Savannah HEALTH PERSPECTIVE©

Heartburn & Cancer: Am I at Risk?

Mark E. Murphy, M.D., F.A.C.P., A.G.A.F.

It's a refrain that gastroenterologists hear every day: "I read somewhere that heartburn can be a sign of cancer. Is that true?"

Physicians have known for years that chronic gastroesophageal reflux disease (GERD) can lead to changes in the type of cells lining the inside of the esophagus, the swallowing tube that leads from the mouth to the stomach. Those changes in the lining (or "epithelium") of the esophagus can result in something called Barrett's epithelium. Such changes are significant because Barrett's epithelium can indeed lead to cancer of the esophagus in some people who have it.

SO WHAT IS BARRETT'S EPITHELIUM?

The esophagus is normally lined by a layer of cells known as squamous cells. Squamous cells are flat, like a fried egg. In many people, gastroesophageal reflux disease ("GERD") does not cause any change in the cell type lining the esophagus. However, in certain individuals, GERD can result in a change in the type of cell that lines the esophagus. These different cells are shaped like cubes, or columns, and are therefore called columnar cells. Columnar cells can look like the kinds of cells normally lining the stomach (gastric-type epithelium) or they can look like the cells lining the small intestine (intestinal-type epithelium). This latter change-intestinal-type cells being found in the esophagus—is called Barrett's epithelium. This term comes from the name of the English physician who first described the phenomenon in the 1950's.

Barrett's epithelium usually begins in the lower esophagus, near the junction of the normal squamous lining of the esophagus and the normal columnar lining of the stomach. This area is called the squamocolumnar junction, and is typically a zigzag line which can be seen with the naked eye. The line of demarcation between the two types of cells is called the "Z-line." Barrett's cells that show precancerous changes on biopsy are termed "dysplastic cells;" the term for having dysplastic cells is "dysplasia."

The diagnosis of Barrett's epithelium is always made on the basis of biopsy findings showing intestinal-type cells, as seen under the microscope. Barrett's can be termed "short-segment Barrett's" (with a length of less than three centimeters) or "long segment Barrett's" (with a length of more than three centimeters). The longer the segment of Barrett's epithelium, the higher the risk that the Barrett's might contain cells that might be precancerous, or dysplastic.

Mark E. Murphy, M.D. F.A.C.P., A.G.A.F.

WHO GETS BARRETT'S EPITHELIUM?

Although anyone with GERD can get Barrett's epithelium, the typical person at risk for Barrett's is a white, middle-aged male. Males with Barrett's outnumber females with Barrett's by a 4:1 ratio. Additionally, persons of Asian and African-American or Native American ancestry develop Barrett's at a much lower rate than Caucasians. The reasons for this discrepancy are unclear, although much of it is likely genetic. Persons with frequent GERD symptoms (several times per week) should be considered to be at risk for the development of Barrett's epithelium, particularly if they are in a high-risk (i.e. white male) demographic group. Advancing age and obesity are also risk factors for developing Barrett's. Both obesity and age greater than 40 independently increased the risk of the development of Barrett's by factors of greater than a factor of two.

It is interesting to note that approximately 40 percent of patients who develop cancer of the esophagus as a result of Barrett's deny ever having typical heartburn or reflux symptoms. Again, the cause for this is unclear.

IF A PERSON HAS BARRETT'S EPITHELIUM, WHAT IS THE RISK THAT THEY WILL DEVELOP CANCER OF THE ESOPHAGUS?

Barrett's epithelium can result in dysplasia, which in turn can progress into invasive cancer, or adenocarcinoma, of the esophagus. Patients with Barrett's epithelium have a 30-40 times greater likelihood of developing adenocarcinoma of the esopha-

gus than those without Barrett's esophagus. Moreover, adenocarcinoma of the esophagus is 8 times more likely to occur in men than in women—a reflection of the greater incidence of Barrett's epithelium in males. Estimates of the frequency of adenocarcinoma in Barrett's epithelium vary, but most sources suggest that the lifetime incidence is between 0.5 and five percent. This may, in fact, be an overestimation. It has been shown on some autopsy studies that as many as 1 in 60 persons in the general population may have Barrett's epithelium, which is much higher than would be estimated by the current medical literature. This means that between 95 and 99.5 percent of persons who have Barrett's epithelium will never develop esophageal cancer.

It should be noted that there is a difference between invasive cancer of the esophagus (adenocarcinoma) and carcinoma-in-situ, or non-invasive cancer. Carcinoma-in-situ is also known as "high grade dysplasia." One of the goals of scope-based surveillance of patients with Barrett's epithelium is the detection of esophageal cancer at these early, non-invasive stages, when it is more easily curable.

Finally, it should be understood that adenocarcinoma of the esophagus is not the only type of esophageal cancer. Another type of esophageal cancer is called squamous cell carcinoma of the esophagus. This type of esophageal cancer is not related to reflux, but is instead associated with tobacco and alcohol use. Currently, adenocarcinoma of the esophagus accounts for about 60 percent of the esophageal cancers seen in North America and Western Europe, and its incidence is rising.

SO IF I AM FOUND TO HAVE BARRETT'S EPITHELIUM, WHAT SHOULD I DO?

The current recommendations are for people with biopsy-proven Barrett's to have surveillance endoscopy (scope testing) done on a regular basis, with biopsies performed in the esophagus to look for evidence of dysplasia. The American College of Gastroenterology (ACG) recommends that patients with biopsy-proven Barrett's epithelium undergo periodic surveillance every three years, although it is also emphasized that surveillance regimens should be individualized for each patient. Endoscopy is performed via esophageogastroduodenoscopy (EGD), where a flexible tube is passed through the mouth and into the esophagus while the patient is under sedation. The test is low-risk, and lasts only five to seven minutes. A standard biopsy protocol is used to insure that errors in sampling of the esophagus are minimized.

WHAT IF I HAVE BARRETT'S AND AM FOUND TO HAVE PRECANCEROUS CHANGES IN THE ESOPHAGUS?

Invasive cancer of the esophagus is treated surgically, with resection of the tumor, in a procedure known as esophagectomy. This is a very complicated surgery that can be dangerous for the patient in the hands of an inexperienced surgeon, although it is a safe, effective and potentially life-saving intervention in the hands of a surgeon who has experience in performing it. Detection of high-grade dysplasia, or early non-invasive cancer, in the setting of Barrett's epithelium affords patients the opportunity to have a less invasive intervention performed. Techniques such as endoscopic mucosal resection,

where part of the lining of the esophagus is removed with an endoscope (without surgery) can be used. Other non-surgical techniques which have been successful in this setting include radiofrequency ablation techniques (i.e. BarrRx), photodynamic therapy (PDT) and thermal ablation techniques. These modalities allow patients to avoid the more arduous surgical resection required for invasive malignancies of the esophagus. It is the early detection aspect of Barrett's surveillance that makes it a useful tool in the treatment of esophageal cancer.

Some have advocated that high-grade dysplasia should be treated surgically in all cases. Certainly, endoscopic therapies can miss islands of invasive cancer (so-called "sampling error"), and there have been cases of PDT-treated high-grade dysplasia resulting in cases of "buried malignant cells," in which cancer cells were found to be present under normal-appearing esophageal lining. Others argue that not all cases of high-grade dysplasia result in invasive cancer, and in fact a significant proportion of high-grade dysplasia patients (39 percent in one study) had spontaneous regression of the dysplasia on medical therapy alone. Nevertheless, when coupled with the inherent risks of surgical esophagectomy, a compelling argument can be made for using less-invasive techniques for the treatment of high-grade dysplasia in the setting of Barrett's epithelium.

SUMMARY OF HEARTBURN AND CANCER RISK

- Chronic heartburn can place patients at risk for the development of Barrett's epithelium, a potentially precancerous change in the lining of the esophagus
- Middle-aged Caucasian males are at the highest risk for the development of Barrett's epithelium
- Patients with chronic reflux should undergo endoscopic surveillance to determine if they have Barrett's epithelium, which is a biopsy diagnosis
- Patients with biopsy-proven Barrett's should undergo regular surveillance of the Barrett's mucosa to insure that no precancerous change (dysplasia) occurs
- Patients with high-grade esophageal dysplasia (early, non-invasive cancer) in the setting of Barrett's epithelium have both surgical and non-surgical options available for treatment.

For more information on heartburn and cancer or other gastroenterological issues, Dr. Murphy can be reached at the Center for Digestive and Liver Health at 1139 Lexington Avenue or call him at (912) 303-4200