

Actualités et controverses en gastroentérologie

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Colites microscopiques

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CHUV

Microscopic colitis

- Definition
- Epidemiology
- Diagnosis
- Etiology and pathophysiology
- Treatment
- Challenges

Microscopic colitis

- **Definition**
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Definition

- Chronic inflammatory disease of colon
- Characterized by watery diarrhea
- F > M
- Middle-aged patients
- Subtypes:
 - lymphocytic colitis (LC):** IEL >20/hpf
 - collagenous colitis (CC):** subepithelial collagen band >10µm
 - incomplete MCi:** MC not otherwise specified, does not fulfill histologic criteria for either LC or CC
- Limited knowledge as of yet

Münch A, et al. JCC 2012;6:932
Veress B, et al. Gut 1995;36:880

Microscopic colitis

- Definition
- **Epidemiology**
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Epidemiology

- Incidence **LC**: 1.1-5.2/100,000/yr
- Incidence **CC**: 3.1-5.5/100,000/yr
- Prevalence: 103/100,000 persons
- Mean age at Dx 65 yrs
- 25% of pts diagnosed before 45 yrs
- Dx in 10% of pts investigated for chronic diarrhea
- Rare in children
- F > M

Münch A, et al. JCC 2012;6:932

Veress B, et al. Gut 1995;36:880

Pardi DS, et al. GUT 2007;56:504

Epidemiology

Table 1 Annual incidence per 100,000 inhabitants in population-based epidemiological studies of collagenous and lymphocytic colitis.

Region and study period	Collagenous colitis	Lymphocytic colitis
Örebro, Sweden 1984–1988 ²¹	0.8	
Örebro, Sweden 1989–1993 ²¹	2.7	
Örebro, Sweden 1993–1995 ¹	3.7	3.1
Örebro, Sweden 1996–1998 ¹	6.1	5.7
Örebro, Sweden 1999–2003 ²	4.7	5.1
Örebro, Sweden 2004–2008 ²	5.8	4.5
Terassa, Spain 1993–1997 ²²	1.1	3.1
Terassa, Spain 2004–2008 ¹⁹	2.6	2.2
Iceland 1995–1999 ¹⁶	5.2	4.0
Olmsted County, Minnesota, USA 1985–1997 ³	1.6	2.7
Olmsted County, Minnesota, USA 1998–2001 ³	7.1	12.6
Calgary, Canada 2002–2004 ²³	4.6	5.4
Calgary, Canada 2004–2008 ¹⁸	7.2	14.0
Zeeland, Denmark 2002–2010 ¹⁷	10.8	6.7

Epidemiology

Table 1 Annual incidence per 100,000 inhabitants in population-based epidemiological studies of collagenous and lymphocytic colitis

Region and study period	Collagenous colitis	Lymphocytic colitis
Örebro, Sweden 1987–1996 ¹⁶	7.1	12.6
Umeå, Sweden 2001 ¹⁵	4.0	2.7
Calgary, Canada 2002–2004 ²³	4.6	5.4
Calgary, Canada 2004–2008 ¹⁸	7.2	14.0
Zeeland, Denmark 2002–2010 ¹⁷	10.8	6.7

Crohn's disease: 1/1,000
 Ulcerative colitis: 1/1000
 Microscopic colitis: 1/1000
 EoE: 1/2000

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Diagnosis: Clinical presentation

- chronic, nonbloody diarrhea
- Sudden diarrhea onset in 40% of pts
- Average bowel frequency 4-9/day
- Diarrhea volume up to 2 liters/day
- Fecal urgency in 70%
- Incontinence in 40%
- Nocturnal diarrhea in 50%
- Abdominal pain in 50%
- Extraintestinal manifestations possible (arthralgia, uveitis, etc)



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Diagnosis: laboratory findings in MC

- Typically non-specific
- Mild anemia
- Auto-antibodies in 50% of pts: RF, ANA, AMA, ANCA, ASCA
- Rarely protein-losing enteropathy
- Fecal exam: eosinophil protein X, myeloperoxidase, and tryptase may be elevated
- Fecal calprotectin: conflicting results regarding use as surrogate marker for microscopic activity

Münch A, et al. JCC 2012;6:932
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Diagnostic workup

Laboratory

- Search for fecal parasites
- Fecal culture (Salmonella, shigella, campylobacter)
- Toxin test for C. Difficile

Endoscopy:

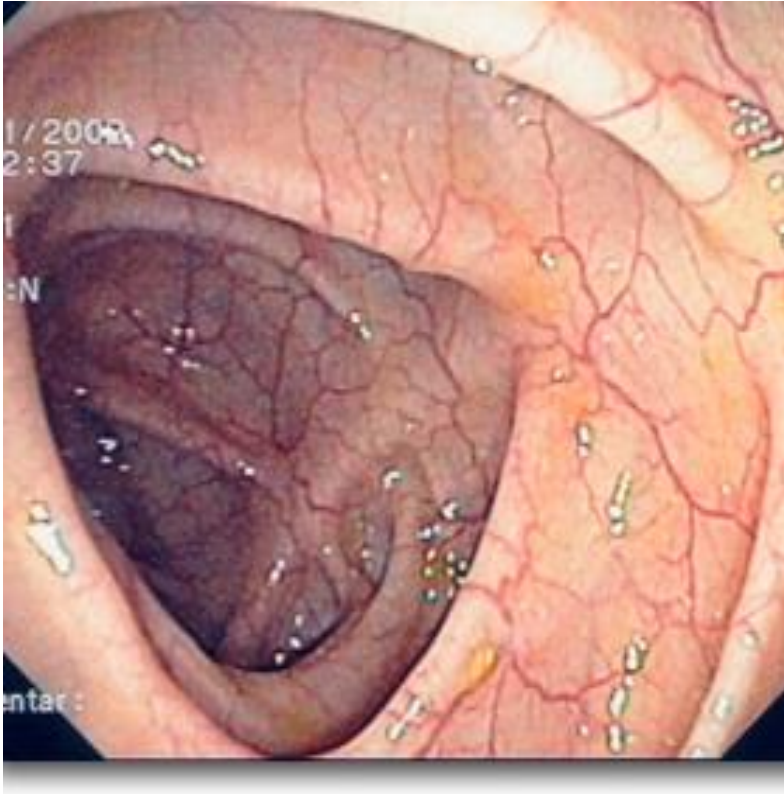
- Normal-appearing mucosa
- Unspecific findings: edema, erythema

Münch A, et al. JCC 2012;6:932
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Diagnostic workup: endoscopy

- Severity of histologic changes declines from proximal to distal colon
- Rectosigmoid biopsies miss Dx of **CC** in 40% of cases
- Highest dx yield if Bx taken from transverse colon (83%) and right colon (70%)
- Lowest Dx yield in bx from rectosigmoid (66%)
- Endoscopy is generally safe

Endoscopy in MC

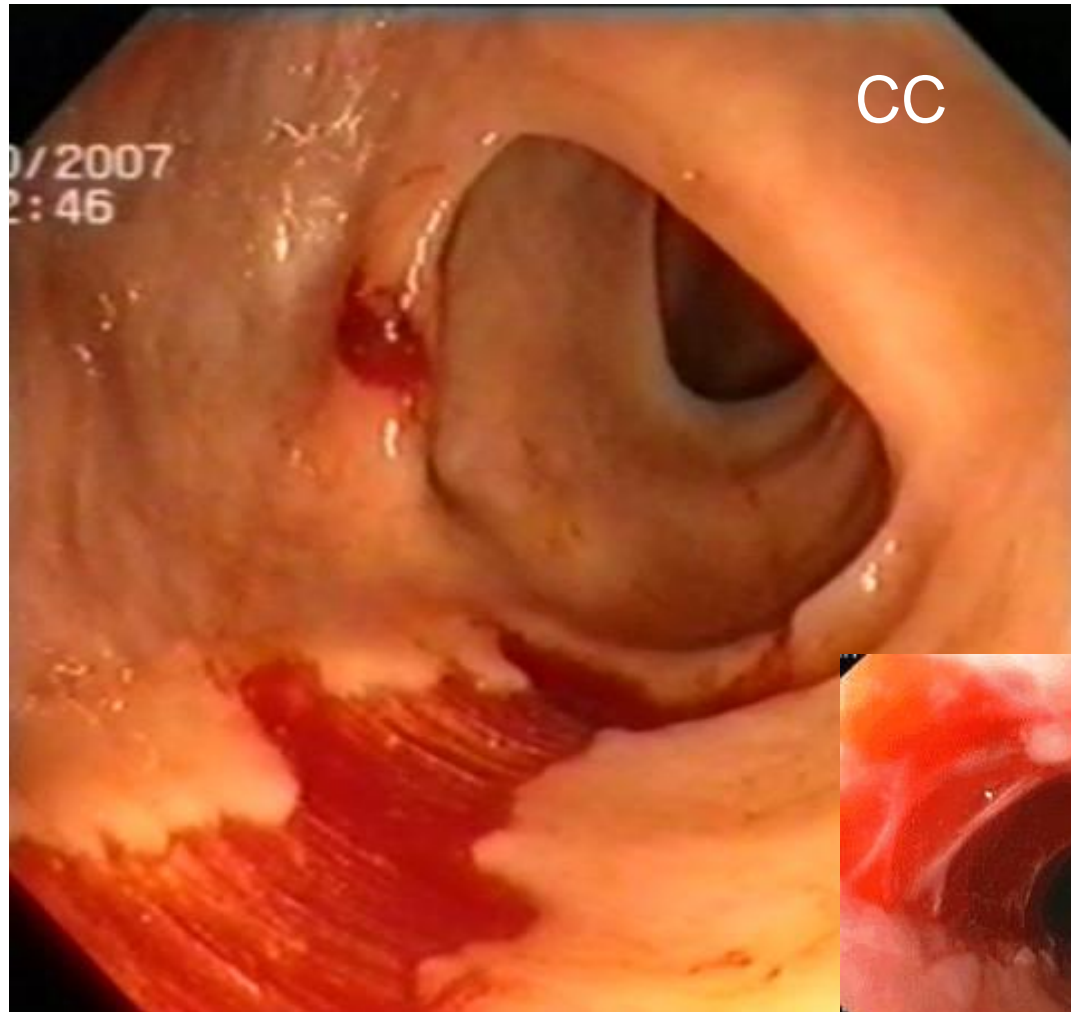


Normal colon

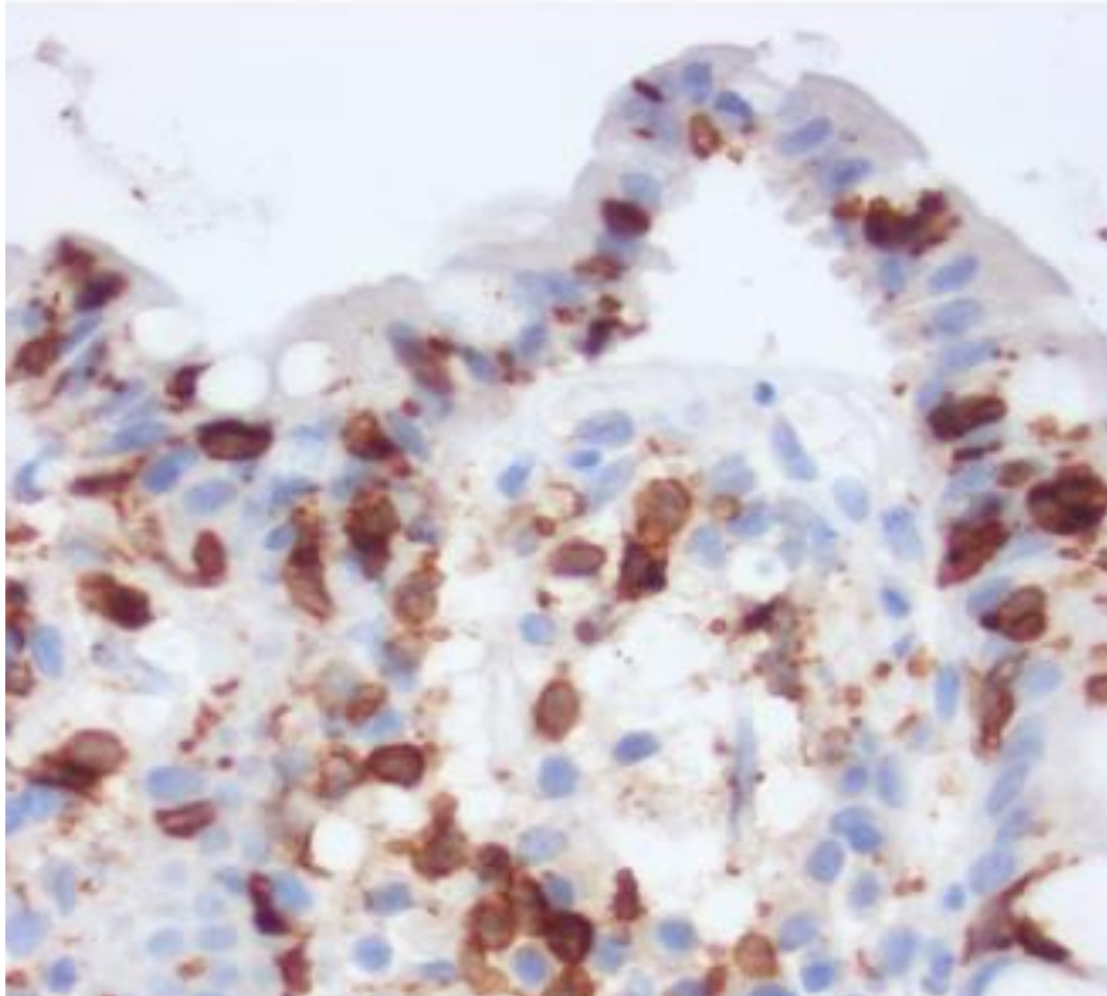


Mosaic pattern in **CC**

Endoscopy in MC: « fractured colon » in CC



Diagnostic workup: histology



LC: increased IEL in CD3 staining
(≥ 20 IEL/100 surface epithelial cells)

Diagnostic workup: histology

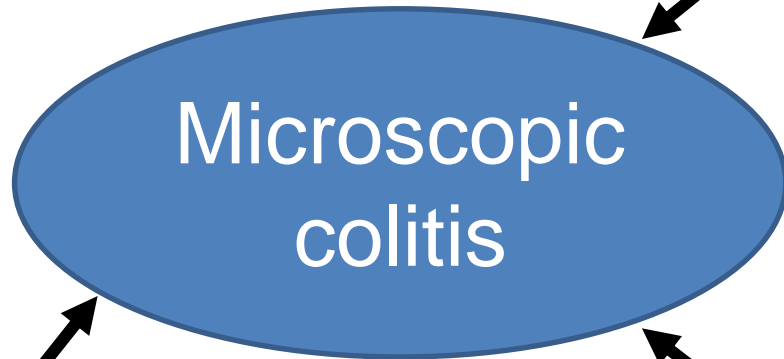


CC: increased subepithelial collagenous layer (EvG), inflammation of lamina propria, intraepithelial infiltration with lymphocytes and epithelial lesions

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Etiology and Pathophysiology: Risk factors



Münch A, et al. JCC 2012;6:932

Etiology and Pathophysiology

Risk factors: Drugs

Table 4 Assessment of the level of likelihood that a specific drug can trigger MC: Review of the literature.¹²⁷.

^aModified from Beaugerie and Pardi.

High likelihood	Intermediate likelihood	Low likelihood
Acarbose ¹²³	Carbamazepine ^{11, 128–131}	Cimetidine ¹³²
Aspirin and NSAIDs ^{118, 133–136}	Celecoxib ¹³⁷	Gold salts ¹³⁸
Clozapine ¹³⁹	Duloxetine ¹⁴⁰	Piascledine ¹⁴¹
Entocapone ¹⁴²	Fluvastatin ¹³⁷	
Flavonoid ^{124, 137, 143–147 b}	Flutamide ^{29, 138}	
Lansoprazole ^{125, 148–151}	Oxetorone ^{152, 153}	
Omeprazole/Esomeprazole ¹²⁶	Madopar ^{154 c}	
Ranitidine ¹²²	Paroxetine ¹¹	
Sertraline ^{11, 127, 137}	Simvastatin ¹⁵⁵	
Ticlopidine ^{29, 138, 156–159}	Stalevo ^{160 c}	

^a This paper used the 'French algorithm' to evaluate causality assessment of adverse drug reactions. This implies the evaluation of seven criteria belonging to two groups: chronological and semiological. Chronological criteria are: Time to onset, dechallenge, and rechallenge. Semiological criteria are: Search for non-drug related causes, evocative semiology of drug responsibility and/or risk factors for drug reaction, and specific validated laboratory test. A bibliographic score taking into account how often the adverse reaction has been reported was used to calculate the total likelihood score of causality.

^b Venotonic drugs containing flavonoids (diosmin, rutin, or hesperidin).

^c Anti-parkinsonian drugs, containing levodopa and benserazide (Madopar^R) and carbidopa, levodopa and entocapone (Stalevo^R).

Etiology and Pathophysiology

Risk factors: smoking

- OR 2.1 (95% CI 1.6-2.9) for smokers for developing MC
- Smokers develop MC 10 years earlier than non-smokers



Yen EF, et al. IBD 2012;18:1835

Vigren L, et al. Scand J Gastroenterol 2011;46:1334

Jessurun J, et al. Gastroenterology 1986

Etiology and Pathophysiology

Risk factors: genetics

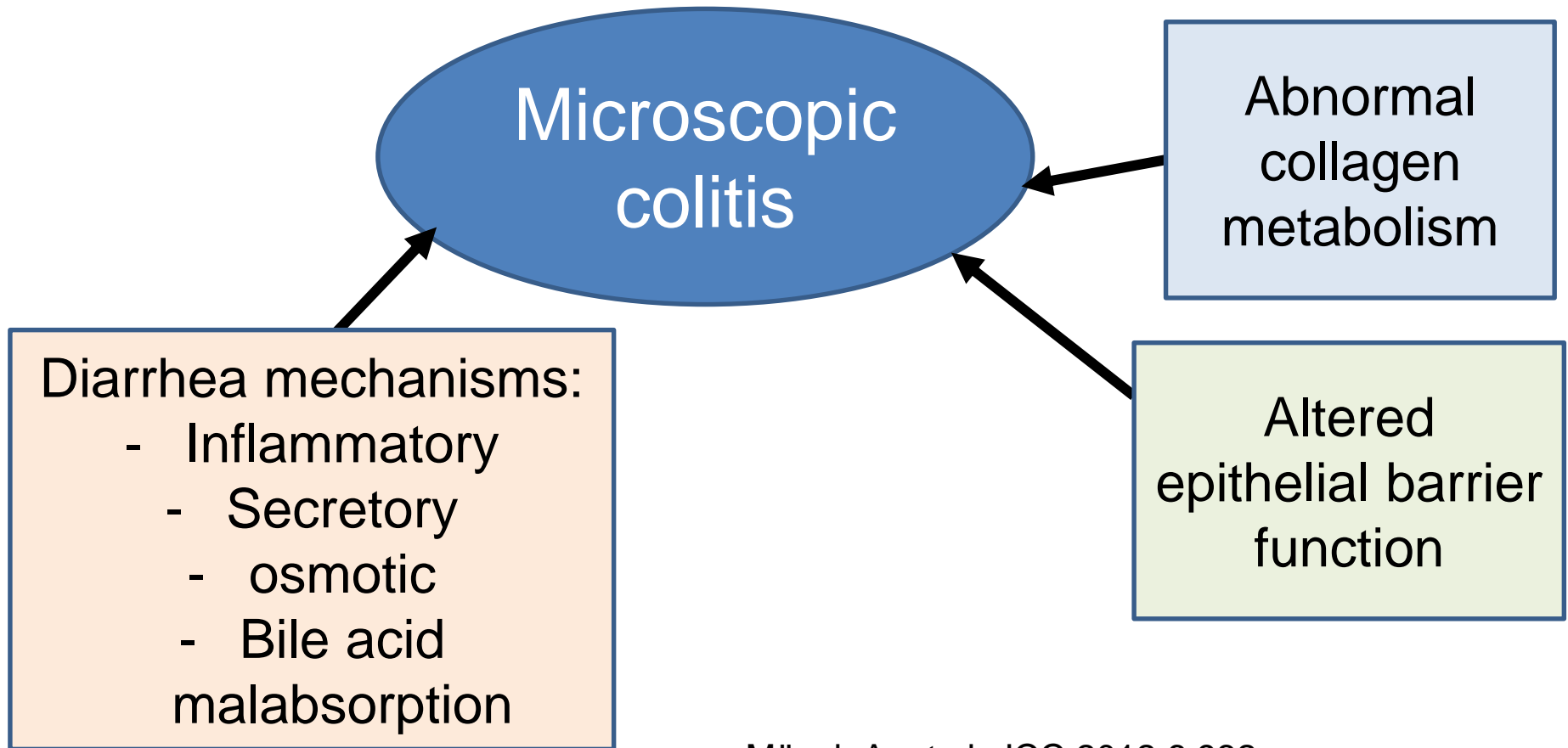


- Familial cases of MC are described
- Different members of family developed either LC or CC => supports similar underlying pathomechanism
- Association of MC with HLA-DQ2 or DQ1/3

Koskela RM, et al. Eur J Gastroenterol Hepatol 2008;20:276
Fine KD, et al. Am J Gastroenterol 2000;95:1974

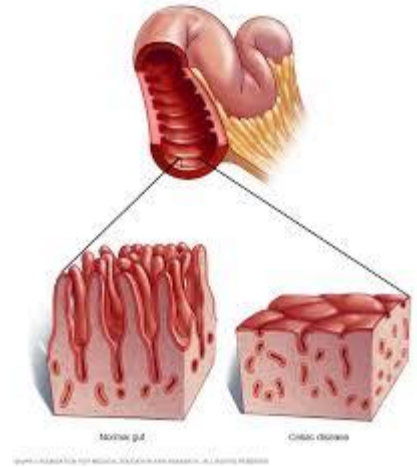
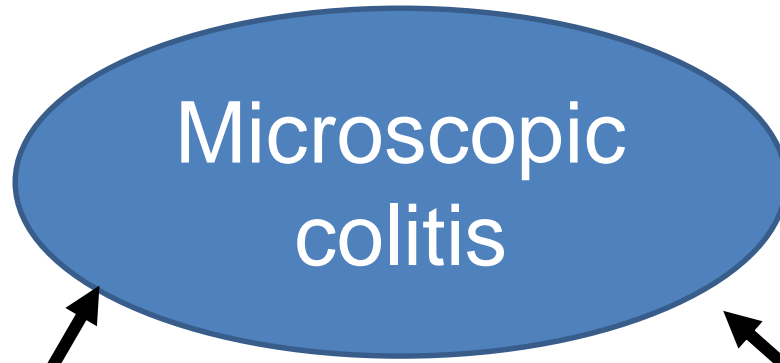
Pathogenesis

Pathogenesis is unclear, it is likely multifactorial, involving mucosal immune responses to luminal factors in genetically predisposed individuals



Münch A, et al. JCC 2012;6:932
Ung KA, et al. Gut 46:170

Associated conditions



TYPE 1 DIABETES
IS AN AUTOIMMUNE CONDITION IN WHICH THE BODY ATTACKS AND DESTROYS INSULIN-PRODUCING CELLS.

INSULIN THERAPY IS THE ONLY EFFECTIVE TREATMENT FOR TYPE 1 DIABETES

ABOUT 1 IN 500 PEOPLE IN THE UNITED STATES HAS THE CONDITION

TYPE 1 DIABETES ACCOUNTS FOR \$14.9 BILLION IN HEALTH CARE COSTS PER YEAR

5% OF PEOPLE WHO HAVE A PARENT OR SIBLING WITH TYPE 1 DIABETES WILL ALSO DEVELOP THE CONDITION

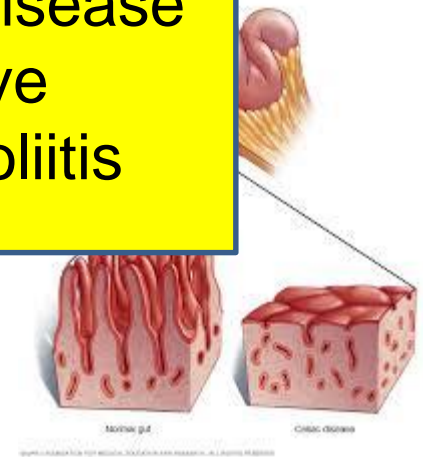
ABOUT 80 PEOPLE GET DIAGNOSED WITH TYPE 1 DIABETES IN THE U.S. EACH DAY



Associated conditions

Microscopic colitis

4.3.% of celiac disease patients have microscopic colitis



TYPE 1 DIABETES
IS AN AUTOIMMUNE CONDITION IN WHICH THE BODY'S INSULIN PRODUCTION IS DESTROYED.

INSULIN THERAPY IS THE ONLY EFFECTIVE TREATMENT FOR TYPE 1 DIABETES

ABOUT 1 IN 500 PEOPLE IN THE UNITED STATES HAS THE CONDITION

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Link with Crohn's disease or UC?

- Rarely microscopic colitis can precede the development of overt IBD (mainly Crohn's disease)
- In CD rarely **lymphocytic** and **collagenous** gastritis are reported

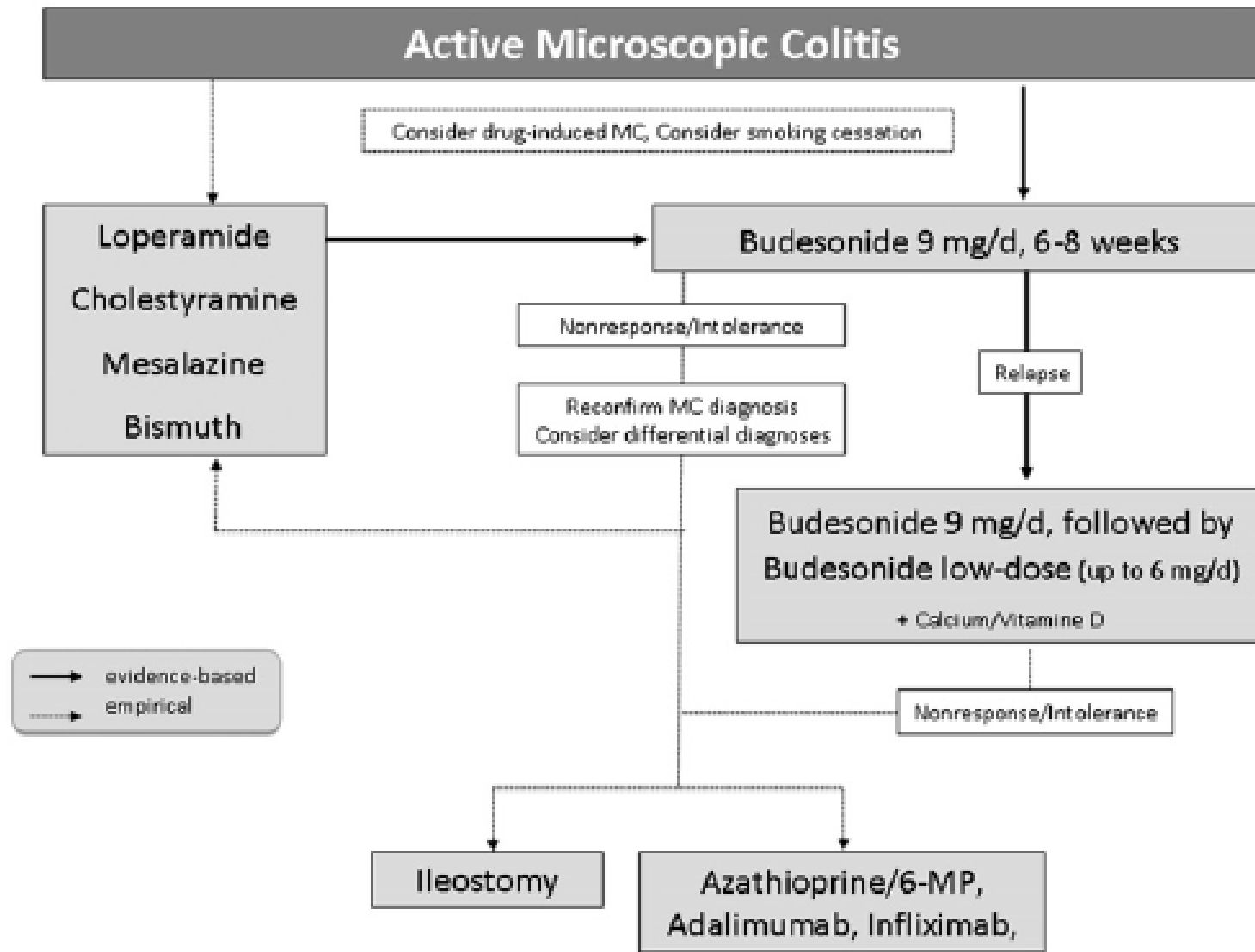


Chandratne S, et al. Digestion 1987;36:55
Chutkan R, et al. Am J Gastroenterol 2000;95:3640

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Treatment



Treatment

No role for the following drugs

- Prednisone (lower response rates than for budesonide)
- Aminosalicylates
- Methotrexate
- Octreotide
- E. coli Nissle

Münch A, et al. JCC 2012;6:932

Münch A, et al. Clin Exp Gastroenterol 2013;6:149

Madisch A, et al. Int J Colorectal Dis 2007;22:1445

Long-term evolution

- Chronic intermittent course
- Relapses are common (30-60% within 12 months)
- 10-year FUP in CC: diarrhea resolved in 50% of pts (under anti-inflammatory treatment)
- No transformation between **LC** and **CC**
- No increased risk for colorectal cancer

Bonderup OK, et al. Eur J Gastroenterol Hepatol 1999
Madisch A, et al. Z Gastroenterol 2006;44:971

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Epidemiology

Pathogenesis



Randomized
clinical trials

Natural history

Thèse: «prévalence et incidence des colites microscopiques dans les cantons de Vaud, Neuchâtel, et Fribourg»



Hugo Maye

Thanks for your attention!

