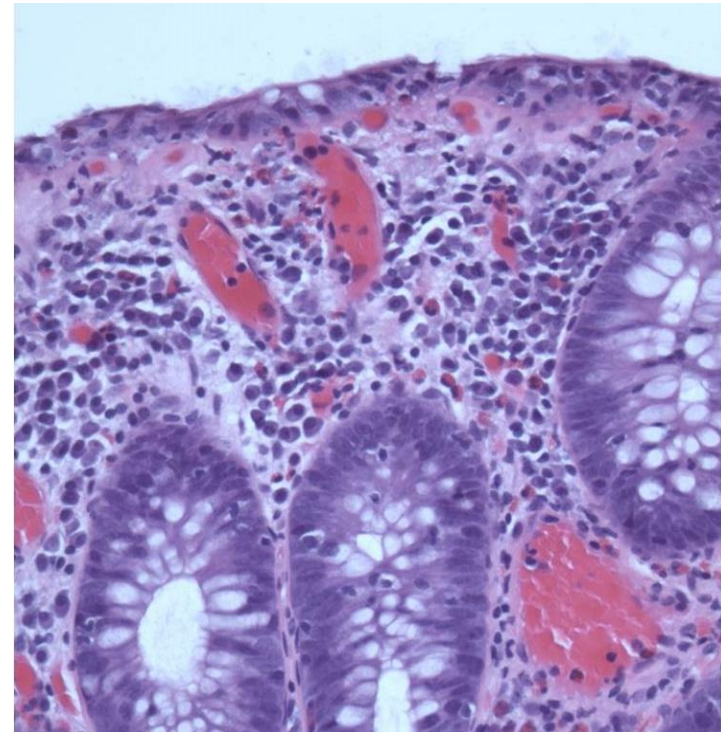
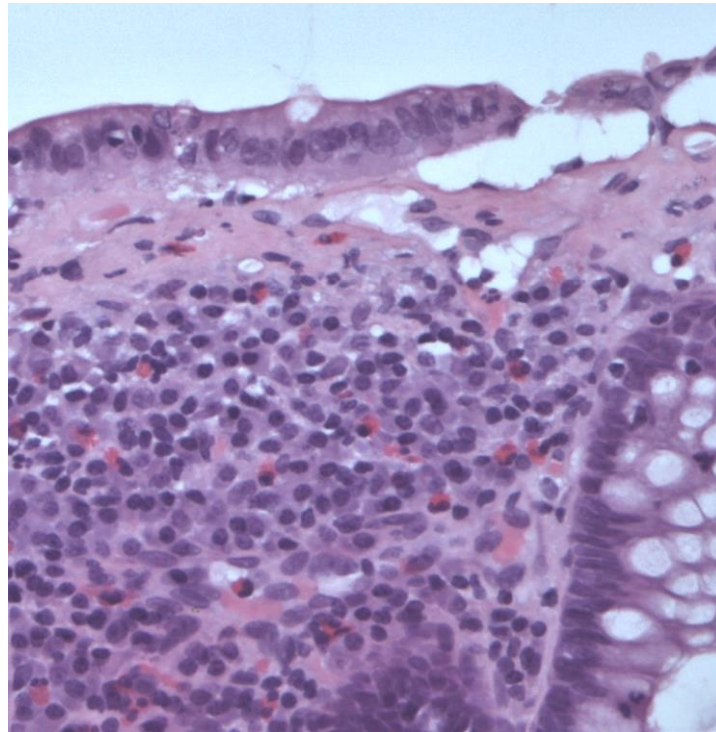


PRO-MC Pathology slide kit



Histology of microscopic colitis (MC) and incomplete forms of microscopic colitis (MCi)



PRO-MC Pathology slide kit



This slide kit is intended to pathologists participating in the PRO-MC study and is based on the article

Langner C et al: Working Group of Digestive Diseases of the European Society of Pathology (ESP) and the European Microscopic Colitis Group (EMCG). Histology of microscopic colitis - review with a practical approach for pathologists. Histopathology 2015; 66: 613-626.

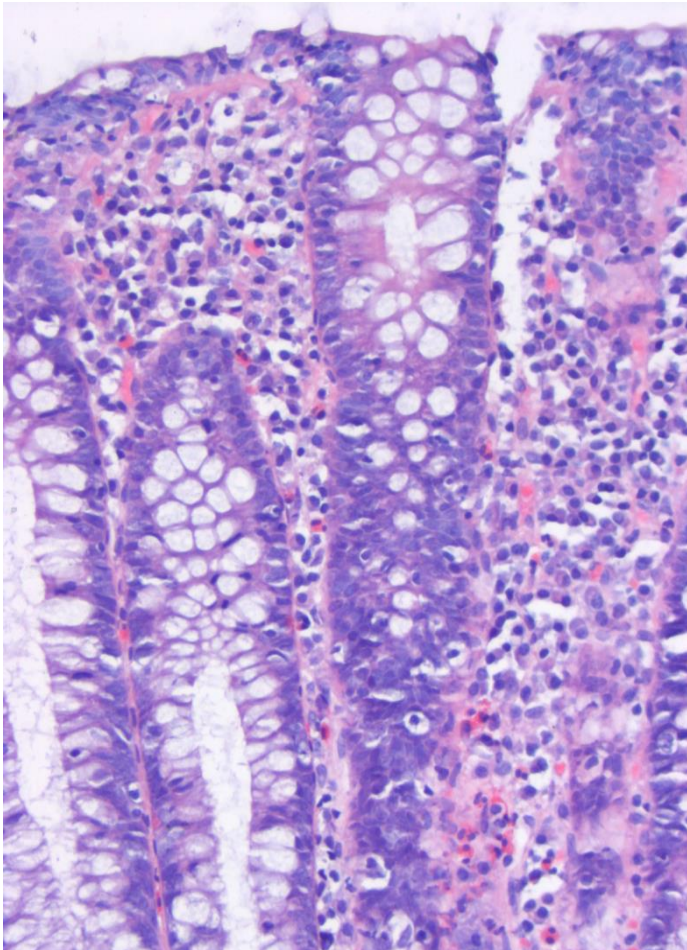
The slide kit was edited by

Peter Engel, Roskilde, Denmark
Cord Langner, Graz, Austria

For further information on the PRO-MC Collaboration please visit

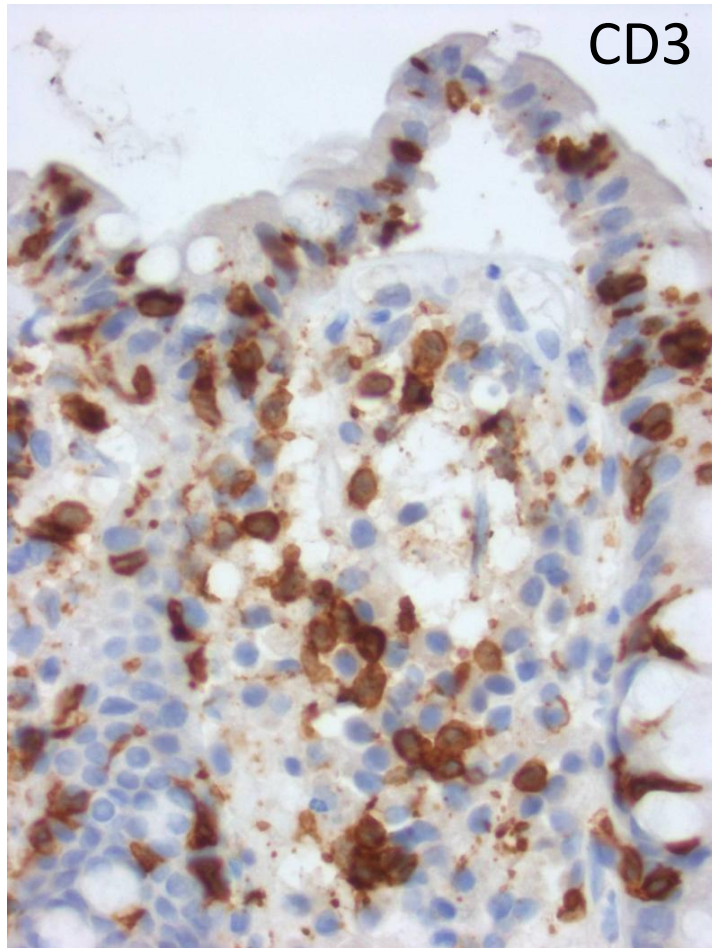
<http://www.emcg-ibd.eu/european-registry-promc.html>

Lymphocytic colitis: Histomorphology



- Increased number of surface intraepithelial lymphocytes (> 20 IELs per 100 epithelial cells)
- Degenerative changes of the surface epithelium
- Normal crypt architecture
- Increased transmucosal infiltrate of lymphocytes and plasma cells
- Granulocytes may be present, but in low number

Lymphocytic colitis: Immunohistochemistry



Immunohistochemical staining for T-lymphocytes (CD3) may be helpful when the pathologist is in doubt of the number of IELs

Differential diagnosis of lymphocytic colitis (1)



- **IBD:**
 - Disturbed crypt architecture
 - Granulocytes in the stroma -> cryptitis -> crypt abscess formation -> crypt destruction -> erosion and ulceration
- **Infectious colitis:**
 - Generally preserved architecture
 - Mucosal oedema, granulocytes in the stroma, cryptitis, crypt abscesses
 - Usually no or only mild increase in lymphoplasmocytic infiltrate
 - IELs missing or less prominent
- **Collagenous colitis:**
 - Cases with mild intraepithelial lymphocytosis (10-20 IELs)

- **Colonic lymphocytosis**

- Mild increase in IELs (10 – 20)
- No increased lympho-plasmacellular infiltration of the lamina propria
- No neutrophils
- No epithelial injury

Conditions associated with colonic lymphocytosis

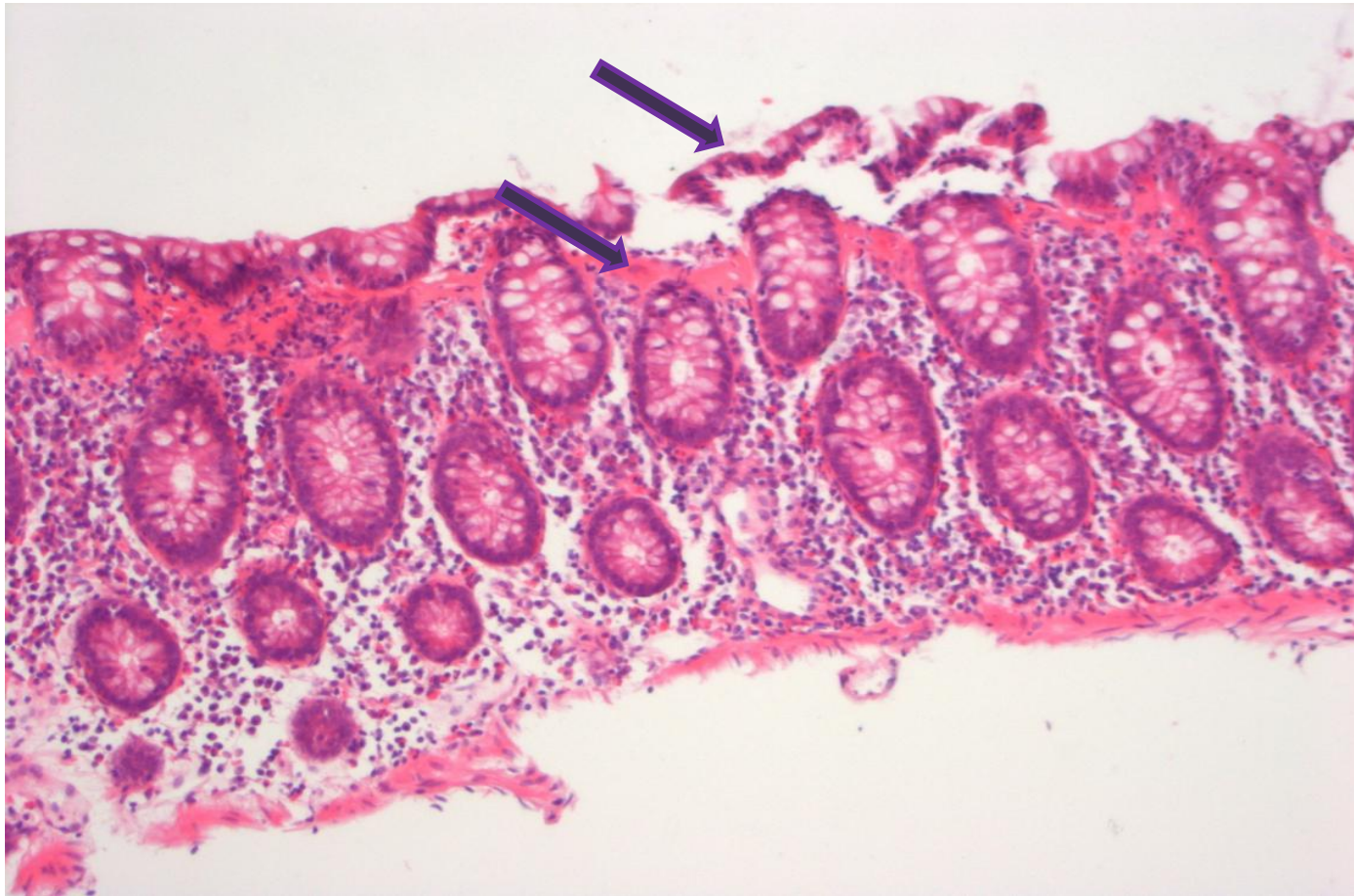
- Incomplete form of LC (LCi)
- Colon involvement in celiac disease
- Medication induced
- Resolving infectious colitis
- Nonspecific changes

Collagenous colitis: Histomorphology



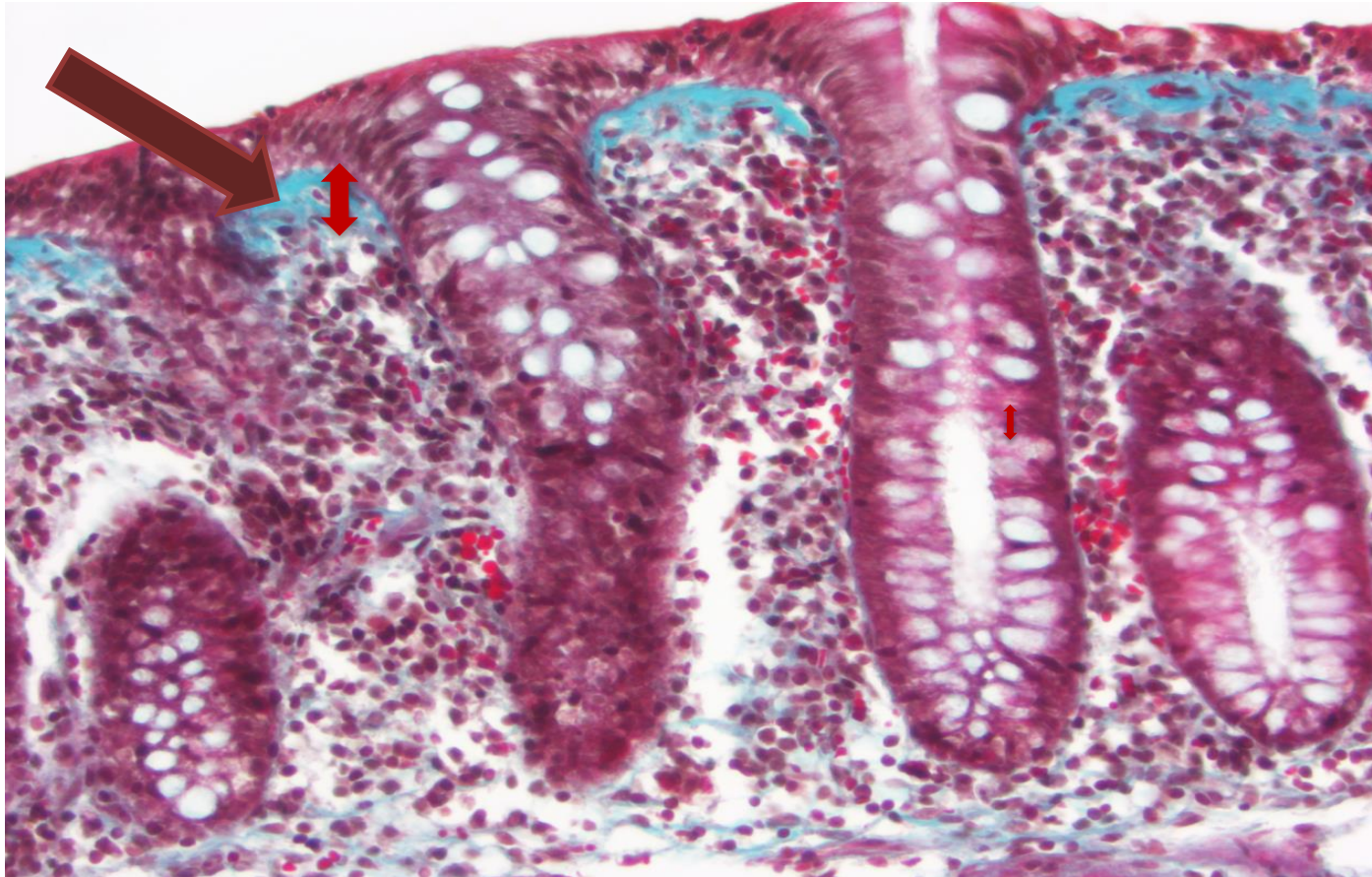
- Increased thickness of the subepithelial collagen band ($>10\mu\text{m}$) and often with entrapped capillaries, blood cells or inflammatory cells.
- No extension of the collagen band into the lamina propria
- Collagen-specific staining may be used for better visualization (*e.g.* Van Gieson, Goldner, Masson Trichrome)
- IELs may be mildly increased (10 – 20/100 epithelial cells)
- Degenerative changes of the surface epithelium, desquamation of the surface epithelium often occur
- Increased transmucosal infiltrate of lymphocytes and plasma cells; stromal eosinophilia may occur

Collagenous colitis: Histomorphology



Arrows mark subepithelial collagen band ($> 10\mu\text{m}$) and degenerative changes of the surface epithelium. HE staining.

Collagenous colitis: Histomorphology



Arrows mark subepithelial collagen band ($> 10\mu\text{m}$). Goldner staining.

Differential diagnosis of collagenous colitis (1)



- **IBD:**
 - Disturbed crypt architecture
 - Granulocytes in the stroma -> cryptitis -> crypt abscess formation ->
 - crypt destruction -> erosion and ulceration
- **Amyloidosis:**
 - Amyloid deposition, not band-like, but in mucosa / submucosa
 - Congo red staining
 - No increase in inflammatory infiltrate
- **Ischemic colitis:**
 - Hypocellular lamina propria
 - Crypt atrophy may be present

Differential diagnosis of collagenous colitis (2)



- **Infectious colitis:**
 - Generally preserved architecture
 - Mucosal oedema, granulocytes in the stroma, cryptitis, crypt abscesses
 - Usually no or only mild increase in lymphoplasmocytic infiltrate
- **Collagen-„mimickers“:**
 - Tangential section
 - Subepithelial edema
 - Warning: Slightly increased subepithelial collagen in hyperplastic polyps
- **Lymphocytic colitis:**
 - Cases with mild thickening of the collagen layer (5 -10 μ m)

Features of incomplete lymphocytic colitis (LCi) and incomplete collagenous colitis (CCi)



- Increased lymphoplasmocytic infiltrate of the lamina propria
- > 10 intraepithelial lymphocytes (IELs), but < 20 IELs per 100 epithelial cells (for diagnosis of incomplete lymphocytic colitis) and/or
- Thickened subepithelial collagen band > 5 μ m but <10 μ m (for diagnosis of incomplete collagenous colitis)
- Degenerative changes of the superficial epithelium
- Granulocytes in a low number may be present
- All features may be patchy throughout the colon

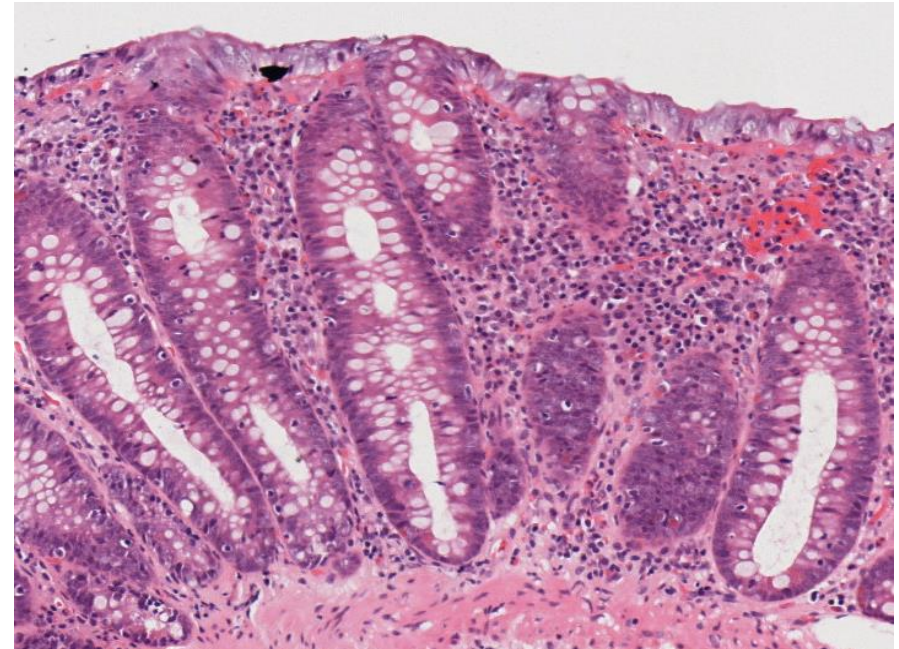
Lamina propria

Normal mucosa



- Normal lymphoplasmocytic infiltrate, with luminal accentuation
- No plasma cells in basal lamina propria
- Infiltrate right colon > left colon

Lamina propria in LCI



- Increased lymphoplasmocytic infiltrate
- Basal to apical gradient less pronounced
- Increased number of eosinophils
- Some neutrophils may be present

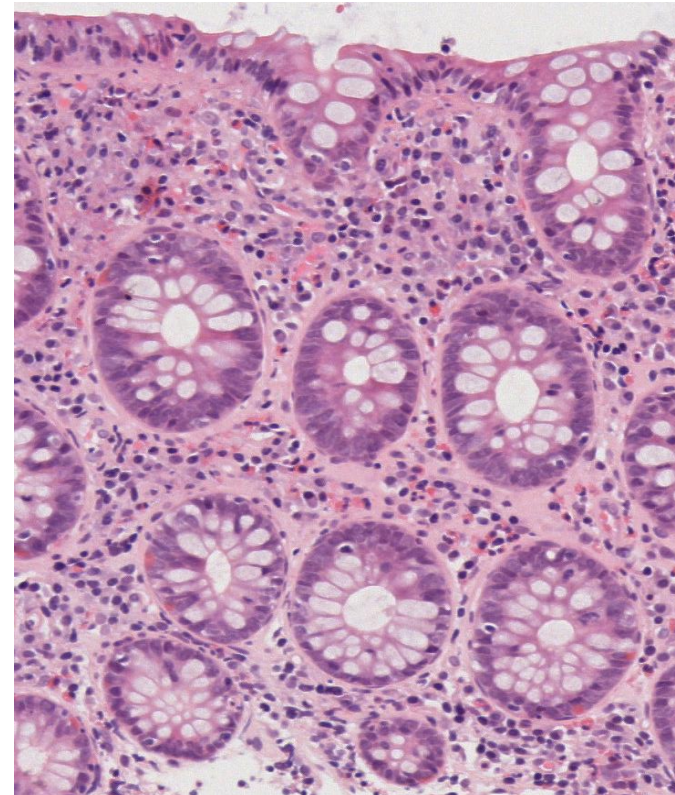
Intraepithelial lymphocytes (IELs)

Normal biopsy



Normal number of IELs

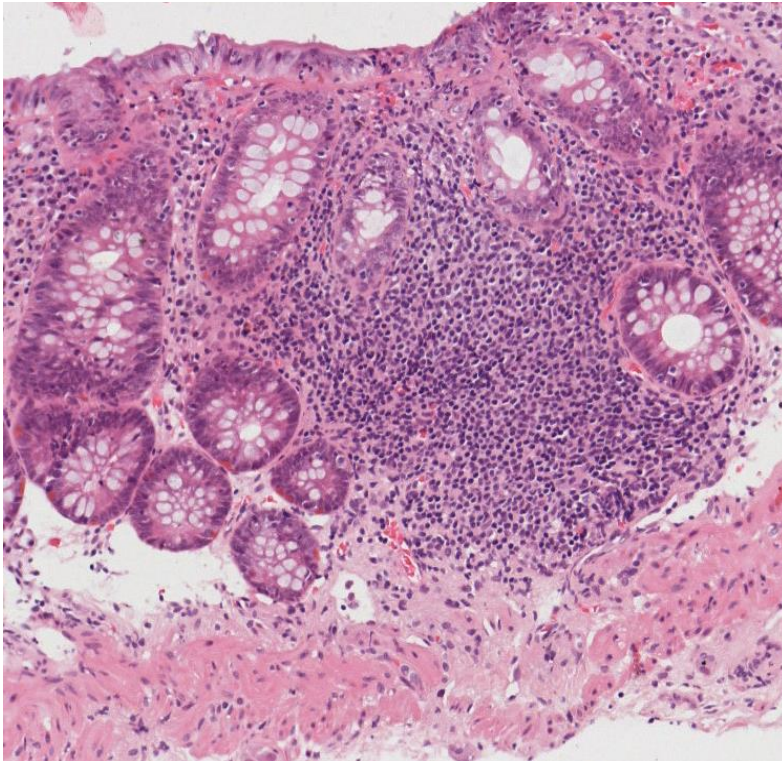
LCi



> 10 IELs and < 20 IELs per 100 epithelial cells

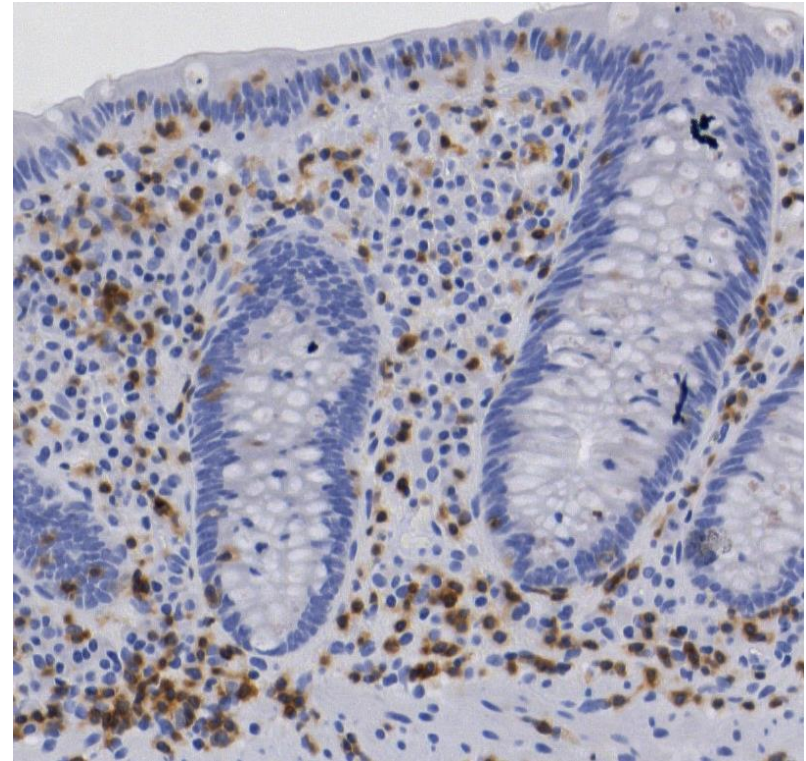
Intraepithelial lymphocytes (IELs)

Normal



Disregard epithelium above lymphoid follicles. HE staining.

LCi



CD3 staining maybe helpful for visualisation of (intraepithelial) lymphocytes.

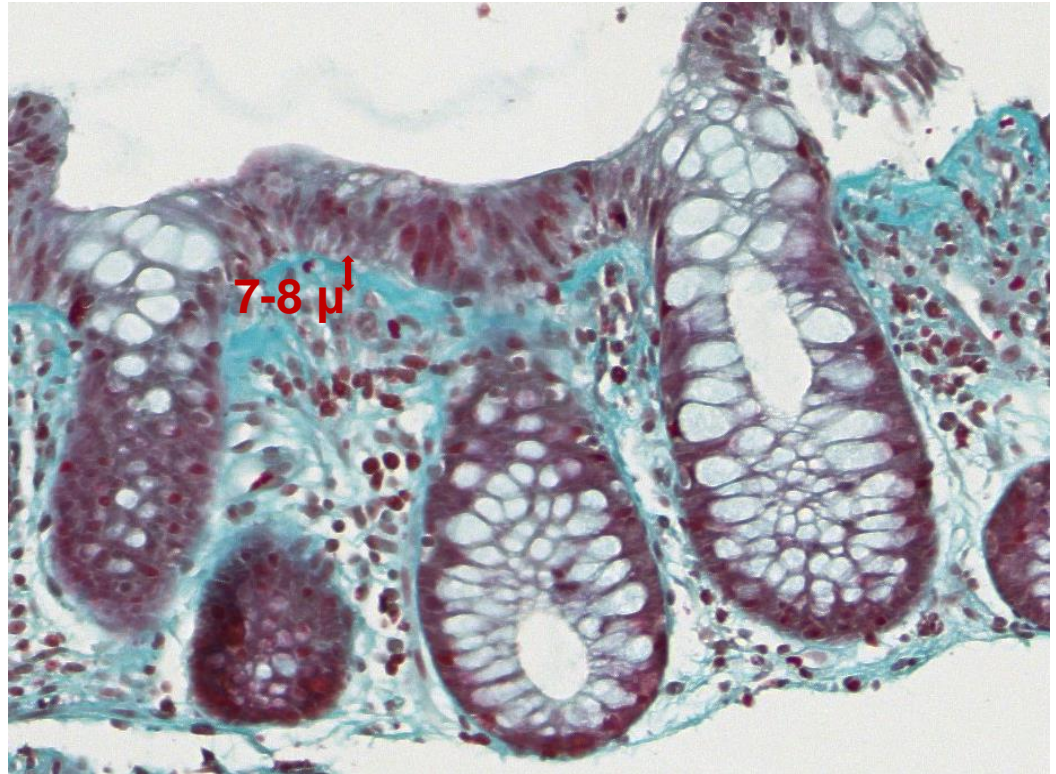
Subepithelial collagen band

Normal



Normal thickness of subepithelial collagen band. HE staining.

CCi



Thickened subepithelial collagen band $> 5\mu\text{m}$, but $< 10\mu\text{m}$. Goldner staining.

Are additional stainings needed in diagnosing MC and MCi ?



- **Not in unequivocal histomorphological cases:**
 - Number of IELs and thickness of collagen band can be assessed on H&E
- **Yes in borderline cases and in clinical trials:**
 - CD3 for counting IELs in LC and LCi
 - Collagen-specific histochemical stains (*e.g.* van Gieson, Goldner, Masson Trichrome) for measuring the collagenous band in CC and CCi
 - Tenascin immunohistochemistry may be useful to detect a glycoprotein associated with the collagen deposition in borderline cases of CC

LC, LCI, CC and CCI: relationship with ulcerative colitis and Crohn's disease

