- Mini Review Article

MUTUALISTIC PRESENCE OF NORMAL FLORA IN HUMAN INTESTINE: A REVIEW

Karishma Kabir Nipa

Institute of Medical Technology, Mirpur-12, Dhaka, Bangladesh

Abstract

Human body contains a huge number of micro-organisms in its intestine. It is ten times more in number compared to the number of human body cells. These micro-organisms are mainly anaerobic bacteria and perform useful functions in relation to development of gut, and production of vitamins and hormones. These bacteria also perform a wide range of metabolic functions. The present article reviews briefly the mutualistic relationship of intestinal flora with human intestine along with their pathogenic behaviour to some extent.

Key words: Human intestine, bacterial flora, mutualism, mutualistic relation.

Introduction

Human body contains about 100 trillion non-pathogenic micro-organisms in its intestine as normal flora, which is ten times greater in number than the total number of body cells (Sears 2005, Steinhoff 2005). These are mainly bacteria. Micro-organisms community maintains a relationship which is not a merely commensal rather a mutualistic relationship (Sears 2005). In healthy individuals these bacteria provide a wide range of metabolic functions (Gill et al. 2006). These micro-organisms are found to perform the useful functions mostly in the human body along with regulating the development of gut (www.pnas.org), producing vitamins like biotin and vitamin K (www.pnas.org; www.clinicalkey.com). They also produce hormones (Gutflora-wikipedia). In humans anxiety disorders are common in patients with disturbed gut flora (Mikocka-Walus et al. 2007). More than 99% of bacteria in the gut are anaerobes (Laurent and Jean-Claude 2004; Gayatri and Hecht 2003). However, in few parts of intestine aerobic bacteria are found with high density (Guarner and Malagelada 2003). This article mainly focuses on the mutualistic association between human intestine and bacteria flora with a little extent of pathogenic action.

Types of Bacterial Flora in Intestine

Members of different species of bacteria can stay fairly overtime and even though some alterations may occur with changes in lifestyle, diet and age (O'Hara and Fergus 2006). Bacterial species are found to belong the genera Bacteroides, Clostridium, Fusobacterium, Eubacterium, Ruminococcus, Peptostreptococcus, Peptococcus and Bifidofacterium (Guarner and Malagelada 2003, Laurent and Jean-Claude 2004). The genus Escherichia and Lactobacillus are found to be present to a lesser extent (Guarner and Malagelada 2003).

Bacterial Flora in Adult Human Intestinal Tract

The upper part of the human intestine contains a few bacteria which are allochthonous and mouth bacteria (Schlegel 1993). However, Costello et al. (2009) reported that the human mouth contains the most phylogenetically similar microbiome. Most abundant microbial populations found in the oral sites were observed in many of the earlier studies (Dewhirst et al. 2010, Bik et al. 2010). Some of the low abundance groups such as Alphaproteobacteria, Coriobacteridae, Acidobacteria, Deltaproteo bacteria and Deinococci

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* Corresponding author E-mail: impelp@yahoo.com

are found in oral communities (Belda-Ferre et al. 2011). Almost similar microbial diversity with oral samples was reported by Ling et al. (2010). Most of the bacteria do not survive passage through stomach because of its high acidic environment (pH 0.5-2.0) (Schlegel 1993). Lactic acid producing bacteria like viridians Streptococci are also found in the duodenum (Schlegel 1993). In the upper part of small intestine (Jejunum) the pH begins to rise; therefore, the food bollus becomes alkaline and the pattern of bacterial flora changes. Bik et al. (2006) reported a greater number of operational taxonomic units in the stomach. However, current studies indicate that bacterial population within the stomach has changed the traditional notion. And it has been found that the upper part of intestine is nearly sterile (Bik et al. 2006, Lawson and Coyle 2010). Anaerobic bacteria like Bacteroides, Eubacterium, Peptostreptococcus and Bifidobacterium gain predominance in the large intestine and 10^5 to 10^7 bacteria/ml are found in the food bolus (Schlegel 1993). In large intestine bacterial density becomes even extraordinary with 10^{11} cells/gm of feces (Schlegel 1993). However, Escherichia coli (E. coli) in colon represent a trace amount of the total bacterial mass (Schlegel 1993). According to Guarner and Malagelada (2003) bacterial density and growth rates are varied along the intestine track.

Infancy and Microbiota

Infant intestines are colonized by large number of E. coli and Streptococci species and within few days their numbers reach 10^8-10^{10}/gm of feces (Andreas et al. 2003, Mackie et al. 1999).These bacteria create an environment, which becomes favourable for subsequent growth of strict anaerobic species belonging to the genera Bifidobacterium, Bacteroides, Clostridium and Ruminococcus (Favier et al. 2002). The diversity of microbiota of feces is significantly higher in adults than in children, although interpersonal differences are higher in children than in adults (Yatsunenko et al. 2012). The study of Yatsunenko et al. (2012) also revealed a high prevalence of enzymes involved in fermentation, methanogenesis and in the metabolism of arginine, glutamate, asperate and lysine in adult microbiomes whereas in baby microbiomes predominate enzymes involved in the metabolism of cysteine and fermentation pathways.

Relationship of Intestine Flora with Diet

Different bacterial genera in intestine microbiota and their association with nutrient intake have been studied and this is composed of mainly of three enterotypes named as Prevotella spp., Bacteroides spp. and Ruminococcus spp. (Wu et al. 2011). Prevotella spp. is related to carbohydrates, while Bacteroides is associated with animal proteins, amino acids and saturated fats (Gutflora-wikipedia). Wu et al. (2011) have said that one enterotype dominate over the other depending on the diet; those who eat plenty of protein and animal fats have predominantly Bacteroides spp. those who consume more carbohydrates Prevotella species dominate in the intestine. Composition of food and reabsorbtion in different regions of intestine have a decisive influence on the microbial activity of the intestinal tract (Schlegel 1993). When excess sugar in the food reach the lower small intestine or the large intestine, these are metabolized by fermentative bacteria with the production of gases like H_2, CO_2 and sometimes CH_4 (Schlegel 1993). Some people produce larger amount of gas due to their less ability to digest few polysaccharides and to absorb sugars (Schlegel 1993). Schlegel (1993) also stated that in normal human intestine many non-reabsorbed metabolites are broken down and therefore little toxic material is produced. However, microbiome in intestine can be changed following a long term diet. Wu et al. (2011) have stated that people whose microbiome is predominantly Bacteroides spp. and change their dietary patterns to a diet based on high level of carbohydrates, they will get a Prevotella spp. enterotype in the long term.

Significant Role of Helpful Gut Flora

In the gut bacteria fulfill a useful function for humans, including digestion of unutilized energy substances (Wynne et al. 2004). These bacteria also perform several functions like suppression of the growth of harmful organisms, development of immune system to respond only to pathogens (Guarner and Malagelada 2003,

Sears 2005, Keeley 2004). By fermentation bacteria turn carbohydrates into short chain fatty acids and the ultimate products are acetic acid, propionic acid and butyric acid (Gibson 2004, Laurent and Jean-Claude 2004). These are used by host cells by providing a major source of useful energy and nutrients for humans (Gibson 2004). These materials also help the body to absorb essential dietary materials such as calcium, magnesium and iron (Guarner and Malagelada 2003). It is also said that bacteria enhance the absorption and storage of lipids (Sears 2005). Bacterial flora is found to increase the guts absorption of water and to simulate the growth of indigenous bacteria (Guarner and Malagelada 2003). Harmful yeasts and bacterial species such as Clostridium difficile are unable to grow excessively due to competition from helpful gut flora species adhering to the mucosal lining of the intestine (Gutflora-wikipedia). The barrier effect protects humans from both invading species as well as the species normally present in the gut at low numbers, whose growth is usually inhibited by the gut flora (Guarner and Malagelada 2003). Indigenous gut flora also produces bacteriocins, which are proteinaceous toxins that inhibit growth of similar bacterial strains and substances.

Significant Role on Human Immunity

Bacterial flora exerts continuous and dynamic effects on the human gut for developing a systemic immune system. Bacteria play key role in promoting the early development of the guts mucosal immune system. The bacteria stimulate the lymphoid tissue associated with the gut mucosa to produce antibodies to pathogen, and the immune system fights harmful bacteria leaving the helpful species alone, due to which a tolerance is developed in infancy (Guarner and Malagelada 2003, Steinhoff 2005, Fergus 2002). After birth of a child, bacteria begin colonizing in its digestive tract. Bacteria can influence the oral tolerance, where the immune system becomes less sensitive to the antigen and this tolerance is mediated partly by gastro-intestinaal immune system and in part by liver which can reduce the over reactive immune response (Jewell 2005). Mantis et al. (2011) have stated that once the host immune system is developed it regulates the bacterial composition in the gut; furthermore, the regulation mechanism like immune exclusion is mediated through neutralizing the action of immunoglobin A (IgA). Immunoglobins are very much essential to maintain the symbiotic balance between microbiota communities of gut and the immune system of host.

Effect of antibiotic therapy

Association between humans and their intestinal flora become obvious when mutualistic relationship is disturbed and bacterial population is eliminated by broad spectrum antibiotic treatment. Levinson (2008) has stated that clindamycin can suppress the predominance of normal flora, and allow a rare organism like Clostridium difficele, which is toxin producer; therefore, overgrowth leads to the development of pseudo membranous colitis. Neomycin orally prior to gastrointestinal surgery to sterilize the gut, which leads to a significant reduction of the normal flora for several days.

Conclusion

In human gut the different species of microorganism live in intestine with a large reservoir for mutual benefit. The micro-organisms benefit the host by providing energy from the fermentation of undigested carbohydrates and by absorption of short chain fatty acids. Intestinal bacteria also play an important role in synthesizing vitamins and metabolizing bile acids, sterols, xenobioties etc. On the contrary the less favourable types of fermentation produce toxins and carcinogens in addition to short chain fatty acids.

Acknowledgment

References

Andreas S, Gruhl B, Lobnitz M, Michel P, Radke M, Blaut M. 2003. Development of the intestinal bacterial composition in hospitalized preterm infants in comparison with breast-fed, full-term infants. Pediatric Research 54(3), 393-399. http://dx.doi.org/10.1203/01.PDR.0000078274.74607.7A

Belda-Ferree P, Luis DA, Ran CR, Hector R, Aurea SS, Miguel P, Alex M. 2011. The oral metagenome in health and disease. ISME J 6, 46-56. http://dx.doi.org/10.1038/ismej.2011.85

Bik EM, Clara DL, Gray CA, Peter L, Joanne E, Emanuel FM, Karen EN, Steven RG, Claire MFL, David AR. 2010. Bacterial diversity in the oral cavity of 10 healthy individuals, ISME J 4, 962-974. http://dx.doi.org/10.1038/ismej.2010.30

Bik EM, Eckburg PB, Gill SR, Nelson KE, Purdom EA. 2006. Molecular analysis of the bacterial microbiota in the human stomach. Proc. Natl. Acad. Sci. USA. 103: 732-737. http://dx.doi.org/10.1073/pnas.0506655103

Costello EK, Christian LL, Micah H, Noah F, Jeffrey IG, Rob K. 2009. Bacterial community variation in human body habitats across space and time. Science 326(5960), 1694-1697. http://dx.doi.org/10.1126/science.1177486

Dewhirst FE, Tuste C, Jacques I, Bruce JP, Anne CRT, Wen-Han Y, Abirami L, Willium GW. 2010. The humane oral microbiome. J Bacteriol 192(19), 5002-5017. http://dx.doi.org/10.1128/JB.00542-10

Favier CF, Vaughan EE, De Vos WM, Akkermans ADL. 2002. Molecular monitoring of succession of bacterial communities in human neonates. Applied and Environmental Microbiology 68(1), 219-226. http://dx.doi.org/10.1128/AEM.68.1.219-226.2002

Fergus S. 2002. The host-microbe interference within the gut. Best Practice and Research Clinical Gastroenterology 16(6), 915-931. http://dx.doi.org/10.1053/bega.2002.0342

Gut flora - Wikipedia, the free encyclopedia.htm

Gayatri V, Hecht DW. 2003. Antibiotics and anaerobes of gut origin. Current Opinion in Microbiology 6(5), 457-461. http://dx.doi.org/10.1016/j.mib.2003.09.006

Gibson GR. 2004. Fibre and effects of probiotics (the prebiotic concept). Clinical Nutrition Supplements 1(2). 25-31. http://dx.doi.org/10.1016/j.clnu.2004.09.005

Gill SR, Pop M, Deboy RT, Eckburg PB, Turnbaugh PJ, Samuel BS. 2006. Metagenomic analysis of the human distal gut microbiome. Science 312(5778), 1355-1359. http://dx.doi.org/10.1126/science.1124234

Guarner F, Malagelada J. 2003. Gut flora in health and disease. The Lancet 361(9356), 512-519. http://dx.doi.org/10.1016/S0140-6736(03)12489-0

http://www.pnas.org/content/28/7/285?ijkey=931998456351a78f5d633e70keytype2=tf_isecsha

https://www.clinicalkey.com/#!/ContentPlayerCtrl/doPlayContent/1-s2.0-S095816691200119X

Jewell AP. 2005. Is the liver an important site for the development of immune tolerance to tumours. Medical Hypotheses 64(4), 751-754. http://dx.doi.org/10.1016/j.mehy.2004.10.002

Keeley J. 2004. Good bacteria trigger proteins to protect the gut. Howard Hughes Medical Institute. Eurek Alert. Assessed January 9, 2007.

Laurent B, Jean-Claude P. 2004. Antibiotic associated diarrhoea. Best Practice and Research Clinical Gastroenterology 18(2), 337-352. http://dx.doi.org/10.1016/j.bpg.2003.10.002

Lawson RD, Coyle WJ. 2010. The noncolonic microbiome: does it really matter? Curr Gastroenterol Rep 12, 259-262. http://dx.doi.org/10.1007/s11894-010-0111-6

Levinson W. 2008. Review of medical microbiology and immunology. 9th edition. Lange Medical/McGraw-Hill, pp. 27-28.

Ling Z, Kong Z, Jia P, Wei C, Wang Y. 2010. Analysis of oral microbiota in children with dental caries by PCR-DGGE and barcoded pyrosequencing. Microb Ecol 60, 677-690. http://dx.doi.org/10.1007/s00248-010-9712-8

Mackie RI, Sghir A, Gaskins HR. 1999. Development at microbial ecology of the neonatal gastro intestinal tract. The American Journal of Clinical Nutrition 69(5), 1035S-1045S.

Mantis NJ, Rol N, Corthesy B. 2011. Secretory IgA's complex roles in immuity and mucosal homeostasis in the gut. Mucosal Immunology 4(6): 603-611. http://dx.doi.org/10.1038/mi.2011.41

Mikocka-Walus AA, Turnbull DA, Moulding NT, Wilson IG, Andrews JM, Holtmann GJ. 2007. Controversies surrounding the comorbidity or depression and anxiety in inflammatory bowel patients. Inflammatory Bowel Diseases 13(2), 225-234. http://dx.doi.org/10.1002/ibd.20062

O'Hara AM, Fergus S. 2006. The gut flora as a forgotten organ. EMBO Reports 7(7), 688-693. http://dx.doi.org/10.1038/sj.embor.7400731

Schlegel, H.G. 1993. General microbiology. 7th edition. Cambridge University Press. p. 655.

Sears CL. 2005. A dynamic partnership: Celebrating our gut flora. Anaerobe 11(5), 247-251. http://dx.doi.org/10.1016/j.anaerobe.2005.05.001

Steinhoff U. 2005. Who controls the crowd? New findings and old questions about the intestinal microflora. Immunology Letters 99(1), 12-16. http://dx.doi.org/10.1016/j.imlet.2004.12.013

Wu GD, Chen J, Hoffman C, Bittinger K, Chen YY, Keilbaugh SA. 2011. Linking long term dietary patterns with gut microbial enterotypes. Science 334(6052), 105-108. http://dx.doi.org/10.1126/science.1208344

Wynne AG, McCartney AL, Brostoff J, Hudspith BN, Gibson GR. 2004. An in vitro assessment of the effect of broad-spectrum antibiotics on the human gut microflora and concomitant isolation of a Lactobacillus plantarum with anti-Candida activities. Anaerobe 10(3), 165-169. http://dx.doi.org/10.1016/j.anaerobe.2004.03.002

Yatsunenko T, Rey FE, Manary MJ, Trehan I, Dominguez-Bello MG, Contreras M, et al. 2012. Human gut microbiome viewed across age and geography. Nature 486(7402), 222-227.