

cases of frontal and parietal lobectomies, if functional differences between the lobes played no role. It is therefore perhaps not without significance that the longest delay in development of discrimination of direction was observed after the temporal lobectomies.

For an evaluation of these observations it may be recalled that a postoperative development of simple CR to sound and light stimuli is possible after decortication or after ablation of the cortical endings of the respective sensory systems and that the acquisition of such reactions is not or only slightly delayed.<sup>6</sup> As pointed out by Jacobsen<sup>7</sup> the fact that such CR may be mediated through subcortical mechanisms in absence of the cerebral cortex does not exclude the possibility that the cortex plays a role in these reactions in the intact brain, as shown by experiences on post-operative retention and forgetting of CR in cortical lesions. Experiments in this direction with CR to labyrinthine stimuli will be reported later.

### 11703

#### **Effect of Denervation of Intestine on its Motor Responses at a Site of Distention.**

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The inhibition of motility at sites between 3 and 20 cm in each direction from a region of distention in the innervated and denervated intestine of unanesthetized dogs has been described.<sup>1</sup> The following is an analysis of responses of the small intestine at the site of distention.

*Methods.* Sixteen dogs with Thiry or Thiry-Vella fistulae of the jejunum as follows were used: 7 with innervated intestinal segments, 2 with both innervated and denervated intestinal segments, 3 with innervated segments that were subsequently denervated, and four with denervated segments only. Several of these animals were the

<sup>6</sup> Poltyreff, S. S., and Zeliony, O. P., *Z. f. Biol.*, 1930, **90**, 157; Culler, E., and Mettler, F. A., *J. Comp. Psychol.*, 1934, **18**, 291; Marquis, D. G., and Hilgard, E. R., *J. Comp. Psychol.*, 1936, **2**, 157; *Brain*, 1937, **60**, 1; Kluever, H., *J. Psychol.*, 1936, **2**, 49; 1937, **4**, 383.

<sup>7</sup> Jacobsen, C. F., *Physiol. Rev.*, 1939, **19**, 303.

<sup>1</sup> Youmans, W. B., Meek, W. J., and Herrin, R. C., *Am. J. Physiol.*, 1938, **124**, 470.

same ones that were used in the former study. Intestinal motility was recorded by a balloon-mercury-manometer system in which the balloon and pressure tubing connecting the balloon with the manometer were filled with water.

Execution of an experiment was as follows. The balloon was emptied by gravity through a side-arm attached to the pressure tubing, and adjustments were made so that the manometer recorded the zero pressure level. The empty balloon was then inserted into the fistula of the unanesthetized animal. Several minutes later 7 cc of water were introduced into the side-arm of the manometer system as rapidly as possible from a 10 cc syringe. This procedure produced

TABLE I.  
Pressures Attained (in mm of Hg.) Following Sudden Filling of Innervated and Denervated Intestinal Segments in Intact Dogs.

Experiment No. and dog No.	Maximum pressure at end of filling	Active increase in response to filling	Absolute maximum if active increase occurred	"Diastolic" pressure at end of 15 min
Innervated segments.				
I, 1	118			42
II, 1	142			36
III, 1	124			54
IV, 1	128			54
V, 1	140			32
VI, 1	162			42
VII, 1	130			34
VIII, 1	130			22
IX, 1	114			44
IX, 2	118			44
X, 1	76			36
X, 2	126			36
XI, 1	162			68
XI, 2	110			56
XI, 3	140			60
XII, 1	168			70
Avg	130			46
Denervated segments.				
VII, 2	170			28
VII, 3	164			30
VIII, 2	144	74	218	58
X, 3	124	20	144	46
X, 4	122			44
X, 5	120			50
XI, 4	160	8	168	92
XI, 5	148	14	162	80
XIII, 1	180	44	224	98
XIV, 1	172			80
XIV, 2	220			91
XV, 1	164	50	214	70
XV, 2	190			74
XVI, 1	158			82
Avg	160			66

a sharp rise in pressure as seen in the illustration. The balloons were of sufficient size to accommodate the amount of fluid used without being stretched. Records were analyzed with regard to (1) pressure at the end of the introduction of the water, (2) maximum pressure attained, and (3) "diastolic" pressure at the end of 15 minutes.

*Results.* The responses of the denervated segments of intestine were found to differ from the innervated with regard to (1) resistance to stretch, (2) excitatory responses to distention, and (3) rate of decrease of the pressure during the sustained distention. Analyses of individual experiments are shown in the table. In innervated intestinal segments the pressure at the end of the introduction of the water into the manometer system ranged from 76 to 168 mm of Hg. with an average of 130 mm of Hg. In the denervated segments the pressures reached at the end of the introduction of the water ranged from 120 to 220 mm of Hg. with an average pressure 160 mm of Hg. The increased resistance to stretch in the denervated intestine may be explained as a true increased tonus of the smooth muscle or as a result of atrophic and fibrotic changes which occur in the unexercised intestine after denervation. An attempt was made to minimize the latter factor by the use of freshly denervated and exercised

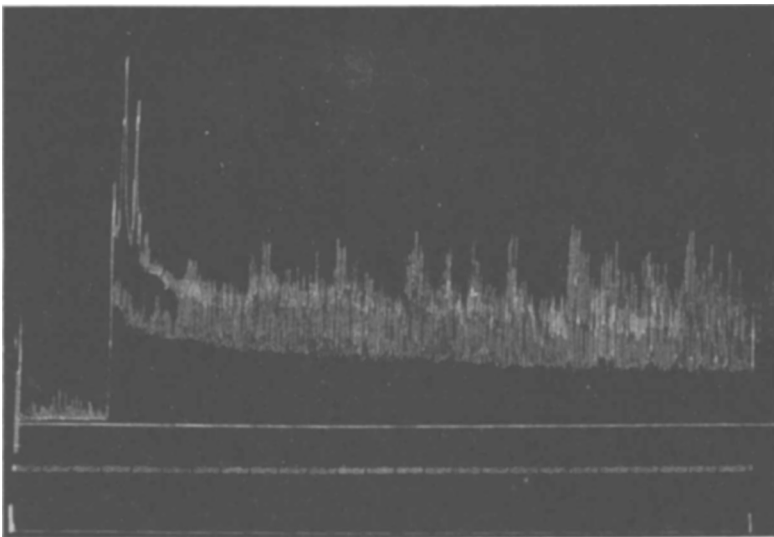


FIG. 1.

Superimposed curves showing differences in pressure changes in the innervated (lower record) and denervated (upper record) intestinal segments of the same unanesthetized dog produced by rapid filling with identical volumes of water. Balloon-mercury-manometer records. Time in 5-second and 1-minute intervals. Base line indicates zero pressure. Further explanations are given in text.

segments. The increased resistance to stretch following denervation was evident in some cases when the segment was used within one week following the operation.

A direct stimulatory effect of distention on the smooth muscle of the intestinal wall was demonstrated. In the innervated intestine the maximum pressure resulted from the resistance to stretch and was attained at the end of the filling with water. This is illustrated in the lower record of the figure. In 6 of the experiments the denervated intestinal smooth muscle responded to the filling with strong contractions so that the pressure was actively increased to still higher levels. This type of response is illustrated in the upper record of the figure. In three instances pressures of 214 to 224 mm of Hg. were produced by the contraction of extrinsically denervated intestinal smooth muscle against the contents of the distending balloon. The high pressures thus produced lasted for less than a minute and were followed by a sharp reduction in pressure. Gradual reduction in pressure continued during the remainder of the 15 minute period.

At the end of 15 minutes the "diastolic" pressure in the innervated intestine was between 22 and 70 mm of Hg. with an average of 46 mm of Hg., while in the denervated intestine it was 28 to 98 mm of Hg. with an average of 66 mm of Hg.

Failure of the innervated intestine to show the strong motor response to distention which commonly occurs in the denervated intestine affords evidence that the innervated intestine at the site of distention is subject to inhibitory influences from extrinsic nerves.

*Interpretation.* The combined results of this and of the previous study<sup>1</sup> provide a basis for description of the sequence of responses of the innervated and the denervated intestine to rapid filling. The pressure or stretch produced by distention stimulates afferent nerve endings, and reflexes are competed over extrinsic nerves rapidly resulting in inhibition of the intestinal smooth muscle along a considerable section including the site of the distention. Denervation of the intestine unmasks a direct excitatory effect of distention on the smooth muscle at the site of distention. A result of these responses is hypermotility of the intestine at the site of distention as compared with the motility in immediately adjacent segments. Therefore, the extrinsic nerves of the intestine contain the pathways for reflexes having a contents-dispersing and pressure-regulating value. Distribution of contents is accomplished in the denervated intestine by the development of relatively higher pressures at the site of distention and by more slowly acting inhibitory influences mediated by local mechanisms.

*Summary.* The role of the extrinsic nerves in the local intestinal

response to filling and distention has been studied by subjecting innervated and denervated intestinal segments of unanesthetized dogs to identical distending forces. Distention acts as a stimulus to the smooth muscle of the denervated intestine so that an active pressure increase may be induced by the stretch and passive pressure resulting from a standard amount of filling. The stimulatory effect of filling is not equally evident in the innervated intestine. This result may be interpreted as indicating that the degree of motility observed at the site of a distention in the innervated intestine depends, in part, upon a balance between direct stimulatory effects and reflex inhibitory effects.

## 11704

## Cobalt Color Reaction of Barbiturates.\*

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Of the numerous analytical methods employed for the determination of barbiturates, those making use of specific color reactions have been most extensively studied. Handorf<sup>1</sup> employed the murxide reaction for the detection of veronal, and Zwikker,<sup>2</sup> Bodendorf,<sup>3</sup> Herwick<sup>4</sup> and Koppanyi, *et al.*,<sup>5, 6</sup> have developed modifications of a color reaction with cobalt salts in conjunction with various bases.

Kozelka and Tatum<sup>7</sup> attributed this color formation to a specific reaction with substances containing one or 2 imide groups. In an investigation of amytal (isoamylethyl barbituric acid) excretion by dogs, using a modification<sup>9</sup> of the reaction designed by Koppanyi

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<sup>1</sup> Handorf, H., *Z. f. d. ges. exp. Med.*, 1922, **28**, 56.

<sup>2</sup> Zwikker, J. J. L., *Pharm. Weekblad.*, 1931, **68**, 975.

<sup>3</sup> Bodendorf, K., *Arch. Pharm.*, 1932, **270**, 290.

<sup>4</sup> Herwick, R. P., *Arch. internat. de Pharm. et de Therap.*, 1933, **45**, 160.

<sup>5</sup> Koppanyi, T., *et al.*, *ibid.*, 1933, **46**, 76.

<sup>6</sup> Koppanyi, T., *et al.*, *Am. Pharm. Assn.*, 1934, **23**, 1074.

<sup>7</sup> Kozelka, F. A., and Tatum, *J. Pharm. and Exp. Therap.*, 1937, **59**, 54.

<sup>9</sup> Krause, R. F., and Riley, Richard F., unpublished work.