of the total number of rats in each experimental group falling within each 5% range of the length of the small intestine traversed by the test meal of charcoal. No essential difference occurred between the intact and sham-operated rats. Partial starvation of both normal and sham-operated rats produced some increase in intestinal motility. However, no significant differences were found

* Many of the experiments were performed by the following graduate students: Milton Stern, Harold Carlin, and Mario M. Boschetti.

TABLE I. Effect of Adrenalectomy or Relative Starvation on Propulsive Motility of Small Intestine in Rats (Expressed as % of Total No. of Rats in Each Experimental Group).

Type of rat	No. of rats in group	% of small intestine traversed by test meal								
		56–60	61–65	66–70	71–75	76–80	81–85	86–90	91–95	96–100
Intact normal	15			13*	20	27	20	20		
Normal starved	6					33	17	33	17	
Sham-operated	19		5	11	11	21	31	21		
Sham-operated starved	12		8		8	25	34	8	17	
Adrenalectomized	30	10	3	3		10	7	23	34	10
Total controls	52		4	8	11	25	27	19	6	

* % given as the nearest whole figure.

among the 4 control groups, and consequently the combined data were used for comparison with the adrenalectomized group.

The adrenalectomized rats differed in two respects from the controls. The small intestines were more active, since 67% exhibited propulsion of the charcoal beyond 85% of the intestinal length. However, 10% had less active intestines than the controls, propelling the charcoal less than 61% of the distance.

The altered propulsive activity of the intestine was not related to the physiological condition of the adrenalectomized rats. For example, severe adrenal insufficiency appeared in approximately one third of those with increased motility and also in the same proportion showing decreased motility. The condition of the other two-thirds in each group varied from poor to fair or good.

Discussion. The increased motility of the small intestine in adrenalectomized rats may be associated with changes in the electrolyte balance in the body. Hyperpotassemia occurs during adrenal insufficiency in rats(5,6) and high potassium may stimulate smooth muscle (7,8). Furthermore, hypomotility occurs in rats during potassium deficiency and potassium injections stimulate active movements(9).

Summary. Adrenalectomized rats showed greater propulsive motility of the small intestine than intact, sham-operated, or partially starved controls. A small proportion exhibited abnormally reduced activity. The altered activity during adrenal insufficiency may be associated with changes in the potassium balance.

1. Stewart, G. N., *Arch. Int. Med.,* 1929, v43, 733.

2. Hartman, F. A., and Brownell, K. A., *The Adrenal Gland,* Philadelphia, 1949, pp. 205, 350, 420.

3. Vogt, M., *J. Physiol.,* 1943, v102, 239.

4. Van Liere, E. J., Stickney, J. C., and Northup, D. W., PROC. SOC. EXP. BIOL. AND MED., 1951, v76, 102.

5. Harrison, H. E., and Darrow, D. C., *J. Clin. Invest.,* 1938, v17, 77.

6. Harrison, H. E., and Harrison, H. C., PROC. SOC. EXP. BIOL. AND MED., 1939, v42, 506.

7. Katz, L. N., and Lindner, E., *Am. J. Physiol.,* 1938, v124, 155.

8. Dawes, G. S., *J. Physiol.,* 1941, v99, 224.

9. Henrikson, H. W., *Am. J. Physiol.,* 1951, v164, 263.

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