

Barrett's Esophagus, GERD and Esophageal Cancer

Barrett's esophagus is a precancerous condition affecting the lining of the esophagus, the swallowing tube that carries foods and liquids from the mouth to the stomach. In a study published in 2005, Barrett's esophagus was estimated to affect approximately 3.3 million adults in the United States.¹ Left untreated, Barrett's esophagus can lead to a dangerous type of cancer called esophageal adenocarcinoma, which is currently the most rapidly rising cancer in the U.S.^{2,3}

Barrett's esophagus is caused by injury to the esophagus resulting from chronic GERD (gastroesophageal reflux disease). Approximately 44% of U.S. adults experience symptoms of GERD almost monthly while 18% experience symptoms weekly.⁴ Approximately 13% of Caucasian men over the age of 50 with chronic GERD will develop Barrett's esophagus.⁵ The disease occurs when normal cells in the esophagus undergo genetic changes, resulting from chronic GERD, which set the stage for cancer.

The lining of a healthy esophagus contains a layer of cells that protects it from injury resulting from reflux of gastric contents. When chronic reflux occurs and exposes the cells to acid, this lining can break down and undergo a genetic change that can lead to cancer.

Studies show that Barrett's is the precursor to esophageal adenocarcinoma. This type of cancer is often incurable as the disease is frequently discovered at a late stage. For a patient with Barrett's, the annual risk of developing cancer is similar to the risk of developing colon cancer for a patient with a colon polyp. Although unlike a colon

¹ "Study provides first estimate of U.S. population affected by Barrett's esophagus." Gastro.org. 2006. American Gastroenterological Association. <www.gastro.org/wmspage.cfm?parm1=1834> Accessed August 2007

² Reid B.J and Weinstein W. M. Barrett's esophagus and adenocarcinoma. *Gastroenterology Clinics of North America* 1987; 38: 477-492.

³ "What Are the Key Statistics about Cancer of the Esophagus?" Cancer.org. 2006. American Cancer Society. <www.cancer.org/docroot/CRI/content/CRI_2_4_1X_What_are_the_key_statistics_for_esophagus_cancer_12.asp?sitearea=> Accessed October 2007.

⁴ Shaheen N, Ransohoff DF. Gastroesophageal reflux, Barrett's esophagus and esophageal cancer. *Journal of the American Medical Association*. 2002; 287: 1972-1981.

⁵ Westhoff B, Brotze S, Weston A, et al. The frequency of Barrett's esophagus in high-risk patients with chronic gerd. *Gastrointestinal Endosc*. 2005; 61:226-231.

polyp, which is removed immediately upon diagnosis, the standard treatment for Barrett's disease is a protocol of "watchful waiting."

A patient with Barrett's visits their doctor at scheduled intervals ranging from every three months to three years for an upper endoscopy and a biopsy of the affected part of their esophagus. The physician inspects the lining of the patient's esophagus and collects tissue samples to evaluate the status or progression of the disease. Patients with Barrett's esophagus who are in surveillance live with the daily fear of the unknown: "Will I develop cancer? If so, when and what can I do to prevent it?" Moreover, people with Barrett's must undergo, on a regular basis, an endoscopic procedure that requires a visit to the hospital, anesthesia, several days of recovery and eating restrictions.

Certain types of advanced Barrett's (high-grade dysplasia) and adenocarcinoma require an esophagectomy, a surgical procedure that involves removing the patient's esophagus. Esophagectomy is a formidable operation with significant risks and a lengthy recovery period. Following esophagectomy, patients may experience swallowing problems, decreased food intake, hoarseness, reflux and diarrhea. The quality of life for patients is poor. The five-year survival rate after developing adenocarcinoma is very low.

In Search of a Solution

Many physicians recognized the need to prevent cancer before it develops and searched for therapies that would allow them to advance the "watch and wait" treatment protocol to a "diagnose and treat" standard of care. Endoscopic ablation—the use of energy to remove the Barrett's cells in the esophagus historically, had not been widely used because previous methods were associated with significant complications, including narrowing of the esophagus (called stricture) and perforation and bleeding. These ablation techniques also did not allow uniform ablation of the esophageal lining, resulting in either excessively deep ablation that damages healthy tissue or shallow treatment that only allows the Barrett's cells to be covered up by new tissue growth. In addition, many of these ablation devices required high operator skill which can lead to variability in therapy. The limitations prevented many Barrett's patients from receiving treatment before their disease became a serious and potentially life threatening problem.

BÂRRX Medical, Inc. developed two endoscopic systems for treating Barrett's esophagus that address the challenges of curing this disease. The HALO³⁶⁰ and HALO⁹⁰ Systems provide uniform and controlled ablative therapy at a consistent depth, which can remove the layer of the diseased tissue and allow the regrowth of normal cells without injuring healthy underlying tissue. The HALO³⁶⁰ System targets a 3 cm circumferential treatment area. The HALO⁹⁰ System is designed for focal ablation of Barrett's and can be used independently or in conjunction with the

HALO³⁶⁰ System. The HALO⁹⁰ System is uniquely able to treat small areas of Barrett's esophagus. Following ablation with either the HALO³⁶⁰ or the HALO⁹⁰ System the diseased tissue in most patients is replaced by new healthy tissue within three to four weeks time. The ability to provide the controlled amount of ablative therapy to diseased tissue significantly reduces the risk of complications normally associated with other forms of ablation therapy.^{6,7}

The HALO³⁶⁰ System has three components: a sizing balloon, an ablative energy generator and an ablation catheter. The HALO³⁶⁰ system was cleared by the FDA in 2001 and became commercially available in the U.S. in January 2005.

Initially, a sizing balloon is used to size the esophagus. A correctly sized ablation catheter is then inflated within the area of the intestinal metaplasia. The HALO³⁶⁰ energy generator is activated to deliver a rapid burst of ablative energy which removes (ablates) a very thin layer of the diseased esophagus. This energy delivery is controlled so as to avoid injury to the normal, healthy underlying tissues. New healthy tissue replaces the ablated Barrett's tissue in three to four weeks for most patients. The procedure, which in clinical studies had a median procedure time of 26 minutes, is performed without incisions using conscious sedation in an out-patient setting.

The HALO⁹⁰ System is an endoscope mounted ablation system. It has two components: an ablative energy generator and an ablation catheter featuring a small electrode that can be mounted on the end of an endoscope. The HALO⁹⁰ system was cleared by the FDA in 2006 and became commercially available in the U.S. in

⁶Ganz RA, Utley DS, Stern RA, et al. Complete ablation of esophageal epithelium with a balloon-based bipolar electrode: a phased evaluation in the porcine and in the human esophagus. *Gastrointest Endosc* 2004; 60:1002-10.

⁷ Sharma VK, Wang KK, Overholt BF, et al. Balloon-based, circumferential, endoscopic radiofrequency ablation of Barrett's esophagus: 1-year follow-up of 100 patients. *Gastrointest Endosc* 2007; 65:185-194.

January 2007. Using standard endoscopic skills, the physician directs the ablation catheter to the diseased area of the esophagus. The HALO energy generator is then activated to deliver a short burst of ablative energy, which removes a very thin layer of the diseased esophagus. The procedure, which in clinical studies had a median procedure time of 15 minutes, is performed without incisions using conscious sedation in an out-patient setting.

Data from several multi-center clinical trials demonstrate that greater than 90 percent of participants were Barrett's-free after one to two treatment sessions (at 30 month follow up).⁸

Today, the standard of care for most pre-cancerous lesions is the removal of that lesion. A colonoscopy is recommended for adults who reach age 50. If a polyp is seen, it's immediately removed when diagnosed despite the fact that the majority are benign. However, untreated colon polyps confer approximately the same risk for developing cancer as untreated Barrett's esophagus: the removal of colon polyps reduces cancer risk by 76-90 percent.⁹ A safe and effective ablation technique that's easy for physicians to use could potentially reduce the risk of developing adenocarcinoma of the esophagus as well as possibly reduce the need for "watchful waiting" an annual expense and uncomfortable endoscopic surveillance for many.

Today, the medical management of a pre-cancerous condition typically follows a "diagnose and treat" protocol. Data show that treating early cancerous changes not only impacts long-term healthcare costs but also improves the quality of life for patients living with uncertainty and fear. Removing Barrett's at an earlier stage—before it advances—may have a high likelihood of preventing progression to cancer. At its current growth rate, adenocarcinoma of the esophagus is on track to exceed the number of deaths from colon cancer within 15 years. Now that technology is available to treat Barrett's disease before it progresses to cancer, there is an opportunity to impact this projection and ultimately improve the quality of life for the millions of Americans living with Barrett's esophagus.

⁸ Fleischer DE, Overholt BF, Sharma VK, et al. Long-term (2.5 year) follow-up of the AIM-II trial for ablation of Barrett esophagus: results after primary circumferential ablation followed by secondary focal ablation. *Gastrointest Endosc* 2007; 65: AB 135.

⁹ Winawer SJ, Zauber AG, Ho MN, et al. Prevention of colorectal cancer by colonoscopic polypectomy. *N Engl Med* 1993; 329:1977-1981.