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Submission date: 10-Jun-2022 11:16AM (UTC+0700)
Submission ID: 1854049394
File name: POST_TURNITIN1_MICROBIAL_NORMAL_FLORA.doc (453K)
Word count: 7308
Character count: 45476

MICROBIAL NORMAL FLORA: ITS EXISTENCE AND THEIR CONTRIBUTION TO HOMEOSTASIS

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Abstract

Normal microflora are a group of various microorganisms that reside in the bodies of all humans or animals. These organisms are consistently exist and relatively stable, with specific genera populating various body regions during particular periods in an individual's life, from shortly after birth until death. The indigeneous normal microbiota provides a first line of defense against microbial pathogens, assists in digestion, and contributes to maturation of the immune system and in general able to assists the anatomy, physiology, susceptibility to pathogens, and even morbidity of the host. Several internal factors like age external factors like geographical position, diets habbits, the condition of stress, infection and even antibiotics consumption, orally or intravenously, are some factors that can affect the function of normal microflora.

Keyword: microbiota, indigeneous, interaction, diets, biological age, stress, antibiotics

Introduction

Normal flora are the microorganisms that live on the surface or inside another living organism (human or animal) or inanimate object without causing disease.[1,2] Sometime it is called commensal because of their permanent presence on body surfaces even if covered by epithelial cells and are even exposed to the external environment (*e.g.,* respiratory and gastrointestinal tract, genital, hair, *etc*.).[3] Normal flora plays an important role inimmunity and inflammation.[3,4]

Significance of the Normal Flora for their host is very important. The normal flora directly influences the anatomy, physiology, immunology, even susceptibility to true pathogenic organisms, and even morbidity-mortality of the host; in short terms, it affects the homeostasis of their host.[3,5,6]

In case of human being, firstly he/she becomes colonized immediately by a bunch of normal microbial flora at the moment of birth and passage through the birth canal; in other words, initial exposure was obtained from the mother.[7] The infant microbiome contributes to his/her future health and its assembly is determined by maternal– offspring exchanges of microbiota.[8] Actually *in utero*, the fetus is sterile, but when the mother's water breaks and the birth process begins, so does colonization of the body surfaces took place. Secondly, in the next stage of life's episode, methods of neonatal care, *e.g*., handling and feeding of the infant right after birth, leads to establishment of a permanent and stable existence normal

flora on the skin, oral cavity and intestinal tract in about the first 2 days post-birth. This process is inflenced by several conditions, *e.g.,* Cesarean section, perinatal antibiotics, and also the practice of formula milk feeding, that have been linked to increased risks of metabolic and immune diseases.[8]

Microbial normal flora has spatio-temporal involvement that differs individually, regional body niche, age, geographical location, health condition, diet and also by type of host.[9-11] Effort has been done through high-throughput sequencing analysis and new software equipment are revolutionizing microbial community analyses.[9] The aim of this short review is to reveal its relative composition, function and contribution to homeostasis and what condition that affect their performance.

Relative Composition

Even without exception to the same individual, relative diversity of the microbial normal flora can possibly differ.[12] The difference is caused by changes due to (1) diet,[13] (2) stress-depression,[14] (3) sexual habits,[15] (4) pharmacology medication,[16] (5) hormonal changes[17] and (6) other host-related factors.[10] Ordinary predominant strain of microbial flora are actually exist in or within body *milleu* and even can shared functional traits.[18]

The exact number of microbial normal flora is difficult to ascertain; but of course the number is exceed the number of cells in human body.[3] The prevailing types of species in humans differ according to the body site or location, *e.g.,* skin, hair-scalp, nose, oral cavity, stomach, ileum, colon or genito-urinary tract. [19]

Mouth/Oral cavity. Normal microbial flora found in the mouth is differ based on location (saliva, tongue, tooth enamel, gingival surface,) and the condition of gingivo-periodontal well-being.[20-22] The composition of normal microbial flora in oral cavity carry a broad spectrum of microorganism, which are predominantly anaerobic such as *Lactobacillus, Bifidobacterium, Actinomyces, Bacteroides, Arachnia, Fusobacterium, Leptotrichia, Peptococcus, Eubacterium, Peptostreptococcus, Selenomonas, Treponema, Propionibacterium,* and *Veillonella*.[21-23] According to Aas *et al*.,[20] 700+ bacterial species or phylotypes, of which over 50% have not been cultivated, actually have been detected in the oral cavity. While to some extent, some genus are general in common and able to be found in most sites that belongs to the mouth, but on the other hand some species were actually very site specific. There is a distinctive predominant bacterial flora of the healthy oral cavity that is highly diverse and site and subject specific.[24] Normal flora in the area of healthy esophagus during upper endoscopy procedures predominantly was found to be *Streptococcus* spp.[25] Species that routinely isolated from tonsils of healthy children are α-hemolytic *Streptococcus* and *Lactobacilli*.[26] An interesting phenomenon that occurs where *Lactobacillus* spp. Can attach specifically to mannose-carrying receptors, *e.g*., *L. plantarum*, have a marked convinience in enduring theirselves in the oral *cavuum* by way of glyceraldehyde-3-phosphate dehydrogenase (GAPDH) assisted adhesion to epithelial cells is considered important for Lactobacillus to exert its probiotic effects.[27]

Effort to compare outcome from profiling predominant flora can be hard to interpret due to the intrinsic variation of (1) subject (*e.g*., age, gender, ethnicity),[28] (2) methods of sampling (by way of flushing of the surface, aspirates or biopsies),[29-31] (3) daily diet,[13,31] (4) sampled

site-location and microbiological assay techniques.[32] All of these four may produce significantly different results.

The Upper Resiratory tract. The human upper respiratory tract is already colonized since very early in life.[33] The composition of microflora is formed by specialized inhabitant organisms (can be bacteria, viral and or fungal assortment, which avert the potency of any pathogens from colonizing, proliferating and even propagating towards the lungs via the blood barrier.[34] Normal respiratory microflora include *Neisseria catarrhalis, Candida albicans, Diphtheroids, alpha-hemolytic Streptococci,* and some *staphylococci*.[35,36]

Anatomically, the evolution and growth of the respiratory system is a complex multistage sequences that happens continously, the sequence of episodes that took place prenatally and also postnatally.[36,37] This maturation process rely, in part, on exposure to microbial, fungal and environmental conditions,[38] including diets,[13] and in turn results in a highly specialized organ properties.[38] Those properties contains several recognizable milleu, each of which is subjected to specialized microbial, cellular and physiological gradients.[39]

The respiratory microflora existence is non-static and influenced by several host and environmental elements, including natural or caesarian birth, feeding pattern, antibiotic consumption and crowding conditions, e.g., the day-care attendance and or presence of siblings.[39,40]

For evey phisicians, they must keep in mind that the presence of normal upper respiratory tract flora is common and should be expected in sputum culture.[40,41]

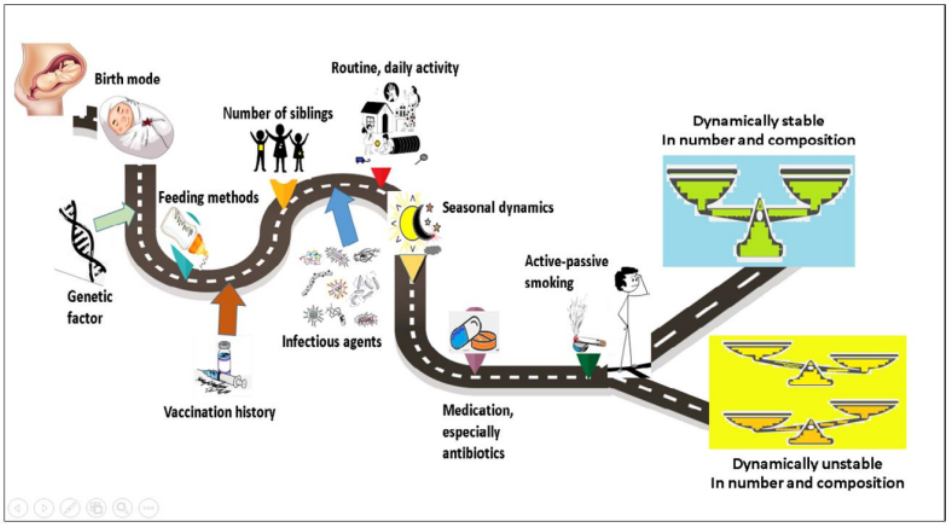

Fig. 1 when a neonates born, its microflora composition formed a highly dynamic communities/network; affected by multiple internal-external factors, including mode of birth, feeding methods,vaccination history, siblings that made crowding situation and medication especially antibiotic treatment. Environmental factors such as seasonal dynamics, pathogenic agents and habbits like smoking can shift number and iversity of microflora, can be directed to a more stable population at equilibrium that make their host able to control the pathogen overgrowth, or, conversely, an

unstable population that is predisposed their vulnerability to recurrent infection and inflammation.[40, with modification]

The Stomach and Intestine. Fewer bacteria actually manage to exist in the stomach due to its harsh environment for organism; where only limited organism have the capability to survive there.[41] Five major phyla have been detected in the stomach: *Firmicutes, Bacteroidites, Actinobacteria, Fusobacteria* and *Proteobacteria*. At the genera level, the healthy human stomach is dominated by *Prevotella, Streptococcus, Veillonella, Rothia* and *Haemophilus*.[10,11,41] The occurrence of *Helicobacter pylori*, the species that has been isolated from specimen that come from peptic ulcers or gastric neoplasia. Actually, *H. pylori* is also able to be found in >60% of healthy individuals. That is why this organism always thought to be responsible for causing gastric abnormalities. Its number increases as it reaches the end of the intestine.[42,43]

The intestine is differ from the stomach, due to the quality and quantity of organisms that they contain. The variety of organisms is also multiplex, mostly there are more anaerobic microorganisms than the aerobes organisms.[44,45] A study found out that the number of intestinal microbial normal flora as much as 10^{11} organisms:gram of feces; and those number is formed by a very diverse composition (>500 different species), with each in number is ranging in different concentrations.[46]

The development of current approachs, methods, techniques and genetic probes has granted finer characterization of organisms that made the normal intestinal flora.[32] The approach conducted by Franks *et al*., that developed several 16S rRNA-targeted oligonucleotide probes actually can detect and confirm the availability of >60% anaerobic organisms in human fecal material.[47] These probes proved to be very important in proving the characterization of the microecologic milleu in the human intestine. Eventhough it is still widely open to conduct more extensive research to provide answers for soem challenging questions about the exact role of normal microflora in digestion or even in intestinal movement.

The Vagina. Previous studies have published the composition of normal microflora in the normal vagina. It is usually a complex combination of aerobic *Lactobacillus* spp., including *L. Acidophilus*, *L. jensenii*, or *L. Rhamnosus*. Some species of lactobacilli, namely *L. Acidophilus, L. crispatus* and *L. Jensenii*, play a crucial role in protecting vaginal surfaces by secreting H2O2.[48,49] This acidic compound prevent the colonization of pathogenic anaerobes and even mycoplasmas.[50,51] Beside preventing colonization, it also inhibits their replication. Lactic acid blocks the enzyme histone deacetylases, thereby magnifying the process of gene transcription and also DNA restoration. The existence of these potential pathogens predominantly associated with vaginal infections such as bacterial vaginitis, *Neisseria gonorrhoeae* or other type of sexually transmitted diseases.[51,52]

The number and composition of vaginal microflora is very dynamic.[53] It has been shown to fluctuate over (1) age (childhood – adolescent – young adult – elderly), (2) routine menstrual cycle, (3) sexual activity (active-passive, promisquity), (4) hygiene habits, (5) fashion related habits and (6) the practice of using intravaginal microbicides, *e.g*., nonoxynol-4.[17,54]

Related to the previously stated dynamics of the presence of vaginal microflora, studies confirmed that most women in healthy condition have short-term switch in vaginal flora composition, which, although not permanent, can cause changes in the local

microenvironment.[54,55] Only a small percentage (22–26%) of healthy women contain lactobacilli-predominant flora. Personal behavior, biological functions including hormones and or other external conditions might contribute to the dynamic pattern of vaginal microflora.[56] Furthermore, the characterization of normal vaginal microflora and its contribution to maintain specific milleu in the vagina is still need to be investigated, especially among specific healthy women population.

The course of the evolution of normal flora is a life long continous episodes that starts immediately at birth process.[57] It is belief that the process of colonization starts during parturition, at the time the neonate's intestine is planted with mostly Gram-positive facultative anaerobes from the mother's vaginal microflora at the time of normal delivery.[58] Close contact is once again responsible for the introduction of normal microflora to the newborn. The vaginal microflora collected from mother's right after delivery was the same in composition as microflora found in the stools of neonates.[59]

The vaginal microflora plays a pivotal role in maternal-neonatal health condition. Dys-balances in this microflora composition and number (dysbiosis) during pregnancy are associated with dismissive reproductive consequences, such as pregnancy loss and preterm birth. Feitas *et al*., [60] who conducted a study of normal flora in pregnant women found out that microflora profiles in general could not be esteemed based on pregnancy status. However, the vaginal microflora of healthy pregnant women had degrade richness and diversity, smaller prevalence of *Mycoplasma* spp. And also *Ureaplasma* spp. but higher bacterial load when compared to non-pregnant women. *Lactobacillus* spp. affluence was also higher in the microflora of pregnant women with Lactobacillus-dominated in comparison with the non-pregnant group.

Neonates born by surgical procedure (caesarian section) usually obtain their first microflora from the *milleu* of the clinical/hospital nursery.[61] Neonates are rapidly inhabited by facultative anaerobes (*E. Coli* and *Streptococcus*), reaching normal concentrations in the stool within the early 1–2 days after birth.[62]

Factors That Contribute to The existence of Normal Microflora

Biological age, not Chronological Age. The diversity of skin microflora in different age groups is vary. Whether with the addition of age is also related with the alteration in its number, its diversity and also to some extent deficits in their function is not well understood. How this change occurs, whether slowly (gradual) or suddenly fast (progressive) is also not known with certainty. The ability to define these deficits in populations of different ages may help determine a chronological age threshold at which deficits occur and subsequently identify innovative dietary strategies for active and healthy ageing.[63] According to Maffei *et al*, increasing biological age in community-dwelling adults is associated with gastrointestinal dysbiosis.[64]

The skin microbiota is also very diverse and varied in different age groups.[63] Diversity in skin microbiota tends to increases with age.[65] The increase in diversity during the first eight years of life is associated with a reduced dominance of the Order *Lactobacillales* (namely *Streptococcus*) and a relatively even increase in other taxa, whereas the reduction in diversity in puberty is due to *Actinobacteria* (such as *Propionibacterium acnes*) becoming dominant.[66]

In case of early infancy, the gut microecology is constructed during this early phase of life by the composition of the normal intestinal microflora.[7,12,13] The diet in pre-weaned babies is mostly influenced by the daily type of diet (breast or formula fed).[1,3,13] Infants usually be inhabited only by three kind of native *Lactobacilli*, and when become older, there is an increased in both quantity of different species and transient nature.[8] Normal gut microflora in geriatry may also differ from younger adults.[67]

Regarding to the genito-urinary microflora, it seems that postmenopausal female have been found to have elevated numbers of microorganisms such as fungi, clostridia and lactobacilli compared to the pre-menopausal group.[49,56,57] Other studies also revealed variation of normal microflora in the older age female, but whether this variation is due to chronological age, medical exposures, or due to illnesses was unclear.

Geography. There are several studies which report differences in normal microflora depending upon geographical setting,[39] one of them was conducted by Benno *et al*.,[68] in elderly Japanese living in urban vs rural region. On the whole, the diversity and counts of stool microflora were similar. Urban people have significantly less *Bifidobacterium adolescentis*, but significantly more total anaerobic bacteria, bacilli and *Clostridium* spp. than those who live in rural areas. These slight differences might be due to different diet (high fiber) in the rural population, eventhough this hypothesis is not in line with data on dietary patterns. One of the crucial topics in the normal microflora research is to characterize what is considered healthy microflora. Recent studies have clarify critical separation in the microflora composition between healthy persons from different race and ethnicity.[39]

The geographical difference on the composition and diversity of normal microflora reported in certain populations are actually not genetically origin, as initially thought, but due to the variation in diet composition.[69] The microflora of the gut varies according to the milieu intereur of the body. Various factors influence the microflora of the oral cavity and the gut. For example, when intestinal microflora is compared for English man living in London and consuming a mixture western diet against Ugandans from the same neighbourhood but consuming only vegetarian diets, and when the stool sample analyzed and the result was as follows: the English people had more *Bifidobacteria* and *Bacteroides* but less *Enterococci, Lactobacilli* and even yeasts than the Ugandans. even though all sample collected in almost at the same time.

The consumption of routine and daily vegetarian foods are related with less number of *Anaerobes* and higher enumeration of facultative and aerobic microbes.[70] It is believed that, one person has a moderately persistent profile of microorganism (qualitatively and quantitatively) that can considered as 'normal microflora'.[10] But, antibiotics consumption can affect the normal microflora composition.[16] Sometime, inter-individual distinction of normal microflora may alter to some extent.[3,10] The comparison of differences in normal microflora composition for various geographic populations is intricated by limitless differences in (1) population characteristics, (2) daily diet, (3) isolation and culturing technique, (4) state of the art technology applied and (5) time when the study conducted.

In connection with those limitations, it is necessary to carry out further research in the context of uniformity of various variables, for example population (same age range, sex, ethnicity, diets), tools applied, materials and methods, time and place of implementation. This approach

may reveal the differences that regularly seen in normal microflora of people from different countries.

Diet. Evidence that comsumption pattern influences normal flora in adults is sparse, but many studies have been conducted in specific populations, *e.g.*, young infants and also animal.[13,71,72] Data from animal study showed us that diet has been shown to change the composition and number of microflora, but unfortunately, data available only limited the mineral calcium, carbohydrates or fiber administration and their direct or indirect effect to microflora. Daily dietary calcium tend to precipitates and induced cytotoxic substances, *e.g.*, bile acids, causing in reduced cytolysis; a condition of changes elicited by inulin and galacto-oligosaccharides consumption.[73] as consequences, fewer intra-lumen cytotoxicity may facilitate and fortify endogenous flora armamentarium.[74] According to the study conducted by Bouvee-Oudenhoven *et al*.,[74] calcium supplementation diets given to animal model (rats) actually reduced inhabitation of *Salmonella enteritidis* in their gut.

The type of diet predominantly affects the composition of microflora in pre-weaning neonates.[75] Infants who are breast-fed contain higher amount of Bifidobacteria.[76] Biochemically, breast milk usually contains minimum protein and on contrary high levels of oligosaccharides and glycoproteins, which facilitates the growth of Bifidobacteria.[77] On the other hand, some studies confirmed that Formula-fed babies have a more sophisticated microflora, namely *Bifidobacterium* spp, *Bacteroides* spp, *Clostridium* spp and *Streptococcus* spp; eventhough the difference in breast-fed vs. Formula-fed infants is not really significant.[78] the higher number of *Bifidobacteria* found in babies fed formula only took place for factory made milk that had only a little buffering magnitude.

Contribution of normal flora to the normal function of the intestine can be summarized as follows: (1) digesting enteric metabolic substrates, (2) resisting colonization by foreign non-self microflora, (3) vitamins assembling, (4) development of attachment sites, (5) facilitates immune system, producing exogenous enxymes, facilitating intraluminal transit, (6) advancement and turn over specific intestinal cells.

Fructo-oligosaccharides (FOS), a specific sugar contained in fruit like bananas, or plants, *e.g.*, fresh onions, artichokes and asparagus, are fermented largely by the bacteria *Bifidobacterium* species, and this turns out to be interrelated and influence each other. in human volunteers, increased consumption of FOS actually expand the levels of *Bifidobacteria* in the intestines for a certain time, but then causing excessive *flattulen* when the amount eaten exceed 20 g daily.[79] FOS was also responsible for the rise of numbers of total *Anaerobes* and *Bifidobacteria*.[80] Beside FOS, sucrose was found to facilitate the escalation of *Bacteroides* spp. and also inulin, specifically was found to escalate mainly *Bifidobacteria*.[81]

Various kind of fiber have the ability to change the levels of *Bifidobacteria* spp, *Lactobacilli* spp and also fungi in animal models (pigs and also rats).[31] Several fermentable fibers may facilitate the expand of normal flora, yielding short chain fatty acid and reduced colonic pH, and by doing it indirectly inhibits the growth of certain bacteria, such as *C. difficile*.[82] Diet containing tea polyphenols given to pigs increased the levels of *Lactobacilli* and reduced levels of *Bacteroides*.[83]

Several studies conducted in newborn in the past showed us that breast-fed babies actually have been found to bear mainly *Bifidobacteria*. While on contrary, a group of formula-fed

babies are inhabited with a broader spectrum of organisms, namely *Bacteroides* spp, *Enterobacteria* spp, and even *Clostridia* spp.

All of those findings provide insight into the role that diet plays critical role in influencing the composition of normal flora, in the context of the digestive tract. There was also a report about consequence of an adapted formula milk, that contain high maltose, on the gut inhabitation of *Bifidobacteria* spp. compared to the group of breast-fed Babies.[78] Breast-fed infants have higher amount of *Bifidobacteria* than formula-fed neonates, even in the very early days of life (4 days).[8] Further study need to be conducted in order to reveal how well-defined diets can modify the amount and also relative composition of normal flora.

Infection. The existence of normal microflora actually also helps their host not to get too easily colonized and infected with enteral parasite.[84] Parasites usually enter the body through the oral fecal route and directly interact with the commensal bacteria of the intestine and causing diarrhea.[84,85] Infection may have obvious clinical manifestations, but it is suspected that there are many more asymptomatic intestinal parasitic infections.[85,86] Normal microflora may increase resistance to parasitic infections at mucosal sites via changes in the composition of intestinal bacteria, and it may also alter systemic immunity to these parasites.[84,87]

Stress. Human beings and their intestinal 'good' bacteria have emited numerous steps to coordinate with and regulate one another.[14] The condition of psychological stress and further depression to some extent can initiate consumption of uncontrolled diets, which directly influencing the growth and the development of microflora.[88] In addition to that condition, stress and depression can reshape the number and composition of normal microflora through thre ways: (1) excessive secretion of stress hormones, (2) initiation of inflammation, and (3) uncontrolled autonomic alterations which can further trigger series of events that can make the condition become worse.

As the consequences, the intestinal bacteria liberate more end-product substance, toxins, metabolites, and even neurohormones that can further alter eating behavior and even appetite and also mood in general.[88,89] Some bacterial species also have the ability to facilitate dysregulated excessive eating, or in other word eating very much.[90] The gut bacteria may also stimulate stress responsiveness by lowering the treshold and in turn heighten the risk for depression, which adding probiotic supplementation may weakened the condition.[88-90]

Antibiotics. Antibiotics that are prescribed to treat pathogenic bacteria also have an impact on the normal microbial flora of the human gut.[16] Antibiotics can alter the composition of microbial populations (potentially leading to other illnesses) and allow micro-organisms that are naturally resistant to the antibiotic to flourish.

For example, oral administration of antibiotics for treatment of urinary tract infections (UTIs) can cause ecological disturbances in the normal intestinal microflora. Poorly absorbed drugs can reach the colon in active form, suppress susceptible microorganisms and disturb the ecological balance. Suppression of the normal microflora may lead to reduced colonization resistance with subsequent overgrowth of pre-existing, instinctively unsensitive microorganisms, such as organisms like yeasts and *Clostridium difficile*.[91] New colonization by resistant potential pathogens may also occur and may spread within the body or to other patients and cause severe infections. It is therefore important to learn more about the

microecological effects of antibacterial agents administration, especially if given long-term, on the existence and performance of human microflora.[88-90]

Actually, some normal microflora have an intrinsic resistance to antibiotics; means that normal microflora harbor specific antibiotic resistance genes to various degrees, and even this condition can took place in any individual with no previous history of exposure to factory made antibiotics.[16] Some condition seem to contribute to the increment of antibiotic-resistant bacteria in feces. One important factor is the repetitive disclosure of the intestinal normal microflora to antibacterial drugs.

The practice of adding certain antibiotics used as feed additives seem to contribute to the development of antibiotic resistance in normal flora bacteria.[92] For example, the use of avoparcin as a feed additive has demonstrated that an antibiotic which was initially considered "safe" is actually responsible for reduced levels of antibiotic sensitivity in the normal flora enterococci of certain animals fed with the antibiotics avoparcin. This reduced sensitivity possibly will be pass to humans which consuming products, *e.g.*, meat or egg, from these animals.

In the context of domesticated animal being consumed by human, other external condition like stress due to ambient temperature, condition of crowding, and perhaps caging management that might contribute to the manifestations of antibiotic resistance in certain normal microflora.[93] The normal microflora of animals has been widely studied in order to screen antibiotic resistance over four decades, but unfortunately, only limited number of studies that focus on intestinal microflora as the main focus. Previous studies contributes to the recent understanding of mobile genetics responsible for bacterial antibiotic resistance. Further study need to be conducted in order to link the number of previous repetitive exposure to the increase in antibiotic resistance of bacterial pathogens.

Bacteria of the normal flora, often disregarded scientifically, should be studied more extensively with the intention of using them as active protection against infectious agents and thereby contributing to the overall reduction of use of antibiotics in both animals and humans.

Another example is the common practice of antibiotics administered orally or intravenously to sterilize and decontaminate the gut in order of patient preparation for intestinal surgery.[94] Common post-surgical complication is infections that was usually of intestinal origin. So previous decontaminating of the intestines with antibiotics might lower the risk. But unfortunately, therre is weakness of the previous statement due to: (1) protective role of normal intestinal microflora and (2) profound disruptive effect due to broad spectrum antibiotic administration. The action of selective gut decontamination actually facilitates 'rebound colonization' with potentially pathogenic organisms, non normal microflora, after surgery procedure.[95] Rebound colonization can possibly took place with dangerous nosocomial aerobic pathogen.[96]

Treatment with the antibiotics, broad spectrum or not, did diminished intestinal microflora, quantitatively and qualitatively, but actually had no effect on the incidence of expected complication, *e.g.*, such as post-surgical infections, sepsis, prolonged wound, pneumonia or fatal organ failure.[94-96] Unfortunately, long term follow up on the practice of gut decontamination among surgical patients did result in higher rates of oxacillin-resistant *Staphylococcus aureus*, which actually used to be part of normal flora but then changed in its

characteristics due to long term antibiotics adminstration. Eventhough one study reported, dose of antibiotics is not merely affected the composition of normal flora.

Most studies of antibiotics and their impact on normal microflora have been aimed at (1) its direct killing ability and (2) the development of antibiotic resistance.[93-96] However, there are a few studies on the impact antibiotics have on normal microflora. There is also a difference of route of adminisitration (Oral vs intravenous) in influencing composition normal microflora or direct effect to state of colonization resistance. So far to my knowleledge, no direct measures on specific strains of normal microflora were done.

Most of the studies regarding normal microflora-antibiotics relationship have been conducted using healthy subjects. One study conducted among healthy volunteers that receive antibiotics revealed that only those respondents that revealed to antibiotics agents were later then found to be inhabited with Gram-negative bacilli.

All of these studies explained how antibiotics consumption may disrupt normal intestinal microflora and may predispose subjects to suffer from disease caused by opportunistic agents.[16,93] Recovery of the colonization resistance brought on by antibiotic exposure may take weeks to months after the discontinuitation of antibiotics. Further studied still need to be conducted, especially on the effect of antibiotics discontinuitation to the diversity and the number of normal microflora.

Conclusion

The 'normal microflora' is the term most commonly used when referring to the microbial collection that consistently inhabits the bodies of healthy human or animal, from shortly after birth until death. The normal flora influences the anatomy, physiology, susceptibility to pathogens, and even morbidity of the host. Diets, stress, infection and antibiotics administration are some factors that can affect the existence and performance of normal microflora.

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