Journal of Pharmaceutical Care
jpc.tums.ac.ir

Pathophysiology, Symptoms and Evolving Treatment for Colonic Diverticular Disease: A Review

Neelottama Kushwaha*, Swatantra K.S. Kushwaha
Krishna Institute of Pharmacy and Sciences, Kanpur, India- 209217.

Received: 2022-05-07, Revised: 2022-07-06, Accepted: 2022-07-13, Published: 2022-09-30

ARTICLE INFO

Article type:
Review article

Keywords:
Diverticulitis;
Inflammatory Bowel Disease;
Colectomy;
Antibiotics

ABSTRACT

The review on diverticulitis disease, is the most prevalent non-cancerous pathology of the colon is diverticular disease and diverticulitis. It has long been thought to be a disease of the elderly, linked to cultural and dietary patterns. Our understanding of this condition, as well as the therapy protocols, has progressed. To give an updated assessment of the epidemiology, pathophysiology, and classification of diverticulitis, as well as to highlight developments in medicinal and surgical management. Treatment of Diverticular Disease represented an important challenge in clinical practice, especially concerning the management of symptomatic uncomplicated diverticular disease (SUDD) and the primary and secondary prevention of acute diverticular disease (AD). Antibiotics and supportive treatments are the mainstays of non-operative treatment, while antibiotics may be skipped in moderate cases. Acute surgery is required for the most severe and refractory cases, whereas elective resections should be considered for chronic, smoldering, or recurrent forms, as well as their associated complications (stricture, fistula, etc.) and patients with factors that are highly predictive of recurrent attacks. Diverticulitis isn't just a condition that affects the elderly. Our growing understanding of diverticulitis as a clinical entity has resulted in a more nuanced approach to its medicinal and surgical therapy. For more than 70% of patients, non-surgical care is still the best option. In the acute, chronic, or elective-prophylactic environment, a segmental colectomy remains the most effective surgical treatment for those with non-relenting, persistent, or recurrent symptoms, as well as those with severe disease and sequelae.

J Pharm Care 2022; 10(3): 136-145.

► **Please cite this paper as:**
Kushwaha N, Kushwaha SKS. Pathophysiology, Symptoms and Evolving Treatment for Colonic Diverticular Disease: A Review. J Pharm Care 2022;10(3): 136-145.

Introduction

The most common anatomical modification in the human colon is diverticula, which are sac-like protrusions in the large bowel wall. Colonic diverticulitis is an inflammatory condition that affects the sigmoid colon the most. The mucosa and submucosa herniate through the muscular layer at places of weakness where blood vessels penetrate the colon wall, forming a pouch-like protrusion. Diverticulosis refers to asymptomatic diverticula, whereas diverticulitis refers to diverticula that are inflamed and can be either complicated (i.e., with abscess, fistula, stricture, or perforation and peritonitis) or uncomplicated (i.e., without abscess, fistula, stricture, or perforation and peritonitis). Due to its relatively high incidence in industrialized places, the western lifestyle has long been regarded as a crucial contributor to the development of diverticulosis (1-3). Diverticulosis is frequently discovered by chance during endoscopy or radiographic exams. Diverticular illness is diagnosed using a combination of clinical symptoms and biomarkers. Cross-sectional imaging, such as ultrasonography, CT, and MRI, are used as biomarkers in the diagnosis of acute diverticulitis (4-5).

Classification of Diverticulosis

As illustrated in figure 1, diverticulosis disease is divided into several categories.

*Corresponding Author: Dr Neelottama Kushwaha
Address: Krishna Institute of Pharmacy and Sciences, Kanpur, India- 209217.
Email: neelottama@gmail.com

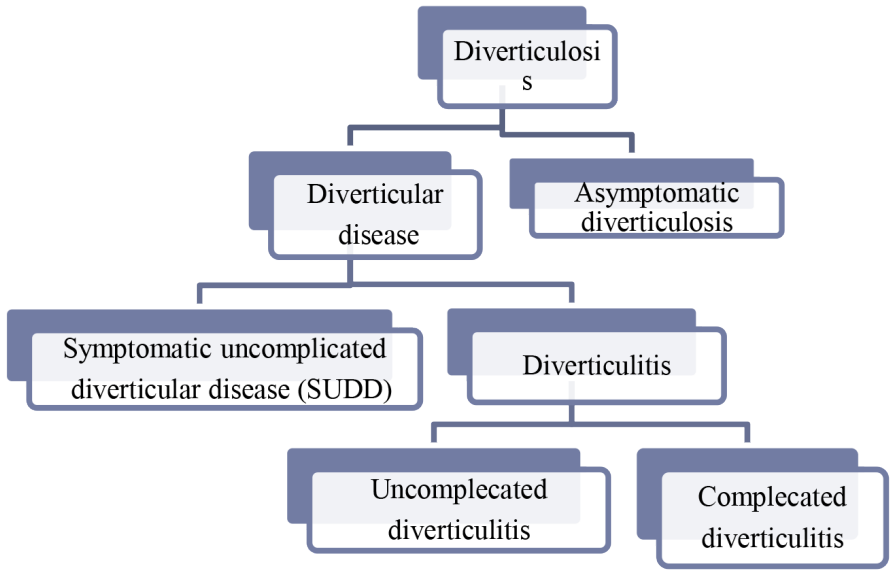

Figure1. Classification of Diverticulosis

Diverticulosis is characterised by the asymptomatic presence of mucosal and submucosal herniations caused by deficiencies in the colon's muscular wall's weaker sections, as depicted in Figure 2.

Diverticular disease encompasses a wide range of conditions, such as diverticular bleeding and diverticulitis (6).

Symptomatic uncomplicated diverticular disease (SUDD) is a kind of diverticular disease characterised by recurring abdominal discomfort but no overt evidence of diverticulitis.

Diverticulitis occurs when the diverticula become acutely irritated, most frequently as a result of faecal debris obstructing the neck and allowing germs to overgrow (7).

Diverticulitis without perforation, abscess, haemorrhage, fistula, peritonitis, or stenosis is known as uncomplicated diverticulitis.

Diverticulitis with complicating characteristics such as perforation, abscess, haemorrhage, fistula, peritonitis, or stenosis; it may be isolated or progress to peritoneal cavity infection; stricture, obstruction, or bleeding may be present; stricture, obstruction, or bleeding may be evident.

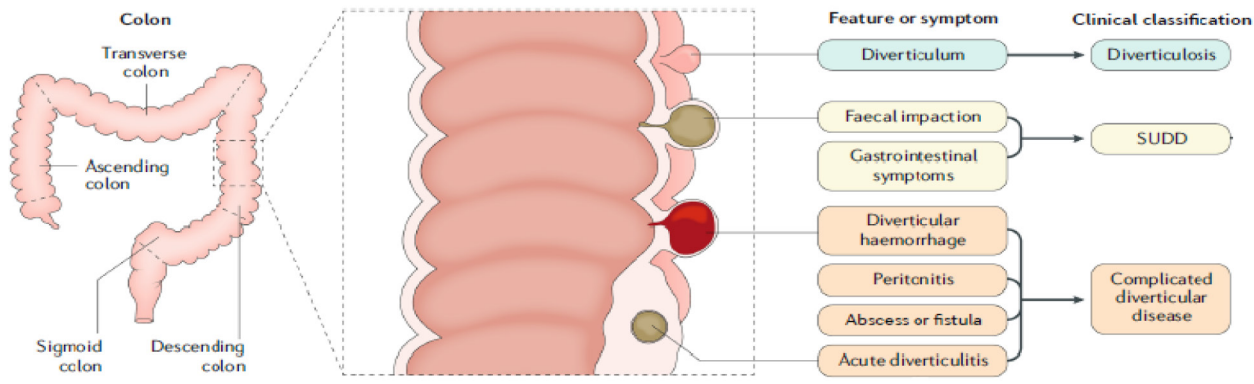

Figure2. Clinical classification of diverticulosis with their symptoms

Table1. Clinical description of Diverticulosis.

Grade	Clinical description	Symptoms
I	Symptomatic uncomplicated disease	Fever, crampy abdominal pain, CT evidence of diverticulitis
II	Recurrent symptomatic disease	Recurrence of above
III	Complicated disease	Haemorrhage, Abscess, Phlegmon, Perforation, Purulent and faecal peritonitis. Stricture, Fistula, Obstruction

Risk factor for developing the diverticular disease

As illustrated in figure 3, there are a variety of risk factors for diverticular disease, including non-modifiable risk variables like age, sex, and heredity, as well as modifiable risk factors like lifestyle (diet and physical activity) and prescription drug use (8-10). The following are some of the most important points:

- Evidence does not support the idea that seeds, nuts, or popcorn promote diverticulitis; rather, the incidence of diverticulitis are rising in tandem with rising obesity rates (11-13).
- Antibiotics are commonly used for outpatient treatment of diverticulitis in the United States, even though little data from randomized trials have cast doubt on their effectiveness.
- Patients with diverticulitis who are treated medically in an outpatient or inpatient environment are less likely to need an emergency colostomy in the future.
- The severity of recurring episodes of diverticulitis is usually the same as the first episode.
- Sigmoid resection with colostomy formation is the safest and most extensively used surgical method for perforated diverticulitis, with better patient outcomes and lower healthcare costs than open surgery (14).

Figure3. Various factors responsible for the development of Diverticulitis

Pathophysiology of Diverticulitis

Diverticulosis' pathogenic etiology is poorly known. Diverticular development, on the other hand, is hypothesized to be caused by three factors: structural abnormalities of the colonic wall increased intraluminal pressure, and a lack of dietary fiber. Based on observation and other research, there is strong evidence that several mechanisms, including pathogenic bacterial overgrowth (due to an impairment in competitive bacterial inhibition) or a decrease in tight junction integrity, lead to the deterioration of mucosal defense as a step toward the development of inflammation in the colon, either alone or in combination (15-16). Diverticulosis is thought to be caused by the following factors: a. in the presence of increased intraluminal pressure, neuromuscular anomalies such as changes in collagen and the enteric nervous system. b. Symptomatic uncomplicated diverticular disease (SUDD) can result from a tachykinin-mediated persistent, low-grade inflammation caused by an altered intestinal flora. Increased nerve sprouting causes visceral hypersensitivity as a result. c. Diverticulitis is thought to be caused by changes in the intestinal microbiota that cause mucosal barrier dysfunction and inflammation, as well as local trauma from a faecalith. d. Asymmetrical vascular thickening leads to diverticular bleeding. Obesity, hypertension, and luminal trauma are all risk factors for vascular injury, which lead to bleeding (17).

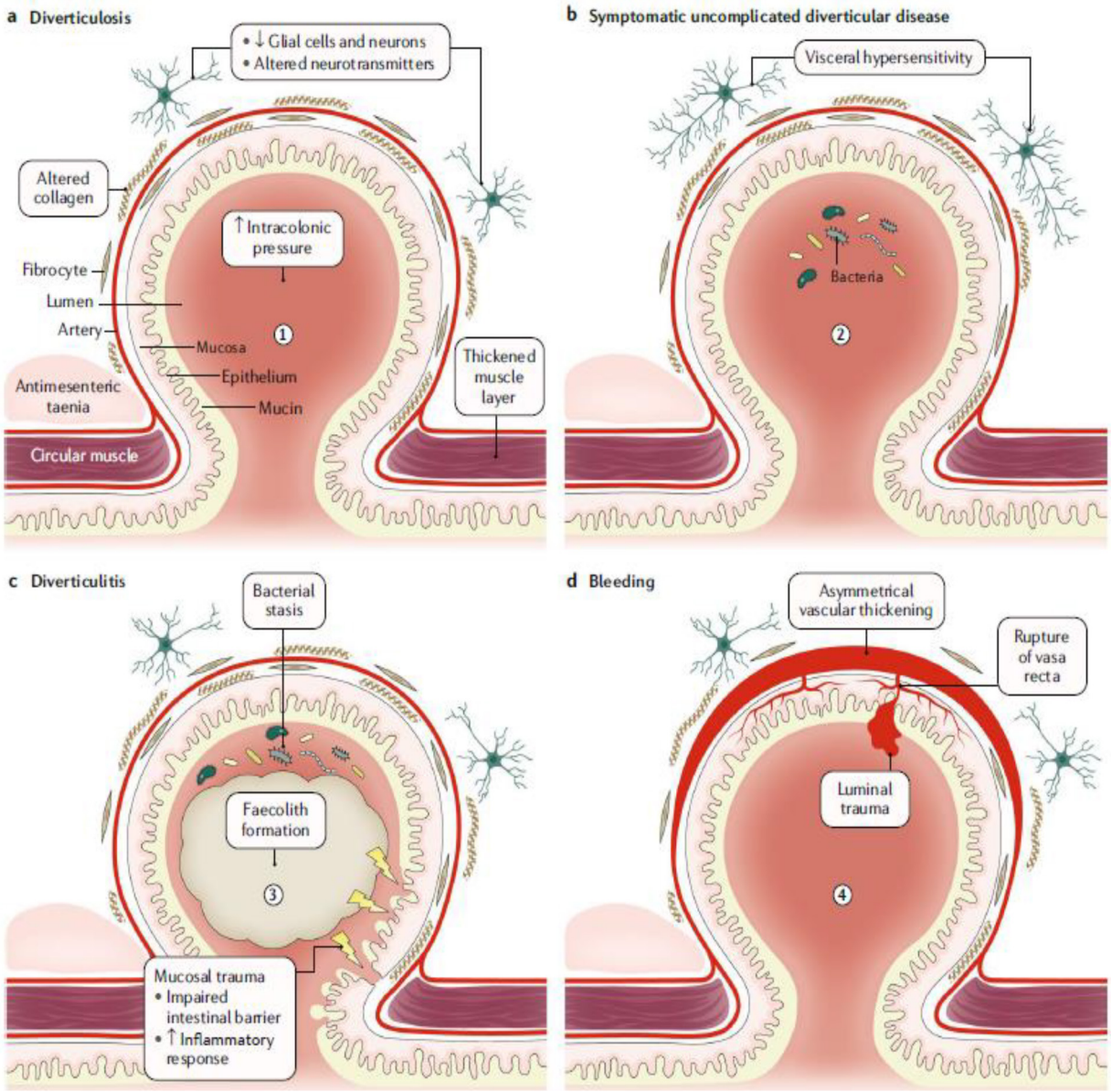

Figure 4. Pathophysiology of Diverticulosis

Diagnosis of Diverticular disease

The clinical presentation includes stomach discomfort, usually in the lower-left quadrant, and fever, as well as changes in laboratory test values, all of which point to an infectious process (18-21). Peritonitis, which is characterized by malaise, decompression abdominal discomfort, and abdominal guarding, can develop if problems arise. It can also be accompanied by lower gastrointestinal bleeding and post-acute diverticulitis stenosis, which necessitates a differential diagnosis with neoplastic illness. Because the clinical presentation of right colon involvement is indistinguishable from acute appendicitis, imaging investigations are required for an accurate diagnosis (Table 2). Hinchey et al. published Hinchey et al. in 1978 to establish a common language among the many professionals (22-23).

Table2. Diagnosis of Diverticulosis

Topic	Diagnosis	Conclusion of recommendation
Clinical assessment	Initial examination Of suspected diverticulitis	The clinical evaluation alone is insufficient for initial diagnosis. Require radiological imaging for diagnostic support
Imaging	Barium CT	No longer indicated: CT is superior Recommended as primary imaging choice (highly sensitive and specific)
Ultrasound	MRI	Use is recommended as an alternative to CT for contraindicated patients or pregnant or fertile women Not widely used
Others	Biochemical tests Colonoscopy	Recommended in routine evaluation but not for diagnosis Colonoscopy after resolution of CT-diagnosed Complicated diverticulitis is recommended in appropriate patients
Management of uncomplicated diverticulitis **Antibiotic therapy**	Non-operative treatment	Outpatient management is safe and recommended in patients without complications, comorbidities, fever and adequate family support Guidelines are yet to implement antibiotic-free strategies but recommend the selective use
Management of complicated diverticulitis	Non-operative treatment Urgent operative Therapy Preferred surgical Procedure	Smaller abscesses (< 5 cm) can be conservatively managed with antibiotics, while larger ones also require percutaneous drainage Recommended in emergency cases of purulent or faecal peritonitis, or when non-operative management fails Both Hartmann procedure and primary anastomosis with or without diversion is indicated. The physician is to determine procedure on a case-by-case basis
Prevention	Vigorous exercise BMI < 30 Avoiding smoking Limiting red meat consumption High fiber diet	Vigorous physical activity is recommended to reduce the risk of diverticulitis Obesity increases the risk of diverticular disease Avoiding smoking reduces the risk of diverticulitis Limited intake of red meat is recommended to reduce the development of diverticular disease A high fiber diet is recommended in combination with healthy lifestyle factors as above

BMI: Body mass index, CT: Computed tomography

Complications of diverticulitis

Perforation: Diverticulitis perforation occurs as a result of severe inflammation of the gut wall layers, which leads to necrosis and loss of intestinal wall integrity. Colonic diverticulitis nearly always causes perforation on the left side (24).

Abscess: Phlegmon and abscess formation can occur as a result of diverticulitis. Phlegmon is identified as an inflammatory mass close to diverticulitis with heterogeneous contrast enhancement, whereas an abscess is often seen as a loculated fluid collection including air. The size of the abscess, as well as its location and the patient's overall medical status, all influence how it is treated (25-28). In abscesses less than 3 cm in diameter, conservative treatment may be considered, however, bigger lesions may require percutaneous drainage or surgical intervention.

Pylephlebitis: Pylephlebitis is a rare consequence of intraabdominal infections, often known as ascending septic thrombophlebitis. Infective suppurative thrombosis of the portal vein or its branches, or both, is the most common symptom. Appendicitis, necrotizing pancreatitis, intestinal perforation, pelvic infection, and inflammatory bowel disease are some of the other underlying causes of pylephlebitis (29).

Bleeding: Up to 5% of patients with colonic diverticulosis experience lower gastrointestinal hemorrhage. Both non-complicated diverticulosis and diverticulitis tend to bleed because the outpouchings, which characterize the diverticula, occur mostly where the vessels pierce the muscular layer of the colonic wall. Consistent bleeding from diverticulitis is a frequent symptom of chronic diverticulitis.

Fistula: After an episode of acute diverticulitis, the rate of fistula formation is around 14%. They arise when the wall integrity of the neighboring anatomic structure is compromised by a diverticular abscess. Fistula formation after diverticulitis may encompass the urinary bladder, ureter, other neighboring intestinal segments, gallbladder, uterus, fallopian tubes, vagina, skin, and the perianal region (30-32). Colovesical, coloenteric, and colouterine fistulas are the three types of diverticulitis fistulas, in order of decreasing frequency.

With open-air in the bladder and thickening of the surrounding bladder wall, a colovesical fistula is present. The presence of stool or air in the urine, as well as several episodes of treatment-resistant lower urinary tract infection, are prevalent symptoms in these patients. Rectal contrast may be useful in tracing the exact path of the fistula tract. The left posterior region of the bladder, which is in close physical proximity to the sigmoid colon, is the most typical location for these fistulas (33). Diverticulitis-related colovesical fistulas differ from those seen in Crohn's disease. The fistula usually forms between the terminal ileum and the right anterior surface of the bladder in Crohn's disease patients. The myometrial abscess might be a sign of a colouterine fistula. If air bubbles are identified within the uterine cavity, CT may reveal them, which is a highly specific result. Colouterine fistula has also been found to be detectable via MRI and sonohysterography (34-36).

Treatments

After two attacks of simple diverticulitis and one attack in patients younger than 40 years, prophylactic colectomy was recommended. The major reasons for doing surgical resection of recurrent diverticulitis are to (1) prevent subsequent attacks and enhance the quality of life, (2) avoid potential complications such as colovesical or colovaginal fistulae, and (3) avoid the possibility of colostomy development during an emergency treatment (37).

A fiber-deficient diet, in addition to encouraging diverticula formation, has been demonstrated to alter the intestinal microbiota, resulting in a drop in beneficial flora and an increase in pathogenic bacteria in other studies. Chronic inflammation and epithelial cell proliferation in the colonic mucosa in and around the Diverticula may result as a result of this (38). If the inflammation is severe and/or prolonged, it can lead to localized necrosis and, eventually, micro- or macro perforation. Bacterial overgrowth, which has been associated with colonic ischemia and diverticula, may be facilitated by the changed microflora and decreased immune tolerance to commensal bacteria.

Recent evidence suggesting the success of new treatment interventions could be explained by these new insights into the biology of diverticular disease. If chronic inflammation and bacterial overgrowth are caused by a change in the colonic microflora, as they are in IBD, it stands to reason that 'normalizing' the flora or using an anti-inflammatory agent (which is effective in IBD) could help treat the symptoms of diverticular disease, prevent the onset of acute diverticulitis, and/or reduce the risk of symptomatic recurrence. This has prompted studies investigating the use of probiotics and 5-aminosalicylic acid (5-ASA) as adjuvant therapies for diverticular disease (39).

Diverticular disease has been linked to abnormalities in motility, which has prompted an investigation into the role of neurotransmitter problems. In resected colonic specimens with diverticulitis, the presence of serotonin-producing cells was shown to be higher. Although it is unclear whether this is a causal link, another study found higher serotonin expression in symptomatic diverticula patients. Another group has proposed that decreased activity of choline acetyltransferase causes hypersensitivity to acetylcholine (40). Additionally, lower nitric oxide activity in the diverticular colon's longitudinal muscle could explain the condition's decreased relaxation and increased muscle spasm (41). While these findings do not prove that the pathogenetic pathways of diverticular disease are mediated by neurotransmitters, they do imply that more research in this area is warranted.

5-aminosalicylic acid (5-ASA): The principal therapy (figure 5) for inducing and maintaining remission of mild-to-moderately severe inflammatory bowel illnesses, particularly ulcerative colitis, is 5-aminosalicylic acid (UC). To minimize inflammation, this therapy acts topically on the

intestinal mucosa rather than systemically (42). Various oral and rectal 5-ASA formulations are available, all of which are effective in treating symptoms and maintaining periods of remission in UC patients while also being well-tolerated. Because of their superior side-effect profiles, newer non-Sulphur-containing medicines are recommended over the classic 5-ASA prodrug, sulphasalazine. Mesalazine (which comes in a variety of formulations with varying release and delivery properties) and the 5-ASA prodrugs olsalazine and balsalazide are among the newer 5-ASA medicines (43).

Rifaximin: It's used to treat a variety of gastrointestinal issues (i.e., acute bacterial diarrhea, portal-systemic encephalopathy). Because of its distinctive pharmacological actions, such as non-systemic absorption, high fecal concentration, and a broad spectrum of antibacterial activity, this medication exerts its gastrointestinal activity (44). Rifaximin also works through a variety of mechanisms: I bacterial growth inhibition; (ii) bacterial infection resistance; (iii) modulatory action of some bacterial species, such as Lactobacillus spp. and Bifidobacterium spp., leading to the so-called eubiotic effect; (iv) bacterial metabolic modulation; (v) anti-inflammatory activity Rifaximin is commonly used in European countries for symptomatic relief in SUDD patients and the prevention of AD for these reasons.

Mesalazine: Combining mesalazine with a broad-spectrum antibiotic may have complementary and possibly synergistic effects, according to some studies. Indeed, in patients with symptomatic, uncomplicated diverticulitis and mild-to-moderate colonic obstruction, the combination of mesalazine and rifaximin was proven to be significantly more beneficial than rifaximin alone in preventing disease recurrence and reducing symptoms (45).

Probiotics in diverticular disease: Probiotics are live microorganisms that, when consumed in large enough quantities can alter the microflora of the host and provide specific health benefits while reducing the risk of antibiotic resistance (figure6). These microbes have been studied for the treatment of gastrointestinal illnesses as well as the avoidance of antibiotic-related gastrointestinal side effects. Bifidobacterium spp., Lactobacillus spp., and certain strains of Escherichia coli, as well as the budding yeast Saccharomyces cerevisiae, are common examples. Inhibition of pathogen adhesion, promotion of immunoglobulin A secretion in Peyer's patches, and improvement of immune system function through modulating the balance of pro- and anti-inflammatory cytokines are all possible effects of probiotic microorganisms. Furthermore, probiotics may disrupt pathogen metabolism (46-47).

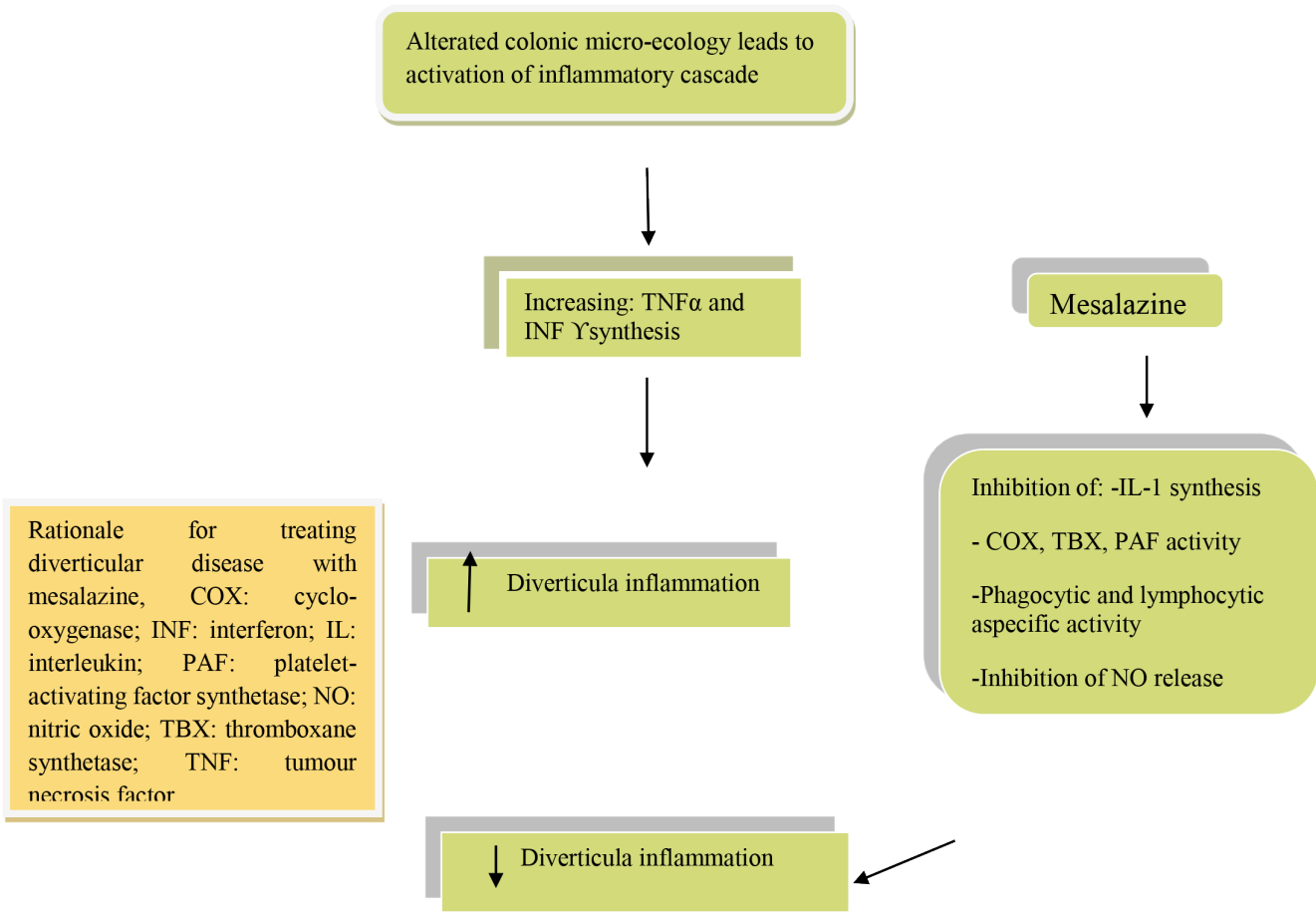

Figure 5. Treatment of diverticulosis with anti-inflammatory agents

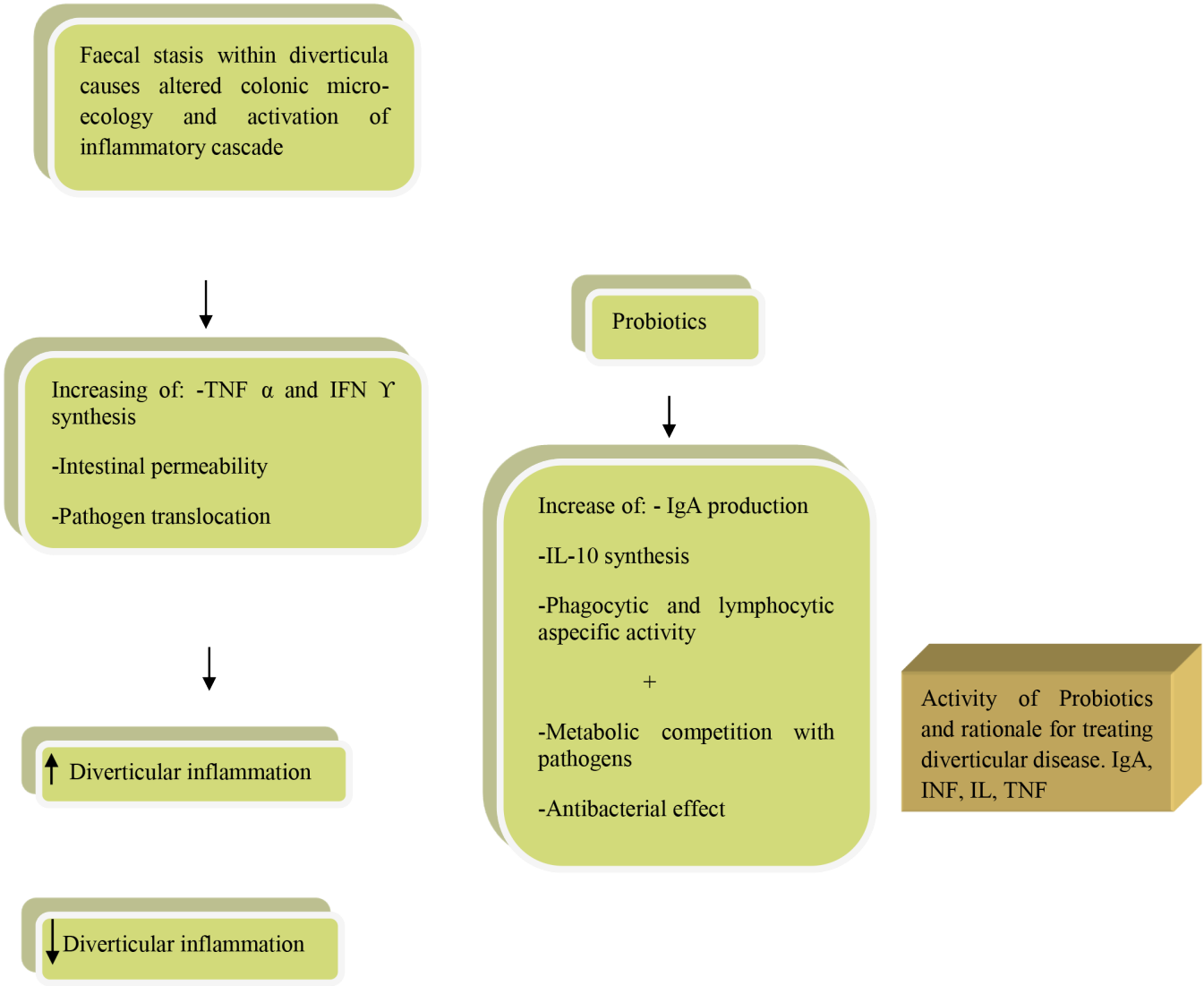

Figure 6. Treatment of diverticulosis with Probiotics

Conclusion

Chronic inflammation and aberrant colonic microbiota are closely linked to the etiology of diverticular disease, according to new research. Diverticular illness, like IBD, appears to be primarily an inflammatory mucosal disease, according to this new pathogenic explanation. However, several issues remain, including: (1) is inflammation caused by the existence of diverticula and/or bacterial overgrowth, and (2) what is the relationship between chronic inflammation and symptoms experienced at different phases of the disease or the risk of recurrence? Alternatively, diverticular illness may cause chronic mucosal inflammation as a result of the high intraluminal pressure. High pressure, rather than the implausible progression from low-grade mucosal inflammation, would be responsible for the advancement from asymptomatic diverticulosis to diverticular perforation in this case. More research is needed to better understand the role of inflammatory alterations in symptom development. Currently, the basis of treatment for diverticular disease is dietary modification combined with antibiotic medication, and antibiotic therapy is expected to remain the mainstay of medical treatment for the diverticular disease in the future. When treating acute, recurring diverticulitis, however, a surgical method is routinely used and is usually suggested after two or more previous occurrences. Surgical intervention is frequently required because one-third of all patients get recurrent diverticulitis within a year of their first episode. This implies that present medical treatment can yet be improved. Because inflammation plays such a crucial part in the pathophysiology of complex diverticular disease, new treatment methods may be necessary. If we consider diverticular illness to be a chronic inflammatory disease, we

need to know how to treat it effectively in all areas. As a result, the outcomes of many ongoing, randomized, double-blind, placebo-controlled phase III studies, including one including patients with painful diverticular disease, will be eagerly anticipated. Widespread use of anti-inflammatory medications cannot be recommended until a definitive solution is available. New research is needed to better understand the classification of diverticular illness as well as new treatment options. The classification and medical management of the diverticular disease are likely to change as this information becomes accessible.

References

1. Harald R. Diverticular Disease- among Myths, Paradigm and Scientific Evidence. Turk J Colorectal Dis. 2020; 30: 210-19.
2. Strate LL, Morris AM. Epidemiology, pathophysiology and treatment of diverticulitis. Gastroenterology. 2019; 156(5): 1282-98.
3. Tursi A, Elisei W. Role of inflammation in the pathogenesis of diverticular disease. Mediators Inflamm. 2019; 2019: 8328490.
4. Zullo A, Gatta L, Vassallo R, et al. Paradigm shift: The Copernican revolution in diverticular disease. Ann Gastroenterol. 2019; 32(6): 541-53.
5. Lambrichts DPV, Bolkenstein HE, et al. Multicenter study of non-surgical management of diverticulitis with abscess formation. Br J Surg. 2019; 106(4): 458-66.
6. Carabotti M, Annibale B. Treatment of diverticular disease: an update on latest evidence and clinical implications. Drugs Context. 2018; 7: 212526.
7. Young-Fadock TM, Solomon CG. Diverticulitis. N Engl J Med. 2018; 379 (17): 1635-42.
8. Rezapour M, Stollman N. Antibiotics in uncomplicated acute diverticulitis: to give or not to give? Inflamm Intest Dis. 2018; 3: 75-79.
9. Slim K, Joris J, Bayer-Berjot L. The end of antibiotics in the management of uncomplicated acute diverticulitis. J Visc Surg. 2019; 156: 373-375.
10. Rottier SJ, van Dijk ST, Unlu C, et al. Complicated disease course in initially computed tomography- proven uncomplicated acute diverticulitis. Surg Infect. 2019; 20(6): 453-9.
11. Bolkenstein HE, Esther CJC, Job VP, et al. Long-term outcome of surgery versus conservative management for recurrent and ongoing complaints after an episode of diverticulitis: 5- year follow-up results of a multicenter randomized controlled trial (DIRECT-trial). Ann Surg. 2019; 269(4): 612-20.
12. Ticinesi A. Diverticular disease: a gut microbiota perspective. J Gastrointestin Liver Dis. 2019; 28(3): 327-37.
13. Hanna MH, Kaiser AM. Update on the management of sigmoid diverticulitis. World J Gastroenterol. 2021; 27(9): 760-81.
14. Hassan AH, Abhilash JP, Samer D, Irshad S. Recurrent Acute Diverticulitis: When to Operate? Inflamm Intest Dis. 2018(3); 3: 91-9.
15. Lopez DE, Brown CVR. Diverticulitis: The most common colon emergency for the acute surgeon. Scandinavian J Surg. 2010; 99(2): 86-9.
16. Tursi A, Papagrigoriadis S. The current and evolving treatment of colonic diverticular disease. Aliment Pharmacol Ther. 2009; 30(6): 532-46.
17. Antonio T, Carmelo S, Lisa LS, et al. Colonic diverticular disease. Nat Rev Dis Primers. 2020; 6(1): 20.
18. Hayley Y, Amy S, Michelle LC, et al. The management of diverticulitis: a review of the Guidelines. Med J Aust. 2020;212(9):434-434.e1.
19. Tonia M, Young-Fadok BM. Diverticulitis. New Engl J Med. 2018; 379(17): 1635-42.
20. Mehmet RO, Erhan A, Ali DK, et al. Diverticulitis: a comprehensive review with usual and unusual complications. Insights Imaging. 2017; 8(1): 19-27.
21. Massimo S, Dieter GW, Yoram K, et al. 2020 Update of the WSES guidelines for the management of acute colonic diverticulitis in the emergency setting. World J Emerg Surg. 2020; 15(32): 2-18.
22. Nicolas DR, Leidy DR, Lizeth G, et al. Review of Hinchey's (diverticulitis) classification and its therapeutic implications. Rev Argent Radiol. 2020; 84: 123-9.
23. Anne FP, Aasma S, Lisa LS. AGA Clinical Practice Update on Medical management of Colonic Diverticulitis: expert review. Gastroenterol.2021; 160(3): 906-11.
24. Mariana MC, Paulina MV. Diverticular Disease of the colon- Recent Knowledge of Physiopathology, Endoscopic Approaches, Clinical and Surgical Treatments provides a comprehensive overview of diverticular disease. Published February 2nd, 2022; ISBN 978-1-83968-579-8.
25. Michael C, Robert SS, Anne FP. Etiopathogenetic Mechanisms in Diverticular Disease of Colon. Cell Mol Gasroenterol Hepatol. 2020; 9(1): 15-32.
26. Amir Q, Itziar EI, Jennifer SL, Nick F, et al. Diagnosis and Management of Acute Left-Sided Colonic Diverticulitis: A Clinical Guideline from the American College of Physicians. Ann Intern Med. 2022;175(3):399-415.
27. Amy ET. Diverticulosis and Diverticulitis. JAMA. 2016; 316(10): 1124.
28. Joel AB, Rafael ACC. Colonic Diverticulosis MSD Manual, Oct 2020.
29. Janson H, Karin H, Sang L, Amy L, et al. The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Treatment of Left-Sided Colonic Diverticulitis. Dis Colon Rectum. 2020; 63(6): 728-47.
30. Thad W, Katherine E, Ruth G. Diagnosis and management of acute diverticulitis. Am Fam Physician. 2013; 87(9): 612-20.
31. Riccardo V, Niccolo F, Matteo B, et al. Role of CT colonography in differentiating sigmoid cancer chronic diverticular disease. Japa J Radio. 2022; 40(1): 48-55.
32. Betul TBS. Computed Tomographic Evaluation of Colonic Diverticulum Complication. Curr Med Imag. 2021; 17(9): 1054-8.
33. Nina C, Carl F, Victor S. Gut wrenching: cases of missed gastrointestinal tumors and their mimics on computed tomography. Emerg Radio. 2021; 28(2): 389-99.
34. Kristopher BP, Olivier M. Diverticulitis of the appendix- case report and literature review. J Surg Case Rep. 2021; 2021(10): 1-3.
35. Morris CR, Harvey IM, Stebbings WSL, et al. Epidemiology of perforated colonic diverticular disease. Postgrad Med J. 2002; 78(925): 654-9.
36. Ahmed FR, Mohamed HK, Khalid A, et al. Small Intestinal Diverticulosis: A rare cause of Intestinal Perforation Revisited. Case Rep Sur. 2020; 2020: 1-6.
37. Elliot CD, Suzanne TC, James HE, et al. Recurrence of Colonic Diverticulitis: Identifying Predictive CT Findings- Retrospective Cohort Study. Radiology. 2017; 285(3): 850-8.

38. VanDijk ST, Daniels L, de Korte N. Quality of life and persistent symptoms after Uncomplicated Acute Diverticulitis. Dis Colon Rectum. 2019; 62(5): 608-14.
39. Jaung R, Nisbet S, Gosselink MP. Antibiotics do not reduce length of Hospital stay for Uncomplicated Diverticulitis in Pragmatic Double-Blind Randomized Trial. Clin Gastroenterol Hepatol. 2021;19(3):503-10.
40. Kim JY, Park SG, Kang HJ. Prospective randomized trial of uncomplicated right-sided colonic diverticulitis: antibiotics versus no antibiotics. Inter J Colorec Dis. 2019; 34(8): 1413-20.
41. Lambrichts DPV, Bolkenstein HE, et al. Multicenter study of non-surgical management of diverticulitis with abscess formation. Brit J Surg. 2019; 106(4): 458-66.
42. Mali J, Mentula P, Leppaniemi A. Determinants of treatment and outcomes of diverticular abscesses. World J Emerg Surg. 2019; 14:31.
43. Seoane UA, Zaffalon D, Pera RM. Routine lower gastrointestinal endoscopy for radiographically confirmed acute diverticulitis. In whom and when is it indicated? Rev Esp Enferm Dig. 2018; 110(9): 571-6.
44. Carabotti M, Annibale B. Treatment of diverticular disease: an update on latest evidence and clinical implications. Drugs in Context. 2018; 7: 212526.
45. Studniarek A, Koehar K, Warner C. Findings on Colonoscopy after Diverticulitis: A Multicenter Review. American Surgeon. 2019; 85(12): 1381-85.
46. Qaseem A, Crandall CJ, Mustafa RA. Screening for Colorectal Cancer in Asymptomatic Average- Risk Adults: A Guidance Statement from the American College of Physicians. Ann Intern Med. 2019; 171(9): 643-54.
47. Mizuki A, Tatemichi M, Nakazawa A. Effects of Burdock tea on recurrence of colonic diverticulitis and diverticular bleeding: An open-labelled randomized clinical trial. Sci Rep. 2019; 9: 6793.