

Fig. 3. 1 h after the injection of glycine- $^{14}\text{C}$  the splenic tissue becomes visibly black. The amino acid distribution is analogous in sham-thymectomized (above) and in thymectomized rats (below). It is possible to notice that the lymphatic follicles acquire glycine in a very low quantity. 30th day of experiment.

The data obtained confirm that the serum-proteic picture of a neonatally-thymectomized animal is unchanged; they also confirm that the process of serum-protidopoiesis remains within the limits of normality; particularly the synthesis of  $\gamma$ -globulins proceeds normally. Thus it is not in this way that the thymus influence on immunogenesis is mediated. The data on the 'humoral' intervention of thymus on immunogenesis<sup>13-15</sup> and the consideration that the  $\gamma$ -globulinopoietic device is probably safe in the thymectomized animal, would suggest attributing to thymus a 'starter' role: in any case, the mode and the exact course of this start to the power of immunological response is still unknown.

**Riassunto.** In ratti timectomizzati alla nascita e seguiti per 2 mesi non si osservano alterazioni a carico del quadro sieroproteico: in particolare i valori delle  $\gamma$ -globuline e l'incorporazione di glicina- $^{14}\text{C}$  in tale frazione sono analoghi a quelli trovati in animali sottoposti a falsa timectomia.

Pure qualitativamente simile appare la distribuzione dell'aminoacido marcato nel parenchima splenico e in quello epatico dei ratti di entrambi i gruppi.

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(Italy), April 9, 1965.

<sup>13</sup> D. OSOBA and J. F. A. P. MILLER, *Nature* 199, 653 (1963).

<sup>14</sup> L. W. LAW, L. TRAININ, R. H. LEVEY, and W. F. BARTH, *Science* 143, 1049 (1964).

<sup>15</sup> L. BUSCARINI, G. BEDARIDA, and P. MARANDOLA, *Exper.* 20, 696 (1964).

## Peristaltic Movement of the Tortoise Intestine

While 5-hydroxytryptamine (5-HT) has an excitatory effect on various intestinal musculatures<sup>1,2</sup>, it was shown that on isolated tortoise intestine<sup>3</sup> 5-HT had a weakly excitatory as well as an inhibitory effect. The different responsiveness to 5-HT in the tortoise intestine prompted us to study the nature of the peristaltic movement and its modification by 5-HT in this animal. In the present study intestinal strips of the tortoise, *Amyda japonica*, which is found in the waters in Korea, were used. To study peristaltic activity, the upper part of the intestine (ca. 5 cm in length) was dissected out and suspended in oxygenated Ringer solution at 25°C, according to the method of TRENDELENBURG<sup>4</sup>, or BELESIN and VARAGIC<sup>5</sup>. To investigate differences in responsiveness of longitudinal and circular muscle of the tortoise intestine, three preparations (circular, longitudinal, and the usual Magnus preparation) were suspended in the same 100 ml organ bath and their responses were examined simultaneously. The circular

preparation was made as follows: after cutting the intestine so as to make a ring of an intestinal segment 5 mm in width, 3 such rings were connected through cotton thread to make a chain, and the chain was suspended in the bath. The longitudinal preparation was made by cutting the intestine in the direction of the longitudinal fibres 5 cm in length and 5 mm in width.

Unlike mammalian intestinal strips, the peristaltic movement could not be induced either by increasing intraluminal pressure (up to 80 mm H<sub>2</sub>O) or by the simultaneous application of pressure and 5-HT (up to 1 mg/ml) on the intraluminal surface (9 experiments). Intraluminal

<sup>1</sup> V. ERSFAMER, *Pharmac. Rev.* 6, 425 (1954).

<sup>2</sup> R. FÄNGE, *Pharmac. Rev.* 14, 281 (1962).

<sup>3</sup> C. C. TOH and A. MOHUDDIN, *Brit. J. Pharmac. Chemother.* 13, 113 (1958).

<sup>4</sup> P. TRENDELENBURG, *Arch. exp. Path. Pharmac.* 81, 55 (1917).

<sup>5</sup> D. BELESIN and V. VARAGIC, *Brit. J. Pharmac. Chemother.* 13, 266 (1958).

application of acetylcholine (up to 100  $\mu\text{g/ml}$ ) and pressure also failed to produce peristalsis. However, addition of 5-HT or acetylcholine in doses as low as 0.01  $\mu\text{g/ml}$  into the bath, i.e. application of the drugs on the serosal surface, in combination with elevated intraluminal pressure (usually 30 mm  $\text{H}_2\text{O}$ ) caused peristaltic movements in all the experiments (27) (Figure 1). Development of the peristaltic activity was not prevented by the local anaesthetic tetracaine (10  $\mu\text{g/ml}$ ).

In the above experiments, the application of intraluminal pressure produced inhibition of spontaneous pendular movements and an increase in the tone of longitudinal muscle. Acetylcholine caused a spasmogenic contraction of the longitudinal muscle, but 5-HT, either with or without pressure, exerted only a transitory weak stimulation. These findings suggested that there are important differences in the responsiveness of circular and longitudinal muscle to 5-HT. To explore this possibility further, the experiments involving three types of preparations described above were employed. 5-HT (up to 100  $\mu\text{g/ml}$ ) did not cause contraction of the longitudinal muscle and the Magnus preparation in most experiments (27 out of 29 cases), but caused contraction of the circular strip with doses between 0.01 and 0.1  $\mu\text{g/ml}$ . An illustrative experiment is depicted in Figure 2. Increasing doses elicited greater responses and the maximal response was usually attained with 10  $\mu\text{g/ml}$ . Acetylcholine (0.1  $\mu\text{g/ml}$ ) caused contraction of each strip; the sensitivity of each muscle layer was not markedly different. Dimethylphenylpiperazinium (1–50  $\mu\text{g/ml}$ )<sup>6</sup> caused contraction of the longitudinal and Magnus preparation without affecting the circular muscle. The contractile response of the circular strip to 5-HT was not affected by pretreating the intestine for 30 min with morphine (10  $\mu\text{g/ml}$ ), atropine (0.01  $\mu\text{g/ml}$ ), hexamethonium (10  $\mu\text{g/ml}$ ), but was either abolished or markedly inhibited by phenoxybenzamine (0.01  $\mu\text{g/ml}$ ) or methysergide (0.01  $\mu\text{g/ml}$ )<sup>6</sup>.

The results indicate that there are significant differences in the peristaltic activity of the tortoise and mammalian intestine. In contrast to the findings in mammals, in which the peristaltic reflex could be produced by the intraluminal application of pressure and 5-HT<sup>7-9</sup>, the peristaltic reflex in the tortoise was not affected by these procedures. Another peculiarity of the tortoise intestine was the difference in the response of the longitudinal and circular muscle to 5-HT. In the guinea-pig ileum, HARRY<sup>10</sup> observed findings contrary to our results, i.e. the longitudinal muscle responded to 5-HT but the circular did not.

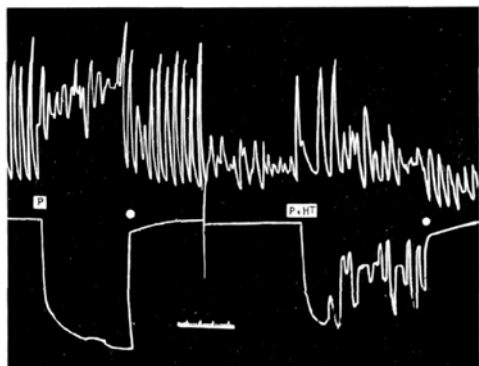


Fig. 1. Effect of 5-HT on the peristaltic movement of the tortoise intestine. Upper record: pendular movement. Lower record: peristalsis. At 'P' pressure of 30 mm  $\text{H}_2\text{O}$  was applied intraluminaly. At 'P + HT' intraluminal pressure (30 mm  $\text{H}_2\text{O}$ ) and 5-HT (0.1  $\mu\text{g/ml}$ ) were applied simultaneously. At white dot, pressure was removed. Time: large division equals 1 min.

According to the 5-HT receptor theory<sup>11,12</sup>, the insensitivity of the longitudinal muscle is interpreted as indicating the absence of the 5-HT receptors in this layer; on the other hand, the high sensitivity of the circular muscle indicates the presence of a large number of these receptors. The inability of morphine, atropine or hexamethonium to block the 5-HT action, in contrast to the blocking effects of methysergide or phenoxybenzamine, suggests that 5-HT receptors in the tortoise circular muscle are located in the muscle structures per se. The failure of dimethylphenylpiperazinium to affect the circular muscle suggests the lack of nervous structures in this tissue. This is supported by the fact that the local anaesthetic, tetracaine, did not block the development of the peristaltic movement by 5-HT. From these observations, it seems that muscular elements played a major role in the development of the peristaltic movement in the tortoise intestine. This may explain, at least in part, the differences in the nature of the peristaltic movement in the tortoise from that of mammals.

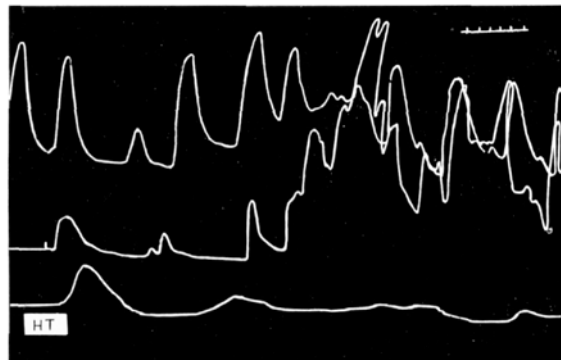


Fig. 2. Response of Magnus preparation (upper), circular strip (middle) and longitudinal strip (lower) to 5-HT. At 'HT' 0.5  $\mu\text{g/ml}$  of 5-HT was applied. Time: 10 sec.

**Zusammenfassung.** Am Schildkrötendarm kann die peristaltische Bewegung weder durch Erhöhung des Binnendrucks, noch durch Kombination interner Applikation von 5-Hydroxytryptamin oder Acetylcholin mit Druck angeregt werden. Druckwirkung auf die Mucosa und Einwirkung von 5-Hydroxytryptamin oder Acetylcholin auf die Serosa war jeweils erfolgreich. Präparate von Längsmuskelstreifen reagierten nicht auf 5-Hydroxytryptamin, während die Ringmuskelstreifen mit Kontraktur antworteten.

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<sup>7</sup> E. BULBRING and A. CREMA, Brit. J. Pharmac. Chemother. 13, 444 (1958).

<sup>8</sup> T. FUKUHARA, S. NAKAYAMA, and R. NANBA, Jap. J. Physiol. 10, 420 (1960).

<sup>9</sup> C. Y. LEE, J. Physiol. 152, 405 (1960).

<sup>10</sup> J. HARRY, Brit. J. Pharmac. Chemother. 20, 399 (1963).

<sup>11</sup> J. H. GADDUM and D. P. PICARELLI, Brit. J. Pharmac. Chemother. 12, 323 (1957).

<sup>12</sup> M. DAY and J. R. VANE, Brit. J. Pharmac. Chemother. 20, 159 (1963).