The Barrett esophagus (BE) was first described in 1950 by a British surgeon whose name has been given to this condition. Barrett believed the condition to be present at birth but in 1953 Allison and Johnston postulated that the condition might be acquired. In 1961 Hayward considered it to be acquired and elegantly described the mechanism of its development as a consequence of destruction of the normal squamous cells lining the esophagus by repetitive reflux of stomach acid, probably over many years. The body’s effort to heal the segment of esophagus in which the normal lining cells (squamous type) are destroyed results in the growth of primitive cells. These evolve into the intestinal metaplasia and other types of columnar cells that replace the squamous cells that were destroyed by acid. These new cells are better able to tolerate an acid environment and thereby can readily grow in the esophagus to heal the damaged areas. A columnar cell variant, so-called intestinal metaplastic type, has the potential over time to become dysplastic (abnormal growth) and later evolve into adenocarcinoma (cancer). Knowledge of the stages of this sequence provides the opportunity for detecting those persons who develop dysplasia and have the highest risk to develop cancer. Current research on genetic markers for predisposition to cancer may provide a means to more precisely identify those at greatest risk.

BE has been recognized with increasing frequency over the past three decades and there is currently no explanation for this phenomenon. Likewise the esophageal cancer that occurs with BE has remarkably increased in frequency. Forty years ago less than 5% of esophageal cancers were of the adenocarcinoma type and 95% were squamous cell cancer. Today over 70% of esophageal cancers in our practice are adenocarcinomas and nearly all of these are associated with BE. Both BE and adenocarcinomas are primarily diseases of white males between 40 and 80 years of age. This condition is less common in females and rare in black persons.

BE is always associated with a hiatal hernia and reflux of stomach contents into the esophagus. This occurrence over time (duration required unknown) leads to destruction of the squamous cells lining the esophagus if the reflux is not treated properly. Most patients with BE have only mild to moderate symptoms of acid reflux, i.e. heartburn, regurgitation, chest pain, or pain on swallowing (odynophagia). Interestingly, it appears that in patients with BE the acid reflux injury likely is related to a predominance of nighttime acid reflux and reduced lower esophageal sphincter pressure. The typical patient controls symptoms by using over-the-counter antacids, baking soda and more recently over-the-counter H2 blockers (Tagamet, Zantac, Pepcid) for many years and has never been bothered enough to seek medical attention. This is probably why most of these patients who develop adenocarcinoma are never seen by a gastroenterologist before the cancer develops. Once the patient develops difficulty swallowing or other telltale symptoms of cancer the chances for cure are very low. The current belief is that early diagnosis and close follow-up by endoscopy and biopsy to detect the pre-cancerous tissue changes (dysplasia) offer the best hope for early curative treatment.

BE is reported to occur in 8 to 20% of patients with reflux esophagitis who are examined by endoscopy with biopsy of the esophagus. In those with esophageal stricture due to reflux the frequency of BE is over 80%. The current procedure is to carefully examine every patient for BE who requires endoscopy for evaluation of their symptoms of acid reflux with special attention to white males because of their predisposition. Our recommendation is that persons over 50 years of age, especially white males, with a long history (over 10 years) of acid reflux (heartburn) should have endoscopy to evaluate for BE. In a recent study researchers detected BE (intestinal metaplasia) by upper endoscopy and biopsy extending above the esophagogastric junction in 25% of subjects over 50 years of age without prior acid reflux symptoms who were also undergoing screening sigmoidoscopy for colorectal cancer. In view of the rarity of esophageal cancer and the low progression rate of BE to cancer further research will be required to determine whether screening for BE should be applied to the general population in this age group.

When BE is confirmed the patient is advised that the relationship to cancer is real. There is a 30 to 40 times greater chance that a patient with BE will develop cancer than a person of the same age, race and sex without BE. If there are no signs of BE on endoscopy and biopsy at this initial examination and reflux symptoms are adequately treated, there is very little chance the patient will later develop this condition. Patients with BE are advised that the proper interval for surveillance endoscopy with biopsy to search for the pre-cancerous dysplasia is every 1 to 2 years initially but if continued surveillance reveals no pre-cancerous changes (dysplasia) this interval can safely be increased to 3 – 5 years. Although at greater risk of developing cancer with BE, it should be reassuring to know that less than 0.4% of patients will develop cancer annually. If severe or high-grade dysplasia is found the patient has about a 30 to 40 % chance of having early cancer in the esophagus at that time.

If either low-grade or high-grade dysplasia (the earliest form of cancer located in the surface cells of BE tissue without any invasion) is found the management scheme becomes more intensive. With low-grade dysplasia, the interval for repeat biopsies is initially reduced to 3 – 4 months to obtain more tissue to examine in search for high-grade dysplasia that may be present but too focal to have been found on the initial set of biopsies. After one year of this schedule the interval is increased to 1 year if no high-grade dysplasia is found.

Because of the cancer risk with high-grade dysplasia a decision regarding therapy should be made after this biopsy diagnosis is confirmed by a second expert pathologist. Currently, there are three acceptable management options for high-grade dysplasia based on experience and medical literature reports over the past decade. A decision on therapy after this biopsy confirmation should be preceded in our opinion by further evaluation that includes repeat endoscopy with four quadrant biopsies of the Barrett segment using large capacity or “jumbo” forceps and a CT scan of the chest and abdomen to search for metastases. If CT scans are negative an endoscopic ultrasound examination of the esophagus should be done to examine for any spread of this presumed superficial cancer to deeper layers or outside the wall of the esophagus. If all findings indicate the high-grade dysplasia or superficial cancer is localized to the inner layer (mucosa), the three options should be explained in detail to the patient and a decision made.

Surgical removal of the esophagus (esophagectomy) remains the treatment of choice in many centers but is a major operation with significant operative mortality and postoperative complications although it does provide the best
chance of a cure. The operative mortality is reported to vary between 3% and 17% depending on the experience of the surgeon and institution where the esophagectomy is performed.

Another acceptable option based on a decade of experience is photodynamic therapy or PDT, a non-surgical procedure, performed through the endoscope that destroys the dysplasia and surrounding tissue of BE in the inner layer (mucosa). The patient is given high dose acid suppressing drug treatment (one of the proton pump inhibitors after PDT). When esophageal acid exposure is reduced or eliminated by this treatment the normal esophageal mucosal cells will regenerate and overgrow the area where the BE cells (intestinal metaplasia) and high-grade dysplasia cells were destroyed. Continued surveillance by endoscopy with biopsy is required after PDT therapy.

Lastly, a recent report of long-term follow-up of high-grade dysplasia with endoscopy and biopsy has shown that many patients are not found to have progression to esophageal cancer. Very close follow-up is required if this course is selected. Further long-term studies are needed to confirm this report.

In patients with BE and no dysplasia the gastroenterologist usually prescribes the most potent drug available (a proton pump inhibitor) to suppress stomach acid and thereby attempt to reduce its’ progression. Whether future development of dysplasia or cancer in BE can be prevented or delayed by maximum suppression of acid is unknown. Evidence to date indicates that as long as the abnormal tissue of BE is present in the esophagus the threat of cancer remains and the need for biopsy surveillance continues.

---

**EXTRAESOPHAGEAL MANIFESTATIONS OF ACID REFLUX**

Milton C. Johnson, M.D.

Gastroesophageal reflux disease (GERD) is the most common cause of “indigestion” in the United States of America. Between 20% and 40% of the adult population have frequent heartburn, but only a few develop significant complications. Classical clinical manifestations include heartburn or pyrosis (burning discomfort behind the breast bone or sternum) and regurgitation (the backflow of stomach acid from the esophagus into the mouth). The presence of abnormal amounts and exposure time of acid reflux in the esophagus may involve other symptoms of GERD that include difficulty swallowing (dysphagia), painful swallowing (odynophagia), and the presence of excess saliva (water brash or salivary rhora) in the mouth or throat, especially in those individuals who have problems with solid foods hanging up or “sticking” in the throat or esophagus.

Gastroesophageal reflux is less commonly manifested by chest pain that mimics pain of cardiac etiology. A prompt cardiac (heart) assessment should always be a prerequisite to a diagnosis of chest pain of “esophageal origin.” A non-cardiac cause of chest pain should be determined early in the evaluation of any patient presenting with “chest pain of undetermined etiology.” Many other atypical manifestations of GERD may be experienced by patients. These are often referred to as “extraesophageal, supraesophageal or extraintestinal manifestations.” Halitosis, laryngitis, hoarseness, vocal fold granulomas or polyps, subglottic stenosis, loss of dental enamel, oral ulcerations, burning in the mouth or throat, sinus headaches, chronic cough, wheezing, and recurrent respiratory infections are examples of a few extraesophageal manifestations of GERD.

A large population-based study evaluated the frequency of GERD in the general population and discovered that asthma was reported in 9% and bronchitis in 20% of patients who also reported symptoms of heartburn. Sixty percent of patients with asthma, bronchitis or pneumonia also had frequent heartburn or regurgitation.1

Prospective studies have demonstrated the presence of GERD in 70-80% of patients with asthma and 20% of patients with chronic cough. Careful evaluation has found that 50-75% of patients with chronic cough or asthma and GERD will have infrequent heartburn. Most patients with pulmonary (airway) symptoms will be more likely to complain of regurgitation rather than heartburn. Clinicians should consider GERD as a cause of symptoms in any patient who complains of a chronic cough who is a non-smoker with a normal chest x-ray without complaints of post-nasal drip, and who does not take an angiotensin-converting-enzyme inhibitor (popular class of drugs with a major effect on the kidneys in the control of high blood pressure). Asthmatic episodes that occur postprandial (after meals), following alcohol ingestion, or which are refractory to bronchodilator therapy should be considered as related to acid reflux. GERD as a cause of symptoms should also be considered especially in adult asthmatics with predominant nocturnal symptoms that have developed asthma later in life and have no history of significant allergies.

Koufman estimates that 4-10% of chronic non-specific laryngeal disorders in otolaryngology (Ear, Nose and Throat or ENT) clinics is associated with GERD.3 The major factors, which have influenced the clinician to associate chronic laryngitis with gastroesophageal reflux include: 1) lack of etiology for chronic laryngeal symptoms and findings; 2) occurrence or persistence of laryngeal symptoms and abnormalities; 3) and successful relief of laryngeal symptoms with empiric anti-reflux therapy in some patients. Koufman demonstrated that of all patients suspected to have otolaryngologic complications of GERD, only 43% had classic symptoms of heartburn, regurgitation or dysphagia. Frequent symptoms associated with extraesophageal manifestation of GERD have included persistent throat clearing, recurrent hoarseness (especially in the morning upon waking), halitosis, and increase volume and thickening of salivary secretions (sialorrhea). It is suspected that the laryngeal manifestations of gastroesophageal reflux disease are more apt to be caused by microaspiration (“small droplet inhalation”) with resulting damage by surface contact. This is also the mechanism proposed to exacerbate asthma. However, a second mechanism based upon a neural reflex (vagus nerve-mediated reflex bronchoconstriction or airway spasm) from an area in the distal esophagus to the tracheobronchial tree (airway passage) has also been hypothesized or speculated to be the trigger point for asthma associated with GERD.3

Our body’s position appears to influence postprandial (after meals) and fasting reflux. Castell’s group demonstrated (10 patients included in study) that the right lateral decubitus (“right side down”) position (during sleep) had a much greater percent time for acid reflux pH <4 and more prolonged time to clear acid from the esophagus compared to the left lateral decubitus (left side down), supine (back down) or prone (face down) positions. Interestingly, they also discovered that acid reflux episodes were more frequent in the supine position (p < 0.04).

Twenty-eight percent of the time reflux episodes occurred within 1 minute after change in sleeping position.5

Review of data from Sue Harding’s group at the University of Alabama reveals that 77% of asthmatics complain of heartburn. Forty-one percent of that group experienced reflux-associated respiratory symptoms. Clinically silent reflux has been demonstrated in 24% of individuals with asthma that has been difficult to control. A significant subset of asthmatics have prolonged esophageal acid contact times when in the supine position (sleep). When adult asthmatics are studied during sleep, it has been discovered that no change in the pattern and rate of airflow through the large and small airway tubes occur as a result of acid reflux. Studies of pediatric asthmatics have revealed similar findings. Acid reflux episodes during sleep are not significantly different in the adult and pediatric asthma groups. The acid reflux events observed did not contribute to the worsening of asthma symptoms of wheezing, cough or shortness of breath in the majority of individuals studied.6

Additionally, Dr. Harding’s research suggests that gastroesophageal circadian (biological rhythm every 24 hours) issues are probably important contributors to worsening of nocturnal (nighttime) asthma by reflux. It has been determined that gastric acid secretion peaks at 9 pm and gastric emptying is delayed when a meal is given at 8 pm as compared to 8 am. This is important since the time to clear esophageal acid is delayed during sleep; but markedly improved during periods of arousal. When these events are coupled with the finding of a decrease in the upper esophageal sphincter (UES) pressure during sleep, microaspiration as a probable cause of supraesophageal symptoms is provided greater support.4 In summary, the results indicate that the potential for acid reflux episodes during sleep is influenced by several physiological (natural occurring) events. Acid reflux events however do not necessarily produce symptoms; and, many times supraesophageal symptoms occur without evidence of acid reflux.
**DIAGNOSIS AND THERAPY**

Twenty-four-hour ambulatory esophageal pH monitoring is the single most important test/study to perform in patients with extragastric manifestations of GERD. This type of prolonged pH monitoring allows the clinician to determine if there is an increase in esophageal acid exposure and whether or not symptoms of chronic cough, wheezing, asthma exacerbation, hoarseness, sore throat, burning in the mouth or throat correlate with gastroesophageal reflux during a 24-hour period. Typically, a two channel pH electrode (sensor) is placed 5 cm (2 inches) above the distal end of the esophagus. The second sensor is positioned 10 cm (4 inches) above the distal sensor. The frequency, duration, and number of acid reflux episodes are measured by the electrodes at their respective sites in the esophagus.

Some advocate the additional use of a monitoring catheter or tube that contains a third electrode (sensor) in the hypopharynx (back of throat) for simultaneous monitoring of acid exposure in the hypopharynx and esophagus during the twenty-four-hour period. Clinical studies have compared the use of 24-hour monitoring catheters designed with two and three electrodes. These studies do not reveal any significant improvement in the detection of acid reflux events related to supraesophageal symptoms regardless of whether or not a catheter with two or three electrodes is used during the monitoring period. The overall sensitivity and specificity of 24-hour pH monitoring is only 80% when evaluating extragastric manifestations of acid reflux.

Endoscopy (use of a lighted tube and camera to view the food tube and stomach on a television screen) is the least sensitive study to indicate the presence of GERD unless esophageal erosions, esophagitis, ulceration, or columnar-lined (Barrett) esophagus (CLE) is present at the time of endoscopic assessment. Endoscopy is therefore not the best, first diagnostic test to confirm GERD as a cause of supraesophageal symptoms. Greater than two-thirds of patients with supraesophageal symptoms will have a normal endoscopic examination.

Aggressive or high dose proton pump inhibitors (twice daily dosing 30 minutes prior to breakfast and dinner) for 12-16 weeks is the best-recognized mode of conservative therapy for the extragastric complications of GERD. Operative intervention by laparoscopic antireflux surgery should be reserved for patients who have signs of overt or obvious regurgitation and/or heartburn symptoms that correlate well with acid gastroesophageal reflux episodes demonstrated by ambulatory 24-hour pH monitoring.

**REFERENCES**

Would you believe...medicine? That's because your bathroom's warm, damp environment can alter chemicals in prescription and over-the-counter drugs — as can exposure to light, air and extreme heat or cold. Poorly stored medicines can become too strong, possibly leading to overdose symptoms (for example, the alcohol in cough syrup can evaporate, concentrating the medicine so that it causes extreme sedation). Or the medicine may become weaker so that your condition won't be cured. What to do? Relocate your prescriptions to a dry, dark room-temperature spot such as a linen closet shelf. (Refrigerate only if recommended.) Keep medicines in their original containers and out of children's reach. If you notice a change in color, odor or consistency (cracked or crumbling tablets, for instance, or clear liquids turn cloudy), show the questionable medicine to your pharmacist.

**SPEECH PATHOLOGY CONSULTANTS FOR OROPHARYNGEAL SWALLOWING DISORDERS**

Speech Pathology . . . . Joy E. Gaziano, M.A., CCC/SLP  
Linda Stachowiak, M.S., CCC/SLP  
Allana Sullivan, M.S., CCC/SLP

**WHAT NOT TO KEEP IN YOUR MEDICINE CHEST**

OFFICE HOURS: 8:00 a.m. 'til 4:30 p.m. Monday through Friday. Telephone hours: 8:00 a.m. 'til 5:00 p.m.

Also, our emergency telephone number for after hours is (813) 974-2201

BILLING: Payment for services rendered is due at the time of your visit. Please be prepared to pay any co-payments due at the time of your visit to the Center.

Patients who have problems with their physician or facility fee bills should contact Gayle Stephens, Financial Specialist, at the University of South Florida Medical Clinics at (813) 974-3575 between the hours of 9:00 a.m. and 4:00 p.m. Monday through Thursday.

For those patients who are from out-of-town, a new toll-free number has been added for you to call with billing questions. The number is 1-888-873-3627. This number is for calls originating in Florida and is only for billing questions and help with insurance authorizations.

HAS YOUR INSURANCE COMPANY OR PRIMARY CARE PHYSICIAN CHANGED? With an ever changing medical insurance market (shopping for the best contract, companies merging, others closing their doors, etc), you may have changed insurance company. If you changed your insurance company you may have a new primary care physician. Maybe you have moved and had to choose a new doctor closer to your home. Regardless of the circumstances we would very much appreciate your contacting our office to let us know, (813) 974-3374. This will not only insure we can obtain the necessary authorizations/pre-certifications and that your medical bills go to the right insurance company but it will help us make sure your medical records are forwarded to the right doctors. Thank you for helping us keep the records straight.