# Pouchitis

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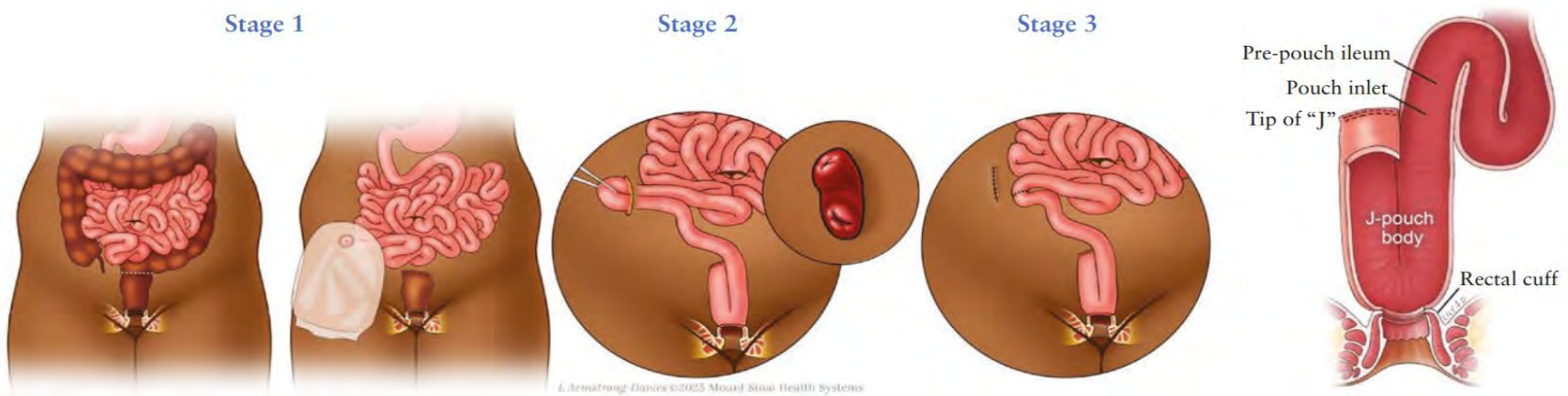
# Introduction

- 10-15% of UC patients require colectomy for medically refractory disease or neoplasia.
- Restorative proctocolectomy (RPC) with ileal pouch-anal anastomosis (IPAA) is the preferred surgery.
- Provides regular, controlled, per anal defecation with significantly reduced risk of colorectal cancer.
- The J-pouch is the most common IPAA configuration.
- Approximately 15-20 cm in length, 4 cm in diameter, and 200 ml in volume.
- Post-operative adaptation occurs after 6-12 months, pouch function is 4-8 bowel movements per day and 0-2 per night.

1. Fumery M et al. Natural history of adult ulcerative colitis in population-based cohorts: a systematic review. Clin Gastroenterol Hepatol. 2018;16:343–356.e3.F
2.de Buck van Overstraeten A, Wolthuis AM, Vermeire S, et al. Long-term functional outcome after ileal pouch anal anastomosis in 191 patients with ulcerative colitis. J Crohns Colitis. 2014;8:1261–1266.

# Introduction

| Restorative procedure | Single-stage | 2-stage | Modified-2-stage | 3-stage |
|---|---|---|---|---|
| | Proctocolectomy and pouch construction without ileostomy | Proctocolectomy and pouch construction with ileostomy | Total colectomy with ileostomy | Total colectomy |
| | | Ileostomy closure | Proctectomy and pouch construction with ileostomy closure | Proctectomy and pouch construction with ileostomy |
| | | | | Ileostomy closure |




Maia Kayal et al. ECCO Topical Review on Pouch Disorders, *Journal of Crohn's and Colitis*, Volume 19, Issue 7, July 2025, jjaf103

# Definitions

- Acute pouchitis- Symptoms < 4 weeks of increased stool frequency, urgency, incontinence, and abdominal/pelvic pain that respond to a 2-week course of antibiotics.
- Intermittent pouchitis- isolated and infrequent episodes of classic symptoms which disappear with/ without treatment, followed by prolonged periods of normal pouch function.
- Chronic Antibiotic Dependant Pouchitis(CADP)- Relapsing or persistent symptoms of pouchitis that necessitate frequent antibiotics (3 or more courses within 12 months) or continuous antibiotics.
- Chronic Antibiotic Refractory Pouchitis(CARP)- Persistent symptoms of pouchitis despite 4 weeks of antibiotics.
- Crohn's Like Disease of the Pouch(CLDP)- One or more of the following features: extensive ulcerations & strictures in the pre-pouch ileum/ pouch body or pouch-related fistulae.
- Cuffitis- Inflammation of the residual rectum used to facilitate the stapled pouch-anal anastomosis.

1. Biancone L, Michetti P, Travis S, et al.; European Crohn's and Colitis Organisation (ECCO). European evidence-based Consensus on the management of ulcerative colitis: special situations. J Crohns Colitis. 2008;2:63–92.
2. Syal G, Shemtov R, Bonthala N, et al. Pre-pouch ileitis is associated with development of Crohn's disease-like complications and pouch failure. J Crohns Colitis. 2021;15:960–968.

# Classification

| Criteria | Category | Additional comments |
|---|---|---|
| Response to antibiotics | Antibiotic responsive | Based on response to a 2–4-week course of a single antibiotic |
| | Antibiotic dependent | |
| | Antibiotic refractory | |
| Disease duration | Acute | Cut-off: 4 weeks |
| | Chronic | |
| Disease pattern | Episodic | Episodes <3–4 per year |
| | Relapsing | Episodes ≥3 per year |
| | Persistent | Constant symptoms and endoscopic inflammation |
| Aetiology | Primary/idiopathic | A classic example is dysbiosis-associated diffuse pouchitis |
| | Secondary | Such as NSAIDs, *Clostridioides difficile* infection |
| Pathogenetic pathway | Microbiome | Gastrointestinal pathogens versus dysbiosis |
| | Autoimmune | Example: PSC-associated pouchitis |
| | Ischaemia | With characteristic patterns of distribution of ulcers |
| | Faecal stasis | Examples: structural or functional obstruction of the pouch outlet |
| Distribution of endoscopic inflammation | Diffuse | Example: PSC-associated pouchitis |
| | Patchy/segmental | Example: ischaemic pouchitis or CDP |
| Segment involved | Pouch body | Diffuse inflammation in the pouch body is classic, microbiota associated |
| | Prepouch ileum | Prepouch ileitis can solely present or coexist with pouchitis, cuffitis or strictures |
| | Pouch inlet | Inflammation or ulcers often coexist with inlet strictures |
| | Cuff | Classic cuffitis is a form of remnant ulcerative colitis; anterior cuffitis can be from structural or functional pouch outlet obstruction |
| | Pan-cuff, prepouch, ileum | Can be seen in patients with concurrent PSC |
| Depth of inflammation | Mucosal and superficial submucosal | Commonly seen in acute antibiotic-responsive pouchitis |
| | Transmural | Commonly seen in chronic antibiotic-refractory pouchitis; mimicking Crohn's disease of the pouch |

Shen, B. Pouchitis: pathophysiology and management. *Nat Rev Gastroenterol Hepatol* **21**, 463–476 (2024)

# Prevalence

- Annual incidence of endoscopy-diagnosed pouchitis is documented to be 17–40%.
- The cumulative incidence of pouchitis is highest in the first year after IPAA surgery.
- Cumulative incidence of approximately 48% within the first two years after IPAA in one study.
- Cumulative frequency rates for pouchitis in 10 years after surgery range from 23% to 60%.
- Approximately 50% of patients who undergo IPAA for UC will develop at least one episode of pouchitis.

Rottoli M, Vallicelli C, Bigonzi E, et al. Prepouch ileitis after ileal pouch-anal anastomosis: patterns of presentation and risk factors for failure of treatment. J Crohns Colitis. 2018;12(3):273-279.

# Risk factors -Acute Pouchitis

- Mutations in NOD2/CARD157.
- Genetic polymorphisms of interleukin 1 receptor, TNF allele 2 and TLR 1.
- Primary sclerosing cholangitis (PSC) and other EIMs.
- First-degree relative with inflammatory bowel disease.
- Positive PANCA and CBir1 serology.
- Pre-colectomy factors- Anti-TNF, Antibiotic use, previous admission for ASUC.

1.Barnes EL, Herfarth HH, Kappelman MD, et al. Incidence, risk factors, and outcomes of pouchitis and pouch-related complications in patients with ulcerative colitis. Clin Gastroenterol Hepatol. 2021;19:1583–1591.e4.
2.Barnes EL, Dunn MS, Ashburn J, et al. Extraintestinal manifestations and family history of inflammatory bowel disease increase the risk of pouchitis in a state-level epidemiology study. Clin Transl Gastroenterol. 2024;15:e00670.
3. Fleshner P, Ippoliti A, Dubinsky M, et al. Both preoperative perinuclear antineutrophil cytoplasmic antibody and anti-CBir1 expression in ulcerative colitis patients influence pouchitis development after ileal pouch-anal anastomosis. Clin Gastroenterol Hepatol. 2008;6:561–568.

# Risk factors-CADP and CARP

**Chronic Antibiotic Dependant Pouchitis**

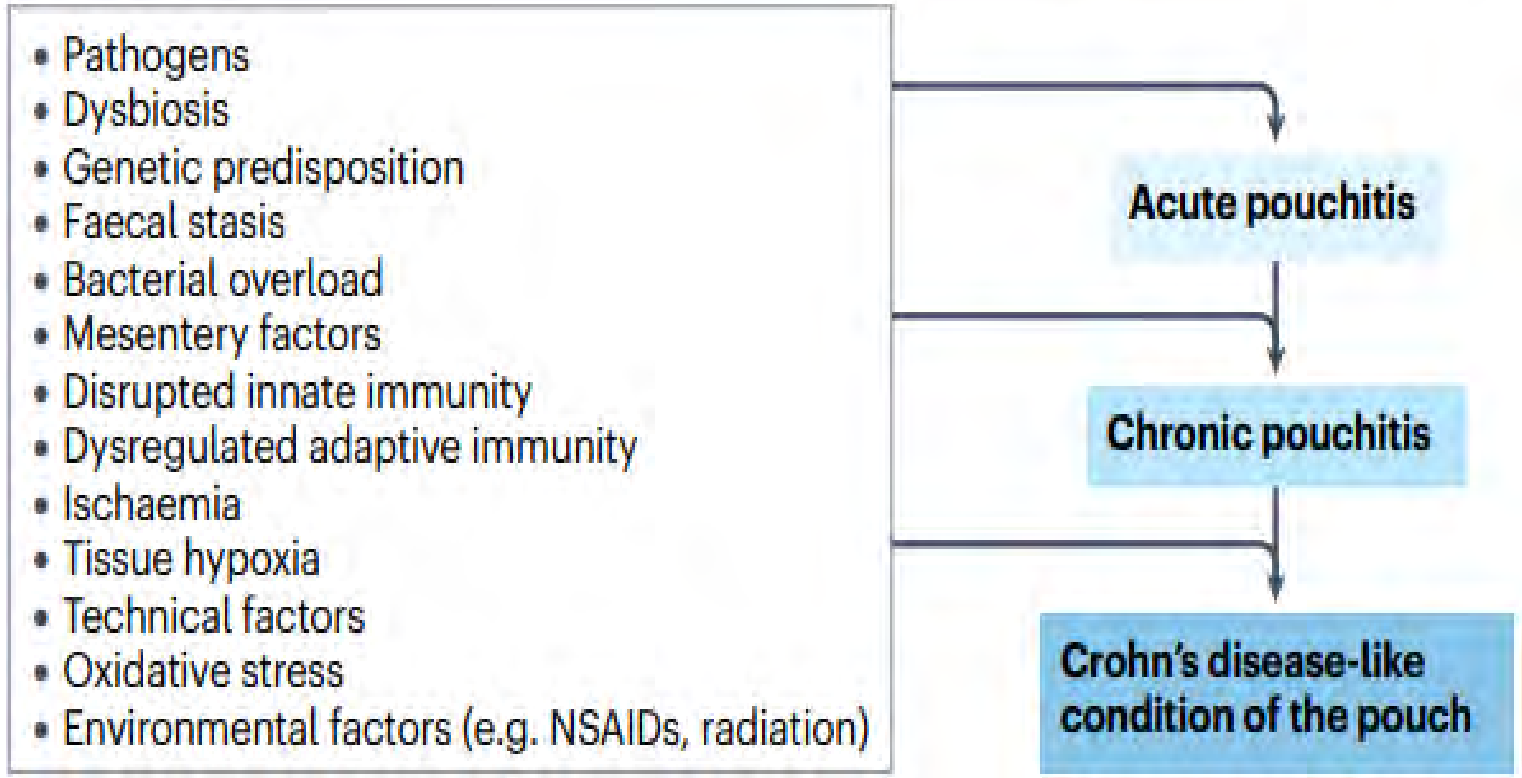
- Pouchitis within the first 180 days of surgery
- Age ≥ 55 years at the time of IPAA
- Primary Sclerosing Cholangitis

**Chronic Antibiotic Refractory Pouchitis**

- Pre-colectomy extensive disease
- Use of biologics
- Primary Sclerosing Cholangitis
- Post-IPAA use of non-steroidal anti-inflammatory drugs.

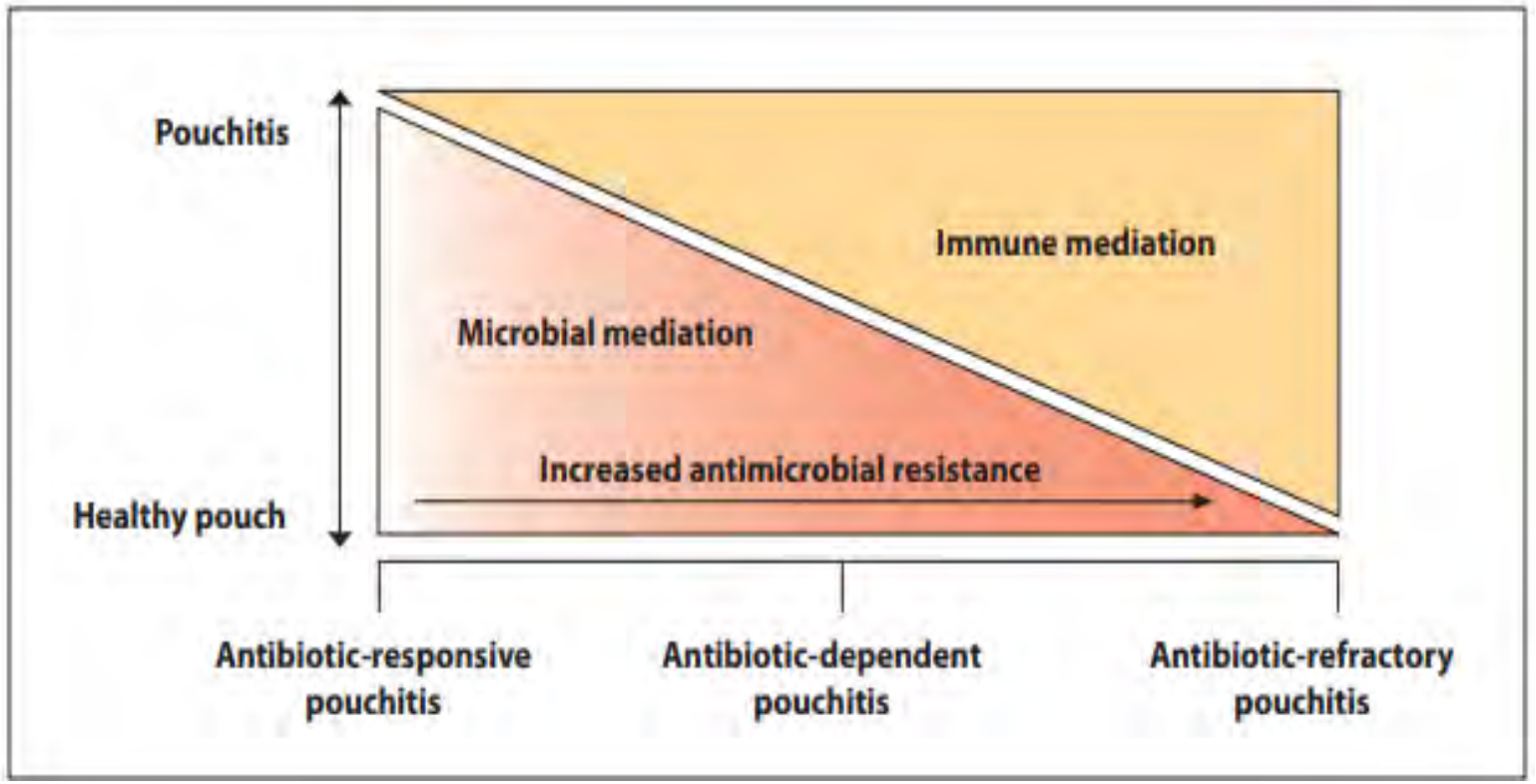
1.Esckilsen S, Kochar B, Weaver KN, Herfarth HH, Barnes EL. Very early pouchitis is associated with an increased likelihood of chronic inflammatory conditions of the pouch. Dig Dis Sci. 2023;68:3139– 3147.
2.Weaver KN, Kochar B, Hansen JJ, et al. Chronic antibiotic dependent pouchitis is associated with older age at the time of ileal pouch anal anastomosis (J-pouch) surgery. Crohns Colitis 360. 2019;1:otz029.
3. Quinn KP, Urquhart SA, Janssens LP, Lennon RJ, Chedid VG, Raffals LE. Primary sclerosing cholangitis-associated pouchitis: a distinct clinical phenotype. Clin Gastroenterol Hepatol. 2022;20:e964–e973.

# Multifactorial Pathophysiology model




Shen B. Pouchitis: what every gastroenterologist needs to know. Clin Gastroenterol Hepatol 2013; 11: 1538–1549.

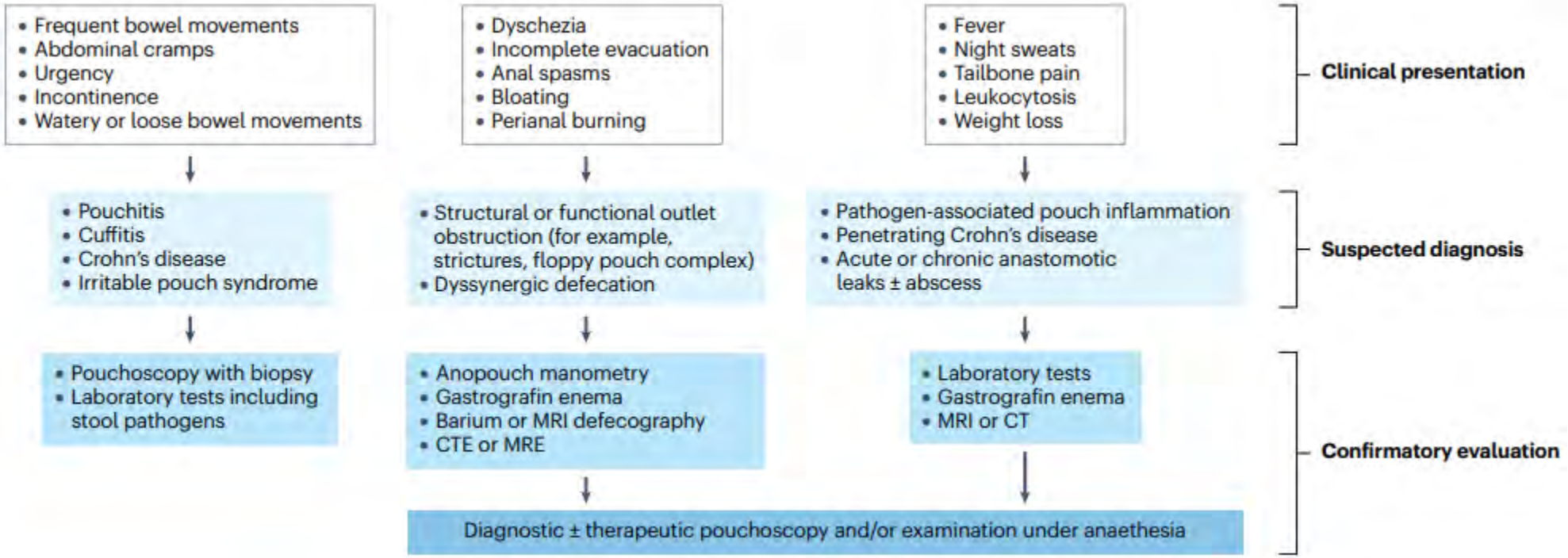
# Pathophysiology





Shen B. Pouchitis: what every gastroenterologist needs to know. Clin Gastroenterol Hepatol 2013; 11: 1538–1549.

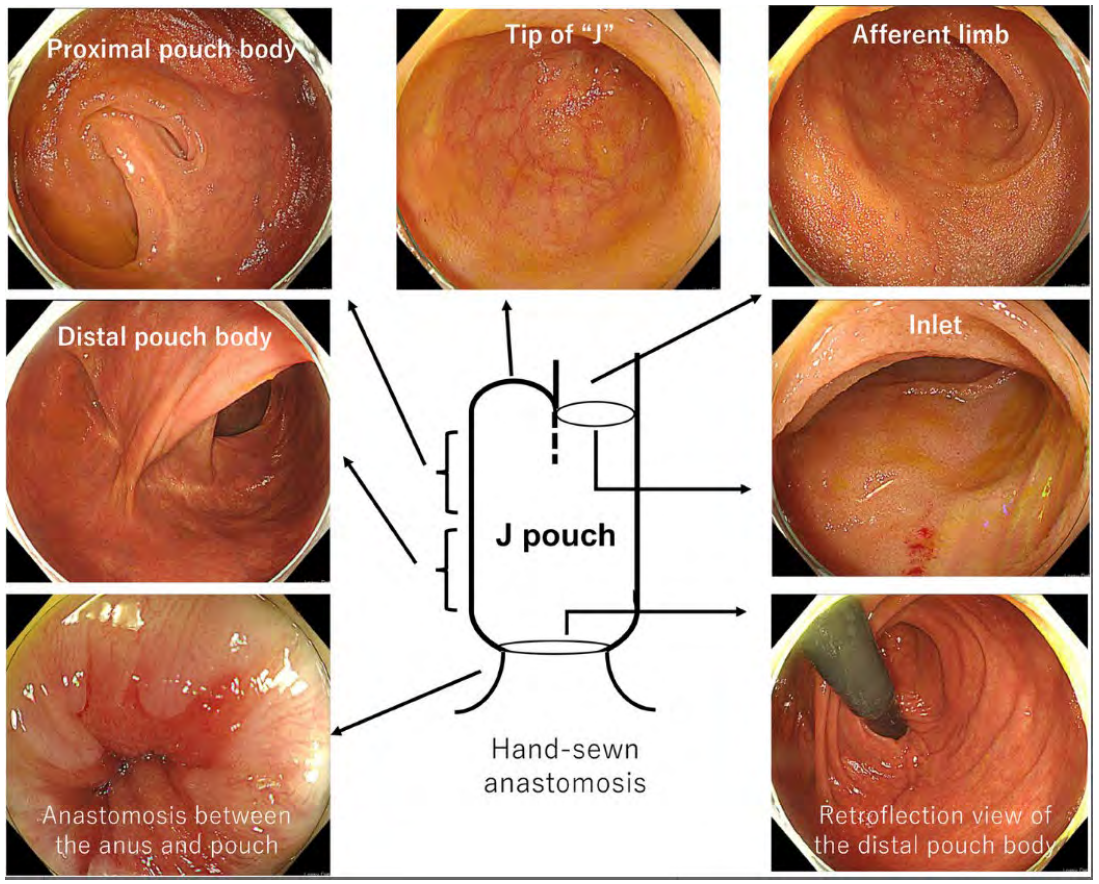
# Diagnostic Algorithm

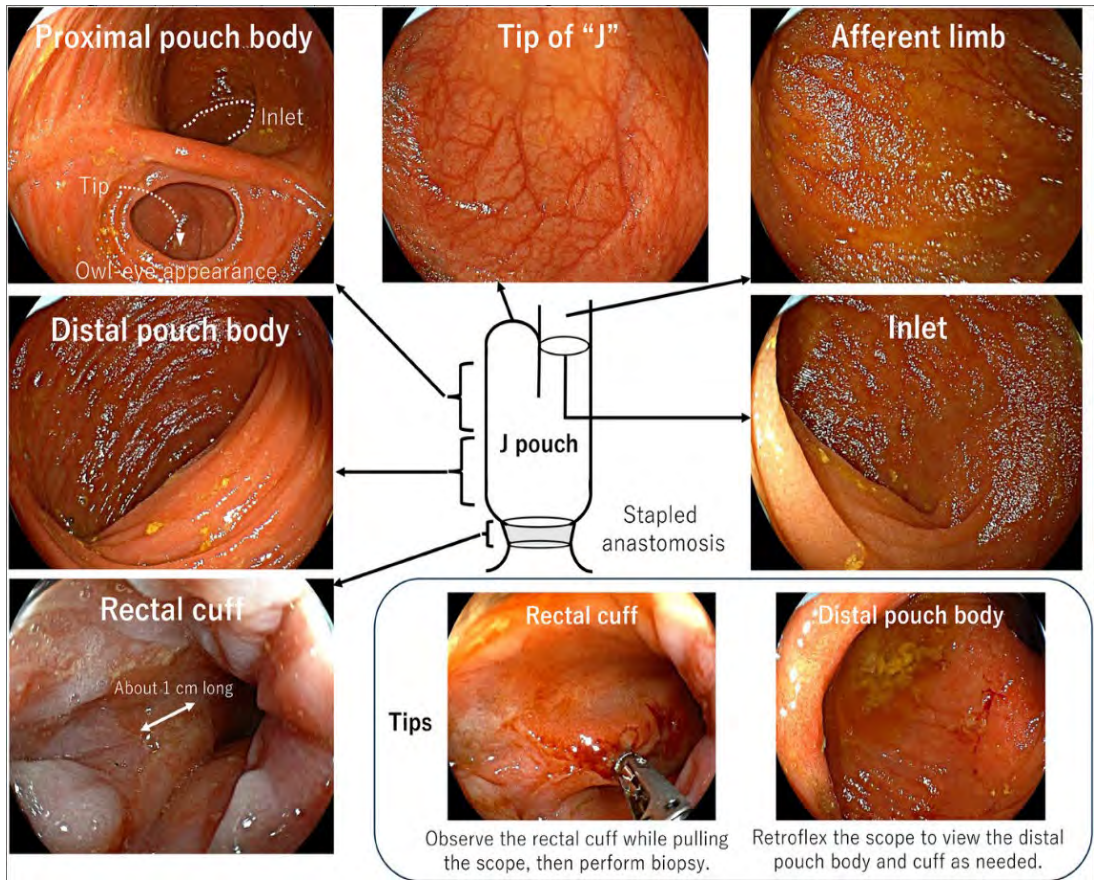





Shen, B. Pouchitis: pathophysiology and management. *Nat Rev Gastroenterol Hepatol* **21**, 463–476 (2024)

# Pouchoscopy- Pouch Anatomy

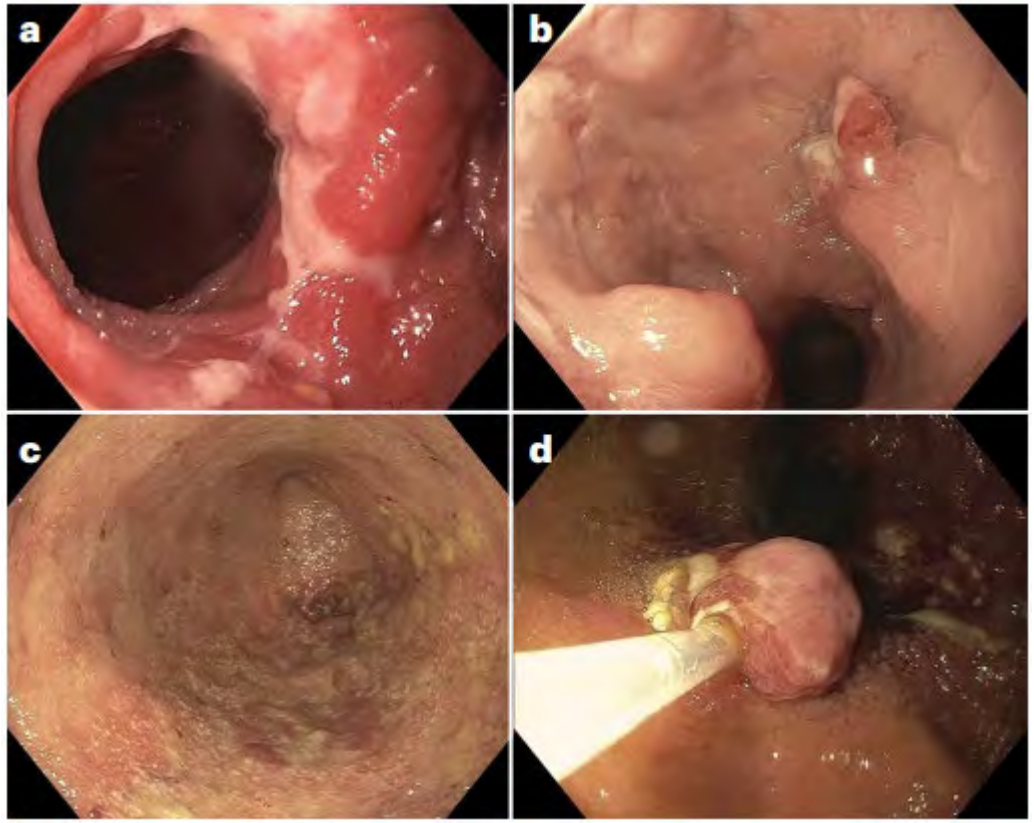





Akiyama, S., Barnes, E.L., Onoda, T., Ishikawa, N., Shiroyama, M., Ito, Y., Rubin, D.T. and Tsuchiya, K. (2025), Endoscopic assessment of the J pouch in ulcerative colitis: A narrative review. DEN Open, 5: e373.

# Pouchoscopy- Endoscopic images


(a) Diffuse pouch inflammation sparing the prepouch ileum. (a) Ischaemic ulcers at the pouch inlet. (b) Faecal stasis-associated pouchitis: anastomotic stricture with prolapse of the cuff. (c) Faecal stasis-associated pouchitis: diffuse pouchitis with mucosal exudates and erythema. (d) Endoscopic removal of a chronic pouchitis-associated inflammatory polyp.

# Pouch Disease Activity Index

| Criteria | Score |
|---|---|
| **CLINICAL** | |
| Stool frequency | |
| - Usual | 0 |
| - 1-2 stools more than usual per day | 1 |
| - >3 stools more than usual per day | 2 |
| Rectal bleeding | |
| - None/rare | 0 |
| - Present daily | 1 |
| Fecal urgency / Abdominal cramps | |
| - None | 0 |
| - Occasional | 1 |
| - Usual | 2 |
| Fever | |
| - Absent | 0 |
| - Present | 1 |

| Criteria | Score |
|---|---|
| **ENDOSCOPIC INFLAMMATION** | |
| Edema | 1 |
| Granularity | 1 |
| Friability | 1 |
| Loss of vascular pattern | 1 |
| Mucus exudates | 1 |
| Ulceration | 1 |

| Criteria | Score |
|---|---|
| **ACUTE HISTOLOGIC INFLAMMATION** | |
| Polymorphonuclear leukocyte infiltration | |
| - Mild | 1 |
| - Moderate + crypt abscess | 2 |
| - Severe + crypt abscess | 3 |
| Ulceration per low-power field (mean) | |
| - <25% | 1 |
| - 25-50% | 2 |
| - >50% | 3 |

***Pouchitis is defined as a total PDAI score of greater or equal to 7.**

Sandborn WJ, Tremaine WJ, Batts KP, et al. Pouchitis after ileal pouch-anal anastomosis: A Pouchitis Disease Activity Index. *Mayo Clin Proc.* 1994;69:409–415.

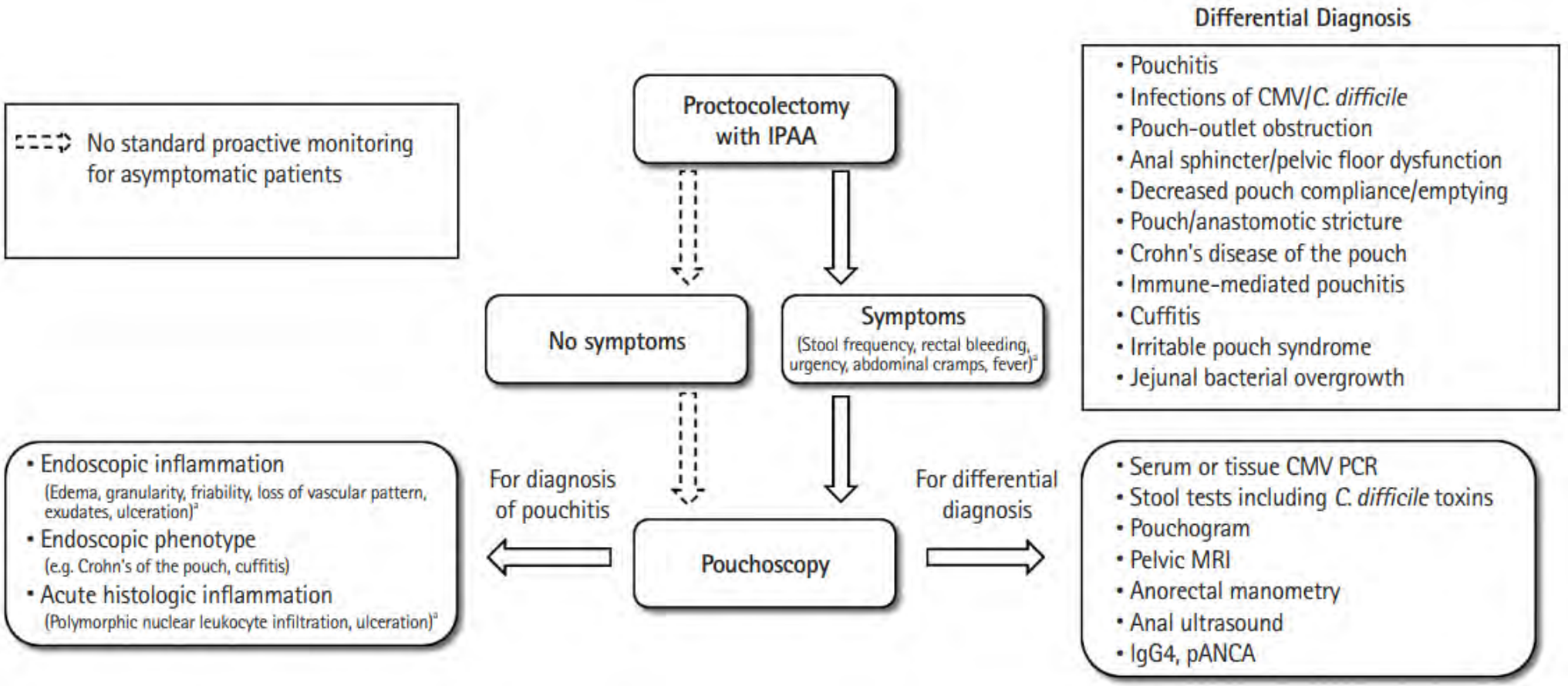
8

# Chicago classification Pouch phenotypes

- Normal pouch
- Afferent limb involvement
- Inlet involvement
- Diffuse inflammation of the pouch body
- Focal inflammation of the pouch body
- Cuffitis
- Pouch with fistulas 6 months or longer after ileostomy takedown

Kayal, Maia et al. Clinical Gastroenterology and Hepatology, Volume 20, Issue 2, 281 - 282

# Differential Diagnosis




Shintaro Akiyama et al, Pouchitis in inflammatory bowel disease: a review of diagnosis, prognosis and treatment. 2021:19(1):1-11.

# Management Approach & Strategies

## Treatment goals

- Goals of treatment
  - ➢ Alleviate symptoms
  - ➢ Improve quality of life
  - ➢ Achieve clinical & endoscopic remission by demonstrating mucosal healing

- Endoscopic mucosal healing
  - ➢ Completely normal mucosa
  - ➢ Absence of erosions or ulcers
  - ➢ PDAI endoscopy subscores of 0 or 1

## Primary prevention of Pouchitis

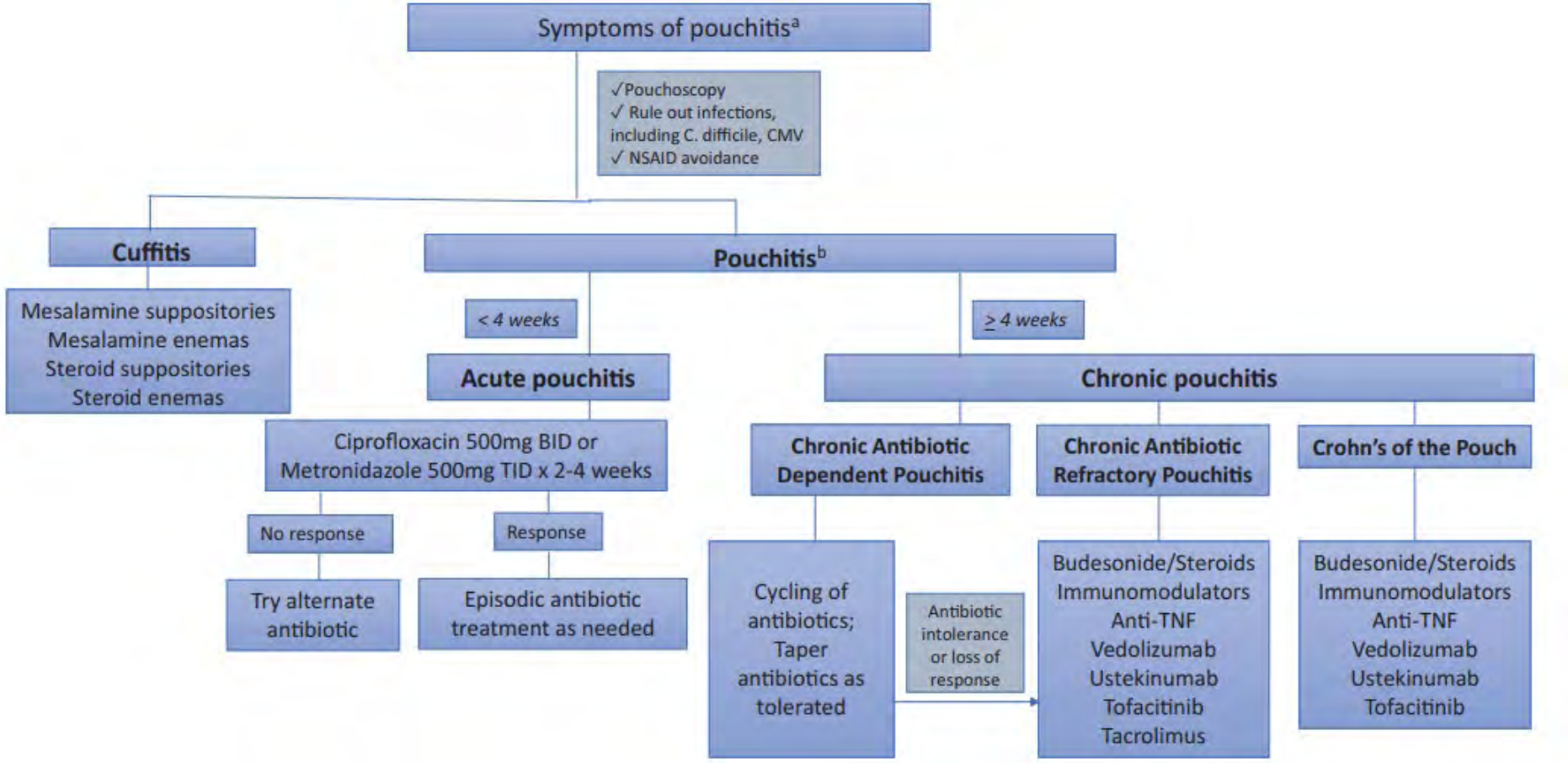
- Goal is to promote optimal pouch function.
- NSAIDs are associated with an increased risk for chronic pouchitis.
- Maintain ideal body weight- Obesity is a risk factor for pouch failure.
- Probiotics and other pharmacologic agents NOT recommended.
- Probiotics are used for secondary prevention of active pouchitis

Achkar JP et al. Differentiating risk factors for Acute and Chronic pouchitis. Clin Gasterol Hepatol 2005; 3:60

# Treatment of Pouchitis AGA recommendations

- Intermittent pouchitis: Antibiotics for treatment. No recommendation for or against probiotics as treatment.
- Recurrent episodes of pouchitis responsive to antibiotics: Probiotics for prevention of recurrence.
- CADP: Chronic antibiotic therapy. Ciprofloxacin 500/250 mg BD or cyclical Abx course(cycling 1 Abx to another every 2 weeks).
- CADP and CARP: Advanced immunosuppressive therapies, biologics.
- CARP: Corticosteroids- controlled ileal-release budesonide(8-12 weeks). No recommendation in favor or against mesalamine, biologics.
- CLDP- Corticosteroids, immunosuppressive therapies, biologics.

# Treatment algorithm for Pouchitis






Rabbenou W, Chang S. Medical treatment of pouchitis: a guide for the clinician. *Therapeutic Advances in Gastroenterology*. 2021;14.

# Management of Acute Pouchitis

- RCT designed to compare the effectiveness and S/E of ciprofloxacin and metronidazole in acute pouchitis.
- PDAI >7and symptom duration of <4 weeks.
- 16 patients randomized to 2-weeks course of ciprofloxacin 1,000 mg/d (n = 7) or metronidazole 20 mg/kg/d (n = 9).
- Ciprofloxacin showed more significant reduction in the total PDAI score, symptoms, endoscopy, and histology sub scores.
  - Total PDAI- 6.9+/-1.2 vs 3.8+/-1.7; p = 0.002
  - symptom score -2.4+/-0.9 vs 1.3+/-0.9; p = 0.03
  - endoscopic score 3.6+/-1.3 vs 1.9+/-1.5; p = 0.03
- No pt in ciprofloxacin group experienced adverse effects vs 3 pts in the metronidazole group- vomiting, dysgeusia, or transient peripheral neuropathy.



Shen B, Achkar JP, Lashner BA, Ormsby AH, Remzi FH, Brzezinski A, Bevins CL, Bambrick ML, Seidner DL, Fazio VW
Inflamm Bowel Dis. 2001;7(4):301.

# Antibiotics in Chronic Pouchitis

- Maintenance ciprofloxacin or metronidazole at lowest effective dose.
- Cycling and tapering to increase tolerability & decrease side effects.
- Metronidazole- nausea, metallic taste, interaction with alcohol, and potential risk of peripheral neuropathy.
- Ciprofloxacin -risk of tendonitis & tendon rupture(pts>60 & steroids users).
- Generally low risk of side effects.
- Alternative- rifaximin, tinidazole, amoxicillin-clavulanate, doxycycline, and vancomycin(data are limited).



Shore BM, Weaver KN, Allegretti JR, et al. 2023. Prevalence of Clostridioides difficile infection after ileal pouch–anal anastomosis in patients with chronic antibiotic-dependent pouchitis and Crohn's-like disease of the pouch. Inflamm. Bowel Dis. 29:932–37.

# Steroids in Chronic Pouchitis

- Prospective study of 20 patients with CARP treated with budesonide.
- 75% achieved clinical remission and the median total PDAI scores decreased significantly from 14 to 3, $p < 0.001$.
- Open-label study of 10 patients with CARP treated with beclomethasone.
- 80% of patients achieved clinical remission, median number of bowel movements decreased significantly from 10 to 6 ( $p < 0.001$) (17).
- Budesonide may be used as induction therapy in CP as a bridge to biologic or small-molecule therapy.
- Maintenance monotherapy with budesonide in CP is not recommended.



1. Gionchetti P, Rizzello F, Poggioli G, et al. 2007. Oral budesonide in the treatment of chronic refractory pouchitis. Aliment. Pharmacol. Ther. 25:1231–36
2. Gionchetti P, Calabrese C, Calafiore A, et al. 2014. Oral beclomethasone dipropionate in chronic refractory pouchitis. J Crohn's Colitis 8:649–53

# Management of Refractory Pouchitis

## Efficacy of Vedolizumab for Refractory Pouchitis of the Ileo-anal Pouch: Results From a Multicenter US Cohort

*Martin Gregory, MD,[*] Kimberly N. Weaver, MD,[†] Patrick Hoversten, MD,[‡] Stephen Bradley Hicks, MD,[‡] Devin Patel, MD,[§] Matthew A. Ciorba, MD,[*,¶] Alexandra M. Gutierrez, MD,[*,¶] Poonam Beniwal-Patel, MD,[††] Sowmya Palam, MD,[‡‡] Gaurav Syal, MD,[§§] Hans H. Herfarth, MD, PhD,[†,‖,**] George Christophi, MD, PhD,[*,¶] Laura Raffals, MD,[***] Edward L. Barnes, MD, MPH,[†,‖] and Parakkal Deepak, MBBS, MS[*,¶]*

# Vedolizumab in Refractory Pouchitis Study highlight

- Effectiveness and safety of vedolizumab in CD of the pouch and CADP/CARP.
- Retrospective, multicentre cohort study  5 referral centres.
- 83 patients treated with vedolizumab. Median follow-up 1.3 years .
- Primary endpoint- clinical response at any time point. Secondary endpoint- clinical remission, endoscopic response, and remission.
- Proportion for clinical response- 71.1%,  19.3% - clinical remission.
- 74 pts with follow-up pouchoscopy, proportion with endoscopic response(54.1%) and mucosal healing(17.6%).



Martin Gregory, Kimberly N Weaver, Patrick Hoversten et al. Efficacy of Vedolizumab for Refractory Pouchitis of the Ileo-anal Pouch: Results From a Multicenter US Cohort, *Inflammatory Bowel Diseases*, Volume 25, Issue 9, September 2019, Pages 1569–1576.

# Summary of the evidence

| Treatment type | Pouch condition | Response or remission rate/ duration of treatment | Primary outcome | Dose |
|---|---|---|---|---|
| Oral antibiotics (ciprofloxacin or metronidazole)[55] | Acute pouchitis | 96%/ up to 14 days | Response to oral antibiotics determined by resolution of symptoms. | Metronidazole 250 mg three times daily for 7 days. Metronidazole was switched to ciprofloxacin 500 mg twice a day for 7 days if patients failed metronidazole or had its side effects. |
| Oral antibiotics (ciprofloxacin and metronidazole)[60] | Chronic pouchitis | 82%/28 days | Remission defined as a combination of PDAI clinical score of ≤2, endoscopic score of ≤1 and total score of ≤4. | A combination of metronidazole 400 or 500 mg twice daily, and ciprofloxacin 500 mg twice daily for 28 days |
| Oral budesonide[62] | Chronic pouchitis | 75%/8 weeks | Remission defined as a combination of PDAI clinical score of ≤2, endoscopic score of ≤1 and total score of ≤4. | 9 mg/day for 8 weeks |
| Infliximab[69] | Chronic pouchitis | 84%[a]/8 weeks 45%[a]/52 weeks | Complete response defined as cessation of diarrhea and urgency. PR defined as marked clinical improvement but persisting symptoms. | 5 mg/kg at weeks 0, 2, 6, then every 8 weeks |
| Vedolizumab[79] | Chronic pouchitis | 40.7%/3 months 39.1%/12 months | Clinical response defined as any improvement in symptoms including a decrease in bowel movements, pain, or fistula drainage. | 300 mg at weeks 0, 2, 6, then every 4–8 weeks |
| Ustekinumab[82] | Chronic pouchitis | 50%/12.9 months (median) | Clinical response defined as any improvement in physician global assessment and the number of bowel movements per 24 hours. | One 90 mg IV loading dose infusion followed by 90 mg injections every 8 weeks |



Akiyama S, Rai V, Rubin DT. Pouchitis in inflammatory bowel disease: a review of diagnosis, prognosis, and treatment. Intest Res. 2021;19(1):1-11.

# Conclusion

- Pouchitis is highly prevalent among patients with IPAA.
- Risk factors could determine pouchitis phenotype.
- Patients who present with symptoms should be evaluated promptly.
- Diagnosis of Pouchitis is aided by pouchoscopy- PDAI-severity & Chicago-phenotype.
- Pouchitis has several differentials that need to be evaluated.
- Treatment of Pouchitis- Antibiotics, advanced immunosuppressive therapies and biologics.
- Biologics are the mainstay therapy for CARP.