REX HEALTHCARE

Laboratory Bulletin...

Updates and Information from Rex Healthcare and Rex Outreach

July 2001 *Issue Number 58*

Gut Check #1 – Barrett's Esophagus

"Distal Esophageal Bx – r/o Barrett's" We receive esophageal biopsy specimens with this request on a regular basis. If this is the only information provided to the pathologist, the ability to comply is limited. The diagnosis of Barrett's esophagus requires knowledge of the precise anatomic location of the biopsy, in addition to the histologic features of the biopsy itself. "Barrett's esophagus" refers to the presence of benign glandular type epithelium lining the tubular esophagus (the esophagus proximal to the gastric folds) generally beginning in (if not restricted to) the distal portion. [1,2] This disorder may arise in patients with symptoms of reflux esophagitis, but many patients are asymptomatic. By definition, the glandular epithelium represents a glandular metaplasia – in that either gastric type or intestinal type columnar cells replace the normal squamous epithelium. The gastric type metaplasia generally resembles normal gastric cardia, although gastric fundic type mucosa may also be observed. The intestinal type metaplasia is usually "incomplete", in that it consists of goblet type cells without Paneth or intestinal absorptive cells. This latter type of metaplasia is referred to by a variety of different names - "incomplete intestinal metaplasia ", "specialized mucosa", "specialized epithelium", "Barrett's mucosa" or "intestinal metaplasia" - depending on the pathologist (Some pathologists define "Barrett's esophagus" **only** when this type of epithelium is present, as this is the only histology which confers a need for special management – vide infra). [3] The diagnosis is complicated by the fact that the squamocolumnar junction ("Z-line") is frequently 2 – 3 cm. proximal to the gastroesophageal junction (GEJ). In this "short" segment between the Z-line and GEJ, the finding of gastric-type mucosa is normal. "Short segment" Barrett's esophagus refers to the presence of "incomplete" intestinal-type metaplastic (IM) epithelium in this interval between the Z-line and GEJ (or the area 2 –3 cm. proximal to the GEJ). [4] Furthermore**, it is important to recognize that the IM histology may also occur in the gastric cardia and thus is not specific for Barrett's esophagus.** [5] The endoscopic appearance of Barrett's may vary from an irregular Z-line to tongues of abnormal pink mucosa directed proximally for distances of 2 cm. or more. In some cases, islands of abnormal pink mucosa may be surrounded by the normal white (squamous) mucosa.[1] The landmarks may be obscured by coexistent disease (esophagitis, hiatal hernia), making it difficult for the endoscopist to be certain of the location of the GEJ and/or Z-line.

For the pathologist confronted with a "distal esophageal biopsy" who sees fragments of gastric type mucosa with areas of "incomplete intestinal metaplasia" (+/- squamous mucosa), the histologic differential diagnosis includes long segment Barrett's, short segment Barrett's, or normal gastroesophageal (GE) junction (with sampling of gastric cardia involved by IM). If a similarly labeled biopsy contains only gastric type mucosa (+/- squamous mucosa), the histologic differential diagnosis includes long segment Barrett's or normal GE junction. [*] Absent knowledge of the specific source of the biopsies with regard to the GEJ, the pathologist will report "Fragments of gastric and squamous type mucosa (with/without focal incomplete intestinal metaplasia)" and direct the reader to a comment which stresses that the anatomic location of the biopsies is necessary for an accurate diagnosis. [3,4] ("Location!

Location!! Location!!!)

The diagnosis of "Barrett's esophagus" is important because of an associated risk of esophageal adenocarcinoma developing in these patients. The likelihood of cancer development in Barrett's is debatable, ranging from 30-350 times that of the general population. [2,3] A recent paper suggested that the risk of adenocarcinoma was overstated due to publication bias and suggested a true risk of 0.5% per patient year. [6] The recognition of precancerous "glandular dysplasia" in a subset of these patients has proved helpful in management of this disorder. In particular, the IM histology is believed to be a marker for those at greatest risk for development of dysplasia, and periodic surveillance endoscopy has been recommended for patients with this histology. [3] The traditional practice of placing patients with the finding of incomplete intestinal metaplasia at the GEJ in this category has been challenged by a recent provocative autopsy study (an oxymoron to some of you, no doubt). The authors found an 11% incidence of IM at the GEJ in 223 nonselected (predominantly white, male) adult autopsies. [5] After careful histologic mapping, only 2% had associated had IM affecting the tubular esophagus. The remaining 92% had associated IM confined to the gastric cardia. The authors reported a strong association of gastric cardia IM with distal gastric IM and distal chronic gastritis ($p < 0.01$) and postulated a link with *H. pylori* infection. [5] (Unfortunately the presence or absence of *H. pylori* type organisms in the distal stomach was apparently not studied further.) This study suggests that most cases of IM occurring at the **GEJ** are of **gastric** origin, and lumping these patients in a "Barrett's esophagus" category with the need for follow-up endoscopy may not be warranted. This study underscores the importance of careful communication between the endoscopist and pathologist in this setting. Each has to know the limitations of the other, and each is dependent upon the other to assure accurate diagnosis. Knowledge of the endoscopic findings and precise site of biopsy is desirable and may be relayed by diagram, written note, and/or photograph. It is particularly helpful to know the distance relationship between the biopsy site(s) and the GEJ. A cartoon drawing of the GI tract is present on the Rex endoscopy requisitions and may be used for this purpose. We would be happy to provide these for our Outreach clients upon request.

John D. Benson, MD

[*] If the specimen had been labeled simply "esophageal bx.", the histologic differential would also include gastric heterotopia ("inlet patch") which is a congenital abnormality arising in the proximal esophagus of little clinical significance other than creating confusion for unwary endoscopists and/or pathologists!!! [7] The author is indebted to Dr. Ron Schwarz for providing reference #7 as a clue to one pathologist in need, some 14 years ago

1. Emory TS et al. *Atlas of Gastrointestinal Endoscopy and Endoscopic Biopsies*. AFIP, Washington, DC, 2000, pp. 13,42.
2. Moskauk C. Biopsy diagnosis of Barrett's esophagus. *Practical Reviews in Pathology* v. 21(12) April 1997.
3. Petras RE. Barrett's esophagus. *Practical Reviews in Pathology* v. 21(8) December 1995.
4. Emory TS. Personal communication (6/26/2001).
5. Ormsby AH et al. The location and frequency of intestinal metaplasia the esophagogastric junction in 223 consecutive autopsies: implications for patient treatment and preventive strategies in Barrett's esophagus. *Mod Pathol* 13: 614-20, 2000.

6. Shaheen NJ et al. Is there publication bias in the reporting of cancer risk in Barrett's esophagus? *Gastroenterology* 119:333-38, 2000.
7. Jabbari M et al. The inlet patch: heterotopic gastric mucosa in the upper esophagus. *Gastroenterology* 89:352-6, 1985.

.

NCEP Adult Treatment Panel III Issues New Guidelines

Introduction: The National Cholesterol Education Program (NCEP) has recently updated the clinical guidelines for cholesterol testing and management. The Adult Treatment Panel III of NCEP issued a special communication in the May 16th issue of JAMA of this year. The major new feature is a focus on primary prevention in persons with multiple risk factors and its impact on LDL cholesterol goals and the cutpoints for initiating treatment. Risk of developing coronary heart disease (CHD) is stratified into three categories. The goals for lowering LDL cholesterol are clearly defined for each category.

Major Risk Factors for CHD[3]

+ 1	Age (men ≥ 45 years, women ≥ 55 years
+ 1	Cigarette smoking
+ 1	Diabetes
+ 1	Family history of premature CHD (male first degree relative <55 years, female first degree relative < 65 years)
+ 1	Hypertension (BP ≥ 140/90 or on antihypertensives
+ 1	Low HDL cholesterol (< 40 mg/dL)
- 1	High HDL cholesterol (≥ 60 mg/dL)

It is advisable to remember that any person with elevated LDL cholesterol or other form of hyperlipidemia should undergo clinical or laboratory assessment to rule out secondary dyslipidemia before initiation of lipid-lowering therapy. Other causes include: diabetes, hypothroidism, obstructive liver disease, chronic renal failure or drugs such as diurectics, progestins, anabolic steroids, and corticosteroids).

New Guidelines at a Glance:

- LDL cholesterol of <100 mg/dl now considered optimal
- HDL cholesterol cutpoint raised from 35 mg/dl to 40 mg/dl because the high number is a better measure of depressed HDL
- Triglyceride classification cutpoint lowered to 150 mg/dl
- Complete fasting lipoprotein screen using total cholesterol, LDL cholesterol, HDL cholesterol and triglyceride recommended for screening
- Diabetes is now considered an equivalent risk for heart attack as coronary artery disease
- New classification of risk created called metabolic syndrome in which individuals are identified as candidates for intensive therapeutic lifestyle changes.
- Framingham Heart Study projections of ten-year absolute coronary heart disease risk now used to identify certain patients with multiple risk factors for which more intensive treatment is recommended
- Recommends treatment for those with triglycerides greater than or equal to 200 mg/dl
- Includes strategies for accomplishing therapeutic lifestyle changes and drug changes.
- Encourages use of plant stanols/sterols and viscous soluble fiber as a

therapeutic dietary option

New Optimal Levels for Lipids – effective August 13, 2001

Lab Value	OLD		NEW
	mg/dl		mg/dl
LDL cholesterol	<130		<100
HDL cholesterol	<35		<40
Triglycerides	<250		<150
Total cholesterol	<200	(no change)	<200

Summary: The third report from the Adult Treatment Panel lowers the optimal level of LDL concentration and encourages more aggressive treatment in all risk groups. Refer to the May 16th JAMA article for a complete discussion. The panel did not make recommendations for elevated levels of Lipoprotein (a), homocysteine or small dense LDL particles. It is likely that these lab values will also be included in subsequent recommendations from the NCEP.

Stephen V. Chiavetta, MD

References:

1. Chiavetta, Stephen, Clinical Value of Lipoprotein Subclassification, Rex Healthcare Laboratory Bulletin, Issue #44, January 2000.
2. Auxter, Sue, "How the New NCEP Cholesterol Guidelines Will Affect Labs", Clinical Laboratory News, vol 27, number 7 July 2001, p 1 – 10.
3. Executive summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III), JAMA vol 285 number 19 May 16, 2001, p. 2486 – 2497.
4. Chiavetta, Stephen, Update on Coronary Artery Disease and Lipids, Rex Healthcare Laboratory Bulletin, Issue #56 May 2001.

For further information, call the Laboratory (784-3040). Telephone extensions are: Pathologists' Direct Line (3201), Sharon Logue (Lab Director 2400), Robin Ivosic (Core Lab Manager 3053), Elaine Patterson (Core Lab Manager 3054), Jackie Okoth (Core Lab PM Manager 4248), Diane Young (Anatomic Pathology Manager 3888), Nga Moore (Customer Service Manager 3396), Kori Horsley (Customer Service PM Manager 4340).