ANALYTICAL PROCESSES IN DIGESTIVE PHYSIOLOGY TODAY

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This article analyzes the main stages in the development of digestive physiology.

The Ancient and Middle Ages laid the foundations for the further development of this scientific field. In the modern era, knowledge continues to accumulate through new theoretical and experimental approaches to understanding processes in the body, and important discoveries are being made. Currently, digestive physiology is a significant branch of physiology.

The purpose of this article is to identify and characterize the main periods in the formation and development of digestive physiology. Comparative historical and analytical methods of historical and medical research were used in writing this work.

The main results include a presentation of the stages in the development of digestive physiology and a description of the contributions of key researchers in this field. The conclusion provides a summary of the formation and development of digestive physiology as a field of medical and biological knowledge.

Keywords: history of science, history of medicine, history of physiology, history of biology, physiology of digestion

The need to understand the functioning of the human body is as ancient as the existence of medicine. In the history of science, the study of the stages of formation and development, as well as the historical and scientific periodization of the development of medical and biological disciplines and fields, is very important.

The history of the formation and development of digestive physiology is an important section of study within university courses such as "History of Medicine," "History of Biology," and "Philosophy and History of Science," as well as in the study of specialized topics in specialized disciplines (gastroenterology, therapy, and others). In V.O. Samoilov's monograph "Illustrative Essay on the History of Physiology" (2005), one section briefly presents the main milestones in the development of digestive physiology.

Over the years, works have been published containing biographical summaries and reflecting the main achievements of leading Russian specialists in the physiology of digestion (L.O. Orbeli [1], I.P. Pavlov [3], L.Z. Morokhovets [4], and others). Lectures on the history of physiology in Russia by Professor Tatyana Sergeevna Sorokina, a leading Russian specialist in the field of the history of medicine [6], partially reflect the achievements of Russian physiologists in the 19th and 20th centuries. The above publications are fragmentary in nature, which in no way diminishes their significance.

In connection with the above, it seems important to create a historical and scientific analytical review of the development of ideas about the physiology of digestion, covering all stages of world history and reflecting the contributions of researchers from different regions, which will be useful for teaching historical and scientific disciplines, as well as for researchers studying the history of physiology. In preparing this publication, we primarily used articles in publications included in the Russian Science Citation Index (RSCI),

PubMed, Scopus, and Web of Science. Preference was given to materials published within the last 10 years.

Results: Background to the Development of Knowledge on Digestive Physiology in the Ancient World

The ancient Egyptians understood the major organs, including the intestines. The Ebers Papyrus (c. 1500 BC) mentions approximately 900 recipes for treating gastrointestinal diseases [5, p. 76].

According to ancient Indian beliefs, the "digestive fire" (agni) plays an important role in digestion. Its main function is to break down food into simple components that can be absorbed by the body. Primary metabolism occurs in the gastrointestinal tract from the stomach to the end of the small intestine [7, p. 26].

In traditional Chinese medicine, each organ of the body corresponds to a specific substance—yin or yang. Thus, the liver corresponds to yin; this organ performs a storage function and does not release the "substance stored within." The stomach, small intestine, and large intestine correspond to yang, as these organs "constantly empty themselves and do not retain anything" [5, p. 113].

The works of Hippocrates (460–370 BC) state that the liver has five lobes. Galen (129–217), whose works were widely respected in the Middle Ages, also held this opinion. However, the Italian physician Andreas Vesalius (1514–1564) wrote that this opinion was based on animal anatomy; the human liver does not have such lobes. Vesalius also noted the inaccuracy of Galen's concept of the liver as the source of veins. He named the heart as the source of veins and arteries [16, p. 42]. The Physiology of Digestion in Modern and Contemporary Times

Ancient concepts were supplemented in the 17th century by the enzyme theory introduced by the Dutch iatrochemist Johann Baptist van Helmont (1577–1644). Later, the Italian priest Lazzaro Spallanzani (1729–1799) was able to demonstrate the existence of such processes in living organisms by conducting experiments on artificial digestion with gastric juice.

It was hypothesized that circulatory movement is characteristic not only of blood and bile, but also of saliva, gastric juice, pancreatic juice, and lymph. The task of evaluating the kinetics of enterohepatic circulation of bile was undertaken by the Italian scientist Giovanni Alfonso Borelli (1608–1679), not only a physiologist but also a mathematician and physicist. He was the teacher of Marcello Malpighi (1628–1694), the renowned Italian anatomist who not only described the microscopic "bile capillaries" of the liver but also demonstrated that it is the liver, not the gallbladder, that produces bile [13, p. 500].

Based on his student's observations of the microscopic anatomy of the liver lobule and the hepatic origin of bile, Borelli concluded that bile flows from the liver into the duodenum, where it mixes with digested food and then passes through pores into the duodenum. The Dutch physician Reinier de Graaf (1641–1673) discovered that pancreatic secretion is actually slightly alkaline, not acidic, as previously believed [12, p. 663].

At the end of the seventeenth century, the traditions of anatomy and chemistry merged to substantiate new theoretical and experimental approaches to understanding processes in the body.

The concept of metabolism was introduced into scientific literature no earlier than 1839 by the German physiologist Theodor Schwann (1810–1882) and the German chemist Justus von Liebig (1803–1873) in 1842. In 1835, Theodor Schwann discovered a substance in gastric juice that he named "pepsin" [14, p. 304].

French physician Claude Bernard (1813–1878) defended his dissertation on the role of gastric juice in nutrition (1843). Bernard's major achievement was the discovery of glycogen. He described the glycogenic function of the liver and elucidated the functions of the pancreas [8, p. 256].

German physiologist and chemist Moritz Schiff (1823–1896) studied enterohepatic circulation in dogs with biliary fistulas. He investigated the glycogenic function of the liver, as well as the influence of the spleen on processes in the duodenum [13, p. 503].

Russian surgeon Vasily Aleksandrovich Basov (1812–1879) was the first in the world to perform an artificial gastric fistula in dogs and later described it in the article "Notes on an Artificial Route into the Stomach of Animals" [6, p. 26].

Russian physiologist Lev Zakharovich Morokhovets (1848–1919) conducted research on the biochemistry of digestion. His primary focus was the biochemical transformations of proteins. He wrote such works as "On the Identity of Nuclein, Mucin, and Amyloid Substance" (1878), "Digestion as a Chemical Method," and "Elastin and Its Derivatives." In 1880, he defended his dissertation on "The Laws of Digestion" (1880).

Lev Zakharovich discovered that the end product of the action of pepsin in gastric juice on proteins is peptones, which are broken down into amino acids in the duodenum [4, p. 575]. The renowned Russian physiologist Ivan Petrovich Pavlov (1849–1936) and his classmate Mikhail Afanasyev, while still students, studied the nerves responsible for pancreatic function.

During their experiments, they discovered a branch whose stimulation was always accompanied by pancreatic secretion. It was then that I.P. Pavlov developed a method for performing permanent pancreatic fistulas, which made it possible to demonstrate the inhibitory effect of atropine on pancreatic secretion [6, p. 59]. The students presented the results of their research in their work "On the Nerves Controlling Pancreatic Function" (1875).

Pavlov's first discovery in this field was the creation of a permanent pancreatic fistula (1879), which made it possible to obtain pure digestive juices and study digestive enzymes and the influence of the nervous system on pancreatic function. Based on his original surgical procedures, the scientist began developing the fundamental principles of physiological surgery of the gastrointestinal tract [6, p. 64].

In 1897, Pavlov published a monograph, "Lectures on the Functioning of the Main Digestive Glands," in which he summarized the results of his research and the work of his colleagues on the physiology of digestion. He later demonstrated that the various reactions of animals to the sight and smell of food are physiological in nature, and coined the term "conditioned reflex" (1901) for this phenomenon [6, pp. 72–74]. For his discoveries in the field of digestion, I.P. Pavlov was awarded the Nobel Prize in 1904. This award was the first Nobel Prize in Russia and the first awarded in physiology or medicine.

Ivan Petrovich produced a galaxy of talented students who continued research into the physiology of digestion.

Boris Petrovich Babkin (1877–1950) completed his first scientific work in Pavlov's laboratory in 1902 on the effect of alkalis on pancreatic secretion [3, p. 18]. He studied the mechanism of pancreatic secretion and gastric juice secretion, as well as the activity of the salivary glands. Leon Abgarovich Orbeli (1882–1958) studied the functions of the stomach, pancreas, and intestinal secretory function [1, p. 27].

Konstantin Mikhailovich Bykov (1886–1959), together with Ivan Terentyevich Kurtsin (1907–?), developed a theory of peptic ulcer development. They also substantiated the physiological significance of mechanical stimulation for gastric secretion. Konstantin Mikhailovich developed a method for obtaining pure gastric juice in humans using mechanical stimulation. He is credited with developing the concept of gastric secretory fields, according to which the glands of the lesser curvature are considered the "pacemakers" of gastric secretion [2].

The German physiologist Carl Ferdinand Lüderitz (1854–1930) published several papers on the sensory and motor components of peristalsis, including a seminal paper on stimulus-evoked muscular responses of the stomach in vivo [15, p. 4]. He provided the first detailed description of muscular responses after dilation of the intestinal lumen with a balloon or by instillation of fluid, emphasizing the importance of internal nerves and other structures in the intestinal wall for reflexes. Lüderitz published his research results several years before William Bayliss and Ernest Starling reached similar conclusions. In the literature, the muscle reactions caused by intestinal distension were called the Lüderitz-Bayliss-Starling reflex.

British physiologists William Maddock Bayliss (1860–1924) and Ernest Henry Starling (1866–1927) discovered special messenger molecules (hormones) in the blood that regulate various physiological mechanisms: secretin was discovered in 1902, and gastrin in 1905, both produced in the intestine.

These gastrointestinal hormones are important regulators of metabolism, growth, and development. Their discovery can be considered the beginning of the scientific field of endocrinology [18, p. 5]. Almost a thousand years after Ibn Sina (980–1037), who asserted in his "Canon of Medicine" that one of the liver's functions is to separate fluid from the blood, Starling confirmed that the liver is the primary source of lymph formation, demonstrating that the walls of liver vessels have a higher permeability to serum proteins than any other source of lymph [10, p. 144].

Polish physiologist Leon Popielski (1866–1920) formulated the stimulating effect of histamine on gastric juice secretion and demonstrated that the regulation of the stomach and pancreas is mediated not only by neuroreflexive mechanisms but also by humoral mechanisms [17, p. 15].

By the beginning of the 20th century, the question of internal secretion, as well as the consequences of its disruption, had been studied in considerable depth. Among the first prominent researchers in this field were the German physiologists Rudolf Peter Heidenhain (1834–1897), who described a new class of clear cells (1868); Paul Langerhans (1847–1888), who identified pancreatic islets (1869); and M. Ciacco (1877–1956), who introduced the

term "enterochromaffin" (1906). In 1897, Russian histologist Nikolai Konstantinovich Kulchitsky (1856–1925) identified the enterochromaffin cell, which served as the basis for the subsequent description of the DNS and provided the cellular foundation upon which the discipline of intestinal neuroendocrinology would be founded [9, p. 109].

Their contributions facilitated Friedrich Feyrter's (1895–1973) description of the diffuse neuroendocrine system (DNS) in 1938, which provided insight into the syncytial regulatory system, which consists of both endocrine and neural components. John Sydney Edkins (1863–1940), building on the discoveries of Starling and Bayliss, observed in a series of experiments that injection of pyloric mucosal extract resulted in secretion of gastric acid and pepsin in anesthetized cats. In 1905, he named this putative active substance "gastrin" [11, p. 233]. Although his ideas were initially accepted, the discovery of histamine in 1910 and the identification that extracts from other tissues had similar physiological effects raised serious questions regarding the validity of gastrin. Later, in 1938, gastrin was identified as a unique antral acid secretagogue, followed by purification and elucidation of its chemical structure in 1964. Edkins's original hypothesis was confirmed, but not until after his death. French physician André Latarjet (1876/7–1947) and American surgeon Lester Reynold Dragstedt (1893–1975) discovered acetylcholine, which increases peristalsis in the stomach and intestines [17, p. 18]. In 1928, Julian Walawski (1898–1975) discovered enterogastrones, hormones that reduce secretion.

Thus, the development of digestive physiology has gone through several stages. Its origins date back to ancient times. During the Middle Ages, empirical knowledge in this area continued to accumulate, but the ban on autopsies in many cultures prevented the acquisition of more reliable information in this area of physiology. Gradually, the erroneous ideas of the ancients, which had held absolute authority for centuries, were corrected and supplemented. The modern era is a period of significant scientific discoveries. Numerous experiments and research are being conducted. The study of digestion draws not only on anatomical data but also on discoveries in chemistry. Today, the study of digestive physiology continues to develop and influences other areas of medical and biological knowledge.

The materials in this article complement existing historical and biological research devoted to the development of concepts in digestive physiology. This work can be used in further research on the formation and development of digestive physiology, as well as as a teaching aid for the disciplines of "History of Biology," "History of Medicine," and "Physiology."

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