Current Problems in Constipation¹

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When Bayliss and Starling stated that “in no other sector of physiology do opinion and fact differ so widely as in the physiology of intestinal motility” in 1899, they could have had no idea that, more than half a century later, the situation would hardly have changed. The physiology and pathophysiology of intestinal motility and of the passage of ingesta through the intestine, have become interesting again in the last decade. Results of animal experiments and clinical findings have often been at odds with the generally accepted teachings. Even today, for example, the opinion is widespread that intestinal hypermotility leads to accelerated passage and thus to diarrhoea, while the intestinal movements in constipation are characterized predominantly by hypomotility and “atony”.

The information on the pathophysiology of intestinal movements is based almost exclusively on results produced by cineradiography and intraluminal manometry. The results can in as much as a definitive judgement is possible at this stage – be summarized by saying that the intestinal transport of ingested material is subject to similar laws as those pertaining to the blood circulation. The dominating factors are the pressure gradients between the proximal and distal parts of the intestine, and the peripheral resistance, which inhibits the transport and which is chiefly based on the segmental contraction of the intestinal wall [16]. Segmental intestinal contractions such as are also manifested in the formation of haustra, are the chief intestinal activity responsible for increasing the intraluminal pressure and can thus be recorded manometrically [15]. Propulsive intestinal movements usually lead to no, or only insignificant, manometric waves. Pressure measurements in the small and large intestines provided apparently paradox results. They showed that in constipation, the intestinal activity tending to promote an increase in pressure, is often increased or normal, while in diarrhoea, a striking manometric “calm” is usually recorded in the intestine. Segmental intestinal activity, which inhibits the passage of ingesta, is thus less often recorded than in healthy persons [2, 5, 7]. Diarrhoea means accelerated passage as a result of reduced local intestinal contractions, while constipation is, in the main, the expression of an obstruction of the passage of ingesta resulting from increased segmental activity. Thus the constipative effect of codein and opium is not – as is generally believed – due to the lowering of the intestinal tone, but results from an increase in the intensity of segmental intestinal contractions [14]. For this reason, anticholinergic drugs can, in cases of constipation not only act “spasmolytically”, but can also accelerate the transit of ingesta so that they usually remain without effect in cases of diarrhoea.

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The influence of sympathetic and parasympathetic nerves on the activity of the intestine in vertebrates becomes progressively less, from the amphibian onwards. In higher vertebrates, when both the sympathetic and parasympathetic nerves supplying the intestine are severed, intestinal activity still continues apparently normally [8]. Sympathectomy has no effect, and vagotomy no clinically recognizable effect on intestinal motility [3] in most cases. In addition to this nervous regulation, the intestinal activity is also influenced by humeral and hormonal factors. Constipation is a symptom of primary hyperparathyroidism and of other hypercalcemia syndromes. A direct effect of the parathormone on the intestinal musculature was not proved. Both acute and chronic hypercalcemia stimulate the gastric secretion of acid and the functional activity of endocrine cells [1, 12]. An increase in the extracellular calcium concentration promotes the inter- and intracellular spread of excitation. In many functions, magnesium acts as an antagonist to calcium. In three separate series of investigations, we examined the influence of acute hypercalcemia and hypermagnesemia on the activity of the intestinal musculature tending to promote an increase in pressure. During intravenous infusion of calcium with subsequent hypercalcemia, a significant increase in intestinal motility (wave frequency, length of activity and motility index) compared with the resting motility and with placebo infusion (fructose) was demonstrated. In the second and third experimental series, hypermagnesemia was induced. The result was a statistically significant inhibition of the resting motility and of the colon motility associated with pressure activity and induced by hypercalcemia (wave frequency, length of activity, motility index and wave amplitude). All in all, these experimental results allow us to draw the conclusion that hypercalcemia stimulates the smooth muscles of the intestine to pressure-active segmental activity, and in this way delays the intestinal passage of ingesta. Hypermagnesemia inhibits both this influence of hypercalcemia and the pressure-active resting motility, and thus produces intraluminal pressure curves such as are often recorded in cases of diarrhoea. Our results are, to some extent, at odds with clinical observations in patients with hypomagnesemia and diarrhea which could only be influenced by the administration of high doses of magnesium [9].

The peptide hormones which influence intestinal motility, include bradykinin, vasopressin and others, as well as gastrin, which has been analysed and synthesized in the meantime. In experiments, both with animals and human subjects, a motility-enhancing effect has been demonstrated in both small and large intestine [10, 11]. As a result of his investigations, Logan [10] has spoken of a physiological mediator role played by gastrin in the gastrocolic “reflex”. Our information on the hormonal physiological regulation of intestinal motility is still completely inadequate. Above all, we know too little about these hormones in the pathophysiology of intestinal movement. The same is true for serotonin, which acts not only as a direct stimulant of the intestinal musculature, but which also works as a carrier substance of the newly discovered nonadrenergic neurons in the myenteric plexus, and thus indirectly inhibits the intestinal musculature. A third point of attack for serotonin is provided by the afferent nerve fibres in the intestinal mucosa, which are stimulated [6, 7]. Scientific interest is at present concerned with the potential