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Histological assessment of oesophageal columnar mucosa

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This review presents the pathological features of Barrett's oesophagus, with an emphasis on the role of pathologists in the diagnosis, surveillance and treatment of the disease. The diagnosis of Barrett's oesophagus is based both on endoscopy and histology. The surveillance of patients relies on systematic biopsy sampling, looking for dysplasia – intraepithelial neoplasia. Well established classifications of dysplasia are now used by pathologists, but there remain problems with this marker. Therefore, many alternative biomarkers have been proposed, that remain of limited interest in daily practice, including DNA-ploidy, proliferation markers, and p53 abnormalities. Endoscopic improvements already allow a better selection of biopsies, and it may be that new technologies will allow 'virtual biopsies'. The role of pathologists is now extended to the evaluation of new therapeutic modalities of early neoplastic lesions in Barrett's oesophagus, especially endoscopic mucosal resection.

Key words: Barrett's oesophagus; oesophageal cancer; dysplasia; intraepithelial neoplasia; intestinal metaplasia.

Barrett's oesophagus (BO) is defined as the change from the normal stratified squamous epithelium of the lower oesophagus to a metaplastic columnar epithelium.[1] It is a consequence of prolonged gastro-oesophageal reflux disease (GORD). Also known as 'endobrachyoesophage' (in France), and columnar lined oesophagus (CLO), it is increasing in incidence. BO predisposes to the development of oesophageal adenocarcinoma, a tumour with a rapidly increasing incidence in most western countries.[2] BO is found in 1.6% of the general population[3] and in 10% of those patients who undergo endoscopy for symptoms of GORD. Follow-up studies have

Abbreviations: BO, Barrett's oesophagus; CLO, columnar lined oesophagus; CK, cytokeratin; EMR, endoscopical mucosal resection; GOJ, gastro-oesophageal junction; GORD, gastro-oesophageal reflux disease; HGD, high-grade dysplasia; IM, intestinal metaplasia; LGD, low grade dysplasia.

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demonstrated in surveillance programs of patients with BO an incidence of adenocarcinoma ranging from one in 52 to one in 441 patients-years, and a 0.5–1% annual conversion rate to malignancy.

Pathologists play a central role in the management of patients with BO. This is especially a crucial diagnostic role, complexified recently, due to changes in the definition of BO, with the emergence of so-called short and even 'ultra-short' segment BO. Pathology is also the base of surveillance, as the only recognised marker for an increased risk of cancer is dysplasia, diagnosed on histological examination of endoscopic biopsies.

The recent development of novel investigative techniques may make the current diagnostic procedures of BO and dysplasia obsolete in the near future.[4] These new technologies already include endoscopic improvements (e.g. chromoendoscopy, narrow band imaging etc.), and in the future entirely new methods that may allow 'virtual biopsies' (e.g. confocal laser microscopy, optical coherence tomography, Raman spectroscopy etc.). These methods may induce major changes in the role of pathologists in BO.

Accompanying these changes in diagnostic procedures, there have been improvements in therapeutic options, with the emergence of various procedures of non-surgical treatment of early neoplastic lesions, either ablative (mainly endoscopic mucosal resection – EMR), or destructive.[5] Again, pathologists play a central role in these new issues, especially when they have to report mucosectomy specimens.

DIAGNOSTIC CRITERIA OF BO

There is a consensus to define BO as columnar metaplasia of the distal oesophagus. Columnar mucosa in the lower oesophagus presents as a red velvety mucosa over the gastro-oesophageal junction (GOJ). It can extend either circumferentially or as one or several tongues, and in some cases as a mixture of these two patterns. It was considered initially that this mucosa had to extend at least on three centimetres over the GOJ to diagnose BO.[1] But this definition has changed, due to the recognition of short segment BO measuring less than three centimetres.[1,6,7] However, as it may be difficult to measure precisely a short segment BO and to localise the metaplastic mucosa, it is now well admitted that the diagnostic criteria of BO include both endoscopic and histological features.

Three types of columnar mucosae can be present in BO, intestinal, cardiac, and fundic (Figure 1).[8] They will be described in the next part of this article. But there is at the present time a controversy to decide whether it is necessary or not to demonstrate the presence of intestinal metaplasia (IM) to diagnose BO. Most definitions proposed by national societies (for example the American Gastroenterological Association, the American College of Gastroenterology, the German Society of Pathology, the French Society of Digestive Endoscopy) or international groups (Amsterdam working group) propose definitions that include both endoscopic recognition of a change in the oesophageal epithelium of any length, and histological evidence of IM.[9–13] However, this strict definition has been challenged by the 'new British Society of Gastroenterology guidelines for the diagnosis and management of Barrett's oesophagus',[14] which consider that 'the presence of areas of IM, although often present, is not a requirement for diagnosis'. An international consensus group recently proposed the term endoscopically suspected oesophageal metaplasia, confirmed as BO when biopsies show columnar epithelium, that can be of intestinal type or not.[15] These varied definitions