Quantitation of intraepithelial lymphocytes in human duodenum: what is normal?

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Background: An increase in intraepithelial lymphocytes (IELs) is mandatory for the histological diagnosis of coeliac disease (CD). Currently, duodenal biopsies are used almost exclusively to establish the diagnosis, yet published work continues to cite an upper limit of 40 lymphocytes/100 epithelial cells, a figure derived from jejunal biopsies over 30 years ago.

Aim: To establish the normal range for IEL counts in distal duodenal biopsies.

Materials/Methods: Twenty subjects (seven men, 13 women; median age, 34 years; range, 20–65) with a normal sugar permeability test and concurrent distal duodenal biopsies were identified. The number of IELs and epithelial cell nuclei in an uninterrupted length of surface (villous) epithelium (> 500 cells) was counted. An image analysis system was used to assess villous architecture by calculating the villous height to crypt depth ratio.

Results: The range of IEL counts in 20 subjects was 1.8–25/100 villous epithelial cells, with a mean value of 1.1 and SD of 0.6. The mean villous to crypt ratio was 1.82 (SD, 0.38; range, 1.22–2.46). There was no correlation between IEL counts and villous to crypt ratio (Spearman rank correlation, −0.066; p = 0.80).

Conclusions: These results suggest that 25 IELs/100 epithelial cells (mean +2 SD) should be taken as the upper limit of the normal range for duodenal mucosa.

DISCUSSION

The recognition of an increased density of IELs is important in the diagnosis of CD and even in the presence of normal villous architecture may reflect lesser degrees of gluten intolerance. On the basis of these results, we suggest that 25 IELs/100 epithelial cells is taken as the upper limit of the normal range (mean +2 SD) for duodenal mucosa when counting profile densities in standard histological sections. Although it has been established that these counts overestimate the absolute IEL to enterocyte ratio by a factor of two, methods that provide absolute values are impracticable for routine assessment. Indeed, we would not advocate that detailed quantification (as performed here) is carried out to corroborate a subjective impression of raised IELs. Having established that 25 IELs/100 epithelial cells is the upper limit of normal, it would suffice in routine practice to estimate whether a density ratio of 1 : 4 lymphocytes to epithelial cell nuclei is exceeded at several points in the surface epithelium. Interestingly, an identical value of 25% has been suggested as the threshold that must be exceeded for the diagnosis of lymphocytic gastritis.

Abbreviations: CD, coeliac disease; IEL, intraepithelial lymphocyte.
**Take home messages**

- An increase in intraepithelial lymphocytes (IELs) is mandatory for the histological diagnosis of coeliac disease
- Although duodenal biopsies are currently used for diagnosis, 40 lymphocytes/100 epithelial cells is used as the upper limit of the normal range, a figure derived from jejunal biopsies over 30 years ago
- Our results suggest that 25 IELs/100 epithelial cells should be taken as the upper limit of the normal range (mean +2 SD) for duodenal mucosa when counting profile densities in standard histological sections

**REFERENCES**


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