Barrett's Esophagus

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International Foundation for Gastrointestinal Disorders (www.iffgd.org)

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Norman Barrett was a pathologist. In 1950, he described an abnormality in the lining of the lower esophagus that bears his name (i.e., Barrett's esophagus). Barrett believed that this abnormality was due to a congenitally short esophagus. [A congenital abnormality is something people are born with.] We now believe that it is due to severe, longstanding, gastroesophageal reflux disease (GERD). Significantly, most people with GERD have no such abnormality. Nevertheless, the presence of Barrett's esophagus is an important observation since those who have it are at greater than normal risk of developing cancer of the esophagus.

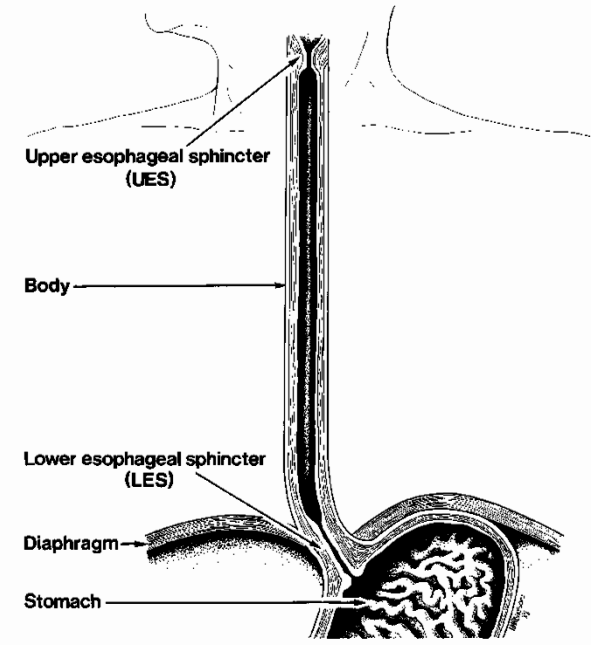

Figure 1

The figure illustrates a normal esophagus, the organ that connects the mouth to the stomach. The lining (epithelium) of the esophagus down to the lower esophageal sphincter is normally squamous. However, in Barrett's esophagus, columnar epithelium extends to varying degree up into the esophageal body.

Anatomy

Figure 1 illustrates the anatomy of the esophagus. Normally, the esophageal lining (the *epithelium*) consists of flat, layered cells similar to those in the skin. This *squamous epithelium* stops abruptly at the junction of the esophagus with the stomach near the lower end of the lower esophageal sphincter. The epithelium of the rest of the gut, down to the anus, consists of a single layer of side-by-side rectangular cells, which is called *columnar epithelium*. Barrett observed that in some people, the transition from squamous to columnar epithelium occurs higher within the esophagus than normal. There may also be islands of columnar epithelium above the normal junction of the stomach and esophagus. Figure 2 illustrates the difference between squamous and columnar epithelium.

Barrett's columnar epithelial cells may resemble those of the colon, small bowel, or stomach. One esophagus may contain several types. The process of cell change from flat, layered squamous to tall columnar epithelium is an example of *metaplasia*. Columnar cells are more resistant to acid and pepsin and the metaplasia may be a defense against refluxed acid. In Barrett's, the cells are usually of a type referred to as *specialized columnar epithelium* (a distinctive type of intestinal metaplasia). They include mucus cells, and have a tendency to resemble cells found in the small intestine.

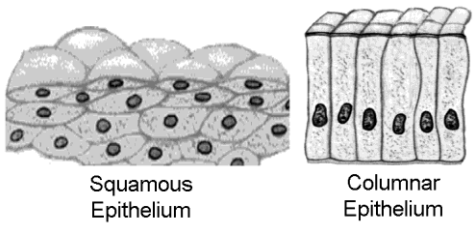

Figure 2

Squamous epithelium, seen in the esophagus and skin, consists of layers of flat cells. Columnar epithelium, characteristic of the rest of the gut, consists of a single layer of tall, rectangular cells. In Barrett's esophagus, the normally squamous epithelium of the lower esophagus becomes replaced with various types of columnar cells, that may predispose to a type of cancer known as adenocarcinoma.

Diagnosis

Barrett's esophagus can only be seen through an endoscope or in surgical tissue specimens (biopsies). Normally, the point where the red tissue that lines the stomach (gastric

mucosa) ends and the paler pink squamous esophageal mucosa begins sharply demarcates the junction between the stomach and the esophagus. In Barrett's esophagus, the separation is above its normal position. It may reach upwards in tongue-like projections of gastric tissue into the esophagus, as islands of gastric mucosa amongst the (esophageal) squamous, or as a sharp demarcation. This abnormal columnar tissue may extend to any level within the esophagus, even as high as the upper esophageal sphincter. The doctor, through endoscopy, can normally recognize the abnormal (metaplastic) tissue, but an overlying inflammation due to reflux may obscure it. Peptic ulcers [sores or erosions] sometimes occur in Barrett's epithelium and can be large.

Esophageal cancer

The importance of Barrett's esophagus is its significantly increased risk of esophageal cancer, though the incidence of this cancer remains low. The exact figure is difficult to obtain because an unbiased estimate of the prevalence of Barrett's esophagus is unavailable. (It can only be diagnosed on an endoscopy and biopsy.) However, the risk is real and is further increased by factors such as tobacco and alcohol use. Also, the risk is greatest if the metaplastic epithelium is of the specialized columnar type and if the area of metaplasia is large.

Changes can be detected in the Barrett's tissue of those more likely to develop cancer. Called *dysplasia*, these changes are an indication for repeated endoscopy and biopsy. [Dysplasia is an abnormal condition in which cells may have altered shape or may divide in a manner that alters the appearance of the tissue or organ. The degree of change ranges from minor to significant changes (low-grade), to serious or very abnormal changes (high-grade) dysplasia.] Low-grade dysplasia can result from inflammation and subside with treatment of the esophagitis. Failure of dysplasia to regress with treatment should prompt close surveillance.

The most common esophageal cancer is a *squamous cell carcinoma* that develops (often also with the help of tobacco and alcohol) in the normal squamous cell lining of the esophagus. This cancer may be treated by radiotherapy or surgery. The cancer developing in the columnar cells of Barrett's epithelium is called an *adenocarcinoma*, and resembles stomach cancer. The incidence of this cancer is increasing in North America especially in white males, and adenocarcinomas do not respond well to radiation treatment.

Endoscopy

Upper endoscopy is a procedure used to identify complications of GERD such as inflammation or tissue damage (esophagitis), stricture, or Barrett's esophagus. An endoscope is a tube-like device with a light on the end through which the examiner can see. The thin fiberoptic tube is used to examine the esophagus, stomach, and upper small intestine. The individual is usually sedated so that the procedure can be performed comfortably. A painless biopsy (tissue sample) may be taken of the lower end of the esophagus to determine if Barrett's esophagus is present.

Treatment of Barrett's esophagus

The management of newly discovered Barrett's esophagus has two objectives: the treatment of the tissue damage in the esophagus (esophagitis) and the early detection or prevention of cancer. Esophagitis is commonly treated with medications to control acid production or secretion (H2 blockers, or proton pump inhibitors). Proton pump inhibitors (PPIs) are recognized as the most powerful and effective drugs used to inhibit acid secretion and allow healing of tissue damage in the esophagus.

Guidelines from the American College of Gastroenterology recommend periodic check-ups (surveillance) or actions as follows:

In the presence of Barrett's esophagus with . . .	**Recommendation:**
No dysplasia	Endoscopic examination every 2–3 years
Low-Grade Dysplasia	Endoscopic examination every 6 months for one year, and if negative results, once per year thereafter
High-Grade Dysplasia	Expert confirmation (second opinion). Depending on individual factors doctor may recommend selective resection (surgical removal of the esophagus) or ablation therapy (endoscopic therapies that remove or destroy the Barrett's tissue). Or endoscopic examination every 3 months

Early detection or prevention of cancer is discussed below.

How can we prevent cancer from occurring in Barrett's esophagus?

Early detection and prevention of cancer are difficult. Since Barrett's esophagus is believed to result from chronic GERD, vigorous treatment of that condition has been tried. However, while proton pump inhibitors improve the esophagitis and heartburn, they fail to reverse the Barrett's

metaplasia. There are reports that anti-reflux surgery has resulted in reversion of the Barrett's epithelium to normal, but this needs confirmation. Even if normality were restored, it would remain uncertain that the cancer risk was abolished.

Risk Factors and Protective Factors
Anything that increases a person's chance of developing a disease is called a risk factor; anything that decreases a person's chance of developing a disease is called a protective factor. Some risk factors can be avoided (e.g., diet or lifestyle), but some cannot (e.g., genetics). Avoiding risk factors and increasing protective factors that can be controlled may decrease chances of developing a disease.

Studies have suggested that risk of esophageal cancer is amplified by factors that either increase reflux (e.g., tobacco, alcohol, high dietary fat, chocolate, caffeine, obesity, certain medications); or are genotoxic, which means capable of damaging DNA (e.g., a diet low in vegetables and fruits, tobacco use, dietary nitrosamines found in cured meat). Measures that may be protective include lifestyle modifications emphasizing controlling reflux, tobacco cessation, improvements in diet (e.g., less fat, more fruits and vegetables), and weight loss if you are overweight.

There have been endoscopic attempts [ablation therapy] to treat the abnormal area with lasers or photodynamic techniques (Photodynamic therapy (PDT) is a two-part treatment using a photosensitizing drug and red, nonthermal laser light). Disappointingly, recurrences are common, and more sinisterly, hidden Barrett's tissue may survive beneath normal-appearing squamous epithelial cells with continued, but hidden malignant potential.

Surgical removal of the abnormal tissue would remove the cancer risk. However, *most people with Barrett's esophagus never develop esophageal cancer*, and such major surgery cannot be justified unless cancer is proven to be imminent. The challenge is the timely discovery of those with Barrett's esophagus that are at risk.

Cancer detection programs employ periodic endoscopic examination of the esophagus and the procurement of tiny tissue samples (biopsies) for the pathologist to examine. For this discussion, Barrett's esophagus is defined as a junction of squamous and columnar epithelium that is three or more centimeters above the normal anatomical junction of the esophagus with the stomach, or the presence of specialized columnar epithelium at any level of the esophagus. In newly detected cases the abnormal segment is systematically biopsied (in four quadrants at 2-cm intervals within the metaplastic esophagus). If there is doubt about the pathologist's interpretation of the biopsies, they should be promptly repeated.

Severe dysplasia seen at multiple sites in a young person may prompt the physician to suggest surgical removal of the lower esophagus (*esophagectomy*). For those individuals for whom surgery is considered too risky, close observation at six-month intervals may be a safer alternative. If low-grade dysplasia persists after adequate treatment of the esophagitis, the patient should be followed yearly with endoscopy and biopsy. Otherwise, all affected persons should be endoscoped and have the affected area biopsied at 18 to 24 month intervals.

Not all the experts subscribe to such an aggressive and expensive program, nor has it yet been shown to save lives or improve quality of life. However, few question the ominous implications of severe or "high-grade" dysplasia. Patients with Barrett's esophagus would not be content to have the condition ignored, so a surveillance protocol is indicated for those who have the condition.

The need for research
In February 2001 representatives from two U.S. National Institutes of Health that sponsor research, the National Cancer Institute (NCI) and the National Institute of Diabetes and Digestive and Kidney Disease (NIDDK), participated in a series of meetings with sixteen experts on GERD, Barrett's esophagus, and esophageal adenocarcinoma with the goal of developing recommendations for a national research agenda.

The working group concluded that data supports the continued development of a national research agenda to establish the factors involved in the development of GERD, Barrett's esophagus, and esophageal adenocarcinoma, and to develop strategies to address the current and increasing public health impact. Research needs to address topics such as identifying who are at risk, causes, risk factors, early detection, prevention, and treatment.

Summary

Barrett's esophagus consists of a change in the normally squamous lining of the lower esophagus to columnar epithelium (metaplasia). Unless there is severe esophagitis, this change can be recognized during an endoscopy. Because there is an increased risk of adenocarcinoma of the esophagus in people with Barrett's esophagus, most physicians recommend regular endoscopy and biopsy of the altered tissue to detect pre-cancerous changes (dysplasia). If these changes persist and are severe (high-grade dysplasia), aggressive treatment is necessary to prevent development of adenocarcinoma.

Suggested Reading

Heartburn: Nothing to do with the Heart, IFFGD Brochure No. 504.

Medical Treatment of GERD: The Proton Pump Inhibitors, IFFGD Brochure No. 505.

GERD, Hiatal Hernia, and Surgery*, IFFGD Fact Sheet No. 523.*
Thompson WG. *The Ulcer Story*. Plenum, New York. 1996. P214-218.

Kahrilas PJ, Hogan WJ. *Gastroesophageal reflux disease*. In: Sleisenger MH, Fordtran JS, editors. Gastrointestinal Disease: Pathophysiology/Diagnosis/Treatment. Philadelphia: WB Saunders, 1993: 378-401.
Barrett's Esophagus. NIH Publication No. 02-4546, June 2002.
Report of the Barrett's Esophagus Working Group, Sponsored by the National Cancer Institute and the National Institute of Diabetes and Digestive and Kidney Diseases, June 2001.

Answers to your Questions about Digestive Health
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If you have a question about your digestive health, please contact us at IFFGD, PO Box 170864, Milwaukee, WI 53217. This information is provided for general information and is not intended to replace your doctor's advice.

Question *– Two years ago I was diagnosed with* ***Barrett's Esophagus****. I had another endoscopy last year and they said it was Reflux Esophagitis. I was wondering: Does Barrett's disappear?"*

Barrett's esophagus is a change in the lining of the lower esophagus that can develop as a result of acid reflux. Patients with Barrett's esophagus have a small increased risk for developing esophageal cancer in that tissue. During an endoscopy, the physician sees a change in the color of the tissue at the lower end of the esophagus. If the biopsies of that tissue show intestinal cells, then the diagnosis of Barrett's esophagus is made. It would be nice if there were a clear demarcation of the normal and abnormal tissue. However, that is not always the case. Barrett's tissue tends to develop sporadically in some patients. It is not at all uncommon for the doctor to take a biopsy of tissue that looks abnormal, but turns out to be normal. But if the biopsy had been taken just a few millimeters away, it would be consistent with Barrett's esophagus. This may occur up to 20% of the time in people with small segments of Barrett's mucosa.

There is still some controversy, as some physicians believe that Barrett's esophagus can regress, or disappear. However, the above explanation seems much more plausible. The bottom line is that you have Barrett's esophagus. The most recent biopsies were fine. Your risk for developing esophageal cancer remains very low, but since it is higher than the general population, you should continue to have an endoscopy every three years.

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The International Foundation for Gastrointestinal Disorders (IFFGD) is a 501(c)(3) nonprofit education and research organization. We work to promote awareness, scientific advancement, and improved care for people affected by chronic digestive conditions. Our mission is to inform, assist, and support people affected by gastrointestinal disorders. Founded in 1991, we rely on donors to carry out our mission. Visit our website at: www.iffgd.org or www.aboutgerd.org.

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