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The role of smoking and alcohol behaviour in the management of inflammatory bowel disease

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ABSTRACT

In the era of increasing use of immunosuppressive and biologic therapy for inflammatory bowel disease, environmental influences remain important independent risk factors to modify the course of the disease, affect the need for surgery and recurrence rates post-surgical resection. The effect of smoking on inflammatory bowel disease has been established over the decades, however the exact mechanism of how smoking affects remains as area of research. Alcohol is also among the socio-environmental factors which has been recognised to cause a flare of symptoms in inflammatory bowel disease patients. Nonetheless, the exact relation to date is not fully understood, and various paradoxical results from different studies are still a point of controversy.

Introduction

Inflammatory bowel disease (IBD) is a chronic idiopathic inflammation of the bowel which comprises of two main subtypes namely Ulcerative colitis (UC), and Crohn's disease (CD) [1,2]. It appears to be the result of complex interplay between genetic and environmental factors. Differences between the two subtypes have been listed in Table 1. Linked to disease development, severity and cause, are various environmental factors, of which smoking remains the most independent prominent established risk factor [3–7] (see Table 2).

In CD, the entire gastrointestinal tract from mouth to anus can be affected. A complex set of phenotypes are recognised including ileal and/or colonic involvement, resulting from transmural inflammation which affects the whole intestinal wall (Table 3) [8,9] (see Table 2).

In UC, the disease is only limited to the colon, and the inflammation is usually limited to the mucosal lining of the colon and rectum. The disease usually starts distally in the gut and progresses to proximal regions in the colon as disease advances [8].

There appears to be shared risk factors in CD and UC and these include: geographic location, western lifestyle, hygiene hypothesis, bacterial gastroenteritis,nonsteroidal anti-inflammatory drug use, vitamin D deficiency and diet: high intake of mono- and disaccharides, and total fat intake are associated with increased IBD prevalence [2,10].

Although the exact aetiologies remain unclear, numerous clinical trials, research in animal models, and human genetics have provided an insight into the pathogenesis of IBD. IBD is characterized by various genetic abnormalities that appear to lead to overly aggressive T-cell responses to a subset of commensal enteric bacteria. The genetic abnormalities associated with IBD can be broadly classified into causing defects in mucosal barrier function, immunoregulation and impaired bacterial clearance [11].

The development and relapse of IBD are triggered by environmental factors that alter the mucosal barrier, stimulate immune responses or cause an imbalance in the enteric bacteria. However, among the many complexities of the pathogenesis of IBD, the environmental factors are the most difficult to determine despite the strong effect of smoking on clinical course of IBD [3].

This review will discuss the effects of smoking and alcohol behaviour on disease course and management of IBD.

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Table 1
Hallmarks of differences between CD and UC [2,3,87].

	Crohn's Disease	Ulcerative colitis
Clinical Features	- Starts in the terminal ileum - Can extend to any part of the gastrointestinal tract - Discontinuous (skip lesions, cobble stone)	- Confined to the colon - Progress from distal to proximal - Continuous
Histology	- Transmural inflammation - Acute and chronic inflammatory cell - Crypt architectural irregularity, ulcus (loss of crypts), cryptitis - Granulomas	- Superficial inflammation - infiltrate Acute and chronic inflammatory cell infiltrate - Cryptitis, crypt abscesses, branched and shortened crypts, crypt regeneration + Paneth cell metaplasia - Mucin granulomas (histiocytic aggregates, giant cells) – Decreased mucus, decreased goblet cells
Immunological response	Th1/17 response Weak association with ANCA	Th2/17 Strong Association with ANCA
Oxidative stress	Infiltration of neutrophils	Infiltration of neutrophils - Increase of 4-HNE-modified proteins in the mucosa
Important differential inflammatory mediators	- CD8+T cell transcriptional signature as a potential immunological marker - Higher levels of CRP in serum, even much higher than UC	LTB4 as a major chemotactic factor for inflammatory cells. Higher levels of IL-13 IL-17. Disease activity correlates with amount of IL-13 and IL-17
Differential risk factors	- Genetic defects: processing of intracellular bacteria, autophagy, innate immunity - Antibiotic exposure, especially early in life - Cigarette smoking: detrimental - Diet: meats, fatty foods, desserts - Stress, depression	- Genetic defects: barrier function - Antibiotic exposure - Cigarette smoking: protective - Diet: Linoleic Acid
Complications	- strictures - Abscess formation - Fistulas - bowel obstruction - string sign on barium studies	- Toxic megacolon - Leadpipe colon on barium xray.
Risk of colorectal cancer	Risk increased	Risk significantly increased
Surgery	Mainly treats complications such as structures, drain abscesses.	Curative

Table 2
Summary of association between smoking and subtypes of IBD.

	Smoking
Crohn's disease	• Increases the risk of developing CD • Increases risk of relapse, and hospitalisation. • Increases requirements for medical therapy including steroids, immunosuppressive therapy and need for biologics. • Increases risk of surgery in an age dependant manner. • Increases risk of re-operation. • Increases risk of postsurgical clinical and endoscopic recurrence.
Ulcerative colitis	• Decreases risk of developing UC. • May affect risk of proceeding to colectomy. • Smoking cessation increases rate of years with major medical therapy including oral, I·V steroids and azathioprine. • Smoking cessation may affect response to medical therapy.

Table 3
Montreal classification for Crohn's Disease [9].

Age at Diagnosis	A1 Below Age of 16 A2 Between Age of 17–40 A3 Above Age of 40
Location	L1 Ileal L2 Colonic L3 Ileocolonic L4 Isolated Upper Disease. (L4 modifier can be added to L1-L3 when concomitant Upper GI disease is present)
Behaviour	B1 non-structuring, nonpentrating B2 Stricturing B3 Penetrating p Perianal disease modifier (Can be added to B1–B3 if concomitant perianal disease present)

Smoking behaviour and its association with inflammatory bowel disease

Smoking as a risk factor in CD

Despite multiple environmental and modifiable risk factors which have an effect on CD, smoking remains the most independent established risk factor [3–7]. A meta-analyses published in 2006 reported significant increased risk of developing CD among smokers ($P < 001$) [6].

Several prospective, multicentred, cross-sectional and cohort studies have reported the detrimental effect of cigarette smoking on CD. [12–15] These studies have reported that tobacco exposure has a significant detrimental effect on course of the disease, manifested with increased risk of relapse, steroid requirements and double the ratio of hospitalisation. Immunosuppressive therapy requirements and need for biologics were also noted to increase in