PRIMEVIEW

BARRETT OESOPHAGUS

nature REVIEWS DISEASE PRIMERS

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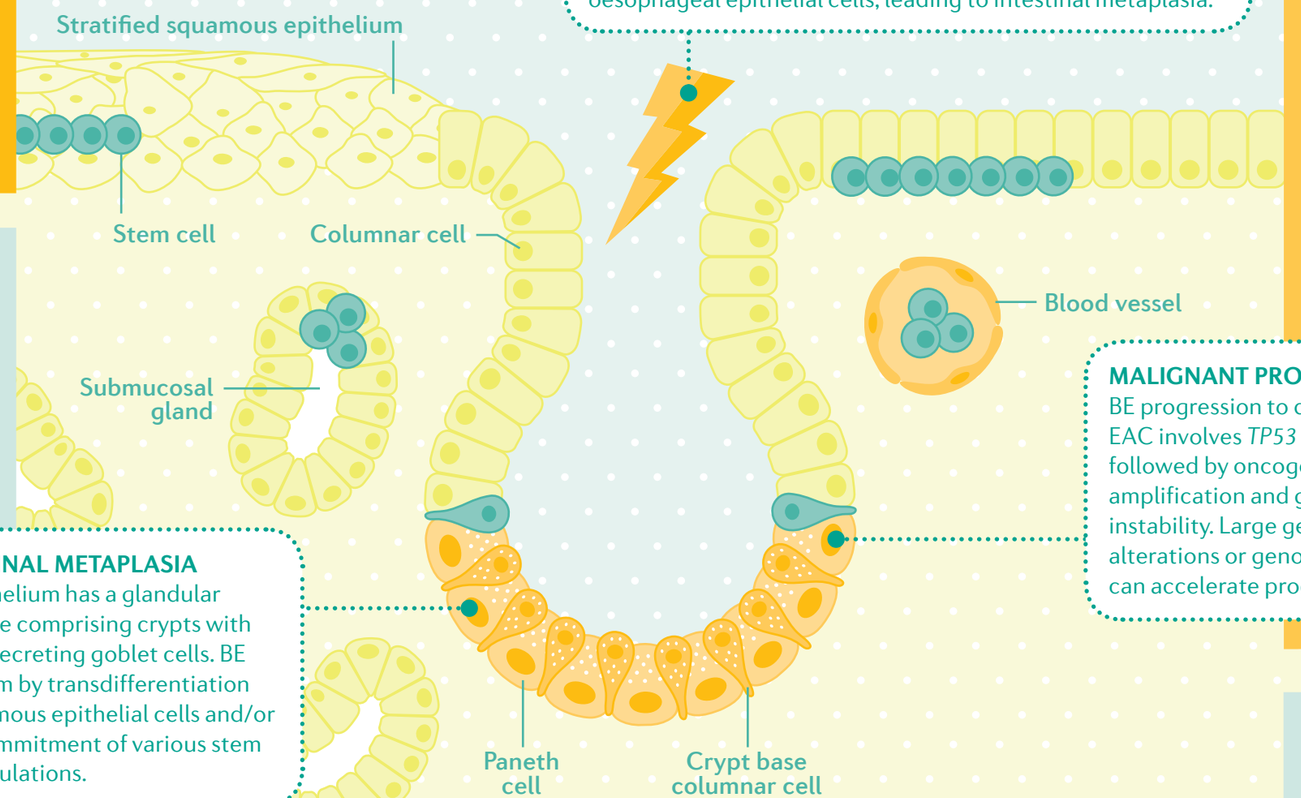
Barrett oesophagus (BE) is the only known precursor of oesophageal adenocarcinoma (EAC), which is rapidly increasing in incidence. BE involves intestinal metaplasia — the replacement of squamous epithelium by columnar epithelium — in the distal oesophagus as an adaptive response to gastro-oesophageal reflux.

DIAGNOSIS

High-definition endoscopy is the gold standard for diagnosis, which is confirmed by histological evidence of intestinal metaplasia in oesophageal biopsy samples, although the precise criteria for both methods are debated. Endoscopy is indicated in individuals >50 years of age with new-onset symptoms of reflux, or at any age if these symptoms persist despite medical therapy or if alarm symptoms (such as weight loss, persistent vomiting and bleeding in the upper gastrointestinal tract) are present. Lifestyle modifications (such as dietary changes, exercise and reducing smoking) can reduce the incidence of BE, as can pharmacological agents such as proton pump inhibitors, NSAIDs and statins, although long-term chemoprevention is not currently recommended owing to potential adverse effects. Screening by upper endoscopy is only recommended in patients with chronic, frequent gastro-oesophageal reflux symptoms and several other risk factors.

PATHOPHYSIOLOGY



OESOPHAGEAL INJURY
Exposure to gastric refluxate increases oxidative stress, activates inflammatory mediators and induces DNA damage in oesophageal epithelial cells, leading to intestinal metaplasia.

INTESTINAL METAPLASIA
BE epithelium has a glandular structure comprising crypts with mucin-secreting goblet cells. BE may form by transdifferentiation of squamous epithelial cells and/or transcommitment of various stem cell populations.

MALIGNANT PROGRESSION
BE progression to dysplasia and EAC involves *TP53* mutations, followed by oncogene amplification and genomic instability. Large genomic alterations or genome duplication can accelerate progression.

EPIDEMIOLOGY

The prevalence of BE is ~1–2% in adults in Western countries, and the rate of progression to EAC is 0.1–0.5% per patient-year. The risk of developing BE is 2–3-fold higher in white individuals than in other ethnicities and twofold higher in men than in women. Age is also an important risk factor, with BE prevalence increasing by 50–100% with every decade of life in adults. BE risk may also have a genetic component, although shared lifestyle elements and increased endoscopic screening in family members of individuals with gastro-oesophageal reflux disease (GERD) are confounding factors.

! Gastro-oesophageal reflux disease (GERD), age, sex, ethnicity, diet, obesity and smoking are important risk factors for development and progression of BE

MANAGEMENT

Histological staging of disease is crucial to guide management. Endoscopic surveillance is recommended in patients with non-dysplastic BE, whereas endoscopic treatment is indicated for low-grade dysplasia (LGD), high-grade dysplasia (HGD) and mucosal or 'low-risk' submucosal EAC. For dysplasia and early EAC, endoscopic mucosal resection is indicated, whereas the more technically demanding endoscopic submucosal dissection is only warranted for bulky lesions or suspected submucosal infiltration. After resection of neoplastic lesions, the remaining BE epithelium is removed by endoscopic ablation. Frequent recurrence of BE and dysplasia after endoscopic treatment mandates regular endoscopic surveillance.

OUTLOOK

The majority of patients with chronic GERD symptoms do not develop BE and most BE cases do not progress to EAC, so further research is needed to understand the molecular mediators of intestinal metaplasia and the inflammatory processes that contribute to BE development and malignant progression. Objective criteria for histological diagnosis of dysplasia are needed, as are better risk stratification tools for selecting populations for screening, which should aid in early diagnosis of BE and dysplasia, thereby improving outcomes. To improve surveillance in patients with BE, additional risk factors for malignant progression need to be identified, which might also forego unnecessary surveillance and intervention in patients at low risk.

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