

The Otolaryngologic Manifestations of Gastroesophageal Reflux Disease (GERD): A Clinical Investigation of 225 Patients Using Ambulatory 24-Hour pH Monitoring and an Experimental Investigation of the Role of Acid and Pepsin in the Development of Laryngeal Injury

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All laryngologists are familiar with the many throat conditions which appear as salient features of underlying systemic states, and yet in the overswing towards localism [specialization], general pathologic data, systemic therapeutics and hygienic aids are not always utilized to the utmost. The laryngologist should continue to be, first of all, a good physician, and after that, something more – a specialist.

William E. Casselberry¹
President's Address, May 22, 1899
American Laryngological Association

ABSTRACT

Occult (silent) gastroesophageal reflux disease (GER, GERD) is believed to be an important etiologic factor in the development of many inflammatory and neoplastic disorders of the upper aerodigestive tract. In order to test this hypothesis, a human study and an animal study were performed. The human study consisted primarily of applying a new diagnostic technique (double-probe pH monitoring) to a population of otolaryngology patients with GERD to determine the incidence of overt and occult GERD. The animal study consisted of experiments to evaluate the potential damaging effects of intermittent GER on the larynx.

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Two hundred twenty-five consecutive patients with otolaryngologic disorders having suspected GERD evaluated from 1985 through 1988 are reported. Ambulatory 24-hour intraesophageal pH monitoring was performed in 197; of those, 81% underwent double-probe pH monitoring, with the second pH probe being placed in the hypopharynx at the laryngeal inlet. Seventy percent of the patients also underwent barium esophagography with videofluoroscopy.

The patient population was divided into seven diagnostic subgroups: carcinoma of the larynx (n = 31), laryngeal and tracheal stenosis (n = 33), reflux laryngitis (n = 61), globus pharyngeus (n = 27), dysphagia (n = 25), chronic cough (n = 30), and a group with miscellaneous disorders (n = 18).

The most common symptoms were hoarseness (71%), cough (51%), globus (47%), and throat clearing (42%). Only 43% of the patients had gastrointestinal symptoms (heartburn or acid regurgitation). Thus, by traditional symptomatology, GER was occult or silent in the majority of the study population.

Twenty-eight patients (12%) refused or could not tolerate pH monitoring. Of the patients undergoing diagnostic pH monitoring, 62% had abnormal esophageal pH studies, and 30% demonstrated reflux into the pharynx. The results of diagnostic pH monitoring for each of the subgroups were as follows (percentage with abnormal studies): carcinoma (71%), stenosis (78%), reflux laryngitis (60%), globus (58%), dysphagia (45%), chronic cough (52%), and miscellaneous (13%). The highest yield of abnormal pharyngeal reflux was in the carcinoma group and the stenosis group (58% and 56%, respectively).

By comparison, the diagnostic barium esophagogram with videofluoroscopy was frequently negative. The results were as follows: esophagitis (18%), reflux (9%), esophageal dysmotility (12%), and stricture (3%).

All of the study patients were treated with anti-reflux therapy. Follow-up was available on 68% of the patients and the mean follow-up period was 11.6 ± 12.7 months. After 6 months of treatment, symptoms had resolved in 85% and medical therapy had failed in 15%. Subsequently, an additional 20% experienced medical treatment failure. Fifteen percent of patients underwent Nissen fundoplication, and all subsequently had resolution of symptoms.

To further investigate the role of gastroesophageal reflux in the development of laryngeal damage, experiments mimicking the effects of intermittent reflux (of acid and pepsin) on the canine larynx were performed. The results of these experiments revealed: 1. Intermittent reflux (three episodes per week) can result in severe laryngeal damage if there is prior mucosal injury; 2. pepsin, and not hydrochloric acid, is the principal injurious agent of the refluxate; and, 3. severe laryngeal damage can occur even when the pH of the refluxate is 4.0.

The manuscript describes the limitations and advantages of standard diagnostic procedures and of 24-hour pH monitoring. The differences between gastroenterology and otolaryngology patients with GERD are emphasized and specific new diagnostic and therapeutic recommendations are made.

INTRODUCTION

Although it has been estimated that 10% of Americans have symptoms of heartburn and regurgitation on a daily basis, and 30% to 50% less frequently,² the epidemiology and the natural history of gastroesophageal reflux disease (GER, GERD) remain incompletely understood. It is often assumed by gastroenterologists and otolaryngologists alike that clinically manifest GERD should be associated with typical gastrointestinal symptoms such as heartburn and regurgitation. However, what if otolaryngology patients with GERD were atypical? What if the standard GER diagnostic methods were insensitive and inaccurate? What if symptoms and complications of GER could result from intermittent reflux? What if occult (silent) GER produced a broad constellation of upper aerodigestive symptoms and sequelae in otolaryngology patients? It is the purpose of this thesis to address these questions.

Case Example

In 1981, a 55-year-old clergyman presented with a recurrent granuloma on the laryngeal surface of the epiglottis (Fig. 1-A). The patient was otherwise healthy and his only symptoms were a sensation of a lump in the throat, chronic throat clearing, cough, and hoarseness. He denied heartburn, regurgitation, or sour taste on eructation.

Three and six months earlier, he had undergone endoscopic (cold knife) removal of the lesion, but it recurred. Histologically, pyogenic granuloma had been found on both occasions. A third endoscopic excision with the carbon dioxide laser was performed. The histologic specimen again demonstrated pyogenic granuloma, and, again, the lesion recurred. An endoscopic epiglottectomy was then per-

formed; however, within 1 week of operation, granulation tissue was forming in the base of the tongue at the surgical site.

A barium swallow esophagogram was obtained and was normal. Nevertheless, because of the intractability of disease and the remote possibility of GER contributing to the disorder, the patient was started on an antireflux regimen, including cimetidine (300 mg q.i.d.). Within 3 weeks (1 year his after initial presentation), the lesion had healed.

For years, otolaryngologists have realized the limitations of the diagnostic tests for GERD and have relied, as in this patient, primarily upon clinical diagnosis. Although the specificity of many of the standard tests for GERD is reasonably good, the sensitivity is often poor. Ambulatory 24-hour pH monitoring (pH manometry; pH-metry) is by far the most sensitive and specific test for GERD currently available.³⁻⁸ At this time, there are scant pH-metry data available in otolaryngology patients with GER-related conditions.

Some GERD syndromes have been well described, including the vocal process granuloma⁹⁻¹⁵ and posterior laryngitis (red arytenoids and piled-up interarytenoid mucosa).¹⁶⁻¹⁹ Even with this information, there is some disagreement. Posterior laryngitis, for instance, which is considered by many clinicians to be virtually pathognomonic for GER, has been found by some investigators not to be invariably associated.²⁰

In spite of the diagnostic limitations, GER has been postulated to be associated with or responsible for an array of upper aerodigestive conditions, including laryngeal carcinoma^{14,21,22} and subglottic stenosis.^{23,24} However, none of the previous reports have suggested that GER-related upper aerodigestive tract conditions may result from occult or intermittent GERD.

HYPOTHESIS

Occult (silent), and sometimes intermittent, gastroesophageal reflux disease is associated with the development of inflammatory and neoplastic disorders of the upper aerodigestive tract.

OBJECTIVES

1. To report the findings (including the incidence of occult and intermittent GER) of 225 otolaryngology patients with GERD-related upper aerodigestive conditions.
2. To describe and contrast the patterns of GERD in otolaryngology patients with those of gastroenterology (esophagitis) patients.
3. To describe the results of ambulatory 24-hour intraesophageal pH monitoring in otolaryngology patients with GERD.
4. To evaluate and report the usefulness of pha-

advice on a day-to-day basis, as well as help in managing many of the more difficult patients.

In the animal laboratory, Dr. Richard Cooper and Janet Talcott made it all possible. As a senior medical student, Dr. Cooper was an endoscopic whiz and helped in every aspect of the animal studies; Janet Talcott kept the animals healthy and ready. Without these two, it would not have been possible for me to do this project while simultaneously maintaining a busy clinical practice. A special thanks to Dr. Kim Geisinger in the department of pathology who adapted the inflammation score for the dog larynges from his previous work with an esophagitis animal model; it

was he who actually examined and scored the larynges.

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