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HISTORY TRACES OF GASTROINTESTINAL MOTILITY IN POLAND

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The objectives of this chapter was to show how motility studies were developed and performed in Poland at the end of century to better understand pathophysiology and improve the clinicians ability to evaluate and treat patients with motility - related disorders. Some of the important historical points along the path to current understanding of the form and function of gastrointestinal motility are presented. Scarce information exists about other than Cracow and Wrocław motility centers in Poland in previous century. Lately sophisticated technology became available in Poland and more centers have begun to yield more effective strategies of treatment and enhanced understanding of the pathophysiologic mechanisms underlying GI motility disorders.

Key words: history, motility, myoelectric activity, MMC, Poland

INTRODUCTION

Neurophysiology of intestinal motility

The importance of the enteric nervous system as a major controlling factor of GI motility has resulted in better understanding of the neurophysiology of intestinal motility.

Twentieth century progress in gastroenterology hinged on a conceptual transition from preganglionic/postganglionic to little brain determination of gastrointestinal behaviour. Gastrointestinal behavior represents two main types of activity in the small bowel local one designed mainly to knead the intestinal contents and rub them over absorbing surface and the other travelling contractions, designed to move material from one segment to the other.

Early in the nineteenth century Beaumont (1) watched the movement of a 10-inch thermometer inserted into the stomach of Alexis St. Martin through an accidentally created gastrostomy. He first recognized the to-and-fro movement of gastric contents. As the nineteenth century ended WB Cannon (2) used one of the first roentgenoscopes in the United States to observe the effects of gastric motor activity. He described peristaltic contraction rings pressing contents toward and through the pylorus and some contents back into the corpus from the antrum. He reported contraction of the fundus uncoordinated with the antrum and noted that antral contractions became progressively more vigorous. The association of most powerful contractions with hunger "pangs" experienced by patients was studied extensively by Carlson (3) and his pupils (4).

Advances achieved in the last century have relied on a confluence of research of smooth muscle physiology, anatomic/mechanical factors, flow dynamics, as well as basic molecular and cellular biology. The measurement of gut motility has been a constant goal during this era, particularly the study of peristaltic contractions by means of recording pressure in the gut lumen. The quantitation of intraluminal pressures started with the use of balloons inflated in the stomach and intestine (*Fig. 1*). Early in the 1920's Wheelon and Thomas (5) came first to the

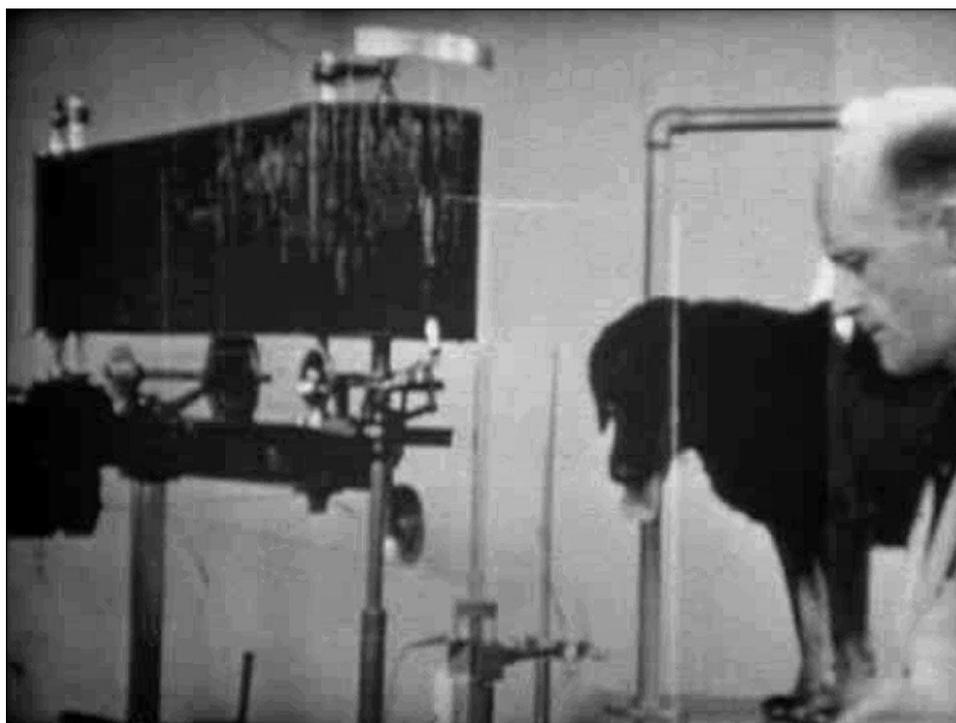


Fig. 1. Gastric motility recorded by Gregory (From "Gastric secretion" edited by Cyril Jenkins ICI Unit Film, 1952)

firm conclusion that the pyloric sphincter was not an independent muscular structure, but contracted in coordination with the distal end of the stomach.

In the 1950's, open - tipped catheters with the continuous perfusion began to be used to study esophageal motility. Improvements include the continuous perfusion catheters with low - compliance Arndorfer pump and the Dent sleeve, which have facilitated the study of sphincters. By 1957 Thomas (6) in an extensive review article concluded that gastric emptying was related to peristalsis and that pyloric closure took place as part of the contraction of the antrum. By the 1990's scintigraphy has developed and used in flow studies of GI tract and become to be performed routinely in clinical practice. Scintigraphy enabled quantitation of esophageal and gastric emptying as well as small bowel and colonic transits. An early description of the motor action of the small bowel was that of Ludwig (7) published in the second volume of the *Lerhbuch der Physiologie des Menschen* in 1861. He described the motor action of the small bowel as consisting of either single contractions limited to one site, or coordinated movements. The latter he stated could be divided into either recurring, stationary, rhythmic and circular contractions or progressive. The last were described as "peristaltic" moving downward or "antiperistaltic" from below upward. Bayliss and Starling (8) in 1899 published the first detailed account of peristalsis in the dog. Their observations led to the formulation of the famous "law of intestine".

Real scientific investigation of gut wall movement began with the use of electrodes and miniature force transducers sewn to the intestinal wall. Alvarez recorded first electrogastrogram in 1921 (9). With his electrical and also mechanical techniques and motion pictures he found that both in man and in dogs there is a definite 11- per - minute rhythm near the cardia of the stomach. In the rest of the stomach there are usually three waves per minute. Electromyography started to be used to enhance our understanding of gut wall motion. In the gut electric slow waves govern the rhythmicity of contractions and slow waves of the stomach and small bowel began to be studied extensively by muscle physiologist in the 1950's and 1960's. In the 1930's, it was believed that gut motor activity occurred as a result of opposition between excitatory parasympathetic and inhibitory adrenergic nerves.

The prevailing concept in the first half of previous century was classical autonomic organization of neural control. Ganglia were parasympathetic and postganglionic parasympathetic neurones released acetylcholine to achieve response from the muscle or/and secretory effectors. Opposite postganglionic sympathetic neurons released norepinephrine to suppress motility and secretion. Automated control functions were wired into the neurons of the central neurones system. No decision-making ability was attributed to the nervous system in the gut. Biggest advance of the previous century was realization that the nervous system of the gut is wired with circuits, which created an independent integrative system.

Langley (10) first recognized that the ganglia of the gut did more than relay information from the brain. He could not reconcile the large disparity between the 2×10^8 neurons in the gut and few thousand fibers in the vagus nerves. In the last decade of the previous century autonomic system new division was accepted as parasympathetic, sympathetic and enteric. The logic of this seems to be simple instead of crowding neurons into the brain and relying on signal transmission, more reasonable is to place integrative neurons at the site of the effectors. Neural networks in intestinal wall generate output signals that keep homeostatic behavior of the effectors system for active computing sensory signals. Extrinsic nerves as shown by Carlson (11) in 1922's are not to be regarded as directly innervating the gastric smooth muscle, but as serving merely as connecting links between the reflex centers in the central nervous system.

Four functions emerge from the "wiring configurations" in the enteric nervous system (ENS). These functions include reflexes, pattern generation, co-ordinated recruitment and gating programs. Reflex behavior is automatic and occurs outside levels of consciousness. The peristaltic reflex circuit is a fixed set of connections confined to short segments of the gut. These sets are repeated serially along the intestine. Synaptic gates that determine a number of propulsive events to occur interconnect peristaltic circuits.

A critical advance toward the minibrain model came in early 1960 with the discovery of some nonadrenergic-noncholinergic (NANC) neurons. The discovery of inhibitory NANC neurons was the legacy of E. Bülbring and her postdoctoral fellows M. Holman and G. Burnstock (12). By 1970 they had evidence that ATP was the transmitter responsible for IJP despite to the widely spread skepticism of the scientific community. S. Said and V. Mutt reported a new vasoactive peptide that was to become the next inhibitory neurotransmitter, VIP. In 1970 and 1980 R. Goyal and G. Macklough implicated VIP in peptidergic neurotransmission in the gut, while pioneering work on new candidate, NO, was done by J. Gillespie in the 1990 (13).

Hormonal regulation of gastrointestinal motility

At 70's hormonal era began in physiology of the GI tract. The importance of GI motility in explaining GI symptoms and disease has been increasingly recognized over the past two decades. There has also been heightened awareness of the symptoms and symptom complexes associated with different motility disorders. At the beginning of the century physicians believed that the GI tract was at rest during fasting. The migrating myoelectric complex (MMC) was first clearly described by Code and Szurszewski in canine studies (14) and by Ruckebusch (15) in sheep studies in France. The MMC was first described in humans in 1975 by Stanciu and Bennet (16) and in 1977 by Vantrappen (17). Differences in fasting and fed pattern of gut motility were firmly established. MMC is seen in all states of prolonged fasting with cycle frequency ranging from

1 - 2.5 hours. Plausible explanation for quiet period of MMC is high activity of inhibitory motor neurons that results in the continuous release of inhibitory neurotransmitters. Quiescence of the circular muscles reflects operation of a neural program that holds all gating points within and peristaltic circuits closed. This is a normal state persisting during phase I of MMC.

Department of Physiology in the Medical School in Cracow at that time was deeply involved mostly in the gastric and pancreatic secretion studies pioneered by S.J. Konturek. I received possibility to work as postdoctoral fellow in Department of Physiology of University of Texas chaired by G. Jacobson. When I arrived in 1975 in Weisbrodt's laboratory in Houston University my new boss was also involved in hormonal effects of myoelectric small bowel activity and published paper showing that pentagastrin and secretin alter electrical activity (18, 19). We started work in dogs (*Figs 2, 3*) on effects of CCK on myoelectric activity of the small bowel and concluded that CCK induced changes may be responsible for change of fasted to fed motility pattern (20). Tolerance to morphine was studied with T. Burks from Department of Pharmacology University of Texas (21). Further studies on gastrointestinal motility become possible in Department of Physiology here in Cracow when prof. Konturek bought equipment, namely Beckman R-611 recorder most precious thing we have

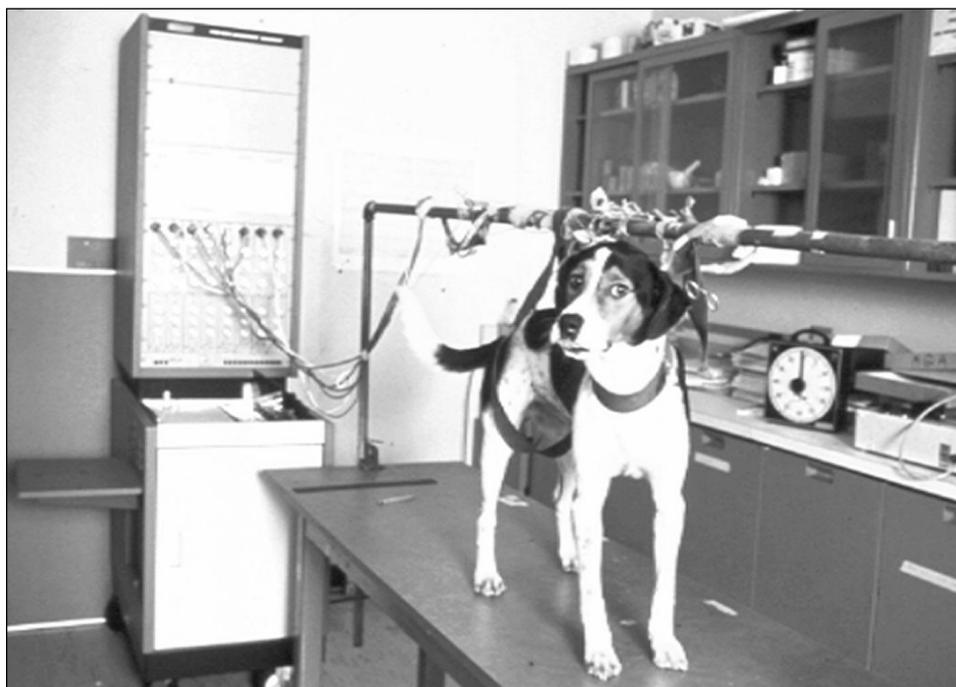


Fig. 2. Recording myoelectric activity in dogs with use of Beckman recorder in 70's in Weisbrodt's motility laboratory.

had at that time in our department. Our Cracow's studies of myoelectric activity of the gastrointestinal tract in the Department of Physiology started in late 70's. At that time first data on role GIP and insulin in glucose induced changes in intestinal motility have shown that duodenal glucose induced marked changes in intestinal motility patterns and in plasma levels of GIP and insulin, however these hormones are not solely responsible factors for the motility changes (22). Continuation of this work was study on effect of pancreatic polypeptide (PP) on intestinal motility. We found that PP does not play any role in fasted intestinal motility but may contribute, at least in part to the postprandial suppression of MMC (23) On the other hand it was found that exogenous PYY inhibits the interdigestive and postprandial motility pattern of the small bowel but does not affect gallbladder motility (24). In series of papers we studied the role of NO in the physiology of myoelectric activity. We found that NO system exerts tonic inhibitory influence on intestinal activity by reducing the frequency of MMC pacesetter and by suppressing the postprandial spike activity (25, 26). Studies on effects of CCK on gastric emptying and secretory response also were continued. We have shown that endogenous CCK released by a fatty meal delays gastric emptying and inhibits gastric acid and plasma gastrin responses in healthy subjects but in DU patients the inhibitory effect of CCK is less pronounced,



Fig. 3. Prof. NW. Weisbrodt in his actual lab.

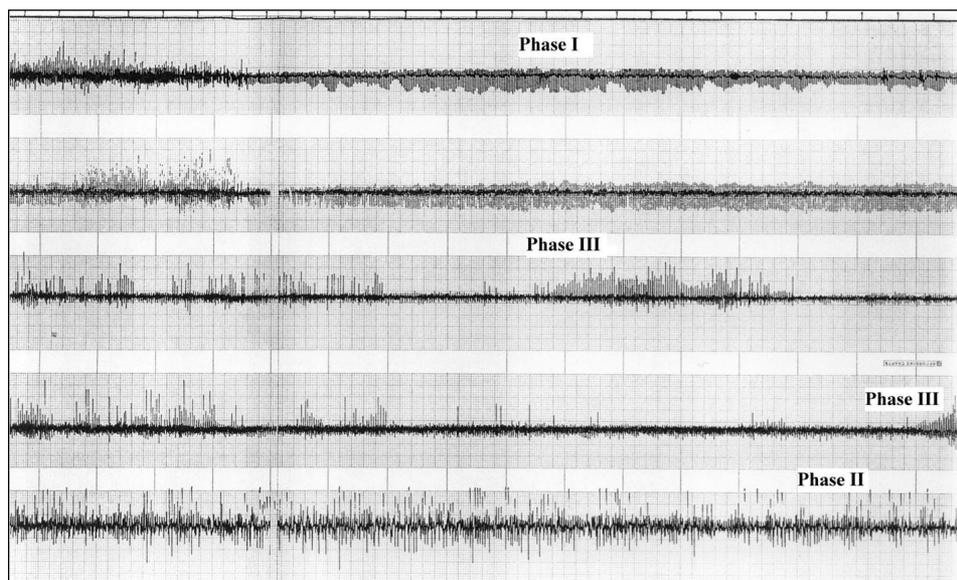


Fig. 4. MMC in dog.

suggesting a defect in the action of this hormone on gastrin release and gastric acid secretion (27). Somatostatin on the other hand induced extraduodenal phases III of MMC by inhibition of activity of the duodenal pacesetter and releasing other areas of enteric innervation (Fig. 4) (28).

Boldyreff phenomenon

The pioneering study of periodic gastro-intestinal motor activity started in the famous Pavlov Physiological Laboratory at St. Petersburg, Russia, where Boldyreff, first noticed the periodic gastric contractions in fasted animals. Feeding inhibited these periodic changes. Boldyreff in 1901-3 made the first definitive study of fasting complex (29). Fasting digestive tract is governed by a regular rhythm that modulates its secretory activity, however magnitude of these changes remains unknown. We found that pancreatic secretion in fasted dogs fluctuates periodically in phase with duodenal motility, but the phase III peak secretory output represents only minute fraction of the maximal pancreatic capacity (30). We have shown that also duodenal alkaline secretion fluctuates cyclically in phase with duodenal motility, which is related to vagal excitation. Similar changes were found in gastric alkaline secretion, which changes in phase with gastric motor activity and is similar in both normal and DU patients. Cephalic phase of gastric and duodenal secretion were related to cholinergic vagal activity and to gastroduodenal motility (31). Motility of the gallbladder in fasted dogs shows cyclic changes with reduction of volume coinciding with the

spontaneous or motilin induced activity front in the duodenum. CCK and muscarinic receptors were involved in these effects (32).

Early in 60's Załucki in Wrocław's Veterinary School started to record gastric motility in sheep and bowel myoelectric activity with special electrodes. In 80's after Leuven training Romański continued their work by recording myoelectric activity in dogs and sheep. Working on Boldyreff phenomenon he found that peaks of plasma bile acid concentration are due to arrival and absorption of bile acids secreted during phase 2 of MMC (33). In series of papers he studied relationship between bile secretion and motilin and pancreatic polypeptide (PP) release in interdigestive period. (34, 35). He noted that poor correlation of plasma bile acid peaks with motilin peaks are probably due to the variability of transport and absorption of bile acid.

Clinical implications of motility studies. Manometry

Small bowel motility is difficult to record and proximal small bowel motility has demonstrated considerable regional variations. However, it has been suggested that manometry may be useful for diagnosing the irritable bowel syndrom (IBS). Current technology enables 24-h ambulatory manometric recording. An example of improving the clinician's ability to evaluate and treat patients with motility-related disorders is combined ambulatory pH and manometric monitoring in-patients with reflux esophagitis.

Electrogastrography (EGG)

Experience with EGG has been extensive and has resulted in the identification of gastric motility pattern in health, nausea and delayed gastric emptying, however, its clinical value remains to be determined.

CONCLUSIONS

Most Polish traces in history of gastrointestinal motility in previous century concern two major topics; 1) hormonal regulation of the gastro-intestinal myoelectric activity in humans and dogs and 2) periodicity of motor and secretory activity of upper gastrointestinal tract and pancreas (Boldyreff phenomenon) in animals and humans realized in Cracow and Wrocław.

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