



The Libyan International Medical University
faculty Of Basic Medical Science

Comprised between ulcerative colitis and crohn's
(Inflammatory bowel disease[IBD])

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Abstract

Inflammatory bowel disease (IBD) is a term for two conditions (Crohn's disease and ulcerative colitis) that are characterized by chronic inflammation of the gastrointestinal tract (GIT). Ulcerative colitis only affects the colon (large intestine). Crohn's disease can affect any part of the digestive system, from the mouth to the anus. Prolonged inflammation results in damage to the GIT, these will lead to many morphological changes. The exact cause of IBD is unknown, but IBD is the result of a defective immune system. A properly functioning immune system attacks foreign organisms, such as viruses and bacteria, to protect the body. In IBD, the immune system responds incorrectly to environmental triggers, which causes inflammation of the gastrointestinal tract. There also appears to be a genetic component—someone with a family history of IBD is more likely to develop this inappropriate immune response. (IBD) is characterized by many symptoms such as recurrent episodes of abdominal pain, bloody diarrhea and weight loss.

Ulcerative colitis is a chronic, relapsing idiopathic inflammation of the rectum and variable lengths of the adjoining colon. Onset usually occurs during the third and fourth decades of life and commonly presents with bloody diarrhea. A diagnosis is made using a combination of endoscopic and histological evidence to distinguish it from other inflammatory colitides, in particular Crohn's disease. The extent of the disease in terms of the amount of colon involved and the severity of the attacks both vary, and treatment is tailored depending on both these factors. Ulcerative colitis predisposes individuals to colorectal cancer, and surveillance is required for most sufferers. Acute severe colitis is the most serious manifestation of the disease and initially requires hospital treatment with intravenous steroids. Emergency surgery in the form of a subtotal colectomy and end ileostomy is vital in those not responding to medical treatment to avoid colonic perforation. There are two major elective procedures: restorative proctocolectomy (ileoanal pouch procedure) and panproctocolectomy. Laparoscopic surgery is now an option for both emergency and elective procedures.

Crohn's disease is a disorder mediated by T lymphocytes which arises in genetically susceptible individuals as a result of a breakdown in the regulatory constraints on mucosal immune responses to enteric bacteria. Regulation of immune reactivity to enteric antigens has improved understanding of the pathophysiological mechanisms of Crohn's disease, and has expanded therapeutic options for patients with this disorder. Disease heterogeneity is probable, with various underlying defects associated with a similar pathophysiological outcome. Although most conventional drug treatments are directed at modification of host response, therapeutic manipulation of the enteric flora is becoming a realistic option.

Crohn's disease is driven by the production of interleukin-12 (IL-12) and interferon- γ (IFN- γ), whereas ulcerative colitis is probably driven by the production of IL-13. A second area of progress is in the identification of specific genetic abnormalities that are responsible for disease. The most important finding is the identification of mutations in the gene that encodes NOD2 (nucleotide-binding oligomerization domain 2) protein in a subgroup of patients with Crohn's disease

Crohns disease	Ulcerative colitis
Can affect any part of the GI tract (from the mouth to the anus)—Most often it affects the portion of the small intestine before the large intestine/colon.	Occurs in the large intestine (colon) and the rectum
Damaged areas appear in patches that are next to areas of healthy tissue	Damaged areas are continuous (not patchy) – usually starting at the rectum and spreading further into the colon
Inflammation may reach through the multiple layers of the walls of the GI tract	Inflammation is present only in the innermost layer of the lining of the colon

Introduction

Inflammatory bowel disease (IBD) is a term mainly used to describe two conditions: ulcerative colitis and Crohn's disease.

Ulcerative colitis and Crohn's disease are long-term conditions that involve inflammation of the gut

Ulcerative colitis only affects the colon (large intestine). Crohn's disease can affect any part of the digestive system, from the mouth to the anus.

Both ulcerative colitis and Crohn's disease usually involve severe diarrhea, abdominal pain, fatigue, bloody stool and weight loss. Ulcerative colitis and Crohn's disease have some complications in common and others that are specific to each condition. Complications found in both conditions may include: Blood clots, Primary sclerosing cholangitis, Skin, eye and joint inflammation, and Colon cancer

The pathogenesis and immune mechanism of IBD: The inflammatory bowel diseases (IBDs) are characterized by intestinal inflammation of unknown etiology. Two distinct disorders, Crohn's disease and ulcerative colitis, have been identified. Three theories of IBD etiology are currently under consideration: 1) reaction to a persistent intestinal infection, 2) existence of a defective mucosal barrier to luminal antigens, and 3) a dysregulated host immune response to ubiquitous antigens. In each of these theories, either pathogenic or resident luminal bacteria constantly stimulate the mucosal and systemic immune systems to perpetuate the inflammatory cascade. Chronicity of inflammation results from an interaction of the persistent stimulus of microbial antigens with genetically determined host susceptibility factors that determine the individual's immune response or mucosal barrier function. The pathogenesis of IBD involves a series of steps, beginning with the breach of the intestinal mucosal barrier by infectious agents or toxins. The defective barrier exposes lamina propria immune cells to the continual presence of resident luminal bacteria, bacterial products, or dietary antigens, which perpetuates the inflammatory cascade. Many immunoregulatory abnormalities are noted in IBD, including the ratio of proinflammatory to immunosuppressive cytokines, selective activation of T lymphocyte subsets, and abnormalities in epithelial antigen presentation. When activated during the initial inflammatory process, macrophages and T lymphocytes secrete a host of cytokines, which recruit other inflammatory cell types, thereby continuing the process. Tissue injury is the net result of the soluble products of the activated inflammatory cells. Knowledge of the pathogenesis in IBD suggests that the ultimate goals of therapy should be to block the pro-inflammatory mediators toward the proximal, rather than the distal, end of the cascade, to decrease the constant antigenic drive of luminal bacteria

Aim of study

The aim of this study to know the inflammatory bowel disease and its pathogenesis, type, morphological changes, and how to reduce its pain

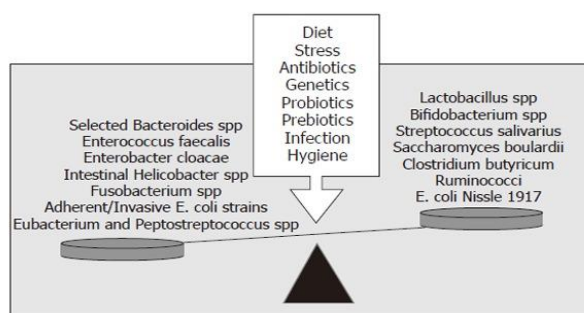
Discussion

At birth, the gastrointestinal tract is a sterile environment. Initial exposure of the gut to microbes occurs during the birthing process from the maternal fecal and vaginal flora. Within a few months after birth, a relatively stable microbial population is established. This abundant, diverse and dynamic intestinal microflora normally lives in a complex, symbiotic relationship with the eukaryotic cells of the mucosa. About 100 trillion bacterial cells benefit from the constant nutrient flow, stable temperature and niches for various metabolic requirements provided by the intestinal environment. Likewise, the host benefits from the ability of the intestinal microflora to synthesize vitamin K, exert trophic effects on intestinal epithelial cells, salvage energy from unabsorbed food by producing short-chain fatty acids, inhibit the growth of pathogens, sustain intestinal barrier integrity and maintain mucosal immune homeostasis. Studies from germ-free animals reveal that the absence of resident intestinal microflora results in significant alterations in intestinal structure and function, including slender villi, shallow crypts, low leukocyte count, a decrease in the number and density of Peyer's patches and decreased stimulation of migrating motor complexes.

In their co-evolution with bacteria, vertebrates develop pattern-recognition receptors, which are activated by specific molecular patterns unique to bacteria, fungi and viruses that are absent in eukaryotes (lipopolysaccharides, peptidoglycan, ssRNA, muramyl dipeptide, flagellins, etc). These include the Toll-like receptors (TLRs) and nucleotide oligomerization domains (NODs). TLRs and NODs are critical for the initiation of innate immune

defense responses. Activation of their signaling cascades usually results in the production of pro-inflammatory cytokines. TLR signaling also provides a link between innate and adaptive immunity, as TLR signaling results in the maturation of dendritic cells, which activate adaptive immune responses [6]. Although stimulation of these receptors in most parts of the immune system results in production of inflammatory cytokines, these ligands are not only tolerated by the gut mucosal immune system, but also essential for adaptation to intestinal bacteria and maintenance of homeostasis. The tolerance to the intestinal microflora is not completely understood, but several aspects of commensal physiology have been defined which contribute to their inability to activate the immune system. Some commensal bacteria can modify TLR ligands, resulting in a hypoactive immune response. For example, the endotoxic portion of LPS is pentacyclated in many *Bacteroides* species, and has minimal toxicity. An important feature of commensal bacteria is their inability to penetrate the intestinal epithelial barrier. If some of these organisms do penetrate, they are usually rapidly phagocytosed by the innate mucosal immune system. Indeed, in a healthy host, the systemic immune system appears to be ignorant of the intestinal microflora. Maintaining tolerance to these intestinal bacteria is a remarkable accomplishment achieved by the mucosal immune system, and disturbances in this bacterial-epithelial homeostasis result in considerable deleterious effects on the host.

Role of the commensal flora in IBD Although many studies have investigated the possibility of a single infectious agent causing Crohn's disease and ulcerative colitis, also called chronic inflammatory bowel disease (IBD), none has yet been discovered. The intestinal bacteria are now believed to be involved in the initiation and perpetuation of IBD. The prevailing theory explaining the development of IBD is that the adaptive immune system is hyper-responsive to the commensal intestinal microflora in genetically susceptible individuals. This hypothesis is supported by several observations: most inflammation occurs in areas with the highest density of intestinal bacteria, broad spectrum antibiotics improve chronic intestinal inflammation, and surgical diversion of the fecal stream can prevent recurrence of Crohn's disease. Most importantly, despite differences in the pathogenesis of chronic intestinal inflammation, a consistent feature of many animal models of IBD (such as IL-10 knockout mice and HLA-B27 transgenic rats) is the failure to develop chronic intestinal inflammation when these animals are raised in germ-free conditions. Dysbiosis is also observed in IBD patients. Adherent and intramucosal bacteria, particularly *Bacteroides* spp, *Escherichia coli* (*E. coli*) and *Enterobacterium* spp are more abundant in patients with Crohn's disease (CD) than in controls. Bacterial overgrowth and dysbiosis are also associated with the development of chronic pouchitis, the inflammation of the ileal reservoir created after ileo-anal anastomosis following colectomy in ulcerative colitis (UC) patients. In addition, several selected commensal bacterial species can induce and perpetuate colitis in genetically susceptible rodent models of chronic intestinal inflammation.



Microbial balance and dysbiosis. The

pathogenic immune responses present in IBD are triggered by the presence of luminal bacteria. The balance of beneficial vs aggressive intestinal microbes is responsible for either mucosal homeostasis or chronic inflammation. A number of environmental and genetic factors influence the balance of beneficial vs aggressive microbes. Adapted from

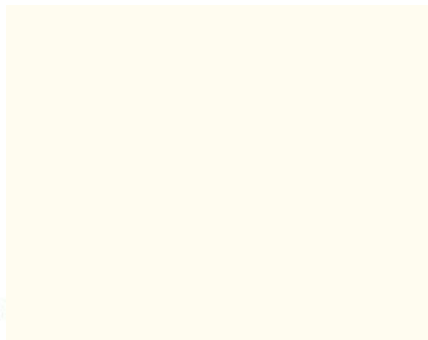
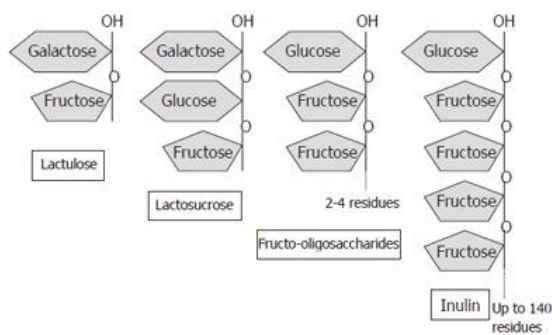
Other immune dysfunctions in IBD include aberrant secretion of pro-inflammatory cytokines and chemokines by intestinal epithelial cells and mucosal immune cells, altered TLR4 signaling, defective antigen presenting cell function and lack of T-cell apoptosis. It is now clear that ignorance of the systemic immune system to commensal intestinal microflora is lost in IBD patients, as shown by enhanced and persistent cell-mediated and humoral immune responses to these bacteria.

At least 7 genetic loci conferring susceptibility to CD, ulcerative colitis (UC) or both, have been identified. Interestingly, such susceptibility genes associated with CD involve polymorphisms of the NOD2 gene (the pattern recognition receptor for muramyl dipeptide) which can result in hampered innate immune functions by impairment of TLR function, defective clearance of invasive bacteria by macrophages, and decreased production of defensins.

The recognition of the compelling association between intestinal microflora and the development of IBD has led to an abundance of studies investigating the therapeutic potential of altering luminal bacteria using probiotics and/or prebiotics.

Probiotics, prebiotics and synbiotics: Probiotics are defined as living organisms in food and dietary supplements which, upon ingestion, improve the health of the host beyond their inherent basic nutrition. Probiotics are typically lactic acid bacteria selected from the gut flora, and are able to survive stomach acid and bile, maintain viability throughout extended periods of storage and are safe for human consumption. Other species have also shown some beneficial effects, such as *E. coli* Nissle 1917 and *Saccharomyces boulardii*. Probiotic bacteria have verifiable beneficial properties, including the ability to improve epithelial barrier function, modulate the mucosal immune system, and alter the intestinal flora.

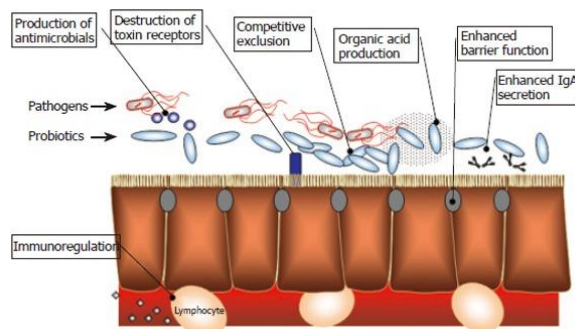
Prebiotics are non-digestible dietary carbohydrates, e.g., lactosucrose, fructo- and galacto-oligosaccharides, inulin, psyllium, bran, germinated barley, which stimulate the growth and metabolism of endogenous enteric protective bacteria upon consumption. Beneficial effects of prebiotics are also associated with changes in colonic short-chain fatty acids (SCFA) due to fermentation by colonic bacteria. Synbiotics are combinations of probiotics and prebiotics, and are also an emerging therapeutic modality. Restoration of normal microflora using probiotics, prebiotics or synbiotics has been investigated in numerous gastrointestinal and other disease states, including infectious diarrhea, *H. pylori* infection, irritable bowel syndrome, colorectal cancer, lactase deficiency, pancreatitis, atopy, and IBD.



Basic structures of various prebiotic substances. Structurally, prebiotics are a mixture of polymers and oligomers comprising branching chains of fructose units.

Protective mechanisms of probiotics by ameliorating chronic intestinal inflammation: Probiotic bacteria have beneficial effects on the intestinal epithelia both directly and indirectly, including enhanced barrier function, modulation of the mucosal immune system, production of antimicrobials, and alteration of the intestinal microflora.

Mechanisms of probiotic activity



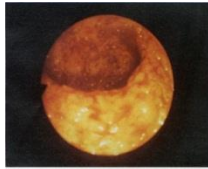
Alteration of the mucosal immune system. The presence of probiotics has been shown to result in several modifications in the mucosal immune response, including augmented antibody production, increased phagocyte and natural killer cell activity, modulation of the nuclear factor kappa-B (NFκB) pathway, and induction of T cell apoptosis. Generally, probiotics increase the production of intestinal anti-inflammatory cytokines (such as IL-10 and TGF-β), while reducing the production of pro-inflammatory cytokines (e.g., TNF-α, interferon-γ, IL-8). Several probiotic bacteria, including *B. breve*, *Streptococcus thermophilus*, *B. bifidum* and *Ruminococcus gnavus* have been shown to secrete metabolites that reduce LPS-induced TNF-α secretion. *L. reuteri* reduces TNF-α and *Salmonella typhimurium* induces IL-8 secretion *in vitro*, by inhibiting nuclear translocation of NFκB and preventing the degradation of IκB. Administration of the probiotic cocktail VSL#3 (consisting of *L. acidophilus*, *L. bulgaricus*, *L. casei*, *L. plantarum*, *B. breve*, *B. infantis*, *B. longum*, *S. thermophilus*) to IL-10 deficient mice results in colitis reduction and a concomitant reduction in mucosal secretion of TNF-α and interferon-γ. *E. coli* Nissle 1917 is able to down-regulate the expansion of newly recruited T-cells into the mucosa and limit chronic intestinal inflammation. In SAMP1/Yit mice, *Lactobacillus casei* strain Shirota inhibits IL-6 production in LPS-stimulated large intestinal lamina propria mononuclear cells and down-regulates nuclear translocation of NFκB. Patients with a recent ileo-anal pouch anastomosis who responded to probiotic therapy have reduced mRNA levels of IL-1β, IL-8 and IFN-γ, and fewer polymorphonuclear cells compared with patients who receive placebo. Probiotic treatment has also been shown to reduce IFN-γ and IL1-α expression and decrease inducible-nitric oxide synthase and gelatinase activities in pouch biopsy samples from patients with pouchitis. In mucosal explants of ileal specimens from patients with Crohn's disease, probiotics reduced TNF-α release and the number of CD4 cells. In addition to live probiotics, components of probiotic bacteria can also exert effects on the mucosal immune system. For example, genomic DNA isolated from VSL#3 inhibits TNF-α-induced IL-8 secretion, mitogen-activated protein kinase activation and NFκB activation in HT-29 cells.

Improved barrier function. Various probiotic bacteria can enhance intestinal epithelial barrier function. For example, oral administration of VSL#3 results in normalization of impaired colonic barrier function and restoration of intestinal epithelial integrity in IL-10 deficient mice and enhancement of epithelial resistance in T-84 cells. Barrier function was enhanced not only by live bacteria, but also by a proteinaceous secreted product of VSL#3. Several strains of lactobacilli are also capable of up-regulating intestinal MUC3 mRNA expression, thereby improving barrier function by increasing the mucus layer. *Lactobacillus GG* (*L. GG*) improves barrier function by inhibiting apoptosis of intestinal epithelial cells. *thermophilus* and *L. acidophilus* have been shown to enhance phosphorylation of actinin and occludin in the tight junction, thereby preventing the invasion of enteroinvasive *E. coli* into human intestinal epithelial cells.

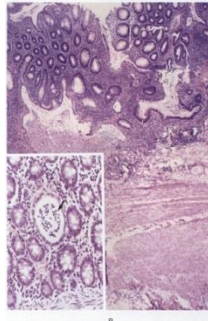
Alteration of the intestinal flora. Probiotics suppress the growth and invasion of pathogens in several ways. They competitively exclude pathogenic bacteria by occupying the limited physical space in the mucus layer and on epithelial cells. They also engage pattern-recognition receptors and consume substrate otherwise available to other (pathogenic) microbes. In addition, probiotics render their microenvironment inauspicious for pathogens by secreting antimicrobial substances such as hydrogen peroxide, organic acids, and bacteriocins. For example, both *in vitro* and *in vivo* experiments demonstrate that *B. infantis* suppresses the growth of *Bacteroides vulgatus*. VSL#3 has been shown to inhibit *Salmonella dublin* invasion into T-84 cells. Patients with pouchitis treated with VSL#3 have been demonstrated to have increased bacterial diversity in the pouch, and decreased fungal diversity.

Probiotics may also alter the intestinal microflora by changing the fatty acid profile in the colon. VSL#3 probiotic strains are also capable of converting linoleic acid to conjugated linoleic acid, a fatty acid with anti-inflammatory and anti-carcinogenic properties.

The morphological changes in IBD : The inflammatory process in ulcerative colitis is confined to the mucosa and superficial submucosa of the large bowel. Although in rare cases ulcerative colitis may spare the rectum,⁸⁶ the process typically extends in a continuous fashion proximally from the rectum. The length of proximal extension varies. The histopathologic features, although nonspecific, are notable for the formation of microabscesses within crypts and the depletion of mucin from goblet cells; the lamina propria is densely infiltrated by neutrophils and lymphocytes as well as other constituents of acute and chronic inflammation. The absence of inflammation in the deeper layers of the bowel is characteristic. As the intensity of the inflammatory infiltrate and the production of inflammatory mediators increase, extensive superficial mucosal ulceration develops. On a macroscopic level, as seen directly through the sigmoidoscope, mucosal granularity and friability are replaced by broad areas of superficial ulceration covered with a mucopurulent exudate. Pseudopolyps are often present. The fundamental histopathologic and endoscopic features of ulcerative colitis



A

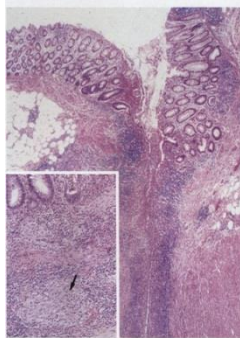


B

Crohn's disease is much more protean in its clinical manifestations than ulcerative colitis, reflecting a seemingly more complex inflammatory process. Active disease is characterized by an infiltrate in which macrophages and lymphocytes predominate. Although the infiltrate present during acute and chronic inflammation in the mucosa can resemble that found in ulcerative colitis, extension of the infiltrate into the deeper layers of the bowel wall is a distinguishing feature; transmural involvement by the inflammatory process is common. Ulceration may occur; early in the course aphthoid-like ulcers can be seen overlying dense areas of lymphoid tissue. In contrast to the superficial ulceration seen in ulcerative colitis, deep linear ulcers, either fissure-like or serpiginous, are present in advanced disease. Extensive linear ulceration with relative preservation of intervening tissue may lead the mucosa to assume a cobblestone appearance. The aggregation of macrophages leads to the development of noncaseating granulomata in approximately 50 percent of patients. In addition, collagen deposition is common and may contribute to the formation of strictures. The salient histopathologic features of Crohn's disease



A



B

Morphological and functional changes were examined in the upper jejunum and terminal ileum of 18 patients suffering from Crohn's disease. Intestinal permeability, biochemical determination of enzymatic activities, and morphologic evaluation of the severity of the lesions were evaluated. Ulcerative colitis and irritable bowel syndrome patients served as controls. We found abnormal lactulose-mannitol tests in all patients with active Crohn's disease. Permeability changes correlated with increased crypt cell proliferation, as indicated by thymidine kinase activity. A significant reduction in brush border enzyme activities was seen in the terminal ileum, but no significant change was observed in the unaffected upper jejunum. The number of mast cells was increased in the diseased ileum. We conclude that the site of inflammation and the healing capacity of the epithelium are important in determining functional and biochemical abnormalities in active Crohn's disease. Changes may be dependent on the type and number of immune cells involved in the inflammatory process

Inflammatory bowel disease (IBD) have become important health problems. Medical therapy for IBD has advanced dramatically in the last decade with the introduction of targeted biologic therapies, the optimization of older therapies, including drugs such as immunomodulators and 5-aminosalicylic acid (5-ASA), and a better understanding of the mucosal immune system and the genetics involved in the pathogenesis of IBD. The goal of IBD therapy is to induce and maintain remission. The current treatment paradigm involves a step-up approach, moving to aggressive, powerful therapies only when milder therapies with fewer potential side effects fail or when patients declare themselves to have an aggressive disease. This review focuses on the current treatments for inflammatory bowel disease

Summarises of clinical pharmacological aspects of thiopurines in the treatment of chronic inflammatory bowel disease (IBD). Current knowledge of pharmacogenetically guided dosing is discussed for individualisation of thiopurine therapy, particularly to avoid severe adverse effects. Both azathioprine and mercaptopurine are pro-drugs that undergo extensive metabolism. The catabolic enzyme thiopurine S-methyltransferase (TPMT) is polymorphically expressed, and currently 23 genetic variants have been described. On the basis of an excellent phenotype-genotype correlation for TPMT, genotyping has become a safe and reliable tool for determination of a patient's individual phenotype. Thiopurine-related adverse drug reactions are frequent, ranging from 5% up to 40%, in both a dose-dependent and -independent manner. IBD patients with low TPMT activity are at high risk of developing severe haematotoxicity if pharmacogenetically guided dosing is not performed. Based on several cost-benefit analyses, assessment of TPMT activity is recommended prior to thiopurine therapy in patients with IBD. The underlying mechanisms of azathioprine/mercaptopurine-related hepatotoxicity, pancreatitis and azathioprine intolerance are still unknown. Although the therapeutic response appears to be related to 6-thioguanine nucleotide (6-TGN) concentrations above a threshold of 230–260 pmol per 8×10^8 red blood cells, at present therapeutic drug monitoring of 6-TGN can be recommended only to estimate patients' compliance. Drug-drug interactions between azathioprine/mercaptopurine and aminosaliclates, diuretics, NSAIDs, warfarin and infliximab are discussed. The concomitant use of allopurinol without dosage adjustment of azathioprine/mercaptopurine leads to clinically relevant severe haematotoxicity due to elevated thiopurine levels. Several studies indicate that thiopurine therapy in IBD during pregnancy is safe. Thus, azathioprine/mercaptopurine should not be withdrawn in strictly indicated cases of pregnant IBD patients. However, breastfeeding is contraindicated during azathioprine/mercaptopurine therapy. Use of azathioprine/mercaptopurine for induction and maintenance of remission in corticosteroid-dependent or corticosteroid-refractory IBD, particularly Crohn's disease, is evidence based. To improve response rates in thiopurine therapy of IBD, comprehensive analyses including metabolic patterns and genome-wide profiling in patients with azathioprine/mercaptopurine treatment are required to identify novel candidate genes

Methods and materials

The article investigated the mucosal flora of washed colonoscopic biopsies of 305 patients with bowel inflammation and 40 controls. The microbial cultures were validated by quantitative polymerase chain reaction with subsequent cloning and sequencing, fluorescence in-situ hybridization, and electron microscopy.

Results

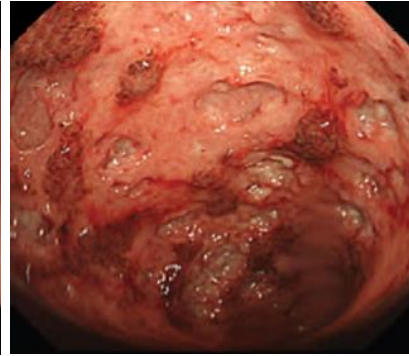
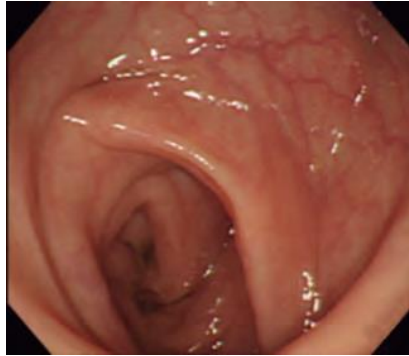
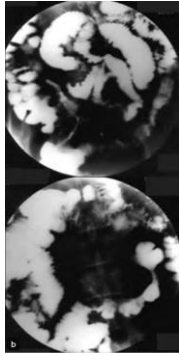
high concentrations of mucosal bacteria in patients with bowel inflammation, but not in controls. The concentrations of mucosal bacteria increased progressively with the severity of disease, both in inflamed and non-inflamed colon. In patients with $>10,000$ cfu/ μ L, a thick bacterial band was attached to the intact mucosa without signs of translocation. Patients with inflammatory bowel disease (IBD) and concentrations of mucosal bacteria $>50,000$ cfu/ μ L had characteristic inclusions of multiple polymorphic bacteria within solitary enterocytes located next to the lamina propria, without or having no contact with the fecal stream. The identified bacteria were of fecal origin.

findings suggest that the changes in the mucosal flora in IBD are not secondary to inflammation, but a result of a specific host response. We hypothesize that the healthy mucosa is capable of holding back fecal bacteria and that this function is profoundly disturbed in patients with IBD.

Conclusion

	Crohn's disease	Ulcerative colitis
LOCATION	Any portion of the GI tract, usually the terminal, ileum and colon Skip lesions, rectal sparing .	Colitis = colon inflammation. Continuous colonic lesions, always with rectal involvement
GROSS MORPHOLOGY	Transmural inflammation: fistulas. Cobblestone mucosa, creeping fat , bowel wall thickening ("string sign" on barium swallow x-ray A), linear ulcers, fissures	Mucosal and submucosal inflammation only. Friable mucosa with superficial and/or deep ulcerations (compare normal with diseased). Loss of haustra: "lead pipe" appearance on imaging.
MICROSCOPIC MORPHOLOGY	Noncaseating granulomas and lymphoid aggregates. Th1 mediated	Crypt abscesses and ulcers, bleeding, no granulomas. Th2 mediated
COMPLICATION	Malabsorption Malnutrition, colorectal cancer (increase risk with pancolitis). Fistulas (eg, enterovesical fistulae, which can cause recurrent UTI and pneumaturia), phlegmon/abscess, strictures (causing obstruction), perianal disease.	Malabsorption Malnutrition, colorectal cancer (increase risk with pancolitis). Fulminant colitis, toxic megacolon, perforation
INTESTINAL MANIFESTATION	Diarrhea that may or may not be bloody.	Bloody diarrhea.
EXTRAINTESTINAL MANIFESTATIONS	Rash (pyoderma gangrenosum, erythema nodosum), eye inflammation (episcleritis, uveitis), oral ulcerations (aphthous stomatitis), arthritis (peripheral, spondylitis). Kidney stones (usually calcium oxalate), gallstones. May be \oplus for anti- <i>Saccharomyces cerevisiae</i> antibodies (ASCA)	Rash (pyoderma gangrenosum, erythema nodosum), eye inflammation (episcleritis, uveitis), oral ulcerations (aphthous stomatitis), arthritis (peripheral, spondylitis). 1° sclerosing cholangitis. Associated with p-ANCA
TREATMENT	Corticosteroids, azathioprine, antibiotics (eg, ciprofloxacin, metronidazole), biologics (eg, infliximab, adalimumab).	5-aminosalicylic preparations (eg, mesalamine), 6-mercaptopurine, infliximab, colectomy.

	<p>For Crohn, think of a fat granny and an old crone skipping down a cobblestone road away from the wreck (rectal sparing). Stones are more common in Crohns</p>	<p>Ulcerative colitis causes ULCCERS: Ulcers Large intestine Continuous, Colorectal carcinoma, Crypt abscesses Extends proximally Red diarrhea Sclerosing cholangitis</p>
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