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Reflux Disease – Historical Overview

Choroba refluksowa – spojrzenie historyczne

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Abstract

The review presents the development and successive changes in the opinion on the essence of reflux disease which took place over the last century. Major milestones increasing our knowledge on the pathogenesis, diagnostics and treatments of this disease were reviewed on the basis of available literature. Special attention has been paid to the role of surgery in treatment of the disease, which is currently considered the most common dysfunction of the alimentary tract (Adv Clin Exp Med 2011, 20, 4, 407–411).

Key words: gastroesophageal reflux disease.

Streszczenie


Słowa kluczowe: choroba refluksowa.

The term gastro-esophageal reflux refers to reflux backflow of gastric contents to the esophagus due to transient weakening or permanent impairment of anti-reflux mechanisms in the lower esophageal sphincter. Transient weakening of the anti-reflux mechanisms occurs in healthy people and it is experienced daily by about 10% of population in highly developed societies and once-weekly by about 20% of the population. On the other hand, permanent incompetence of anti-reflux mechanisms within the lower esophageal sphincter leads to the development of pathological reflux, i.e. prolonged and frequent exposure of the esophageal mucosa to gastric refluxate. In consequence the patient develops a set of clinical symptoms and/or complications associated with the backflow which is referred to as Gastroesophageal Reflux Disease – GERD. Most common GERD symptoms include heartburn, regurgitations, odynophagia (painful swallowing) or dysphagia (difficulty in swallowing). Some patients may develop other symptoms, mainly from the respiratory system (dyspnœa, cough, hoarseness), or dental symptoms in the form of damaged dental enamel. The complications of GERD include severe lesions within the esophagus, from inflammatory conditions in the esophageal mucosa of varying intensity, to ulcerations, reflux-induced cicatrical strictures of the esophagus or Barrett’s esophagus (changes of the epithelial cells from squamous to intestinal columnar epithelium in distal esophagus). Barrett’s esophagus is considered a precancerous condition and, if left untreated, it may lead to esophageal adenocarcinoma.

First descriptions of gastro-esophageal reflux can be found in literature from about 100 years ago, when Walter B. Cannon observed episodes of gastric contents backflow to the esophagus in contrast radiography of the upper gastrointestinal tract in animals [1]. Almost simultaneously, in 1906, first descriptions of peptic esophageal ulcers in humans were presented by Tileston, a pathologist from Harvard [2]. The discoveries of both scholars, Cannon as well as Tileston, were met with indifference, or even were denied, as there were no diagnostic tools to confirm reflux.
The formulation of the concept of reflux disease is attributed to Aster Winkelstein from Sinai Hospital in New York, who in 1934 presented a group of patients with typical symptoms of reflux esophagitis confirmed radiologically and endoscopically (by means of a rigid endoscope) and concluded that inflammations and the symptoms of heartburn or retrosternal burning pain should be attributed to the irritating effect of hydrochloric acid and pepsin on the esophageal mucosa [3]. Winkelstein’s theory of association between clinical symptoms in the form of retrosternal pain and burning, and the presence of reflux disease were confirmed in the studies by Bernstein and Baker, who introduced a test differentiating sternocordial pains of cardiac origin from pains associated with reflux esophagitis. The authors also pointed out a very important issue, that the reflux symptoms are not always correlated with lesions in the esophageal mucosa observed on endoscopic examinations [4].

From the present perspective we know that the authors described a form of GERD, so-called non-erosive reflux disease (NERD). Since that time both, reflux esophagitis as well as burning retrosternal pains (heartburn) have found their place in professional literature on GERD.

The notion of hiatal hernia, which for many years was identified with reflux disease and considered the main cause of reflux esophagitis, is closely associated with Philip Allison, a thoracic surgeon from Leeds, Great Britain. Allison believed that the presence of hernia facilitates backflow of the stomach contents to the esophagus [5]. He also denied the presence of lower esophageal sphincter [6]. It was Eddie Palmer who demonstrated in his studies that reflux may be associated with other factors than hiatal hernia. The author presented evidence that not all the patients with reflux present with hiatal hernia, and on the other hand, not all patients with hiatal hernia develop reflux disease [7].

Thanks to the rapid progress in diagnostic methods – flexible endoscopes, manometry, motor activity, pH-metry of the esophagus – the presence and role of the lower esophageal sphincter (LES) as well as the significance of duration and incidence of pathological reflux in patients with GERD could be confirmed [8–11]. The introduction of a flexible endoscope to the diagnostics of upper gastrointestinal tract in clinical practice not only enabled to visualize lesions in the esophageal mucosa, but also prompted implementation of endoscopic criteria in the evaluation of severity of esophageal lesions – Savary-Miller classification and Los Angeles classification [12–14]. The latter is also used currently.

The history of the notion of Barrett’s esophagus, which is nowadays used to denote one of the complications of reflux disease, and which has been widely investigated, is very interesting. In 1950 Norman Barrett, a surgeon from St Thomas Hospital in London, described the presence of glandular epithelium in the esophagus [15]. Barrett believed that glandular epithelium present in distal portion of the esophagus in fact is a part of the stomach and results from a congenital defect in the form of a short esophagus. Barretts even assumed the possibility of metaplasia, i.e. transformation of squamous epithelium to columnar epithelium. Further studies confirmed that metaplasia results from gastro-esophageal reflux, moreover, the histological picture in Barrett’s esophagus was found to contain metaplastic lesions in the form of gastric metaplasia, intestinal metaplasia, or combination of both types [16, 17]. Intestinal metaplasia is believed to be most commonly associated with neoplastic transformation [17]. At present Barrett’s esophagus still remains the subject of multi-directional interest to numerous scholars [18–21].

Further rapid progress in diagnostic techniques has contributed to broadening and verification of opinions on the pathogenesis of GERD. It was shown that low initial LES tension is not always correlated with pathological reflux, and it was transient lower esophageal sphincter relaxations (TLESR) that were found to be the main causative factor in this type reflux [22–24]. Introduction of new examination techniques, such as 24-hour pH-metry, the Bilitec system and impedance method enabled quantitative evaluation of the exposure of esophageal mucosa to hydrochloric acid (pH-metry), biliary reflux monitoring (the Bilitec system) and detailed registration of the esophageal motor activity on passage of the alimentary stimulus with a simultaneous analysis of chemical composition of the refluxate (impedance) [25–27].

From the historical perspective, treatment of reflux disease did not always develop in parallel to good understanding of its pathogenesis. Even an opinion may be ventured that in many instances it followed the route of sheer coincidence. It was by chance that Nissen’s fundoplication has become a recognized surgical modality in the treatment of reflux disease. Rudolf Nissen, who operated on a patient with ulceration in distal esophagus penetrating towards the pericardium, performed fundoplication in order to prevent a possible fistula in the anastomosis [28]. It appeared that not only immediate outcome of the surgery, but also its remote results were satisfactory. Moreover, the patient did not complain of any symptoms of reflux. Nissen method as well as subsequent modifi-
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Cations of this modality (gastropexy, Hill’s operation, Mark-IV, Toupet posterior fundoplication, Jezioro fundoplication) are still used by surgeons in the treatment of reflux disease and hiatal hernia, also as a laparoscopic variety [24, 29, 30, 31].

Contemporary medicine also offers low-invasive anti-reflux procedures, thanks to unbelievably rapid progress in medical techniques that took place in recent years. They include endoscopic anti-reflux plication within esophageal-gastric junction, endoscopic injection techniques within the lower esophageal sphincter (Enteryx, Gatekeeper or Hydrogel prosthesis), and endoscopic delivery of radio high-frequency energy to the esophageal-gastric junction (Stretta procedure) [32, 33].

Surgical management of reflux disease has not been the only method used in treatment of this condition. Constantly arising new achievements and discoveries in the field of GERD pathophysiology have contributed to the search for new pharmacological preparations apart from neutralizing agents that would be effective in combating GERD symptoms. Among them, H₂ blockers, the efficacy of which was estimated at about 50%, were the first ones to be introduced [34]. But the true turning point in GERD therapy was the introduction of proton pump inhibitors (PPIs), which, contrarily to H₂ blockers, appeared exceptionally effective in significant inhibition of gastric secretion for many hours [35–37].

However the enthusiasm which had accompanied implementation of PPIs into GERD therapy has diminished slightly with time, as it appeared in remote studies that PPIs are effective in eliminating GERD symptoms in about 70% of patients [34, 35]. The remaining sufferers do not benefit even with highest doses of the drug, and some of them, despite treatment, even develop severe complications, such as esophageal ulcerations, bleeding, post-reflux cicatrical strictures, or Barrett’s esophagus, which call for other therapeutic modalities, including severe surgical interventions [38–42]. It was also shown that GERD involves not only esophageal symptoms, but also induces extra-esophageal, mainly respiratory symptoms [43].

The knowledge on GERD gathered in that past years, as well as an urgent need to standardize opinions on the pathogenesis, clinic and therapy for this disease were the impulse for a group of specialists to meet in Montreal in 2005. The Global Consensus Group developed consensus on GERD and presented a generally acknowledged definition of this disease [44]. The Montreal consensus is now used to define and classify GERD.

The presented overview illustrates changes in our knowledge on the essence of reflux disease throughout many years – from the search for one causative factor to understanding of a complex, multifactorial pathogenesis of this disease, from a disease, which was considered extremely rare 100 years ago, to the most common gastrointestinal dysfunction in the contemporary world.

References


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