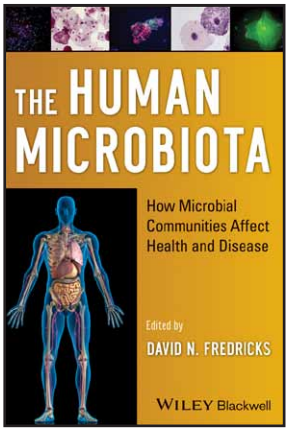
Beneficial Microbes, March 2014; 5(1): 89-94

Wageningen Academic Publishers

K. Venema

Beneficial Microbes Consultancy, Wageningen, the Netherlands

BOOK REVIEWS



The human microbiota
How microbial communities affect health and disease

D.N. Fredericks (editor)

List price: 104.40 Euro (hardcover) / Euro 89.99 (e-book)
Hardcover / e-book: 389 pages
Publisher: Wiley Blackwell, Hoboken, NJ, USA
ISBN: 978-0-470-47989-6
eISBN: 978-1-118-40980-0

Introduction

This book on the human microbiota of 389 pages is intended to 'provide an overview of the microbial diversity found in humans and to describe efforts linking microbial communities to human health'. The book contains 14 chapters that try to cover this broad range of topics. Answers to many different questions are provided, ranging from 'How do communities differ across body sites?' to 'Which microbial profiles are associated with health and disease?'

The human microbiota – introduction and methods to characterise the microbiota

The first four chapters deal with an introduction on the human microbiota (based on the NIH Human Microbiome project [HMP]) and methods to study the composition and activity of the microbiota. The introductory chapter provides an overview of the HMP. Within this project samples from as much as 18 different body sites from 300 individuals have been taken and analysed with respect to composition of the microbiota (based on sequencing of variable regions of the 16S rDNA gene) as well as (potential) activity (through metagenomics). In addition, the total genome of a large collection of reference strains (at the time of writing ~800) was sequenced, and more were planned. The chapter was written in the early phases of the HMP and little concrete data are shown. Currently, there is an explosion of data coming out of this project, but this is not part of this book chapter. The 'future directions for human microbiome research' section is interesting to read. Chapter 2 reviews methods for characterising microbial communities associated with the human body. Most are based on using phylogenetic markers, and the most frequently used marker is the 16S gene. However, functional analyses are used more and more frequently and include simple cloning of (potential) functional genes, metagenomics, functional arrays, and single-cell genome amplification and sequencing of microbes that are hard to culture. Chapter 3 continues to describe how to characterise the microbiota, but specifically using phyloarrays. It is a brief chapter explaining the design, use and benefit of such arrays, but it is not comprehensive. Chapter 4 describes mathematical approaches for describing microbial populations. It is a very good introduction to description of microbial communities by numbers but it is a bit out of place in this book, as it does not describe the microbial diversity found in humans nor efforts linking microbial communities to human health, which the book intends to do.

The human microbiota on different body sites

The next five chapters describe the human microbiota at various body sites. Chapter 5 deals with the enteric microbiota and its role in inflammatory disease, specifically Crohn's disease (CD). This is a disease that cannot be described according to Koch's postulate, i.e. not a single microorganism is responsible for the disease but rather

pathogenic microbial communities are. Besides a microbial component there has also to be an underlying genetic defect in the host, moreover, environmental factors are important too, although the exact interplay between these is not yet established. Chapter 6 describes the human airway microbiome. Very little is known about the role of the microbiota in lung diseases, although certain genera and species have been associated with e.g. ventilator-associated pneumonia, cystic fibrosis, or asthma. The next chapter deals with the oral microbiota, on which a separate book has been reviewed in this issue of Beneficial Microbes. It goes without saying that in this single chapter there is much less information than in the complete book. However, it contains some nice overview figures, and it also describes the links of the oral microbiota with systemic disease. Chapter 8 describes the microbiota of the genitourinary tract. A fair amount of research has been done on the vaginal microbiome, and this chapter is the most extensive out of the five chapters in this section. The chapter ends with a perspective of vaginal health in 2025, which is a nice outlook based on our current understanding of the urinary tract microbiome in women. Chapter 9 focuses on the intestinal microbiota in health and disease, broader than just CD in Chapter 5. In fact, it starts in the mouth and tonsils and then slowly makes its way down to the lower intestines. It has some very beautiful fluorescent micrographs of biofilms in the different parts of the gastrointestinal tract. The authors make a distinction between the gut wall-associated microbiota and the lumen microbiota (i.e. which likely have a different functionality). For all these five chapters one could write complete review books that could all be thicker than the 389 pages of this book. It is therefore clear that limited information is provided.

Models for the human microbiota

There are two chapters on the use of animal models (from fly to human) to study the human microbiota. In Chapter 10 models of the fruit fly *Drosophila*, zebra-fish and mice are discussed with their similarities and dissimilarities, and advantages and disadvantages. Briefly for each disease, the role of the microbiota in inflammatory bowel disease, multiple sclerosis and diabetes are discussed. However, the microbiota has been implicated in many more diseases and disorders, up to autism, but unfortunately the chapter does not deal with these. Chapter 11 continues the description of animal models and shows significant overlap with the previous chapter, although many more animal models are mentioned, including squid, nematodes and termites. The chapter focuses on interaction of the microbiota with the host, how to visualise this and how to identify important host genetic determinants, using animals with certain genes knocked out.

Isolation and cultivation of the human microbiota

There are two chapters on isolation and cultivation of members of the microbiota that have not been cultured before. Both are short and should have been taken together as a single chapter, or perhaps not even included in a book that intends to describe the microbial diversity found in humans. Chapter 13 shows some methods that could be used but also misses a number of recent developments, and is therefore far from complete.

Manipulating the microbiota using probiotics, prebiotics or synbiotics

There is one chapter that discusses the manipulation of the human (gut) microbiota using probiotics, prebiotics or synbiotics (which are a combination of pro- and prebiotics). It describes primarily gut-related diseases in which probiotics have been shown to be beneficial, but also includes allergy-related diseases and ageing. The use of prebiotics and the combination of probiotics and prebiotics (synbiotics) are also briefly discussed.

Conclusion

Overall, this book provides a concise overview of the human microbiota in and on different body sites, a bit too concise for me. It fulfils the intention to discuss many different body sites but in doing so neglects to get to the detailed description of the human microbiota, let alone to give a good overview of their role in health and disease. There is very little attention to microbial activity, which in my opinion is more related to disease than composition. As an example, the phrase butyrate is mentioned only 3 times in the book, as are short-chain fatty acids. These play a major role in health of the gut.

Oral microbial ecology
Current research and new perspectives

N.S. Jakubovics and R.J. Palmer Jr. (editors)

List price: 319 USD (hardcover/e-book)
Hardcover / e-book: 232 pages
Publisher: Caister Academic Press, Norfolk, UK
ISBN: 978-1-908230-17-1
eISBN: 978-1-908230-82-9

Introduction

This book on oral microbial ecology of 232 pages is intended to be essential text for scientists interested in oral microbiology, bacterial communities and biofilms, and is recommended reading for anyone working in the areas of oral health, and the pathogenesis of dental caries and periodontal disease. The book contains 14 chapters that try to cover this broad range of topics.

Oral microbial populations – composition and activity

The first chapters deal with the composition and activity of oral microbes, with Chapter 1 on microbial populations in biofilms. The chapter, however, focuses almost entirely on oral streptococci and specifically the species *Streptococcus mitis*, while from recent evidence it is not obvious that streptococci are the most important species present in the oral cavity in terms of health and disease. Yet, the chapter nicely reviews the knowledge on survival and transmission of this species, initial adhesion, persistence and avoidance of immune detection. Adherence occurs to both soft tissue and dental surfaces, where different species of streptococci are involved. Interestingly, oral streptococci have been shown to be present intracellularly in buccal epithelial cells. The largest part of the chapter deals with immune evasion or mechanisms through which oral streptococci remain unaffected by the mounted immune response. The second short chapter describes the detection and culture of novel species and genera. Although the introductory sentence describes the fact that there are also fungi, protozoa and viruses present in the oral cavity, the chapter unfortunately does not deal with this. The third chapter deals with the activity of the oral microbiota on salivary substrates. The authors state that these are the major substrates for oral microbes, as dietary components are quickly cleared from the oral cavity. If this is true, I do not see why there is so much hassle on sugar-containing soft drinks and why that would be bad for your teeth. I thought it was the quick scavenging of simple sugars by oral microbes and the production of acids from these that play a large role in tooth carries, and what not? Nonetheless, the chapter describes the use of *N*- and *O*-linked glycans in salivary secretions.

Biofilms – structure and matrix components

The next three chapters describe in more detail the structural organisation of oral biofilms and the role of bacterial components in the biofilm matrix. Chapter 4 deals with differences in structure between supragingival and subgingival plaque. It starts by describing the methods available to study this, and continues to describe how biofilms are formed in a stepwise manner. It contains some nice photographs, although one has to thumb through to the end of the book to see them in colour. The next chapter describes the role of extracellular polysaccharides (EPS) in oral biofilms, with a focus on virulent biofilms, although I am not sure we currently can discriminate between virulent and avirulent biofilms. This EPS forms a matrix in which eventually the oral microbes are trapped. It provides structural integrity, cohesion and protection against antimicrobials. The EPS is produced by certain oral bacteria by glycosyltransferases (Gtf) that are present at the outer surface of the bacteria and coat them with a layer of an almost impenetrable layer. Sucrose is one of the substrates used by Gtf. Other components have also been shown to be present in the biofilm matrix, such as proteins, lipids, nucleic acids and lipo-oligosaccharides. Chapter 6 deals with the presence and role of proteins and DNA in the matrix of biofilms. Apparently, these molecules play a key role in maintaining the structure of oral biofilms. The extracellular DNA is thought to (1) play a role in gene transfer between streptococci, (2) be a source of nutrients in an otherwise nutrient poor environment due to the impenetrability of the biofilm, also for nutrients, and (3) play a role in interactions with the host and (4) biofilm structure. The role of extracellular proteins is less clear, apart from those that play a role in the structure of the matrix.

Communication between bacteria and with the host

There are three chapters on communication aspects of oral microbes with each other and with their environment (including the host). Chapter 7 is on interspecies communication within dental plaque. It describes the metabolic and autoinducer-mediated interactions between species in the stepwise formation of the oral biofilm. Chapter 9 continues on this subject but then specifically for *Streptococcus mutans*. The various mechanisms important for survival and persistence in an oral biofilm are reviewed, including production of antimicrobials to get competitive advantage over neighbouring microbes and metabolic cross-feeding to help others. Based on the knowledge on communication across species, new strategies to control a cariogenic community are discussed as well. Chapter 8 describes the mechanisms by which the oral streptococci sense their environment in the oral cavity. Several mechanisms are entertained by oral streptococci to sense the environmental conditions, and the different species are geared towards this by the presence of signalling and sensing machinery encoded in the bacterial genome. Apart from nutrient sensing, stress sensing (and acting upon, or adapting to it) is very important in oral microbiology too, and is reviewed is Chapter 8 as well.

Oral microbiology in health and disease

The remainder of the chapters focus on health and disease, although that also is part of the preceding nine chapters of course. Chapter 10 deals with biofilms in health and disease and is a bit of a repetition of earlier chapters. Several factors playing a key role, particularly in disease, are described, mostly because we cannot yet define health other than the absence of disease (although within the TI Food and Nutrition (Wageningen, the Netherlands) a large consortium is working on getting more insight into oral health). Using the latest molecular technology our insight in oral microbiology increases and microorganisms other than streptococci are found to be important in establishing disease. Chapter 11 describes the role of periodontal biofilms in immunity, especially evasion of detection by select pathogens. Apart from evasion mechanisms, some pathogens, such a *Porphyromonas gingivalis*, exploit innate immune receptors to actively undermine the host immune response. It is believed that by its activity in modulating the immune system *P. gingivalis* allows the survival and persistence of other oral microbes. The next chapter continues on this theme by describing how the oral biofilms acts as a reservoir for extraoral pathogens, with the example of ventilator-associated pneumonia to illustrate this. Chapter 13 is an interesting chapter that describes the use of the oral biofilm as a vehicle for chemotherapeutic agent. The concept is based on the hypothesis (already proven for fluoride) that after mechanical cleaning of teeth (i.e. brushing) a residual biofilm will grow out again in periods between cleaning. Adhesion of antibacterial agents (e.g. from toothpaste) to this residual biofilm will result in their slow release over time at bioactive concentrations. Examples of these are shown in this chapter. The last chapter describes the potential use of probiotics as a tool in oral health care. Even though the title ends with a question mark, I believe there is increasing evidence that probiotic strains may be efficacious. However, this is clearly (as for other diseases and disorders where probiotics are active) species-dependent. The mechanisms described in the chapter include competitive exclusion, production of toxins and other antimicrobials, immune modulation, and modulation of the epithelial barrier function.

Conclusion

Overall, this book is a nice collection of subjects regarding oral microbial ecology. It is an exciting, though complex, field hampered by the fact that no single effect on disease (carries, periodontitis, etc.) can be explained by Koch's postulate, which says that a single microorganism is responsible for disease. In oral disease (and in other diseases where the microbiota plays a role), this turns out to be much more complex. The subject of probiotics could have been expanded to my view but perhaps I am biased since I am working on beneficial microbes. However, recently there is a lot of interest in the role of oral microbes for health and disease, not only for the oral cavity, but also beyond that. A role of the oral microbiota in type I and type II diabetes has been described, likely through the influence of the oral microbiota on systemic immunological parameters. In Beneficial Microbes several recent contributions dealt with oral microbiology and the role of probiotics (Burton *et al.*, 2011; Güngör *et al.*, 2013; Stamatova *et al.*, 2012). So, even though the book is essential text for scientists in the area, there also is a lot of available recent research that is just as essential and shall not be overlooked.

References

Burton, J., Wescombe, P., Cadieux, P. and Tagg, J., 2011. Beneficial microbes for the oral cavity: time to harness the oral streptococci? Beneficial Microbes 2: 93-101.

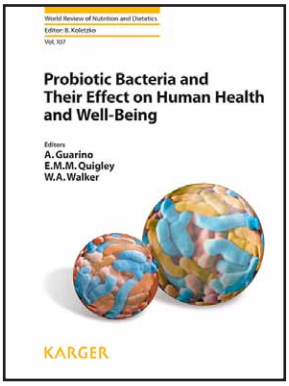
Güngör, Ö.E., Kırzıoğlu, Z., Dinçer, E. and Kıvanç, M., 2013. Who will win the race in childrens' oral cavities? Streptococcus mutans or beneficial lactic acid bacteria? Beneficial Microbes 4: 237-245.

Stamatova, I., Kari, K., Hervonen, L. and Meurman, J.H., 2012. Dietary sugar utilisation by putative oral probiotics. Beneficial Microbes 3: 221-227.

Probiotic bacteria and their effect on human health and well-being

World Reviews of Nutrition and Dietetics, volume 107

A. Guarino, E.M.M. Quigley and W.A. Walker (editors)



List price: 163 Euro (hardcover/e-book)
Hardcover / e-book: 202 pages
Publisher: S. Karger A.G., Basel, Switzerland
ISBN: 978-3-318-02324-4
eISBN: 978-3-318-02325-1

Introduction

This book on probiotics and human health and well-being of 202 pages provides 'an update on probiotics'. It is volume 107 of the World Reviews of Nutrition and Dietetics directed at physicians, biologists, biotechnologists and researchers working in the food industry, agriculture, and the environmental, basic sciences and health care. The book contains 21 unnumbered chapters in 6 sections that try to cover a broad range of topics. Given the limited number of pages and the large number of chapters, it is clear that the content scratches the surface, but reference is made to earlier reviews and the book indeed provides an update on these earlier published overviews. The list of contributors is impressive, with most of the top-notch researchers in particular areas contributing to this volume.

Composition and modulation of intestinal microbiota

The first five chapters deal with composition and modulation of the intestinal microbiota by probiotics, where the first chapter discusses the definition and taxonomy 10 years after the FAO/WHO guidelines. The readers are pointed to the original guideline documents when it comes to the definition of probiotics, and are reminded that in the FAO/WHO guidelines the definition is restricted to 'use in food', and not as a biotherapeutic. Correct taxonomic identification is also discussed, which has become important also in claim substantiation, when EFSA dismissed certain dossiers based on insufficient taxonomic characterisation. The second chapter deals with the composition of the microbiota in children. Unfortunately, this chapter (and many other chapters) still use the word microflora, which has become outdated already a decade ago. Other than that, the chapter gives a succinct update on the composition in children, describing how the microbiota changes from birth to adulthood. Differences in formula-fed and breast-fed babies are discussed, as well as eubiosis and dysbiosis and the consequences of the latter in infants. The following chapter is on the microbiota composition in adults. Apart from bacteria, the presence of *Archeae*, fungi, protists, and viruses and phages are mentioned as well. This is usually overlooked by most researchers. Diversity and function of the gut microbiota are discussed. Logically, the next chapter deals with the gut microbiota in ageing. The microbiota of elderly and centenarians (people over 100 years) have been studied. Clear differences with the microbiota from adults were observed. The fifth chapter in this section deals with the shaping of the microbiota through co-evolution with the host. The chapter discusses how innate immune receptors, focused on Toll-like receptors and Nod-like receptors, are critical for maintaining intestinal homeostasis.

Functions and dysfunctions of intestinal microbiota

The next three chapters describe functions that have been assigned to the microbiota, and also describe what happens if things go awry. The first of these chapters describes the necessity of early microbial colonisation for intestinal immune development. It contains a very nice graph depicting changing functions of the innate immune system over time, from the prenatal period into adulthood. This graph includes amongst others epithelial cell proliferation, production of antimicrobial peptides, innate immune sensing of the microbiota, and secretion of IgA. Neonatal crosstalk between microbiota and epithelium is discussed, including induction of regulatory T cells. Another interesting area is the effect of the microbiota on behaviour and brain development. This is reviewed in the second chapter of this section. This research is still in its infancy, as so far experiments have only been done in animal models. The authors hypothesise on the importance of certain microbial metabolites, such as short-chain fatty acids, serotonin and γ-amino butyric acid in modulation brain activity. They also link production of (some of these) microbial metabolites to pain perception in irritable bowel syndrome, but they acknowledge that these are at most suggested mechanisms and no scientific evidence is currently available. The last chapter in this section reviews the evidence in the gut-airway axis, where the composition and activity of the gut microbiota is thought to play a role in pulmonary diseases. Here, the evidence is also still thin, but it is an interesting link that needs to be further explored. The difficulty with the gut-brain and gut-airway axis is

that, when certain microbes correlate with the disease or disorder, it is unclear whether the changed microbiome is a cause of consequence of the disease or disorder.

Probiotics in prevention and treatment of disease

The next section contains five chapters on the use of probiotics in prevention or treatment of disease. Each of these chapters starts with explaining the disease and underlying physiological parameters, while the part on the potential benefit of probiotics is relatively short. The first of these chapters is on inflammatory bowel disease. Prevention in this case should be taken as the prevention of flare-ups in Crohn's disease or ulcerative colitis. Treatment has so far been unsuccessful, although in the future the use of recombinant bacteria or new species such as *Faecalibacterium prausnitizii* may be efficacious. The second chapter deals with functional gastro-intestinal (GI) disorders in children, encompassing various disorders, including diarrhoea, constipation, vomiting, and colic and abdominal pain. The third chapter in this section is on GI disorders in adults. Specifically, functional dyspepsia, irritable bowel syndrome, constipation and bloating and flatulence are discussed. The latter two chapters are on metabolic syndrome and obesity in children and adults, respectively. The evidence that the microbiota plays a role in these is increasing, although there is not yet a consensus on the mechanism. I believe it is likely that there are multiple, not mutually exclusive mechanisms. Especially for adults, there have been a number of recent studies to examine the effects of probiotics on obesity, ranging from studies in mice to those in man. These are nicely reviewed in the last chapter, which is the largest chapter of the book.

Specific bugs for specific diseases

There are three chapters in a section entitles 'Specific bugs for specific diseases'. This title is inaccurate. It suggests, at least to me, that specific probiotic strains have been shown to be efficacious in very specific disease, but this is not what is shown in this section. The first of the three chapters is on a specific disease, namely neonatal necrotising enterocolitis. The author concludes that the evidence for probiotics (and prebiotics and postbiotics) is questionable. The other two chapters are on more general disorders, allergies and respiratory infections, respectively. Although LGG remains the best studied strain for allergies, it is not efficacious in all allergies. This strain and others have also been studied for respiratory tract infections. There is some recent interest in this, which is reviewed in the last chapter of this section.

Probiotics in food

There are two chapters in a section entitled 'Probiotics in food'. This title is also misleading. The two chapters deal with dose-response and safety of probiotics, respectively. Few dose-response studies in man have been done. The chapter contains a nice overview of those instances where dose-response was studied, although the table is incorrectly titled 'survival', as all that was studied were the number of viable counts in faecal samples. Unfortunately, no correlation between dose and clinical benefit has been provided in this table. Two studies where dose and effect have been studied, are reviewed, both on diarrhoea. The chapter closes with a section that is entitled 'Is too much of a good thing a bad thing?'. This nicely feeds into the next chapter on safety of probiotics. Here, adverse events during clinical trials, translocation over the gut barrier, and transfer of antibiotic resistance are discussed, as well as issues regarding long-term use of probiotics. The chapter contains a table with case reports of 'probiotic-caused sepsis'. This title is also misleading. It suggests that in all those cases (29 case reports!) the probiotic strain caused the sepsis, but this is far from clear. I suppose the title that should have been there ('Case reports in which sepsis occurred when the individuals were taking probiotics, in which case the probiotic likely translocated over the gut barrier as a co-passenger', or something like) was considered to be too long as a table heading.

The future

There are three chapters that discuss the future (of probiotics). The first is on probiotics for elderly. Since the world population is quickly ageing (that is, the average age increases), this is an interesting and promising field for probiotics. The chapter also discusses some challenges faced by the probiotic industry in terms of the EFSA not having approved a single claim on probiotics so far. The second chapter is on the 'use of microbes to fight microbes'. The approach taken is to use antimicrobial factors, such as bacteriocins, to specifically eradicate pathogenic microbes from our gut (or other body sites), or to have probiotics help the host fight the pathogens by e.g. immunomodulation. Therapies derived from the ever-increasing knowledge that we get from our (gut) microbiome is discussed in the last chapter. The 'hot topics' for use of probiotics that are discussed here are also reviewed elsewhere in the book.

Conclusion

Overall this book should be taken as it is intended: an update on probiotics. Due to the many different items discussed and the need to introduce those diseases and disorders properly, there is very little room for an in-depth discussion on the effects of probiotics, although some chapters manage to do so. If you need a good overview on the effect of probiotics on human health and well-being, I would also advise you to read other books, those that are referred to by the authors of this book. This book manages to capture the recent evidence.