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George Sclavunos (1869-1954): Anatomical Insights and his contribution into the "Magenstrasse of Waldeyer"

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Abstract

The purpose of this article is to present a well-known physician and highlight his contribution into an essential, but neglected anatomical feature. George Sclavunos (1869-1954) was a 20th century Greek physician, whose scientific work was a significant milestone in global medical knowledge. In 1899 he became Professor of Anatomy and Head Director of the Department of Anatomy. In 1906 Sclavunos G. published the first volume of the three volume book "Human Anatomy" (1906-1926), which is characterized by its unparalleled illustrations. For more than a century it was the most important book of medical literature in Greece. In 1926 he became a Full Member of the Academy of Athens and was named Life Partner of the International Anatomical Society. His interests included Anatomy, Physiology, Histology, as well as Osteology and Syndesmology. In his book "Human Anatomy", he described for first time the "Sialine Groove of the Stomach", which was described by Waldeyer-Hartz almost at the same time as the "Magenstrasse", a German word that means "stomach road". It is a ribbon-like path that extends along the lesser curvature of the stomach from the gastric cardia to the antrum and releases the gastric content directly into the small intestine. Its importance is confirmed by its association not only with drug delivery, but also with anti-obesity surgical techniques. The old German term has come back into common medical usage in view of the commonly performed Magenstrasse and Mill procedure, a form of bariatric surgery. **Conclusion:** Sclavunos G. managed to observe an anatomical structure that has remained of great importance until today.

Key Words: George Sclavunos ▪ Magenstrasse ▪ Stomach ▪ Bariatric Surgery ▪ Biography.

Introduction

George Sclavunos, a distinguished physician of his time, influenced numerous other physicians through his knowledge and anatomical research. By studying his bibliography, it becomes clear that his holistic perception of medicine was what led him to occupy himself with numerous medical domains of his time (1-4). Generally, his field of interest included anatomy, physiology, histology, embryology, osteology and syndesmology (1-3). Throughout his life he was well-known for the numerous books and scientific works he wrote in Greek and German (1, 4-6). Some of them show a familiarity with Galen's works: "On Anatomical Operations", "Medical Terminology", "On the Dissection of Muscles", and "On the Necessity of the Molecules in the Human Body" (4, 5).

Among others, Sclavunos was involved in anatomical research of the human stomach, and in his book "The Anatomy of Man", he described its anatomy thoroughly (1). However, while most of his scientific work is described in detail in published records, little is known about his contribution to the research of the "Magenstrasse". This is a very important but frequently neglected anatomical feature. Its association not only with drug delivery but also with bariatric surgery prompted us to delve deeper into the issue.

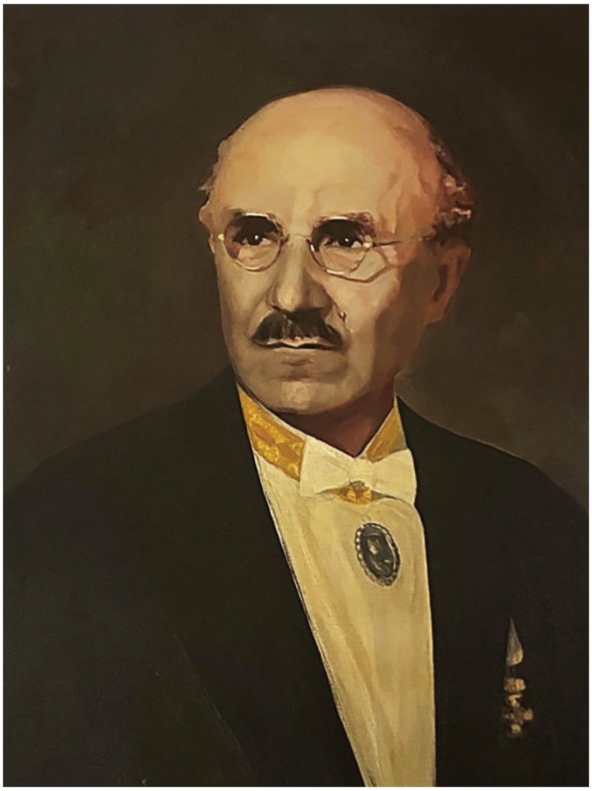

Figure 1. George Sclavunos. Oil painting of Sclavunos G. by an unknown artist. Adapted from the Department of Anatomy of the National and Kapodistrian University of Athens.

The aim of this paper is to shed light on the life and works of a charismatic figure. From our study of his scripts and the bibliography, his significant contribution into the anatomical research of "Magenstrasse" is indisputable.

Sclavunos' Life and Works

George Sclavunos was born in Tithorea on October 16, 1869. He graduated from Thebes School and in the academic year 1884-1885 he enrolled in the Philosophy School of the University of Athens. He then transferred to the Law School. A year later Sclavunos went to Zurich for eight months and later to Würzburg in Bavaria, where he studied Medicine. He graduated in 1891 with a doctorate on the thesis "On elaidin and the keratogenic process of the cardiac fate of the stomach of mammals"(1, 5, 6). In 1891 he passed his practical examinations and worked for two years as an assistant at the anatomical institute of the famous Swiss historian and great anatomist Rudolf-Albert von Köliker in Würzburg (5). He collaborated with the great anatomists Johannes Sobotta, Max Schultze and Hermann Braus, who are the authors of well-known contemporary anatomical textbooks and atlases.

In 1892 he returned to Greece for family reasons. Upon his return to Athens, he was appointed assistant professor of anatomy and curator of the Anatomy department. In 1893 he was appointed as an anatomy lecturer, in 1895 curator of the anatomy laboratory and in 1899-1900 he was elected as a professor and director of the Institute of Anatomy (5, 6). Sclavunos introduced anatomical research and many anatomical terms into the Greek medical literature (4-6). Greek anatomical science began to be comparable to its Western counterpart. In 1906 Sclavunos published the first volume of his monumental three-volume scientific work "The Anatomy of Man" (1). To illustrate his book, he borrowed anatomical paintings from W. Spalteholz, prosector at the University of Leipzig, and histological and anatomical images from J. Sobotta, prosector at Würzburg and later professor at the University of Königsberg and University of Bonn, and O. Schultze, also professor at the University of Bonn. The 48 illustrations in Sclavunos' book were illustrations of his own preparations and they are astonishing in their accuracy of detail. In 1899 he became full professor as the chair of Anatomy and Physiology (5). From the 1933-1934 academic year he was Dean of the Dental School. He retired from the University of Athens in 1938. During his presence at the University he ordered new anatomical casts from abroad while he inaugurated the new Anatomy in Goudi (4, 6).

George Sclavunos used the technique of pyrography to describe the adhesion of muscles to bones by representing the cauterized points which were the points of attachment of the muscles. At that time, the use of the Teichmann technique for injecting a colored substance into corpses was introduced, and this technique was applied first in Greece and afterwards in Europe (1-4).

He taught Anatomical and Physiological Histology and gave demonstrations with microscopic presentations of embryological preparations, anatomical and histological exercises, as well as anything that had to do with osteology and syndesmology, and taught anatomy courses at the School of Fine Arts (1-3, 5).In 1897 he was elected a life member of the International Anatomical Society and the German Anatomical Society, and from 1926 he was a member of the Academy of Athens. He passed away on May 13, 1954 in Athens (4, 5).

Sclavunos G was married and had four children, including Themistocles Sclavunos, professor of medicine at the University of Athens, and Konstantinos Sclavunos, professor of the Agricultural School of the University of Thessaloniki (5, 6). Last but not least, in 2010, a museum was opened in his honor in Amfikleia. The museum, which bears the name of the late academician, was created jointly by the Municipality of Amfikleia and the School of Medicine of the University of Athens (5, 6).

Sclavunos' Contribution to the Anatomical Research of the Magenstrasse

According to Sclavunos' book "The Anatomy of Man", our internal gastric anatomy is very complex. In particular, the internal surface of the stomach displays folds. In an empty stomach 11 plications are created in total by the contraction of the muscularis mucosae (mucosal plications). Some disappear when the stomach is full and expands, some correspond to pachynsis or strangulation of the muscular coat, and others are created by the retraction of the entire gastric wall (total folds) (1).

Mucosal folds are found circularly from the center of the stomach towards the gastric body, helically and towards the pylorus, in parallel and in a straight line. Their helical construction in the gastric body creates a network of anastomised folds which contributes to the collection of food there. Along the lesser curvature, there are two to four elongated folds independently of one another (non-anastomised), from the heart to the antrum or the pylorus. This anatomical structure was observed in infants by G. Sclavunos and was described in his three-volume book, published in 1906. He named it the "sialine groove of the stomach" (1). Almost at the same time, it was also observed in adults and described by Wilhelm Waldeyer-Hartz (1836-1921). At that time it was believed by anatomists that in animals, water or aqueous food is transported from the heart straight to the antrum or the pylorus, and from there to the small intestine, without admixtures with the remaining content of the stomach. Waldeyer-Hartz decided to write a detailed paper to demonstrate that this phenomenon also happens in human beings. In particular, in 1908 he described how food follows the groove arrangements along the lesser curvature of the stomach, and called this passage the "Magenstrasse" (7). Magenstrasse is a compound word from the German "Magen" meaning stomach and "Strasse" meaning road or street. Therefore, Magenstrasse means stomach road (8).

This gastric tract is shown more clearly through a cross-section of an empty stomach, near the angular incisure (Figure 2). The cavity of the stomach appears to be divided by two folds, in two unequal parts, the upper or gastric tract at the lesser curvature or folds. This is the part which expands when the stomach fills with food content, resulting in the disappearance of the folds. On the other hand, the gastric tract is preserved and the folds remain with the filling of the stomach, advancing the content directly to the small intestine (1).

Apart from the folds, the internal surface of the stomach also shows square or hexagonal eminences. As has been seen microscopically, these eminences are created because the glands which flow into the stomach at intervals and in groups press down on the gastric mucosa towards its inside. These gastric depressions are divided by thin septulums or folds, called gastric ridges. In the pyloric segment of the stomach, the septulums are deeper and the ridges higher, resembling the villi of the intestine. For this reason they are named villous folds (1).

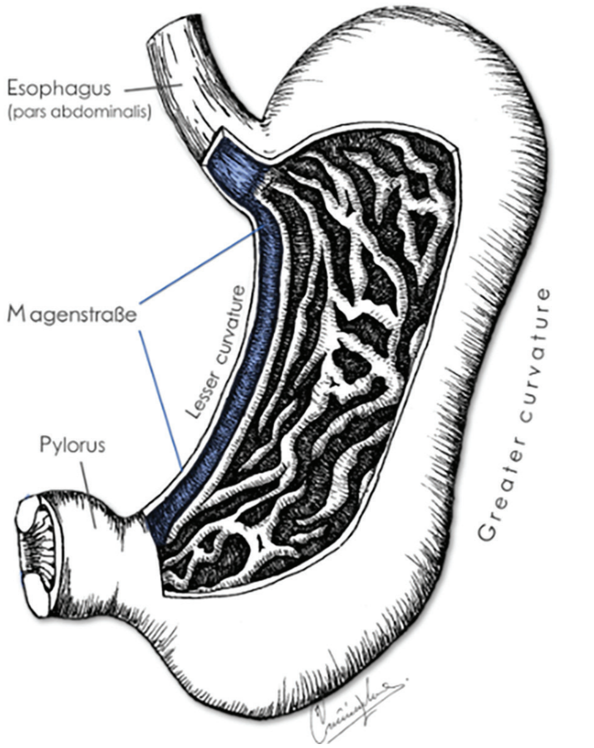

Figure 2. Brief explanation of the Magenstrasse, created by Ioannis K. Antonopoulos.

The empty and relaxed stomach during fasting is shaped like a flattened pipe, with the front wall coinciding with the rear. In contrast, the empty, but contracted stomach during hunger takes the shape of round pipe. During the filling of the empty and relaxed stomach the food goes into it as if entering an empty sack up to the antrum. Inside an empty but systaltic stomach, a bolus encounters resistance because of the cavity created when the front wall falls onto the rear (1).

The human stomach is a multifunctional organ responsible for delivery of nutrients and drugs to the intestines. The digestive gastric process occurs through chemical and mechanical functions, namely, nutrient-stimulated duodeno-gastric reflexes and muscle contractions. There are two types of gastric muscle contractions: the slow volume-reducing contractions of the fundus, and the peristaltic contraction waves in the antrum (ACW). According to the classical description of gastric function, the fundus is a supplier of liquid content to the antrum. The chyme is then mixed, thanks to the action of ACWs, and released into the duodenum. Gastric content released into the upper stomach from the esophagus can take hours to enter the small intestine. This happens because the content stored in the fundus is delivered to the antrum from above and then empties from the antrum into the duodenum. In contrast to the traditional description of gastric emptying, a new path was discovered which was none other than the "stomach road", or "Magenstrasse" that Sclavunos first described (9).

Many years later, Li et al. examined the mixing and emptying of gastric content in the human stomach using a Computational Fluid Dynamics (CFD) method, in order to understand the Magenstrasse phenomenon better. Their study also confirmed the existence of a fast pathway close to the lesser curvature of the stomach. This result is in accordance with the study by Pal et al. (9, 10).

However, as Li et al. first observed, this phenomenon does not occur when gastric contents with different properties are mixed. In contrast, a retropulsive flow is produced, by a terminal antral contraction (TAC), that leads the food contents to the proximal antrum. This contributes to the mixing of water with light gastric contents, but not with the heavy ones, and as a consequence, layers of different food contents are created. In particular, this phenomenon is produced thanks to the gastric motility, the high viscosity of the content and the food matrix that is created by heavier gastric contents. Due to the higher viscosity, gastric wrinkles and food matrix show lower resistance in water than in light gastric contents. In addition, it is impossible for the gastric contents to fill the gastric wrinkles completely. Thus, flow resistance in the food matrix is higher than in the gastric inner surface. Consequently, water is forced to empty immediately near the gastric inner surface trough the Magenstrasse (10).

The Magenstrasse and Drug Delivery

As previously outlined, the importance of the Magenstrasse is clear, regarding the pharmacokinetic properties of various drugs. For this reason, researchers have tried to study this phenomenon thoroughly. On the basis of the studies by Winter et al. and Kiyota et al., the Magenstrasse is of great importance for drug absorption in humans who are being fed, as it represents a shortcut through the fed stomach and carries fluids rapidly allowing the rapid onset of drug plasma levels (11, 12).

The importance of this road was also confirmed by Grimm et al., who conducted an MRI study to demonstrate that gastric emptying of water, in a fed state clinical trial, was as fast as under fasting conditions (13).

Processes such as secretion, digestion, and gastric emptying occur at the same time in the postprandial stomach. Thanks to the Magenstrasse, water is emptied rapidly within 15–45 min from the stomach, even under postprandial conditions. As a result, this road may have essential consequences for the drug plasma concentrations after fed-state administration of immediate release medications. If a drug is taken under postprandial conditions with water, the direct increase of drug plasma concentration is likely to occur, similar to fasting conditions. This observation clearly reflects the presence of the Magenstrasse. In particular, it means that the drug is rapidly transported to the small intestine, through the gastric road, without losing time by mixing with gastric contents. In the case of pain medication for example, where we desire immediate results, this road seems quite useful. Undoubtedly, gastric emptying in fasting and postprandial conditions is quite difficult to study. For this reason, in 2019 Schick et al. developed a simulation model, the GastroDuo, to examine the presence of the stomach road and predict the in vivo performance of oral drugs. According to their experiments, there is clear association between the drug plasma concentrations and the gastric emptying of dissolved and undissolved medications (14).

Kilian et al. conducted a study in humans with radiolabelled paracetamol to assess gastric emptying in fasted and fed conditions. Unexpectedly, the absorption of paracetamol was similar between the pre- and post-prandial state, or even faster in the fed state. The authors hypothesized that this reflected the Magenstrasse phenomenon, suggesting that the fast dissolution of paracetamol occurred at the top of the stomach, and paracetamol moved along the Magenstrasse with the liquid content of the stomach directly into the duodenum (15).

One year later, this model was used by the same investigator in order to examine the performance of a fast disintegrating and dissolving Aspirin® tablet (FDDT) under fasted and fed conditions, and compare it to a regular Aspirin® tablet (RT) administered in the fed state. The FDDT showed faster drug release and improved emptying kinetics in the GastroDuo. The early tmax observed for the FDDT under fed conditions could be related to the presence of the Magenstrasse. Thanks to this road, the drug is released rapidly when it is co-administered with water. In contrast, drug release from the RT resulted in later tmax, because it was insufficient to allow gastric emptying via the Magenstrasse. Therefore, this work highlights the biopharmaceutical significance of the Magenstrasse for oral drug therapy (16).

This result is definitely in accordance with the study by Vrbanac et al. They mention that in the postprandial stomach, fast emptying of ingested liquids is accomplished thanks to this road and this definitely has an impact on the therapeutic onset of co-administered drugs. The motor activity of the fasted stomach is carried out in cycles (MMC), characterized by fluctuation of the muscle contraction intensity. Different intensities of motility patterns can have an influence on the disintegration time and distribution of a drug and the formulation of particles within the various stomach regions (17).

Paixao et al. created a mass transport model (MTM) that reflects drug distribution along the different regions of the stomach as a consequence of random dosing relative to the different contractile phases of the migrating motor complex (MMC). According to this model, drug distribution along the different regions of the stomach can result in the inhomogeneous (i.e., not well mixed) presence of the drug in the stomach. This depends on the time of administration relative to the MMC phase. To capture the drug concentrations (in particular phenol red) in the different segments of the GI tract both in fasted and fed state conditions, it was essential to include a bypass flow compartment. This bypass road is the Magenstrasse, and it facilitates the transport of the drug directly to the duodenum (fasted state) or antrum (fed state) (18). It is also worth mentioning, that the study by Henze et al. showed that the Magenstrasse phenomena reported in humans, may also occur in landrace pigs (19).

The Magenstrasse and Bariatric Surgery

In parallel, the importance of the Magenstrasse was also confirmed by its association with bariatric surgery. Obesity is a worldwide epidemic and, over time, numerous types of anti-obesity procedures have been described. One of the first surgical techniques was Vertical Banded Gastroplasty (VGB). Biliopancreatic diversion with a duodenal switch (BPD/DS) was an additional procedure for food restriction and ulcer reduction (20).

In general, anti-obesity techniques should not only be effective in weight loss, but also safe, with minimal side-effects and metabolic sequels. Johnston et al. tried to evolve a simpler type of gastroplasty in order to satisfy these criteria. They described the Magenstrasse and Mill procedure (M&M), which was first carried out in 1987 in England (20). In this operation, a long narrow stomach tube (namely, the Magenstrasse) is formed around a bougie, and the stomach is stapled and divided from the incisura angularis to the angle of His. Unlike the previous techniques, it does not leave foreign material within the abdomen (21). It was generally shown that this procedure achieves acceptable weight loss, while preserving gastric emptying mechanisms and thus minimizing possible side-effects, such as vomiting, dumping and diarrhea (22). Moreover, Carmichael et al. showed that the M&M operation reduces levels of plasma leptin, and improves the fibrinolytic activity, factors that are associated with morbid obesity and coronary heart disease (22, 23).

In order to reduce severe gastrointestinal and hydroelectrolytic disturbances, surgeons adopted the Roux-en-Y gastric bypass (RYGB). The RYGBP horizontal pouch is better than the RYGBP vertical pouch, because fewer marginal ulcers have been reported after this procedure. This happens because, as Berger first described in 1934, the proximal Magenstrasse contains many more parietal cells than the fundus (24). A technically less demanding operation that gained rapid acceptance was Sleeve Gastrectomy (SG). According to this technique, a circular opening is created in the stomach at the junction between the corpus and the antrum. The stapling then progresses along the small gastric curvature and a tubular pouch, similar to a sleeve, is created (20). 80% of normal stomach is actually resected and this leads to restriction and a decrease in ghrelin levels, and significant weight loss (25). This procedure could be performed safely laparoscopically with satisfactory results (20).

In 2016, Bessemans et al. compared the efficacy of three procedures in obese patients: RYGB, SG and M&M gastroplasty. Their study showed that classical SG provides almost similar results to RYGB and appears to be slightly better than the M&M procedure (26). In addition, three years ago, an interesting experimental study with rabbits was conducted by Sümer et al. in order to compare the SG with the M&M gastroplasty. It was found that weight loss was achieved with the first method, whereas weight did not decrease with the second. M&M leaves the large curvature of the stomach in place. Since the connection between the tube and the large curvature remains open, it can be considered that food also accumulates there, which hinders the restrictive function (27). SG was actually an evolution of the M&M procedure, and is the most popular anti-obesity operation nowadays. Perhaps its success is not purely due to the surgical technique, but especially due to the part of the stomach that remains, which is none other than the Magenstrasse.

Conclusion

To conclude, George Sclavunos was undoubtedly a great Greek physician and professor of his time, whose work contributed to the gradual formation of the foundations of modern anatomy science. His field of interest was extensive and among others, he described the "stomach road", a tubular portion of the stomach, which is a route favored by fluids. Waldeyer-Hartz described it almost at the same time and named it the Magenstrasse. Although it is an anatomical feature that is frequently neglected, its importance is indubitable, in relation not only to drug delivery, but also anti-obesity surgical techniques. We suggest that further studies are required for a more extensive understanding of its function.

What Is Already Known on This Topic:
There are articles regarding the Magenstrasse and its association with drug delivery and different bariatric surgery techniques.

What This Study Adds:
In the existing literature, there is nothing written about George Sclavunos and his contribution to knowledge about the Magenstrasse. We suggest that it is wise to consider the work of men like him. For this reason, the scope of our article is double. First, to present this distinguished physician and secondly, to underline the overall importance of the Magenstrasse. Moreover, this anatomical feature might be the reason of the success of Sleeve Gastrectomy, which is the most common bariatric surgery today.

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Conflict of Interest: The authors declare that they have no conflict of interest regarding the publication of this article.

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