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Nutrition, gut microbiota and immunity: Therapeutic targets for IBD, J.D. Lewis, F.M. Ruemmele, G.D. Wu, editors (Karger, Basel, Switzerland) 2014. 166 pages. Price: US$ 59.00 / CHF 50.00 / EUR 47.00
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There has been a recent upsurge of interest in the human gut microbiome because of potential new treatments in the form of faecal microbial transplant (FMT) for diverse conditions ranging from inflammatory bowel disease (IBD) to recurrent *Clostridium difficile* infection (CDI). The impetus into this field came with the introduction of the 16S rRNA gene sequencing which by virtue of its species-specific signature sequences replaced the old culture technique of identifying the gut bacteria. Growing evidence suggests that the human microbiome may play an important role in several diseases other than IBD.

This book gives a broad outline of the interplay between these factors and suggests future therapeutic targets for the treatment of IBD. It is divided into three sections: the initial chapters deal with the pathogenesis

of IBD followed by an intermediate section dealing with the manipulation of the gut microbiome as a potential therapy for IBD. The final section deals with the future of nutritional therapy in IBD. In the chapter on epidemiology of IBD, the author brings forth the argument that the increase seen in the incidence of IBD in many areas of the world could be attributed to the improved access to healthcare and availability of improved diagnostic tools. Increased awareness of IBD among clinicians coupled with changes in cultural norms where people have a greater willingness to discuss their bowel symptoms could also be contributory factors in the "pseudo increase" in the prevalence of IBD. In line with Western literature, the author gives evidence for the role of prior enteric infections as a risk factor for the development of IBD. The biggest stumbling block to this argument would remain that the prevalence of IBD is lowest in those areas of the world where enteric infections are most prevalent such as in Asia and Africa.

In the chapter on design of clinical trials for IBD, the author makes a strong case for the cluster randomization trials as the preferred modality for future clinical trials as these are particularly useful to evaluate complex interventions such as treatment algorithms. The superiority of the Mayo Clinic score over the Truelove-Witts criteria as a measure of outcome in Ulcerative Colitis (UC) has been highlighted as it takes into account both the symptoms as well as the endoscopic findings. It has been suggested that in the future, endoscopic assessment may be the only outcome measure in UC given that there is a good relationship between endoscopic activity and severity of symptoms.

The next chapter discusses the composition of the microbiome in healthy individuals which differs from those with IBD. While a high bacterial diversity with predominance of Bacteroides and Firmicutes is seen in healthy individuals, the dysbiosis in IBD is characterized by decreased bacterial diversity and certain Clostridial subsets notably *Faecalibacterium prausnitzii*. *F. prausnitzii* is an efficient producer of short-chain fatty acids (SCFA), which have a protective effect on the mucosal barrier function. SCFA are also critical for the development of tolerance to gut commensals. The high bacterial diversity in a healthy microbiome is responsible for the resistance to colonization by *C. difficile* unless the balance tilts in its favour by exposure to broad-spectrum antibiotics. Infants exposed to antibiotics in early life are more prone to IBD at a later stage. Similarly the response to gluten is determined by the age at the time of exposure, as infants exposed during 1-3 years of age are most vulnerable to develop celiac disease followed by those exposed after the age of 7 months.

The role of the cross-talk between gut bacteria and the immune regulatory cells in mucosal homeostasis and immune tolerance is well discussed. Crohn's disease is proposed to be the end result of an overly aggressive TH1/TH17 cell response to a subset of luminal bacteria in the background of innate immune dysfunction. Susceptibility is determined by defects in genes involved in immune response, mucosal barrier function or enteric bacterial clearance. Correction of the dysbiosis in the gut microbiome by customized approaches, to an individual's unique bacterial profile offers an attractive target for novel approaches to treat IBD, as discussed in the second section. Metabolism of bile acids by the gut microbiota has been shown to modulate the inflammation in patients with IBD. The beneficial role of exclusive enteral nutrition with an elemental diet in patients with Crohn's disease also suggests a causative role of the gut bacteria.

Of the estimated heritability risk of IBD, as derived from twin and hereditary studies, only less than 30 per cent is explained by genetic variants discovered in genome wide association studies (GWAS). This has led to the suggestion that heritability assessments have been overestimated. Determining which IBD associated SNPs in coding regions result in functional consequences and which non-coding SNP variants regulate gene expression are important future endeavours.

Environmental factors may also alter the composition of the gut microbiome. This explains why immigrants from regions of low prevalence of IBD to Western countries progress to the same rate as the host country in the second generation. Dietary factors such as a diet rich in fruits and vegetables may have a protective effect considering that the Western diet is rich in total fats and deficient in dietary fibre.

FMT is now an established form of therapy for recurrent and difficult to treat CDI with cure rates of > 90% and a favourable safety profile. Whether the success of FMT in CDI can be repeated in case of IBD remains to be seen. The logistic, legal, social and ethical issues are well discussed in the chapter on FMT.

The last chapter of the book deals with the new targets and unmet needs in the field of IBD therapy.

The gastroenterologists have borrowed the concept of "treat to target" from rheumatologists wherein the treatment is stepped up to achieve a defined target by using objective outcome measures.

All chapters provide a brief overview of the topics without going into the finer details of basic sciences thus enabling the physician / gastroenterologist to gain an insight into the topic. All those who have an interest in the gut microbiology especially those planning to initiate research in this exciting field should read this book.

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