Dear colleagues,

Normal anatomy and physiology are the basis of medicine, without which it is impossible to understand the pathological physiology of diseases, and therefore determine the correct diagnosis and prescribe a pathophysiological treatment. Before a discussion of an article by Wood et al, I offer a review on the normal physiology of the esophagus and esophageal-gastric junction (EGJ), as well as the pathological physiology of gastroesophageal reflux disease (GERD) and achalasia.

1. Normal physiology of the esophagus EGJ at rest.

The esophagus and lower esophageal sphincter (LES) on an empty stomach are in a closed state, regardless of body position. It is known that at rest, the pressure in the esophagus above the LES is less than in the stomach [1]. The constant contraction of LES prevents the reflux of the contents of the stomach into the esophagus. However, smooth muscle LES can not be in constant contraction around the clock. It must relax in order to regain its contractile potential (ATP). Like the postural reflex of striated muscles, different groups of smooth muscle fibers are in a contracted state at different time intervals in a closed circle. This occurs under the control of Cajal cells. While one group of cells is in a contracted state, other groups restore their contractile potential. Thus, a continuous contraction of LES can be explained. Other reflexes provide LES contraction with minimal energy consumption.

The motility of the proximal stomach is regulated by reflexes: receptive relaxation and gastric accommodation. Receptive relaxation is manifested by a decrease in the tone of the proximal part of the stomach during swallowing. Stomach accommodation is described as a proximal relaxation reflex in response to stomach distension. Unlike receptive relaxation, this reflex is independent of stimulation of the esophagus [2]. Thus, more than a liter of nutrients can enter the
stomach without increasing intragastric pressure, which facilitates the antireflux function of the LES.

Shafik et al. in experiments on dogs showed that balloon distension of the stomach walls causes an increase in LES tone after 20 ml of water is introduced into the balloon. The tone of the LES continues to increase with increasing balloon volumes to 110-120 ml [3]. This reaction of LES can be explained by the fact that in response to increased pressure in the stomach, reflex contraction occurs not only of those bundles of muscle fibers that are ready for contraction, but also those that are almost ready for contraction. The tone of the LES is enhanced by the contraction of more muscle fibers. Naturally, this reaction has a limit on the magnitude of the pressure in the stomach and the duration of the provocation.

Each 3-5th peristaltic wave of the stomach closes in the antrum of the stomach with the formation of a closed (antral) cavity between the antral and pyloric sphincters. When the antrum is contracted, high pressure arises in it, which leads to the opening of the pyloric sphincter, after which the contracting antrum injects its contents into the duodenal bulb (Figure 1). The normal function of this mechanism protects the LES from high pressure [5].
Conclusion: The normal function of LES is to completely prevent gastroesophageal reflux, except for extra ordinal cases after overeating, physical exercises after eating, etc. This is confirmed by histological studies of Chandrasoma, which showed that reflux begins with the acid being thrown into the abdominal part of the LES when the acid still does not enter the esophagus [4]. The notion that acid reflux is normal is a mistake that arose initially when selecting patients to determine the normal pH range in the distal esophagus. Since the absence of complaints, as well as the absence of visible pathology during a gastroscopy (without histology) does not exclude GERD, patients with GERD were selected as healthy. As a result of this error, pH-metry diagnoses GERD only in patients with severe form [6].

2. The function of the esophagus and EGJ in a horizontal position
In a horizontal position, the bolus moves along the esophagus from the upper esophageal sphincter to the LES by a peristaltic wave in accordance with the Bayliss-Starling gut law. The wall of the esophagus is contracted proximal to the
bolus and relaxes distally of him [7]. A strong contraction of the last peristaltic wave causes the opening of the LES. At this point, the pressure in the esophagus is higher than in the stomach, as the lumen of the esophagus is blocked by a contracting wave above the bolus. The force of contraction of the last peristaltic wave is great. An increase in gastric pressure, which causes an increase in the tone of the LES, does not stop the movement of the bolus through the EGJ. Therefore, it is impossible to detect and measure LES in healthy people.

With GERD, an aggressive reflux agent (hydrochloric acid, pepsin, bile acids) causes inflammation both in the esophagus and in the LES. This leads to the expansion of the esophagus and the weakening of its peristalsis. In such cases, a weak peristaltic wave cannot overcome the tone of the LES and the bolus (barium) stops over the contracted LES (Figure 2).

![Figure 2](image)

We measured the length of the LES in 28 patients of different ages examined for various reasons. They had no clear clinical symptoms of GERD. However, unlike the norm, LES contracted in response to abdominal compression. The measurement results (Table 1) corresponded to the normal length of the LES measured during manometric studies [8,9]. Therefore, we concluded that these patients had the initial stage of GERD and the LES had not yet has changed relative to the norm [10,11].

Table 3. Normal length of LES (cm) in different age groups.
### 3. The function of the esophagus and EGJ in a vertical position

With the continuous intake of liquid barium in the esophagus, a column forms with a liquid level at the level of 4 thoracic vertebra, after which the LES opens and the contrast medium falls into the stomach. Probably, the hydrostatic pressure of this column creates a threshold pressure for the disclosure of the LES. Single swallows evacuates from the esophagus using peristalsis.

### 4. Pathological physiology of GERD

GERD begins with the penetration of aggressive gastric contents into the lumen of the abdominal part of the LES, causing an inflammatory reaction that weakens the function of this part of the sphincter [4]. At first this is manifested by the disclosure of the abdominal part of the LES only during a rise in pressure in the stomach. Over time, the abdominal part of the LES does not close at all and represents the walls of the stomach. Moreover, the total length of the LES is shortened by almost 2 times. The pathogenesis of GERD is presented in Figure 3.

![Figure 3](image-url)

**Figure 3.** The scheme of the pathogenesis of GERD. (A) Norm. LES (brown line) is located both above and below the diaphragm (d). The part of the LES

<table>
<thead>
<tr>
<th>Age</th>
<th>Up to a year</th>
<th>1-3 years</th>
<th>4-7 years</th>
<th>8-10 years</th>
<th>11-15 years</th>
<th>2 – 65 years</th>
</tr>
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<tbody>
<tr>
<td>Limits</td>
<td>0.7 – 1.0</td>
<td>1.2 – 1.5</td>
<td>1.5 – 1.8</td>
<td>1.9 – 2.3</td>
<td>2.3 – 2.9</td>
<td>3.2 – 4.2</td>
</tr>
<tr>
<td>Average</td>
<td>0.86±0.03</td>
<td>1.40±0.02</td>
<td>1.72±0.07</td>
<td>2.10±0.05</td>
<td>2.45±0.11</td>
<td>3.60±0.08</td>
</tr>
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located below the diaphragm is slightly longer than the rest one. (B) Reflux of aggressive gastric juice (yellow) initially starts only within the abdominal part of the LES. In this case, a weakening of some part of the LES occurs. It expands, ceases to fulfill the antireflux function and becomes the wall of the stomach (white line). (C) In more severe cases, the reflux agent penetrates the esophagus. The inflammatory process affects the entire intraabdominal part of the LES (LES ia), and this part ceases to function as a sphincter. In the inflamed and extended part of the LES, folds appear. In the process of development of GERD, the angle of His increases and the esophagus expands. The dependence of the length of the LES on the pressure in the stomach in patients with GERD is seen in Figure 4.

Figure 4. Radiographs of the EGJ in a patient with GERD, performed in the process of receiving barium (a-b) and schemes for them (c-d). When the volume of barium increased in the stomach, which led to an increase in pressure, the abdominal part of the LES open and the total length of the LES decreased.

GERD is part of the picture of disease caused by hyperacidity of gastric juice. It is often accompanied by gastritis and impaired gastric emptying due to impaired formation of the antrum. If during the contraction of the antrum chamber the antral sphincter does not completely close (see Figure 1), then the pressure in the chamber does not increase to a threshold level to open the pyloric sphincter, which drastically slows the evacuation from the stomach. Secondly, the pressure in the body of the stomach increases, which increases the load on the LES.

In the stage (Figure 3.C), when the chyme penetrates the esophagus, it causes an inflammatory reaction, resulting in the esophagus is dilated and the peristaltic wave is weakened. To create a threshold pressure for the disclosure of LES, the mechanism of the phrenic ampulla arises. The phrenic ampulla is the last peristaltic wave in the dilated and weakened part of the esophagus. It is closed
proximally by a functional proximal sphincter (PS), as a result of which, during a bolus advancement, at some point, a closed cavity appears between the PS and the LES. During its contraction, a threshold pressure arises in it, which leads to the opening of the LES and a contracting ampulla injects a bolus into the stomach (Figure 5).

Figure 5. Radiographs of the EGJ of patients with GERD, in which a functioning phrenic ampulla is fixed. (A) The moment of formation of a closed cavity between the PS (yellow arrow) and the LES (red arrow) was recorded. (B-C) The wide esophagus is filled with barium without signs of peristalsis (B); the last portion of barium is injected into the stomach with a contracting ampulla. The pressure in it is maintained due to the contraction of PS (C). (D-E) The longer the LES, the narrower the esophagus and the smaller the phrenic ampulla (a).
In patients with GERD, a chronic inflammatory process leads to swelling and thickening of the esophagus wall and LES. They lose elasticity. Along with this, there is an expansion of the lumen. Therefore, when the esophagus and the LES are in a closed state, folds form in them. The mucous folds at the level of the LES are rougher than in the esophagus due to a higher tone. X-ray studies and literature analysis, which are given in 6 proofs [6], confirm the results of endoscopic and histological studies Chandrasoma and DeMeester. Their studies reject two false dogmas that result in two widely believed fundamental errors: (1). These are the belief that the cardiac epithelium normally lines the proximal stomach and (2) that the GEJ is defined by the proximal limit of rugal folds [12].

If the esophagus is too wide and the proximal sphincter does not function, a threshold pressure to open the LES is created throughout the esophagus between the upper and lower esophageal sphincters (Figure 6. A-B). In other, more rare cases, sclerotic changes occur in the wall of the proximal sphincter, leading to the narrowing of this zone with the formation of the Schatzki ring (Figure 6. C).

**Figure 6.** Radiographs of EGJ in patients with GERD. (A-B) The esophagus is expanded with signs of esophagitis. Barium is evacuated to the stomach without the formation of a phrenic ampulla. Threshold pressure is created along the entire length of the esophagus. (C) The Schatzki ring (SR) is at the level of the proximal sphincter. (a) phrenic ampulla.

Analysis of the literature and our own radiological studies have allowed us to come to the following conclusions [6]:
1. The stomach does not move into the chest either in healthy or in patients with GERD. What is called a hiatal hernia is an esophagus ampoule. Detection of an ampoule of any size is evidence of GERD. In a chronic progressive process, the proximal sphincter, which limits the ampoule from above, is gradually replaced by connective tissue. The lumen of the esophagus at this level can be wide, although narrower than the ampoule. In rare cases, it is very narrow, which is defined as the Schatzki ring.

2. The esophagus is not shortening in either healthy or in patients with GERD. The complex (esophagus + LES) is shortening due to the shortening of the LES.

3. As a result of the initial erroneous selection of patients to determine the normal border of pH-metry, only severe forms of GERD are diagnosed with this method. In principle, the pH-metry cannot diagnose the initial forms of GERD, when the reflux agent enters only within the abdominal part of the LES, i.e. it does not enter the esophagus. Healthy individuals do not a “physiological” gastroesophageal reflux.

5. Achalasia

The problem of achalasia of the NPS should be divided into two historical periods. The first period is the development of the doctrine of idiopathic achalasia with the gradual accumulation of scientific facts. It lasted until about the 1980s. After this time, the diagnosis of achalasia began to include not only idiopathic achalasia, but also functional impairment of passage through the EGJ. To the pseudo achalasia, one should add the violation of the passage as a result of narrowing by tumors, or Chagas disease.

First period

Idiopathic achalasia was first described and termed by Sir Thomas Willis in 1674. It is a primary esophageal motility disorder of unknown etiology characterized manometrically by esophageal aperistalsis and insufficient relaxation of the lower esophageal sphincter (LES) in response to deglutition. It is a rare disease with an annual incidence of approximately 2/100,000 and a
prevalence rate of $10/100,000$. Studies have shown that peak incidence occurs between 30 and 60 years of age [13]. In the manometric study Shafik, it was found that in normal subjects, esophageal distension caused a significant decrease in LES pressure. In EA (esophageal achalasia) patients, the resting LES pressure was significantly higher than normal ($p < .01$). Upon esophageal distension, the LES pressure increased [14].

**Clinical presentation primary (idiopathic) achalasia** is insidious, usually with dysphagia, regurgitation, foul breath and aspiration [15,16]. In other textbook, the usual presentation is of a slowly increasing dysphagia, caused by solids and liquids [16]. None of the radiological and internal textbooks and in 6 observations described before 1980 had complaints of chest pain, in the abdomen, or heartburn.

**The characteristics of achalasia in barium esophagogram [17].**

- Dilatation of esophagus beginning in upper 1/3, ultimately entire length.
- Small / absent gastric air bubble.
- Stasis in thoracic esophagus filled with retained secretions + alimentary residue.
- Absent of primary peristalsis below level of cricopharyngeus, nonperistaltic contractions.
- “Bird beak” / “rat tail” deformity = V-shaped conical + symmetric tapering of stenotic segment with most marked narrowing at GE junction [Figure 7].
- Hurst phenomenon = temporary transit through cardia, when hydrostatic pressure of barium column is above tonic LES pressure.
- Sudden esophageal emptying after ingestion of carbonated beverage (e.g. Coke).
- Vigorous achalasia = numerous tertiary contractions in nondilated distal esophagus of early achalasia.
- Prompt relaxation of the LES upon amyl nitrate inhalation (smooth-muscle relaxant).
Figure 7. Radiographs of the lower part of the esophagus in patients with idiopathic achalasia. These radiographs from various articles demonstrate the symptom of “Bird beak”. Please note that these radiographs which were done in the 2nd period ignore other significant symptoms: the presence of a gas bubble of the stomach, the rate of evacuation of barium from the esophagus.

The diagnosis was based on a combination of clinical symptoms, a typical x-ray picture, and the absence of mechanical obstruction in esophagogastroscope.

Last period

This period began with the substitution of the concept of achalasia as a diagnosis, with achalasia as a functional state, where the selection of patients focused on the symptom of dysphagia. Spechler et al compared two groups of patients with achalasia. In one group of patients, the heartburn preceded the dysphagia. These patients had lower basal LES pressures than patients who had achalasia without this symptom. For patients with heartburn, it is speculated that achalasia develops in the setting of underlying GERD [18].

Now the concept of achalasia is as follows: “A diagnosis of achalasia should be considered when patients present with dysphagia, chest pain, and refractory
reflux symptoms after an endoscopy does not reveal a mechanical obstruction or an inflammatory cause of esophageal symptoms. Manometry should be performed if achalasia is suspected. Randomized controlled trials support treatments focused on disrupting the lower esophageal sphincter.” [19].

**Clinical presentation** already includes chest pain and refractory reflux symptoms in patients of all ages. There is no room for radiologic study in this concept of achalasia. Gastroscopy is designed to rule out inflammation and mechanical obstruction. The diagnosis and indications for surgical treatment are carried out based on a manometric study.

First, all the symptoms that are attributed to achalasia are characteristic of GERD.

Secondly, gastroscopy cannot rule out GERD. The chronic inflammatory process is visible only with histological examination [20]. Third, dysphagia is a difficulty in swallowing. It may be a sensation that suggests difficulty in the passage of solids or liquids from the mouth to the stomach. However, without an X-ray examination, it is impossible to determine the presence and rate of evacuation from the esophagus. Barium esophagogastrography allows you to objectively evaluate what is subjectively defined as dysphagia. For example, in an article by Gupta et al from 5 radiographs presented as cases of achalasia, in 3 cases is a typical X-ray picture of GERD (**Figure 8. a, b, c**) [21].
Figure 8. Radiographs of the esophagus and EGJ; (a-c) from an article by Gapta et al [21]. Radiographs are made in a horizontal position. (d) A patient with GERD (Our observation).

(a) Presented as secondary achalasia. True height D-11≈ 2cm. The esophagus is slightly expanded. The contracted LES contains barium. Its length (≈ 2 cm) is 2 times shorter than normal. (b) Presented as primary achalasia. Good evacuation from the esophagus. The moment of contraction of the short LES with folds was recorded. (c) Presented as primary achalasia. Good evacuation from the expanded esophagus. During an increase in pressure in the stomach, the LES was fully opened, except for the area at the diaphragm. (d) Good evacuation of barium from the expanded esophagus. The length of the LES is within normal limits. But there is a deformation of the folds, which indicates an inflammatory process. The gas bubble of the stomach is normal in size.

Radiographs from an article by Gapta et al [21] identify irrefutable symptoms of complicated GERD in at least 3 out of 5 cases with so-called achalasia. In a horizontal position with a wide esophagus, the function of the esophagus ampoule is absent. The threshold pressure for the opening of the LES is created all over the esophagus from the upper to lower esophageal sphincters. Therefore, evacuation takes place in portions and the esophagus is much wider than when examined in an upright position. When a portion of barium enters the stomach, the pressure in the esophagus decreases and the LEC is contracting. The presence of barium in the contracted sphincter and the more so “tram-track appearance” indicates an inflammatory process. Based on a manometric study, in the similar x-ray pictures in the case (a) secondary achalasia is diagnosed, and in case (b) - primary achalasia.

It seems that all the scientific information bit by bit collected over many generations was lost for modern researchers. Why does a manometric study determine the diagnosis and treatment tactics of patients with dysphagia?

1. The selection of volunteers as healthy individuals is erroneous. First, gastroesophageal reflux disease (GERD) for a long time can proceed without clinical manifestations. So, for example, with a screening gastroscopy examination of 6,683 healthy Koreans, 14.66% had GERD diagnosed [22].
Secondary, gastroscopy without histological examination does not exclude the presence of GERD [20]. For example, Pandolfino et al. produced concurrent high-resolution manometry (HRM) and fluoroscopy studies in eighteen asymptomatic volunteers. On radiographs, a typical picture of GERD with the formation of a phrenic ampulla and shortening of the LES is recorded [23].

2. HRM has low sensitivity in determining anatomical parameters. For example, in the article Silva et al there is a wide range of individual indicators. (Total LES length -3.82±0.95; range -1.6-5.7 cm) (Basal pressure -77.41±63.13; range -12.2-309.3 mmHg) [23]. The normal LES has a certain anatomical length as the anal canal or 1st lumbar vertebra. It cannot differ in different individuals by 3.5 times [25]. At the same time, in different countries (China, Taiwan, Brazil, India, etc.) researchers set their normative values for the water-perfused HRIM.

3. The study of esophageal peristalsis with a probe is not physiological since the probe stretches the esophagus wall all along its length and disrupts peristalsis. Secondly, the probe occupies a significant and always different lumen of the LES, which affects the results of manometry. If there is a narrowing of its lumen, then the probe can block the lumen of the LES and create an erroneous idea of obstruction. The cause of the narrowing can be not only a high tone of the NPS (idiopathic achalasia) or sclerotic changes in its wall but also inflammation and swelling, which can be treated conservatively.

4. The definition of achalasia as esophageal motility disorder characterized by impaired gastroesophageal junction relaxation and the absence of normally propagated peristaltic contractions without a structural explanation and its division into three types has no pathophysiological basis.

The initial selection of patients with dysphagia to determine pathological characteristics was carried out without objective criteria.

a) The symptom of dysphagia is a subjective, not clearly limited sensation. It may be a sensation that suggests difficulty in the passage of solids or liquids from
the mouth to the stomach, a lack of pharyngeal sensation or various other inadequacies of the swallowing mechanism.

b) The authors of the method did not perform diagnostic studies (histology of the mucous of the esophagus and pH-metry. X-ray examination was carried out based on erroneous ideas about the physiology and pathology of EGJ. As shown above, the limits of norm HRM were determined with gross violations.

c) In this randomly collected community of patients without a pathogenetic diagnosis, there are no coincidences of the manometric indicators with known diagnostic criteria for idiopathic achalasia. Therefore, all the diagnostic signs of idiopathic achalasia accumulated by many generations of scientists are not published and are not known to modern researchers.

d) Among patients with "dysphagia", researchers found 3 varieties of manometric indicators, "without a structural explanation", which are so inconsistent that each time proposing a new version, conference participants vote on which of the amendments to accept. What is determined by voting is not related to science [26].

Conclusion

HRM is not a diagnostic method. Most patients with manometric signs of achalasia suffer from complicated GERD at different stages of the disease. We need to treat the disease, not the symptoms.

Michael Levin, MD, PhD, DSc. Radiologist,

nivel70@hotmail.com; michael.levin@dorot.health.gov.il

https://orcid.org/0000-0001-7830-1944

https://www.anorectalmalformations.com

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