



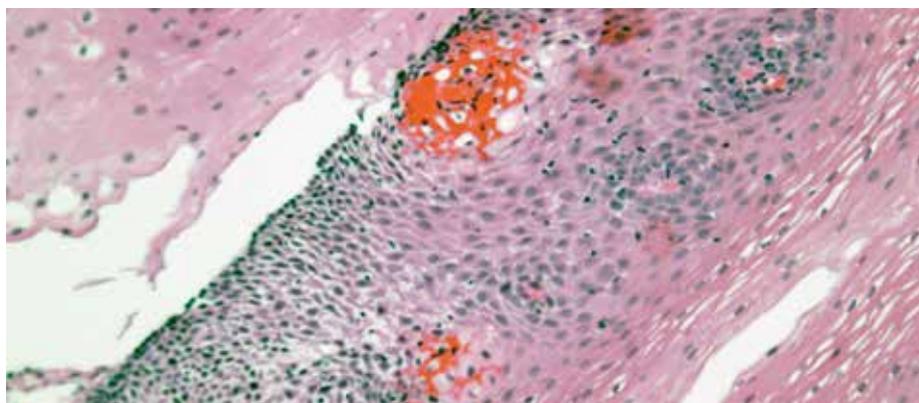
# Lymphocytic Oesophagitis

The importance of eosinophils and neutrophils infiltrating oesophageal squamous epithelium as markers for reflux, eosinophilic oesophagitis, and infection are well entrenched, although traditionally less attention has been paid to lymphocytes. Small numbers of lymphocytes are normally seen in oesophageal epithelium including CD4 helper and CD8 positive cytotoxic lymphocytes. However, isolated increases in lymphocytes in the oesophageal epithelium, outside the context of entities such as lichen planus and graft versus host disease, have been less well recognised until recently.

The criteria for a diagnosis of lymphocytic oesophagitis (LE), where lymphocytes numbers are markedly increased with few or no eosinophils, is not strictly defined since this is still a reaction pattern and not a specific diagnosis per se, and thresholds vary from study to study. The strictest definition requires at least 50 intraepithelial or peripapillary lymphocytes per HPF with few or no granulocytes.

The term lymphocytic esophagitis was originally coined in 2005 by Rubio et al to describe a histological reaction pattern in the esophagus of a series of 20 patients. The patients had a high number of peripapillary lymphocytes (mean number 55.1/HPF in selected cases) and a lack of neutrophils and eosinophils. The papillae are projections of lamina propria, containing capillaries, which project a short distance into the epithelium of the normal oesophagus. The pattern of LE showed an association with Crohn disease (CD), though not a completely specific one. Of the 20 patients, 11 were age 17 or younger and of these, 8 (40%) had Crohn disease; 20% had manifestations of reflux and the remainder a mixture of conditions including celiac, gastroduodenitis, and Hashimoto thyroiditis. A similar study of 40 patients in 2008 was unable to confirm these findings.

Looking at it from a different angle, Ebach et al studied 60 paediatric patients with known Crohn disease and control groups and found an association. LE which was found in 28% of patients with Crohn disease (mean age 13.3) but in only 2/30 patients with ulcerative colitis. A 2014 study of 580 paediatric patients confirms the association with Crohn disease, but also shows the non-specific nature of LE. This found 31 patients with LE and 49 with CD. Six of the 31 LE patients (19%) and 43 of the 514 non-LE patients (8.4%) had CD. The remaining LE patients had other diagnoses with no significant clinical correlates. Conversely, LE was identified in 12.2% of



**Oesophageal epithelium with congestion, spongiosis and increased intraepithelial lymphocytes in adult female patient with dysphagia.**

the patients with CD. Thus, there were still more LE patients without CD than with CD. The other associations included a diverse range of clinical diagnoses, some with no readily explainable association with LE (such as functional abdominal pain), and many had normal endoscopy.

In adults, the association with Crohn disease is not seen but there appears to be an association with oesophageal dysmotility. A 2011 study of over 129,000 patients from a large outpatient private GI pathology lab service revealed LE in only 119 patients, 60% female. Most patients had symptoms of oesophageal disease such as dysphagia or odynophagia, with dysphagia being the most common complaint, and around 20% complaining of reflux. Endoscopically, around a third of patients were suspected of having eosinophilic oesophagitis (including 'feline oesophagus' where the oesophagus has rings resembling that of a cat's oesophagus), around 20% were normal, 18% had features suggestive of reflux, and 10% had stricture. However, none had Crohn disease or an association with *Helicobacter gastritis*. Although this study drew no firm conclusions as to the nature of lymphocytic esophagitis

in adults, the prevalence of dysphagia as a presenting complaint, and the number of patients with findings reminiscent of eosinophilic oesophagitis were noted.

The association with dysmotility is enhanced by the finding that in adult patients, a lymphocytic oesophagitis with a complete absence of granulocytes was mostly seen in older female patients who presented with dysphagia and had an oesophageal motility disorder. CD4 and CD8 predominant LE occurs with roughly equal frequency. However, patients with CD4 predominant LE are more likely to be female (71%), and have a motility disorder (90% of those tested). This suggests a new entity of 'dysmotility lymphocytic oesophagitis'.

In summary, the reaction pattern of lymphocytic oesophagitis appears to be real, however, the term cannot be used as a wastebasket and true increased numbers of IELs must be seen. Clinical and endoscopic correlations determine the significance of a pathologist comment on increased numbers of lymphocytes in the epithelium.

*References available on request.*

## Lymphocytic Oesophagitis

**Definition:** Increased numbers of intraepithelial lymphocytes in peripapillary oesophageal epithelium. Number of lymphocytes required varies, depending on study, from impression of heavy lymphocytic infiltrate in papillae and peripapillary epithelium with spongiosis, to a strict count of at least 50 intraepithelial lymphocytes with few granulocytes.

**Incidence:** 0.1% unselected adult biopsies; higher in pediatric series.

**Associations:** Pediatric Crohn disease (19 – 40%) in some studies; with miscellaneous other associations not reaching significance. Adult: clinical dysphagia in 53%; dysmotility disorder, and endoscopic features resembling eosinophilic oesophagitis.