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(Article Review): Crohn's Disease

(Review about Crohn's Disease and Its Relation with Immunity)

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ABSTRACT

Background: *Crohn's disease is a form of inflammatory intestinal illness can effect in in all region of the gastrointestinal tract. Also consider autoimmune disease . it causes has a complex genetic and environmental basis, but its precise cause is still idiopathic (unknown). The disease appears to be origin by an unsuitable intestine's immune system for medications, toxins, infections, or intestinal bacteria in a genetically susceptible host. Crohn's illness is a complex disease with no notable cause. It is think to produce from a aggregation of genetic , immune, and microbial environmental factors. Crohn's sickness is distinguished by presence mucosal ulceration and inflammation that can occur anyplace on the gastrointestinal tract, while most effect usually in the distal small intestine. Characterized by discontinuously transmural inflammation relate with whole thickness of the intestine wall and an inflammatory response related with granulomas and lymphoid aggregative , that can generate many disorder like fistulous , abscesses and fibrotic strictures. Can diagnosed by many methods like Laboratory examination , Histopathological examination Endoscopic examination and X-ray. Until this moment the treatment of CD are yet under experience also can usage medication such as corticosteroids, immunosuppressants, anti-inflammatory drugs and biological medicines to monitoring and decrease the symptoms.* ***Concolusion :*** *Crohn's illness is a chronic inflammatory sickness of the gut, considered an autoimmune disorder that mean , immune system erroneously attack healthful tissue in human body. The cause of Crohn's disease is due to a chronic inflammatory response that specifically impacts T lymphocytes, such as CD4 T lymphocytes. Activation of lymphocytes is the primary function of T cells; for Crohn Disease patients, T lymphocytes mainly produce IL-12, IFN-alpha, TNF-gamma, IL-1, IFN-gamma, IL-2.*

Keyword: Crohn's disease, Transmural inflammation, Fistulas and Neutrophils.

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INTRODUCTION

Crohn's illness is a chronic inflammatory sickness of the gut, considered an autoimmune disorder that mean , immune system erroneously attack healthful tissue in human body (Gordon *et al*.,2023). It is cause extra-intestinal multiple disorder. The inflammation can happen at any location from oral cavity to anal cavity (White race more vulnerable (Wang *et al*, 2013). Crohn's illness predominately found insidious also it can found as an acute toxicant sickness. Diarrhea , abdominal pain, rectal hemorrhage, pyrexia, weight loss and tiredness , it is very

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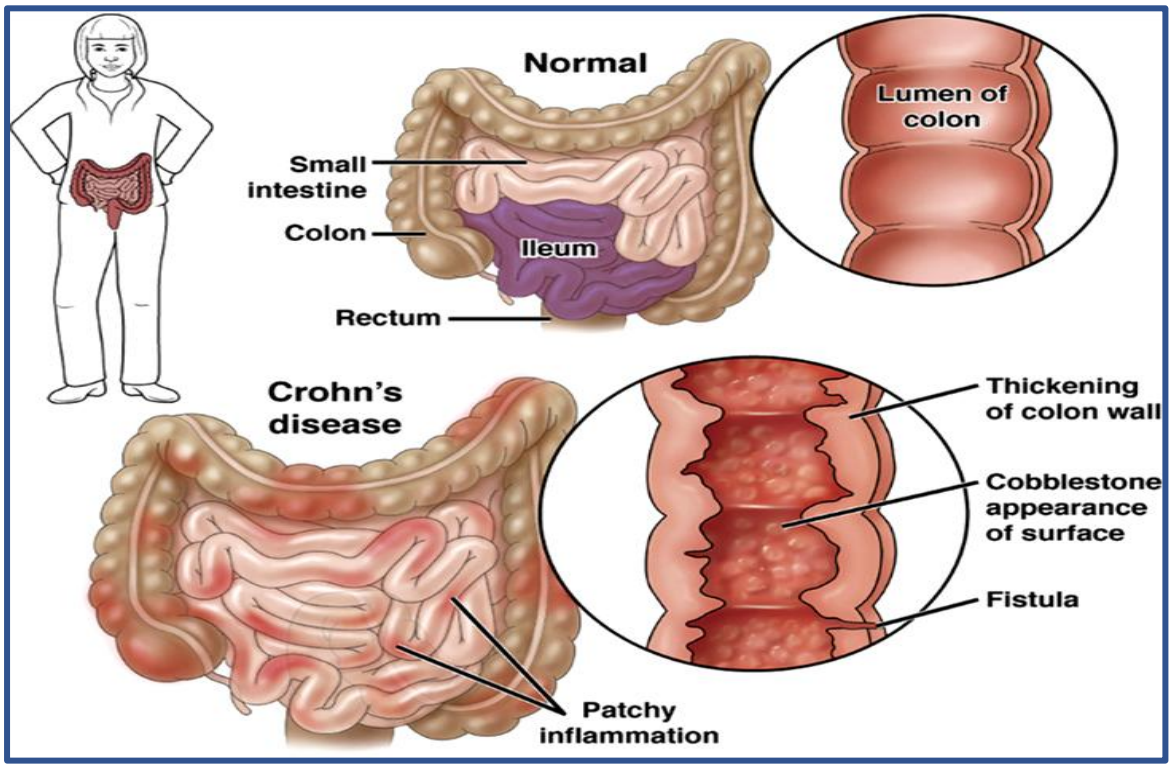
common symptoms (Lichtenstein *et al*.,2018). Crohn's disease is a weaken and irremediable chronic inflammatory intestine illness effecting many individuals about (2.5 million) in the occidental world , increment relative incidence in the developing worldwide (Molodecky *et al*., 2012).

Crohn's disease is distinguished by mucosal ulcer and inflammation, which can happen in any part on the gastrointestinal tract but most usually effect the distal small intestine. Identifying characteristic like interruption transmural inflammation in whole thickness of intestine wall and an inflammatory response related with granulomas and lymphoid aggregate (Abraham and Cho, 2009). Transmural inflammation occurs in intensifying in the gut wall and lumen narrowing . when Crohn illness development lead to blockage or deep sore that progression to fistulous by manner of the sinus tracts penetrating the serosa, microperforation presence (tiny holes or leaks in the intestine wall leading to abscesses or fistulas, adherence and malabsorption. Intestine obstruction is origination initially by oedema formation in the mucosa and related spasm of the gut. Obstruction is sporadic and can be rearward by means of modest measures and anti-inflammatory agents. With illness advance, the obstruction turn into chronic because of stricture formation narrowing luminal of gut and fibrotic scarring (Kornbluth *et al*.,1998).



Crohn illness was first discovered by Dr Burrill B. Crohn and coinmates in 1932. With sore colitis development to chronic idiopathic inflammatory intestine disease. The inflammatory intestine illnesses are chronic intestinal disease a typically classified in to two sub types: Crohn's disease and ulcerative colitis.Ulcer colitis is restricted to the colon, with mucosal inflammation in superficial layer , can pass proximally in a contiguous way that cause sore, strong hemorrhage, toxical mega-colon and fulminant colitis. while Crohn's illness can infected any region in the gastrointestinal tract in a non-contiguous way that contain transmural inflammation that can lead to fibrotic strictures, fistulous and abscesses (Mitsialis *et al*., 2020).

Difference between Ulcerative Colitis and Crohn's Disease

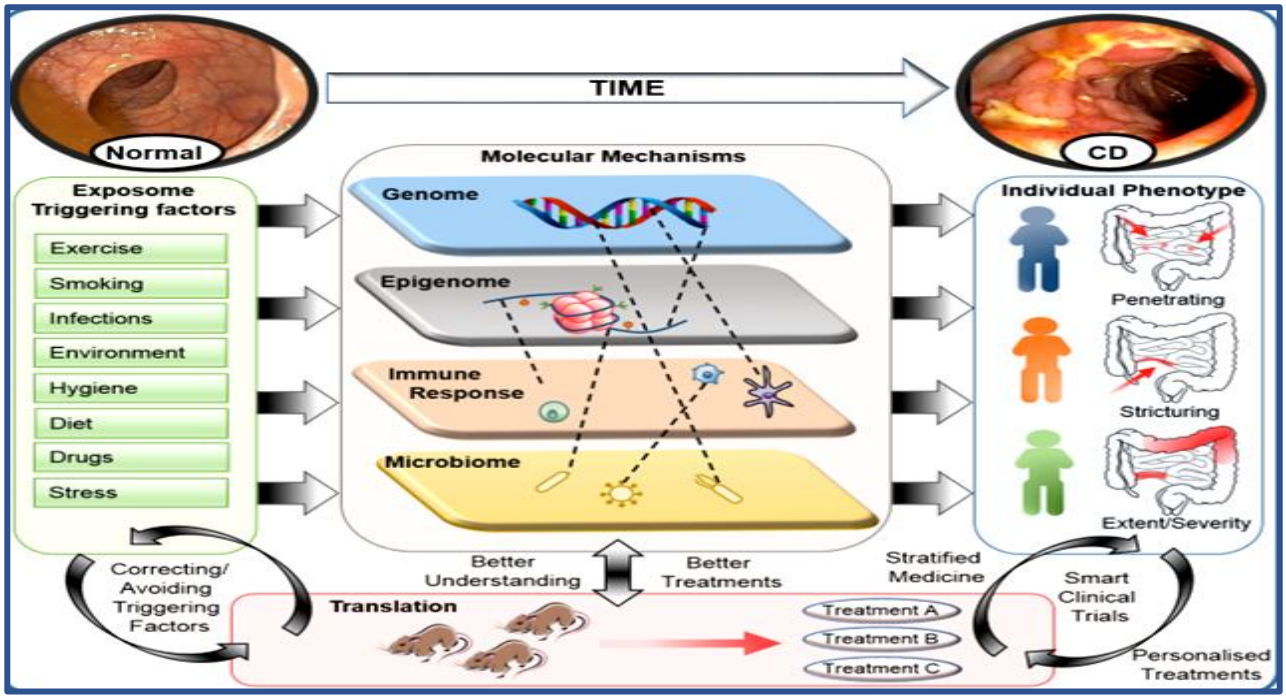
Both diseases affect the bowel in slightly different ways. Ulcerative colitis and Crohn's disease difference are as follows:

Elements	Ulcerative colitis	Crohn's disease
Disease Location	Colon	Entire gastrointestinal tract (anywhere from the mouth to the anus)
Distribution	Complete and continuous inflammation of the colon	Inflammation occurs in between the healthy areas of the GI tract
Extent of damage	Only the innermost lining of the colon will be affected	It affects all the layers of the bowel wall (serosa to the mucosa)
Perianal disease, fistulae and stricture	Absent	Present
Prominent symptoms	Bloody diarrhoea, urgency in defecating, abdominal cramping, weight loss due to severe diarrhoea	Abdominal bloating, fissures with anal bleeding, weight loss due to severe diarrhoea

Pathogenesis

Depend on the interactions between immune system, environmental factors, genes susceptibility and changes in host's microbiome that leading to damage in intestinal mucosa. The function of inflammatory cells in keeping an activist sickness is famed and all of the therapies used to finish the action of inflammatory and pro-inflammatory-cytokines.

Crohn's illness treatment is multidisciplinary that included medical management concentrated on mucosal healing and signs decrease and surgery maintains in treat complications like stricture, perforations, fistulous and abscesses. Surgical repetition is notable to infect over 80% of the operated patients (Assche *et al*.,2004; Rutgeerts *et al*.,2005)



Crohn's illness lead to many complications

1. Strictures: Chronic inflammation that form scar tissue in the intestines, resulting in strictures that narrow the bowel and can cause obstructions (Sutherland *et al*.,2003)

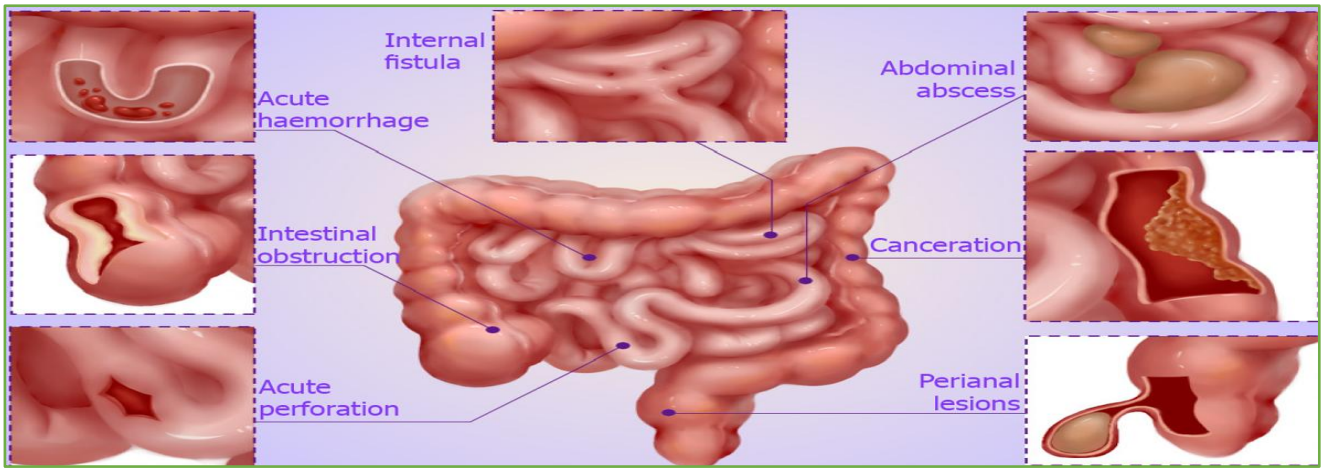
2-Fistulas: abnormal link that can found betwixt various regions of the intestine or betwixt the gut and urinary bladder or vagina. Fistulous can make infections and many complications (Sutherland *et al*.,2008).

2. Abscesses: Inflammation can lead to the formation of pus-filled pockets (abscesses) in the abdomen or near the anal area, which may need drainage and antibiotics (Ghosh *et al*.,2010).

3. Malnutrition: according to inflammation and symptoms such as diarrhea, patients with Crohn's sickness may struggle to absorb nutrients properly, leading to deficiencies (Horne *et al*.,2014).

4-Colon Cancer: Crohn's sickness affect on the colon that increment danger for colo-rectal cancer (Itzkowitz,2004).

5-Extraintestinal Apparent: Crohn's sickness can effect on different parts of the body, that produce many complication (arthritis, skin disorders and eye inflammation (Biancone *et al*.,2015)..



Side effects and complications of crohn's illness in the gut

1. Cramping and abdominal pain : Patients often experience significant abdominal discomfort, which can be intermittent or constant, stools pass so difficult and cramps in the abdomen also incomplete bowel evacuation and hemorrhage in the rectum (Hanauer, 2006).

2. Fistulas and Abscesses: Chronic inflammation, in the form of fistulous (abnormal link between organs) and abscesses (pockets of infection). In fistulae the inflammation range in to intestinal wall, mesentery and surrounding lymph nodes. Reducing in fat may be occur when the mesentery coiled around the intestine surface.The inflammation in serosal layer form adhesions (Plevris *et al.*, 2010).

3. Diarrhea: Frequent and urgent diarrhea is a specialized sign of Crohn's sickness which may be accompanied with mucus or blood (Kappelman *et al*., 2007).

4. Fatigue: fatigue and a general sensation by malaise when effect by Chronic inflammation, often exacerbated by anemia due to nutrient malabsorption (Ananthakrishnan *et al*., 2013)

5. Weight Loss: malabsorption of nutrients and reduced appetite may loss the weight (D'Haens *et al*., 2011).

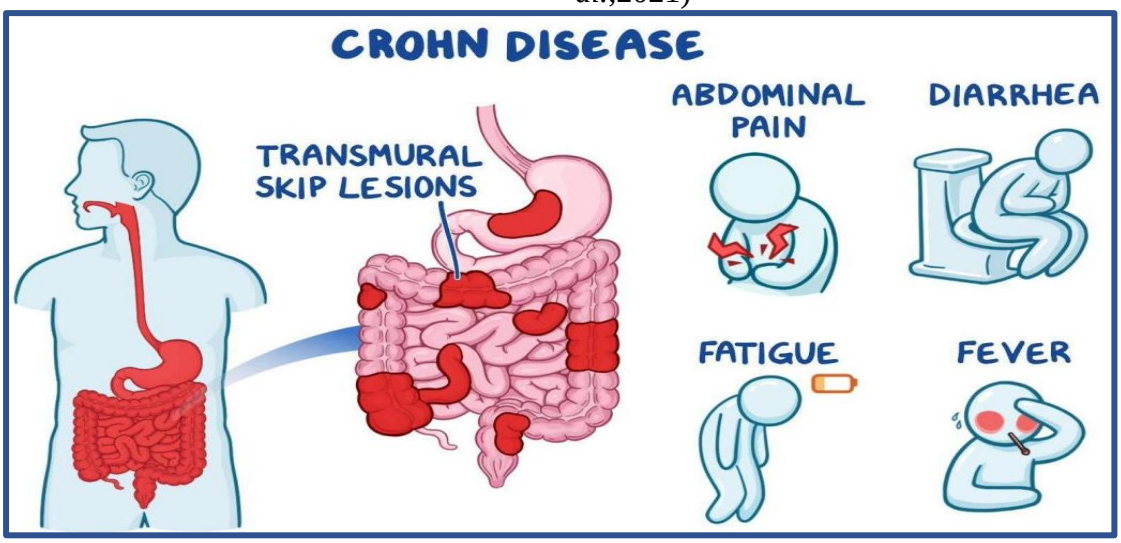
6. Nutritional Deficiencies: Malabsorption can lead to a decrease in minerals and vitamins

(vitamin B12, iron, calciumand vitamin D (Ghosh *et al.*, 2011)..

7. Colon Cancer: permanent inflammation in the colon lead to colorectal cancer (Itzkowitz and Harpaz,2004).

8. Joint Pain and Inflammation: Some patients may experience arthritis or joint pain as an extraintestinal appearance of crohn's sickness.

9-Intestinal obstruction is a commonest complication of Crohn's disease, especially fibrosis-associated intestinal stricture (Ou *et al.*,2021)



Based on the location and characteristics of the inflammation the crohn's disease is classified into several types

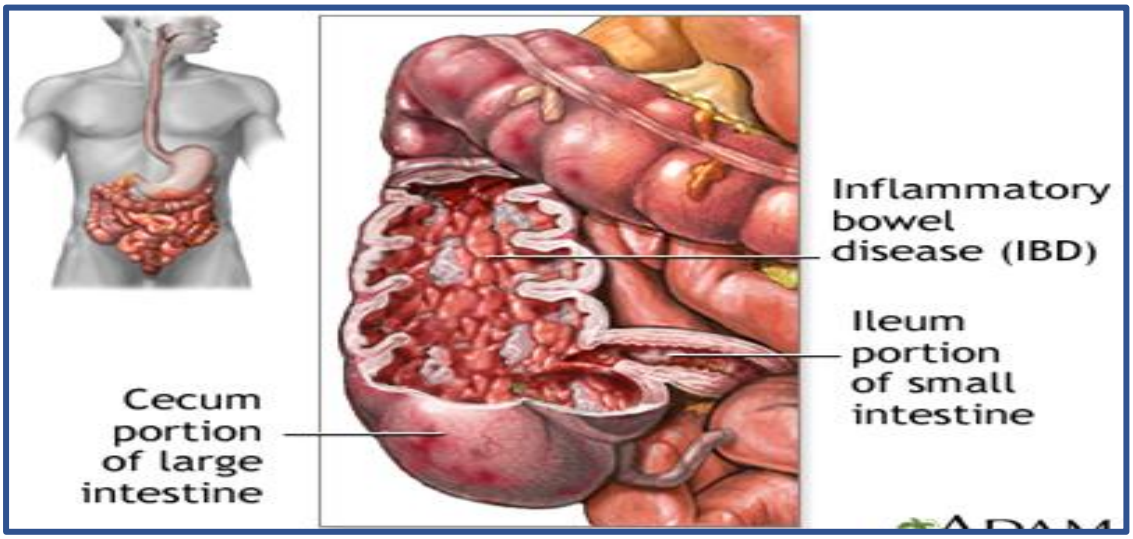
1. **Ileitis:** This type affects on ileum, it is the last region of the small intestine. It is most common forms of crohn's illness (Targan et al., 2007).

2- **Ileocolitis**: This type involves (ileum and the colon region). It can lead to significant symptoms due to involvement of both areas, causes inflammation of the colon (large intestine) and the terminal part of the ileum (small intestine) (Hanauer,2006).

3-**Colitis** (granulomatous): This type primarily effects on colon (large intestine) and can lead to inflammation and ulceration in this area (Kappelman et al., 2007).

4. **Jejunoileitis**: This type primarily effects the jejunum, which is the middle region of the small intestine, and can cause intermittent flare-ups (D'Haens et al.,2011)..

5-**Gastroduodenal**: This less common type effects the stomach and the first part of the small intestine (duodenum) (Aghdassi et al.,2015).



Crohn's Disease and Immunity

Crohn's disease targets healthy bacteria within the gastrointestinal tract, and the cause of Crohn's disease is due to a chronic inflammatory response that specifically impacts T lymphocytes, such as CD4 T lymphocytes. B lymphocytes act primarily to mediate humoral immunity, meaning the B cells do not impact CD development or progression. CD4 T lymphocytes serve as the dominant effector lymphocyte type found in intestinal inflammatory tissue. Activation of lymphocytes is the primary function of T cells; for Crohn Disease patients, T lymphocytes mainly produce IL-12, IFN-alpha, TNF-gamma, IL-1, IFN-gamma, IL-2, and other cytokines during the effector phase of immune response (Bamias et al., 2003). Neutrophils are also important mediators of inflammation; they can stimulate and resolve immune responses. One key action of neutrophils is their phagocytic or pro-inflammatory state as they are clearing and degrading pathogens. Macrophages are critical in switching from a pro-inflammatory state of the tissue to a tissue-repairing state.

In IBD patients, macrophages balance the continuum between damaging the intestinal tissue and healing the intestinal tissue. Dendric cells are considered the primary antigen presenting cells, which regulate the crosstalk between innate and adaptive immunity (with T lymphocytes), while innate lymphoid cells mediate mucosal repair processes and preserve and maintain the integrity of epithelial structures.

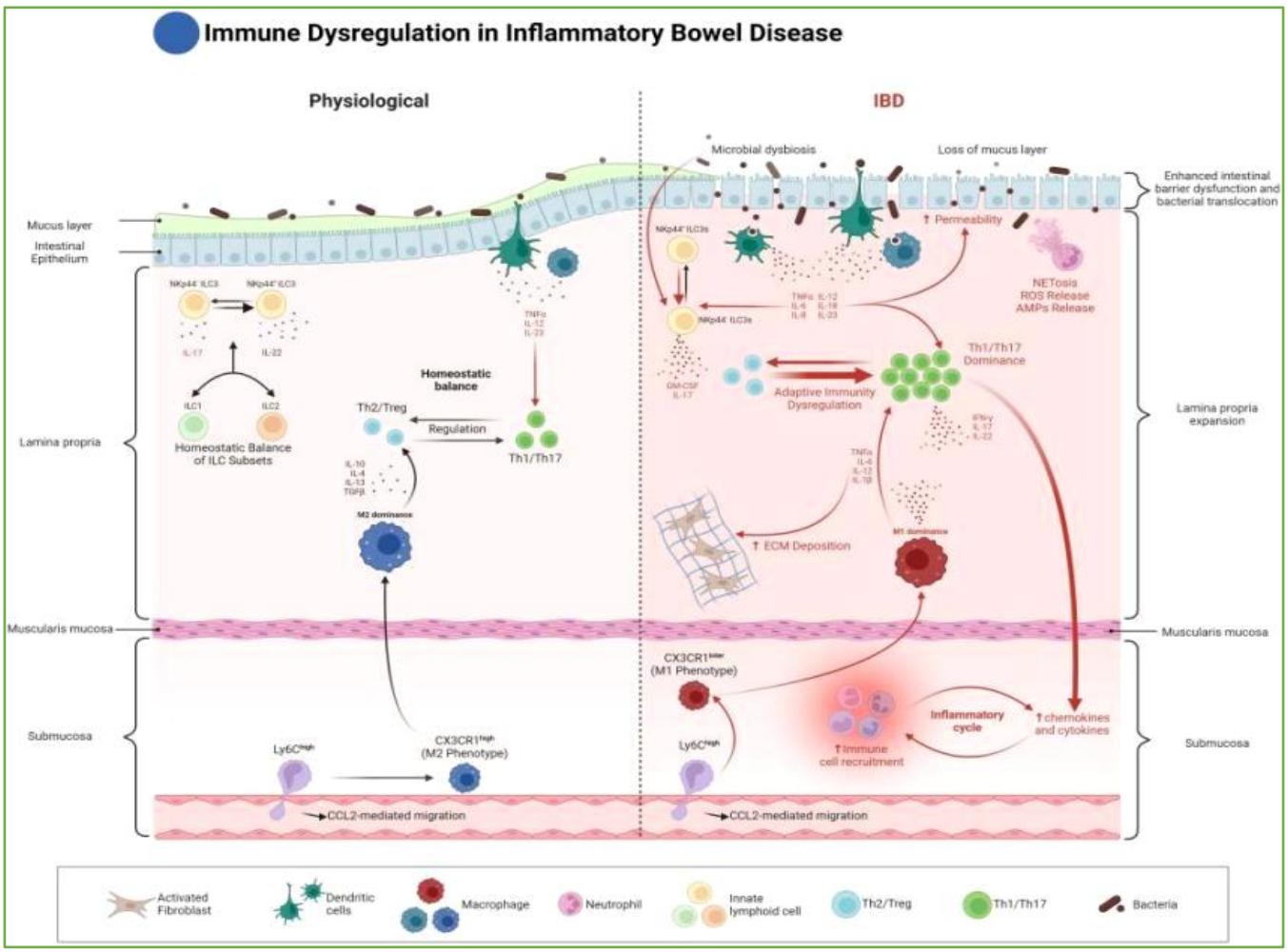
Neutrophils have a double effect in the context of the intestine. Due to their ability to kill microorganisms by way of releasing the Neutrophil Extracellular Traps (NETs) and degranulation, neutrophils are critical to eliminating microorganisms and providing a protective mechanism to the intestinal barrier to protect against invading pathogens (Urban et al., 2009; Chen et al., 2022). Neutrophils respond to the physiologic process of apoptosis (a form of programmed cell death) under normal conditions post-inflammation and are taken up by macrophages (this is called efferocytosis) to restore tissue homeostasis. In inflammatory bowel disease, the metabolic processes of neutrophils and macrophages described above are sub-optimal and cause significant damage in intestinal inflammation and flare-up periods. In ulcerative colitis (UC), neutrophils are the dominated population in the inflammatory infiltrate found in the intestinal tissue, and their activation patterns become prolonged and dysregulated, reduced apoptosis contribute to chronic inflammation (Kucharzik *et al*., 2003; Lin *et al*., 2020).

Neutrophil Extracellular Traps contribute in thrombosis, a common complication in inflammatory bowel disease. The pro-thrombotic activity of NETs has been linked to their ability to trap platelets and promote coagulation, which can lead to an increased risk of thromboembolic events in IBD patients. Studies have shown that NETs can enhance procoagulant activity and support fibrin formation, highlighting their role in the intersection between inflammation and thrombosis in IBD.

This dual role of NETs as both pro-inflammatory and pro-thrombotic mediators underscores the complexity of their function in IBD and suggests that therapeutic strategies targeting NETs could be beneficial not only for controlling inflammation but also for reducing thrombotic risk (Drury *et al* ., 2021)

Dendritic cells (DCs) are pivotal mediators of the immune responses, acting as a bridge between innate and adaptive immunity, and their dysfunction is central to the pathogenesis of Inflammatory Bowel Disease (IBD). They are constantly replenished in gut-associated lymphoid tissues, such as Peyer's patches and isolated lymphoid follicles, emphasizing their essential role in intestinal immunity (De

Schepper et al., 2018). DCs interact with the microbiome to maintain intestinal homeostasis, and disruption of these interactions contribute to chronic inflammation in inflammatory bowel disease (Bernardo et al., 2018, Hedl et al.,2014)



Diagnosis of Crohn's disease

1-Laboratory examination
2-Histopathological examination
3-Endoscopic examination
4-X-ray
5-Computed tomography
6-Ultrasound examination
7-Magnetic resonance imaging (Pasternak *et al*.,2023).

Crohn's disease treatment

Until this moment the treatment of CD are yet under experience also can usage medication to monitoring and decrease the symptoms .

1- Corticosteroids : Used for management due to their anti-inflammatory properties(Lichtenstein *et al*., 2009).

2-Immunosuppressants and Immunomodulators : azathioprine and mercaptopurine, which assist to inhibit the immune response (Biancone *et al*., 2015).

3- Anti-inflammatory drugs: Aminosalicylates (5-ASA): These are anti-inflammatory medications usually utilized in mild to medium of CD (Hanauer *et al.* ,2006).

4-Biological medicines : Targeted therapies like anti-TNF agents (infliximab, adalimumab) and inhibitors of integrin (vedolizumab) (Feagan *et al.*, 2014).

5-Nutritional therapy can make a crucial function in control of symptoms and providing adequate nutrition, especially during flare-ups (Maconi *et al*.,2009).

6-Surgery required to patients when not react to medical therapy or who develop complications such as strictures or fistulas (Marshall *et al*., 2010).

7-Lifestyle Change : often informed the patients to changes dietary , control stress and avoid smoking to help control symptoms (Dyerb et al., 2011).

DISCUSSION

Crohn's illness occurring most frequently between ages 15 and 30 and 40 and 60. Crohn disease is a form of inflammatory bowel disease (IBD) like ulcerative colitis, though Crohn disease often presents more subtly. Crohn disease is an immunologically mediated inflammatory gastrointestinal condition, with pathology involving the entire thickness of the bowel wall (Ghersin et al.,2019). About half of all patients experience an intestinal complication, such as fistulae, phlegmons, strictures, and abscesses,Crohn disease may also have extraintestinal manifestations, which often involve the eyes, skin, liver, and joints. Crohn's illness can infected any region in the gastrointestinal tract in a non-contiguous way that contain transmural inflammation that can lead to fibrotic strictures, fistulous and abscesses (Mitsialis *et al*., 2020).

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CONCOLUSION

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