

## Commentary

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# The columnar lined oesophagus: a riddle wrapped in a mystery inside an enigma

Just a few years ago, the definition and pathogenesis of Barrett's oesophagus seemed straightforward. Barrett's oesophagus was the condition in which metaplastic columnar epithelium replaced oesophageal squamous mucosa that had been damaged by exposure to refluxed gastric juice. The condition was sought primarily in patients with gastro-oesophageal reflux disease (GORD), and was identified when endoscopic examination revealed long segments of columnar epithelium extending well up the oesophagus. Biopsy specimens taken from the oesophageal columnar lining usually showed a peculiar form of intestinal metaplasia called specialised columnar epithelium or specialised intestinal metaplasia. In patients who developed adenocarcinomas in Barrett's oesophagus, the columnar epithelium surrounding the oesophageal tumour invariably contained specialised intestinal metaplasia that often exhibited dysplastic changes. Eventually, Barrett's oesophagus with specialised intestinal metaplasia became recognised as the major risk factor for adenocarcinoma of the oesophagus and oesophagogastric junction.<sup>1</sup>

Over the past two decades, the incidence of adenocarcinoma of the oesophagus and oesophagogastric junction has been rising dramatically in the United States and Western Europe.<sup>2,3</sup> Patients who have oesophagectomy for adenocarcinoma at the oesophagogastric junction often do not have endoscopically apparent Barrett's oesophagus, but rather have short, inconspicuous segments of specialised intestinal metaplasia found on histological examination of the resected specimens.<sup>4</sup> In 1994, investigators who were aware of this phenomenon reported the results of a study designed to estimate the frequency of metaplastic changes in the distal oesophagus.<sup>5</sup> In this study, consecutive patients scheduled for elective endoscopic examinations in a general endoscopy unit had biopsy specimens obtained at the squamocolumnar junction in the distal oesophagus (the Z-line) irrespective of its appearance and location. Among 142 patients who did not have endoscopically apparent Barrett's oesophagus (that is, <3 cm of the distal oesophagus lined with columnar epithelium), the investiga-

tors were surprised to find that 26 (18%) had specialised intestinal metaplasia in biopsy specimens from the Z-line.

Four similar studies, including one by Trudgill *et al* in this issue (see page 585), have been published since 1994 in peer-reviewed journals.<sup>6-8</sup> The results of the five studies, all of which included consecutive, unselected patients seen in general endoscopy units, are summarised in table 1. The studies show clearly that short, inconspicuous segments of specialised intestinal metaplasia can be found frequently at the squamocolumnar junction in predominantly white patient populations. This may be the only clear point that emerges from these studies however. If specialised intestinal metaplasia indeed develops as a sequela of GORD, then one might expect an association with the symptoms and signs of reflux oesophagitis. However, only one study found a significant association with GORD symptoms whereas three did not, no study found any association with endoscopic oesophagitis, and only two of the four studies that sought an association with histological oesophagitis, found it. These observations challenge the traditional notion that oesophageal columnar metaplasia develops as a consequence of GORD, although further studies that include protracted oesophageal pH monitoring will be needed before this issue can be resolved. The potential contributions of *Helicobacter pylori* infection, inflammation in gastric cardiac epithelium, advancing age, race, and sex to the development of specialised intestinal metaplasia also are unclear. One study has suggested that the pathogenesis and epidemiology of specialised intestinal metaplasia at the squamocolumnar junction may vary substantially with the location of the Z-line.<sup>8</sup> In this study, only white patients with GORD symptoms had specialised intestinal metaplasia found at the squamocolumnar junction when the Z-line was located within the distal oesophagus, whereas specialised intestinal metaplasia was found with similar frequency in both black and white patients irrespective of GORD symptoms when the Z-line was located precisely at the anatomical junction of oesophagus and stomach. For future studies, investigators will need to document meticulously the

TABLE 1 Results of studies on the prevalence of specialised intestinal metaplasia (SIM) among unselected patients in general endoscopy units

Study first author	Spechler	Johnston	Nandurkar	Chalasanani	Trudgill
Year of publication	1994	1996	1997	1997	1997
Country	USA	USA	Australia	USA	UK
Number of patients	142	170	158	87	120
Prevalence of SIM at squamocolumnar junction	18%	9%	36%	18%	18%
Association of SIM with GORD symptoms	No	Yes	No	-	No
Association of SIM with endoscopic oesophagitis	No	No	No	-	No
Association of SIM with histological oesophagitis in squamous epithelium	Yes	No	Yes	-	No
Association of SIM with inflammation on columnar side of squamocolumnar junction	-	-	Yes	-	-
Association of SIM with <i>Helicobacter pylori</i> infection	-	-	No	-	No
Association of SIM with advancing age	No	No	Yes	-	Yes
Association of SIM with male sex	Yes	No	No	-	No

location of the Z-line with respect to the oesophagogastric junction. Finally, the cancer risk for patients with short segments of intestinal metaplasia in the distal oesophagus is not known. Considering the high prevalence of specialised intestinal metaplasia at the Z-line, and the infrequency of cancers at the oesophagogastric junction (despite the rising incidence rate), it would seem that the risk imposed by these short segments of specialised intestinal metaplasia is relatively small.

Today, the definition and pathogenesis of Barrett's oesophagus no longer seem straightforward. Recent studies have raised far more questions than they have answered. If, as some have suggested, one defines Barrett's oesophagus by the presence of any specialised intestinal metaplasia regardless of extent, then the aforementioned studies suggest that approximately one in every five patients seen in general endoscopy units has Barrett's oesophagus. This definition does not seem appropriate. It seems preferable to call the condition "columnar lined oesophagus with specialised intestinal metaplasia", rather than to use the artificial and emotionally charged term "Barrett's oesophagus" that implies a strong association with GORD and cancer.<sup>9</sup> Clearly, we have much to learn about the columnar lined oesophagus.

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- 1 Haggitt RC. Adenocarcinoma in Barrett's esophagus: a new epidemic? *Hum Pathol* 1992; **23**: 475-6.
- 2 Blot WJ, Devesa SS, Kneller RW, Fraumeni JF Jr. Rising incidence of adenocarcinoma of the esophagus and gastric cardia. *JAMA* 1991; **265**: 1287-9.
- 3 Tuyns AJ. Oesophageal cancer in France and Switzerland: recent time trends. *Eur J Cancer Prev* 1992; **1**: 275-8.
- 4 Cameron AJ, Lomboy CT, Pera M, Carpenter HA. Adenocarcinoma of the esophagogastric junction and Barrett's esophagus. *Gastroenterology* 1995; **109**: 1541-6.
- 5 Spechler SJ, Zeroogian JM, Antonioli DA, Wang HH, Goyal RK. Prevalence of metaplasia at the gastro-oesophageal junction. *Lancet* 1994; **344**: 1533-6.
- 6 Johnston MH, Hammond AS, Laskin W, Jones DM. The prevalence and clinical characteristics of short segments of specialized intestinal metaplasia in the distal esophagus on routine endoscopy. *Am J Gastroenterol* 1996; **91**: 1507-11.
- 7 Nandurkar S, Talley NJ, Martin CJ, Ng THK, Adams S. Short segment Barrett's oesophagus: prevalence, diagnosis and associations. *Gut* 1997; **40**: 710-5.
- 8 Chalasani N, Wo JM, Hunter JG, Waring JP. Significance of intestinal metaplasia in different areas of esophagus including esophagogastric junction. *Dig Dis Sci* 1997; **42**: 603-7.
- 9 Spechler SJ, Goyal RK. The columnar lined esophagus, intestinal metaplasia, and Norman Barrett. *Gastroenterology* 1996; **110**: 614-21.