Chapter 3
Dysbiosis, Probiotics, and Prebiotics: In Diseases and Health

Contents

Abstract The microbiome like any other components of the body undergoes numerous challenges during the life-span of a human being. These complications may involve injuries, aggression by pathogens, pollution, hormonal variations, genetic pre-disposition, unbalanced nutrition and onset of diseases. Although the microbial reconfiguration provoked by these stressors are not immediately evident as in the case of an afflicted visible organ where the abnormality is readily observable, the biological perturbations induced manifest themselves in form of various illnesses. The disruption of a working microbiome is referred to as dysbiosis and is a condition whereby the fine balance between the microbial communities and the host is distressed. Diseases such as cancer, irritable bowel syndrome, rheumatoid arthritis, acne, gastric ulcers, obesity and hypertension can ensue. The pathogeneses of some pulmonary disorders, digestive complications and neurological

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abnormalities can be traced to the imbalance in the constituents of the microbiome. However, rebiosis, the re-establishment of the native microbiota is proving to be an excellent remedy against this condition. Probiotics, prebiotics, and synbiotics are potent therapeutic tools designed to rectify this situation. Probiotics such as *Lactobacillus* spp are more or less like stem cells utilized to replenish and rejuvenate the microbiome while prebiotics like fructose oligosaccharides (FOS) are microbiome fertilizers akin to mineral supplements or energy nutrients aimed at promoting the proliferation of select microbes in the invisible organ. Synbiotics is a combination of both probiotics and prebiotics in a proper dosage aimed at remedying dysbiosis. The molecular understanding of dysbiosis and rebiosis will offer a very effective non-invasive means in preventing and curing diseases with probiotics and prebiotics. This will have a dramatic impact on our well-being.

Keywords Microbial imbalance · antibiotics · cancer · obesity · anti-oxidant · drug activation

3.1 What Happens When the Invisible Organ Is Distressed? The Disruption of Our Microbial Communities and Common Diseases

As our microbiome accomplishes a variety of critical tasks for us, it is clear that we will not be the way we are without the microbes inhabiting in and on our body. Without this microscopic support, our anatomical constituents and our diet would have been completely different. The diets of carnivores and herbivores are also dependent on the microbial helpers these animals possess. The cows we see grazing would not be engaging in such an activity if it was not for the microbe-laden stomach they have. Indeed, humans also have evolved to be reliant on microbes to carry numerous functions they are not able to execute without the assistance of their traditional organs. Without the presence of these microbes, human anatomy and physiology would have been entirely different; we would not have been biologically the way we are. Thus, it is not surprising that if this harmonious relationship is perturbed, major complications may arise with disastrous consequences to the bodily operation. In fact, the delicate balance among the microbial ecosystems needs to be preserved if the body is to function normally. The metabolically compatible members of this community work in harmony and as they are assigned a specific job that enables the community to function properly. This synergy breeds inter-dependence and a specialization of functions. The community forges a collective work ethic amongst all the stake-holders. Constant interspecies communication ensures that their activity is controlled and excessive growth is under check. However, perturbation of this fine microbial-balancing act can result in debilitating impact on the host.

The increase in some bacterial species with the concomitant decrease of others triggers abnormal signals that can be the harbingers of diseases. This situation is similar to the operation of our social communities. For instance, if there is an excessive amount of doctors and limited number of nurses and other health professionals, the medical delivery system becomes sick. The disruption in the microbial community is bound to create a shift in the families, genera or species of the resident microbes. This can be fatal or make the business of living unpleasant. Numerous diseases are known to be triggered by the disturbance of microbial population within the body. The imbalance of the microbiome is referred to as dysbiosis (Fig. 3.1). Diet, physical stress, exercise, psychological distress, radiation, flying, humidity, geographical location, age and medications including antibiotics have been shown to exert demonstrable change in the microbial landscape in the body. For instance, ampicillin utilization leads to a sharp decrease in the gut microbiome, while the antibiotic, cefoxilin perturbs the fine balance by promoting the proliferation of *Clostridium difficile* at the expense of other microbes. The amount of some *Lactobacillus* species is sharply diminished during flight and may lead to anxiety associated with air travel. The increased levels of catecholamine produced during stress trigger the growth of pathogenic microbes like *E.coli* and impede the proliferation of good microbes like *Lactobacillus* and *Bifidobacteria*. Farm workers who are exposed to pesticides suffer a similar diminution in *Lactobacillus* and *Bifidobacteria*. Exposure to metal pollution like cadmium limits the amount of micro-organisms belonging to the family of *Bacteriodes* that in turn is reflected in reduction of metabolites like SCFA (short-chain fatty acids), contributors to numerous pivotal functions in the body as we have seen before. These changes lead to various abnormalities (Fig. 3.2).

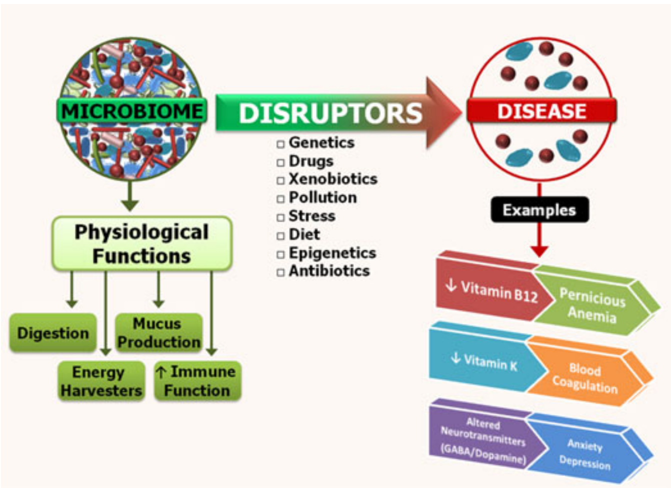


Fig. 3.1 Factors resulting in the disruption of the microbiome lead to dysbiosis. (Note the lack of microbial diversity in the distressed microbiome)

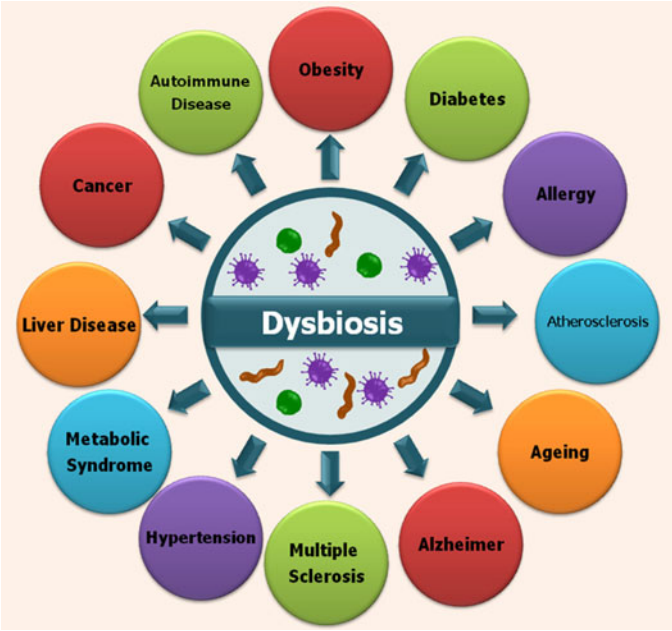


Fig. 3.2 Diseases and dysbiosis. (These medical complications can be initiated by dysbiosis)

3.2 Dermal Dysbiosis Leads to Acne and Eczema

The skin is the primary contact with the external environment and is constantly exposed to a variety of fluctuating conditions that affect the microbial communities residing on it. Humidity, temperature, clothing, cosmetics, soaps, age, and personal hygiene are some of disruptors of the skin microbiome leading to the onset of various abnormalities (Box. 3.1). Acne is a common skin complication that afflicts primarily adolescents. During puberty there is a major change in the landscape of the skin with the increase of hair follicles and the maturation of the pilosebaceous glands. These oil-producing vesicles enrich the nutritional content of the skin and trigger the proliferation of oil-loving microbe like the *Propionibacterium acnes*. These microbes secrete lipases and proteins that enable them to gobble oil. Unfortunately, these molecular scissors also bruise the tissues adjoining the oily glands. Such an unintended assault compels the body to unleash its own guards to defend itself, with devastating outcome. This counter response to the shift in microbial population results in the formation of those unwelcomed blemishes on the face. Hormonal imbalance may also aggravate this problem (Fig. 3.3).

Box 3.1 Disruptors of the Skin Microbiome

The dermal microbiota is prone to disruption by a wide variety of factors as it is permanently exposed to the external environment. Geography, pollution, ultraviolet radiation (UV-R), occupation and the host biology are major contributors to the skin microbiome. Injury, chronic conditions, infection, cosmetics and the use of hygiene products may result in a shift in the bacterial communities. UV-R promotes the release of anti-microbial peptides that may block the body's immune system and creates an environment for the cancer-causing viruses to flourish. Chemicals like triclosan, a common ingredient in household products like soap and toothpaste can perturb the fine microbial balance. This is further compounded by the inherent diverse landscape that the skin offers; the face is oily, hairy and exposed to environment while the axilla is occluded, moist and laden with microbial nutrients. The dysbiosis triggered by the host of environmental and microbial-driven features are at the origin of numerous skin diseases. For instance, the atopic dermatitis that is a chronic pruritic inflammatory disorder is characterized by an overwhelming increase in *Staphylococcus aureus*. A decrease in filaggrin, a microbial sensing protein coupled with a decrease in dermicidin, a peptide defending bacterial invasion results in this lack of microbial diversity and the proliferation of a select few microbes. Prebiotics like fucosylated oligosaccharides derived from chicory roots and probiotics like *Staphylococcus epidermis* are being introduced in cream to fight dermal dysbiosis.

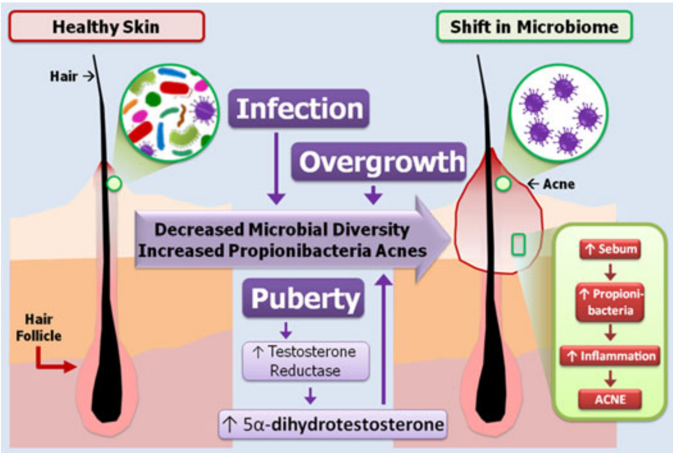


Fig. 3.3 Hormonal and nutrient fluctuations trigger acne. (The dysbiosis caused by these events provokes inflammation)

Eczema is another common skin ailment that finds its origin in the imbalance of the dermal microbial community. It is a chronic, recurring skin disorder that is more prevalent in children compared to adults. This disease is characterized by a major shift in the microbial population resulting in diminished biodiversity. Such a situation promotes the unchecked growth of the microbe, *Staphylococcus aureus*. Increased colonization by this organism provides a fertile landscape for the nasty *Streptococcus* to proliferate. The tight-knit functional community is unraveled. The new uncontrolled colonizers secrete toxins that induce the degranulation of the dermal mast cells and force the body's immune system to respond. This change in landscape is partly responsible for the dry red spots that are characteristic of eczema. These patches are sometimes accompanied by local inflammation.

In the case of psoriasis, a disease that is prevalent world-wide, similar conditions conspire to create a dramatic shift in the harmonious microbial population. The ensuing diminished biodiversity propelled by the over-representation of the genera *Staphylococcus* belonging to the *Firmicutes* family automatically leads to a reduction in other family members that had bonded into this dermal community and learnt to live in harmony. In this instance, the territorial presence of members belonging to the *Acetinobacteria* family is restrained. Thus, begins the initiation of psoriasis. Environmental factors like temperature, humidity or presence of cosmetics on our skin may hasten the onset and the severity of this malady. The establishment of the unbalanced microbial community residing in the psoriatic lesions generate antimicrobial peptides and other modulators that hyper-activate the body's immune system. This reaction modifies the life-cycle of the skin cells that respond by growing rapidly, a situation culminating in itchy, dry, red plaques. These become the hub of other uncontrolled microbial activity and can aggravate into psoriatic arthritis. Wound healing in diabetic patients is a problem as cuts on the skin of these individuals take unusually longer time to repair. Here again the inability to effectively recover from wounds is again due to the uncontrolled proliferation of certain microbes at the expense of others. The sugary environment provided by the diabetic blood and the presence of other nutrients create an ideal ecosystem for the multiplication of *Staphylococcus*. This nutrient-rich landscape on the skin-cut acts as a magnet for some bacteria and disrupts the harmony among the otherwise orderly community members. This microbial imbalance is a recipe for disaster and opens the body for invasion as some of our trusted partners are either too small in numbers to make any difference or are completely wipe-out of our intimate landscape by the opportunistic intruders. And wound healing becomes a very abnormal exercise for the body to partake in the absence of some of the invisible allies.

3.3 Distressed Microbial Communities in the Mouth: A Smelly and Painful Concern

The mouth is another part of the body that lends itself to constant contact with the invisible world. As it is an extension of our environment, the microbial traffic is high. Anytime we open our mouth to eat, drink, laugh, smile, yawn or cry, we are

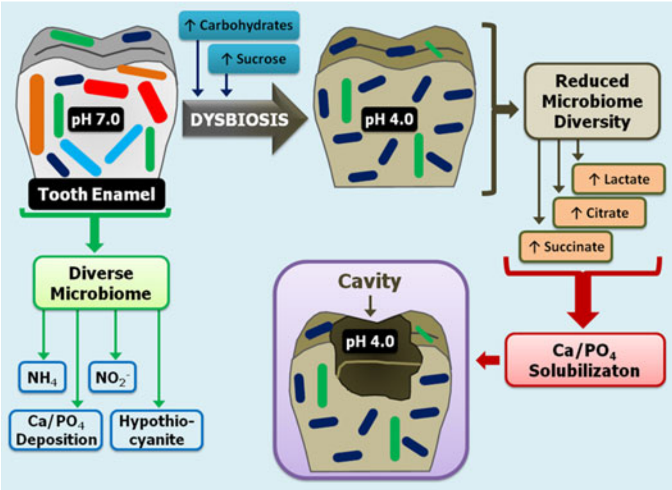


Fig. 3.4 Sugary diet and dental cavities. (The organic acids produced by the imbalanced microbial community decrease the pH and attack the enamel; hypothiocyanite is a potent antimicrobial agent)

enabling millions of microbes to access our body. However, due to the vigilant watch of resident oral microbes and their anti-microbial components, only a select few can contemplate to occupy a piece of the real estate either in our mouth or lungs. The microbial communities composed of diverse constituents that set foot are scrupulously and carefully interrogated by our molecular sentinels. Interactions with prospective residents are permitted only if they work for a common purpose. Only when a member can contribute to a specific function that the community depends on, the microbial member is accepted and a shelter is made available. The contribution of each of the member is critical for the functioning of the community.

However, this situation can rapidly change specially in the mouth where there is a constant flux of diverse exchanges occurring with respect to microorganisms. Furthermore the buccal chemical landscape also undergoes tremendous fluctuation due to the regular intake of foods and drinks. This situation can be complicated if one allows any food component to remain in the mouth for too long. Carbohydrate-rich nutrients become easy prey on which some opportunistic microbes can thrive. Despite the vulnerability of the mouth to possible invisible intruders, the microbial population is kept in check by the watchful guard of other community members including the host. For instance, in the establishment of dental caries, the *Streptococcus mutans* utilizes these sugary goodies stuck on the tooth to produce lactic acid, an event that increases the acidity of the buccal ecosystem. This presents an opportune situation for other microbes like the *Veillonella* and *Lactobacillus salivarus/acidophilus* to colonize this territory and further aggravate the affliction on the tooth (Fig. 3.4). The fine microbial balance that is perturbed as a result of ensuing chemical change in the mouth is an ongoing concern for people especially children with poor dental hygiene. This disruption and the resulting medical complication can be averted by controlling the chemical

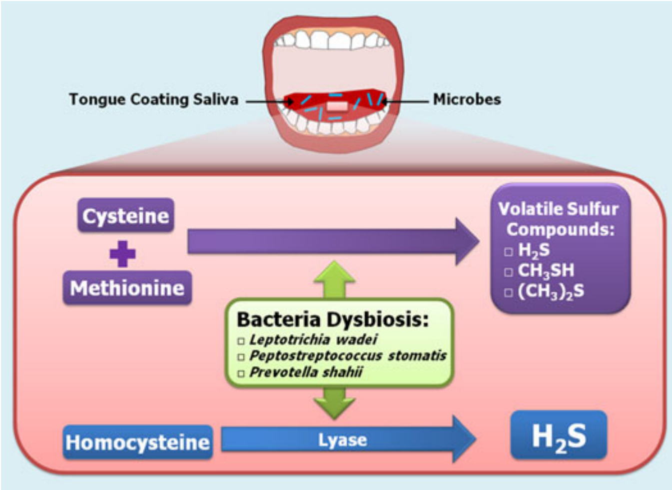


Fig. 3.5 Halitosis: bad breath and oral microbes. (The volatile sulphur compounds are the leading cause of bad breath, dysbiosis also impedes the production of antimicrobials like hypothiocyanite)

landscape in the mouth. Halitosis is also caused by microbial disruption that results in the increase in H_2S, a molecule responsible for smelly breath. This may also be aggravated by the genetic make-up of the host (Fig. 3.5).

The perturbation of controlled microbial growth in the oral cavity is known to trigger the gum disease referred to as periodontics. The homeostatic equilibrium in the microbial community for a healthy gum is maintained partly by the body's own immune system. This is upset by the invasion and colonization of *Porphyromonas gingivalis*, a microbe responsible for the destruction of gum tissues. These degraded components create a nutrient-rich environment that becomes a breeding ground for other opportunistic organisms that are usually kept at bay by our oral microbiome and the lack of appropriate nourishments they can thrive on. This feeding frenzy results in the overpopulation of some species compared to others and give rise to a misfit community of microbes. Bacteria such as *Prevotella* and *Desulfobulbus* are two culprits that exploit this situation and assist in the task of invading the gum. Thus, dysbiosis an uncontrolled microbial proliferation resulting from the temporary nutritional change in the oral ecosystem is at the root cause of numerous complications that ache both the hard and soft components belonging to this part of the body. The lack of microbial biodiversity in the crypts of the soft tissue like the tongue is at the origin of halitosis, an affliction that emanates unpleasant smell that most of us find repulsive (Box 3.2).

Box 3.2 Salivary Microbiome and its Health Impact

The mouth has the second most diverse microbiota in the body with over 700 species. The chemical landscape of the saliva plays an important role in the establishment of the microbial communities that reside in the buccal

(continued)

Box 3.2 Salivary Microbiome and its Health Impact (continued)
cavity. Nearly 10^8 microorganisms are found in one milliliter of saliva, a fluid rich in proteins, lipids, carbohydrates and enzymes. The presence of lactoferrin, lysozyme and lactoperoxidase act in concert to dissuade the colonization by fortuitous bacteria. Hydrogen peroxide, hypothiocyanite and nitric oxide derived from nitrate in foods are potent antimicrobial and are part of the defense armoury deployed to fend against cariogenic intruders. However, poor hygiene, nutritional habits, smoking and diseases like diabetes tend to weaken this defense. The presence of increased glucose level generates acidic metabolites that drop the pH of the mouth from 7.0 to 4.0. This promotes the acid tolerant microbe like *Staphylococcus mutans* and results in an increase in the *Firmicutes* family coupled with a decrease in the *Bacteriodetes* family. The solubilization of calcium and phosphate is preceded by a variety of dental diseases. Furthermore, the dysbiosis created by this situation leads to reduction of nitrate reducing bacteria, a situation restricting the output of nitric oxide, NO. This has major health impact including cardiovascular complications. The use of chlorhexidine containing mouthwash also has a negative influence on NO-producing bacteria. Hence, the saliva and its microbial residents are an important contributor to a healthy outcome.

3.4 Pulmonary Dysbiosis, Asthma, and Cystic Fibrosis

The mouth and the nostrils are constantly providing the lungs the air we need to live. Without this obligatory and mundane routine we will not be able to produce energy (ATP) that keeps our body machine active. This process is hard-wired in our brain that we keep on doing until we are no more alive. Thus we are constantly exposed to the microbes and chemicals in the environment where we are studying, sleeping, playing, working or just relaxing. The lungs are permanently bombarded with the myriad of micro-organisms our surroundings have to offer. Although the microbial populations in the lungs are well-maintained, these communities can be harassed by medications we ingest and by the chemicals in the air we are surrounded by. Farmer workers, employees in factories and other industrial organizations are at high risk in this regard as they are surrounded by chemical constituents that affect the microbial composition of the lungs. The development of asthma is triggered by the decrease in the diversity of the pulmonary microbial ecosystem.

The release of nutrient-rich mucus during lung infection aimed at arresting the proliferation of intruders can also inadvertently act as a magnet for some opportunistic microbes that further compound the problem. A shift in the microbial community favouring a group of *Lactobacillus* is observed during the onset of chronic obstructive pulmonary disease (COPD). During cystic fibrosis (CF) the viscous sputum allows the rapid growth of *Pseudomonas aeruginosa*, a microbe that is controlled in non-CF lungs. This microbial imbalance generates chemicals like alginate that further aggravates the situation. The nearly unimpeded pathway of the air tract between the mouth, lungs and the environment render these organs an easy target of dysbiosis. These body parts are challenged on an ongoing basis with changing microbial population and environmental factors such as chemicals and gaseous pollutants that make them a fertile ground for microbial disharmony. Hence, it is critical that the crevices in the mouth do not have nutrients stuck for long as these are perfect ingredients that can dislodge the well-established functional microbial communities and inflict us with diseases. The mouth and nose gears are a common sight in cities around the world with high level of pollution.

In Beijing, New-Delhi and Mexico City, citizens are often seen wearing these protective screens in an effort to limit the intake of the polluted air in order to diminish its influence on the lung microbiome. During outbreaks of microbial diseases such as severe acute respiratory syndrome (SARS) or influenza, this phenomenon is observed around the globe in order to ensure that the lungs are not further burdened by air loaded with viruses as these will undoubtedly promote dysbiosis. The mouth and lungs are the first line of defence to combat the growth of opportunistic microbes lurking around in the air. Thus, oral hygiene and the quality of air one breathes in will go a long way in helping maintain the proper microbial balance required for a healthy body. However, if these conditions are not met, microbial disruption resulting from the reduction of biodiversity in the pulmonary and oral landscape can be a cause of concern. It is not surprising that the deteriorating quality of the air across the planet has led to sharp rise in asthma and other lung-related illnesses (Fig. 3.6, Box 3.3).

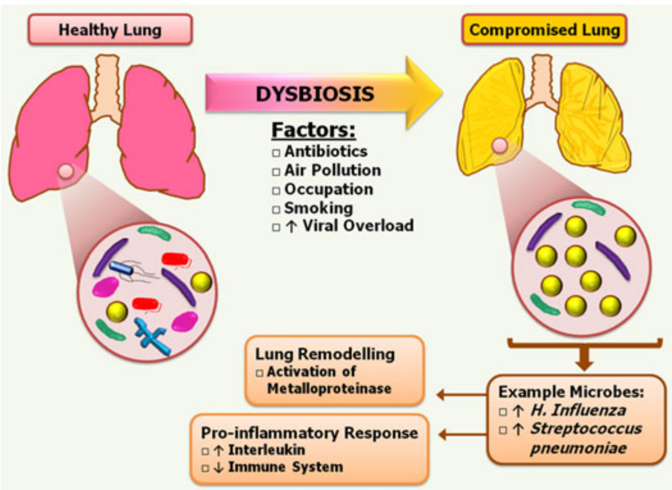


Fig. 3.6 Chronic obstructive pulmonary disease and the lung microbiome. (The remodelling of the lungs leads to decreased functional capacity)

Box 3.3 Microbial Link to Rheumatoid Arthritis and Asthma
Rheumatoid arthritis (RA) is a debilitating autoimmune disorder associated with the inflammation of the joints that can lead to bone erosion and deformity. The hyperactive immune response can also damage other parts of the body like the eyes, lungs and skin. This dysregulation of the immune system triggers pro-inflammatory tendencies with an increase in T-lymphocytes and self-reactive antibodies. Although genetic factors may contribute to this disorder, a major shift in the constituents of the microbiome is observed in RA patients. There is an overrepresentation in the *Provetella* species including *Provetella copri*, an increase in *Clostridium* spp and a reduction in *Bacteriodes* spp. This dysbiosis evokes the elevated production of homocysteine, hydrogen sulphide and lipopolyssacharide (LPS) that all known to promote inflammation, a feature culminating in the attack of one's own body part. Probiotics like *Lactobacillus casei* has been shown to mitigate symptoms associated with RA. Asthma is another inflammatory disease where the respiratory airways are challenged by the aggressive action of the immune system. There is an overproduction of mucus and an intense remodeling of the airway wall ensues. The presence of dust, pollen and spores tend to aggravate this situation. However, this disease is characterized by a marked change in the lung microbiota. In children there is reduction in such microbes as the *Faecalcibacteria*, *Veillonella* and *Rothia* while in adults an increase in *Proteobacteria* and a decrease in *Bacteriodetes* and *Firmicutes* are common. Hence, restoration of the microbiome with probiotics and prebiotics can be an alternative therapy.

3.5 Microbial Imbalance in the Digestive Tract: Gastric Complications

The digestive tract is the home of most bacteria in the body. Although the vast majority is housed in the intestine, some do find refuge in the stomach. Despite the inhospitable environment presented by this acidic organ, the microbes belonging to the *Helicobacter* spp have set-up their home here. They have done so by learning how to tame the low pH these environs are immersed in. They cling to the mucus of the cell-wall where the acidity tends to a bit more manageable. By neutralising this unfriendly territory, these microbes are able to develop a friendly habitat where they can reside. Even with these territorial adjustments, the stomach is the organ that harbours the least amounts of bacteria. However, the perturbation of this microclimate can quickly change this microbial landscape. The intake of medications like the proton pump inhibitors and antibiotics tend to promote a shift in this microbial population to the upper confines of the gastrointestinal tract. Once, this uncontrolled colony is established, it produces ammonia that compels an empty

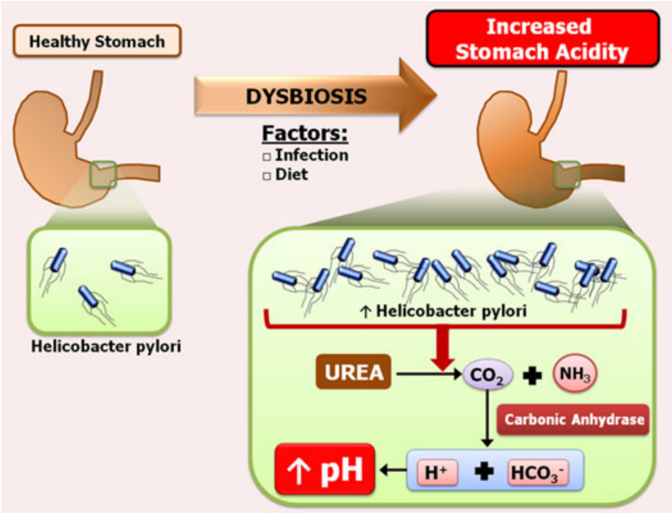


Fig. 3.7 Gastrointestinal microbiome and stomach diseases. (The disruption of the pH is the main culprit)

stomach to generate acid. It is critical that this digestive compartment is acidic only when it has food in its midst. Any change in the acidity in the absence of food distresses this organ. It is more or less like the stomach is chewing itself. This becomes the genesis of aches and heartburns that result into peptic ulcers. There is a rise in this microbially-induced disease around the world and the disruption of the fine working arrangement struck among the invisible residents may be at play. It is not surprising that the majority of ulcers can be cured by antibiotics and not by drugs aimed at diminishing the acidity of stomach, a finding that has dismayed many pharmaceutical companies as they have invested heavily on the incorrect cause of the disease. The understanding of how the disruption of these gastric microbial communities will pave the way for better remedies (Fig. 3.7).

3.6 Food Intake, Gut Microbiome and Diseases

The majority of the constituents of our microbiome is lodged in the small and large intestines with the latter harbouring the bulk of the invisible partners. Once the colonies are established in these locations, the stability of the residents is constantly being questioned due to the passage of foods and other edibles that transit through. This environment is under constant flux due to our daily intake of foods that can come in all shape, size, content, well-done, rare, or raw. The colonizers have to adapt. Low carbohydrate, high fat, high protein, dietary fibres, medications, antibiotics, sugary drinks all have major impact on the ecosystem. This constant pounding by these diverse ingredients, roughly around 60 tons during our

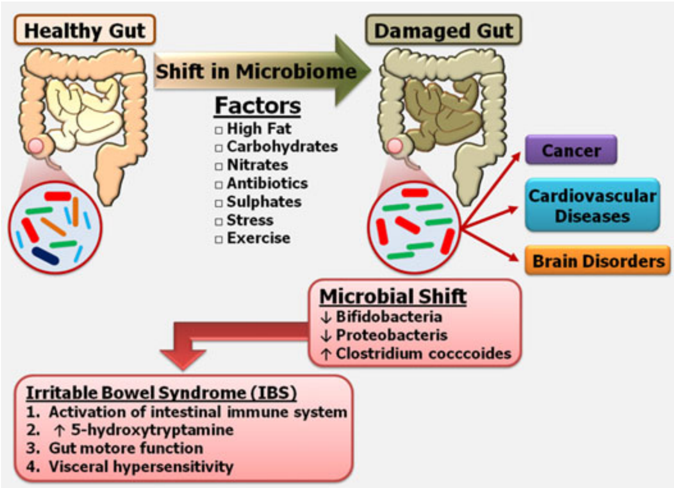


Fig. 3.8 Irritable bowel syndrome. (A reaction to microbial perturbation leading to inflammation and damage in the intestine)

life span is bound to take its toll on these miniscule residents within. Such a situation is akin to us changing our clothes conatantly in response to temperature changes in the environment. How would you feel if you have to face snow, rain, sun and fog on an ongoing basis and keep modifying your outerwear continually (Fig. 3.8).

Whether the food is starchy, oily or meaty; the microbes have to adjust. A shift from a high fat/high sugar diet to a regime of low-fat/plant-based polysaccharides can change the gastrointestinal microbial ecosystem in a matter of days. For instance, while *Bacteriodes* spp thrive in people who consume high fat foods, *Prevotella* spp dominates the guts of individuals who eat more carbohydrate-rich products; refined sugar intake on the other hand favours *Clostridium* spp. The lovers of vegetarian diets are host to less pathogenic bacteria while protein-rich nutrients tend to provoke increased activity of enzymes like nitroreductases derived from microbial sources. This situation contributes to the weakening of the inflammatory response and prevents the metabolism of short-chain fatty acids (SCFA). Remember the oxidation of SCFA like butyrate provides the intestines with an important source of energy and perturbation of this process can result in abnormal physiological functions. Preserved foods, dehydrated vegetables and alcoholic drinks with their high content in sulphate provide a fertile ecosystem for suphate-reducing bacteria like *Desulfovibrio* spp to thrive and distress the body. These micro-organisms generate metabolites that restrict the growth of probiotics that help us execute numerous tasks. Medications like opioids and the popular diabetic drug metformin impair the mobility of the gut. These are also responsible for shifting and deranging the community-like environment that good bacteria nurture. This disruption provides an opportune situation for bad microbe like the *Clostridium difficile* to multiply. Even psychological stress that is known to trigger the production of signaling chemicals like catecholamines has an impact on the microbiome. Well-established microbes like *Lactobacilli* and *Bifidobacteria* that are known to confer a number of healthy attributes in the body tend to diminish (Box 3.4).

Box 3.4 Food Additives, Dysbiosis and Health Impact
Numerous chemicals are introduced into foods to improve taste, to extend shelf-life, to add volume, to enhance appearance and to impart a variety of other properties. Some of these are known to interact with the microbial communities in the gut and perturb the fine communal balance. Dietary emulsifiers like carboxymethyl cellulose (CMC) is one of the additives that is widely utilized in foods, cosmetics, and hygiene products. Ice-cream, cookies, toothpaste and laxatives are some of the products where this polysaccharide provides texture, viscosity and structural integrity. Despite being mostly composed of glucose, CMC cannot be digested either by the visible or the invisible organs. However, it creates a major ecological change in the gut by interfering with mucin, a natural barrier lining the gut. Mucin is heavily glycosylated and act as a potent fence against any opportunistic pathogens to access the inner walls of the intestine. It inhibits the absorption of dietary flavonoids and also promotes the proliferation of microbial flora desired by the body. These functions are perturbed by CMC as it shares some chemical and physical features with mucin. This disruption results in dysbiosis leading to the multiplication of pathogens and their translocation into the intestinal tissues. There is an increase in *Proteobacteria* spp and inflammation ensues. Chronic intestinal complications have been attributed to these additives.

3.7 Microbiome and Global Epidemics: Obesity and Cardiovascular Diseases

Hence, it is not surprising that these chemical, environmental and behavioural changes that the gut microbiome has to contend with invariably lead to the disturbance of the delicate balance cementing the microbial communities and the host in an effective functional relationship. This flux in the gut ecosystem creates conditions for the abnormal proliferation of some members at the expense of others. The subsequent activation of enzymes and production of disease-causing factors can contribute to such maladies as irritable bowel syndrome (IBS), colorectal cancer, rheumatoid arthritis (RA), Type 2 diabetes, obesity, cardiovascular complications and neurological disorders. Some of the metabolic diseases like diabetes, obesity and heart ailments have reached an epidemic proportion globally. A recent report revealed there are more obese people than underweight individuals, a phenomenon that is a first for human history. An average person has become 1.5 kg heavier over each decade. Thus, if your grand-father was say 50 kg, your dad is 65 kg and you will be 80 kg at the same age of course. This scenario will be true if nothing else changes. The study on body mass index that was done over 40 years in 186 countries is alarming indeed. Policies on food and the quality of food we have access to will help to some extent. It is not surprising to see various North American cities are imposing an obesity tax aimed at sugar-laden soft drinks.

Examining the role of our microbial ecosystem is also pivotal if this issue is to be remedied. The gut microbiome is an important participant in the manner we digest food, extract the maximal energy and nourish the rest of the organs. A disruption in the microbial landscape can trigger metabolic diseases. For instance, during irritable bowel syndrome (IBS) microbes belonging to the *Firmicutes* family decrease while an increase in members of the *Bacteroidetes* family is observed. This disorder in the intricate microbial balance propels a concomitant rise in facultative bacteria like the *Enterobacteriae* spp. The unregulated establishment of the microbial community tends to impair the integrity of the mucus lining of the intestine. This shift perturbs the ability of the resident intestinal microbes to properly communicate with the mucosal barrier; such a situation results in the inability of the body to tolerate the harmless bacteria and neutralize the invading squatters. Following this distress imposed on this natural fence, conditions are perfect for the release of signals and chemical shuttles by the microbes to enable their migration across the intestinal defensive wall. This sequence of events forces the host to activate its guards with no clear mandate on the proper target and the result is an unintended inflammation giving rise to Crohn's disease and ulcerative colitis. These are the two most prevalent forms of IBS that can be traced to the perturbation of microbes residing in the gut. In fact, these diseases can be mitigated by increasing the presence of *Firmicutes* in the gastro-intestinal tract. It is clear that the conditions promoting the opportunistic microbes and the colonizing factors they produce are at the root cause of these disorders and re-establishing the original microbial communities goes a long in alleviating the pain of individuals suffering from these complications.

Obesity is a major problem afflicting the world. The rise in overweight individuals has been staggering and this malady attacks regardless of any economic and geographical boundaries. Almost all countries surveyed are experiencing the ill-effects of this metabolic disease. A variety of elements such as diet rich in simple carbohydrates, low in vegetables and fibres; life-style and genetic factors may be at play. However, the disturbance of the microbial harmony in the body cannot be discounted as a potential trigger responsible for the soaring rate of obesity around the globe. There is a clear distinction in the microbial landscape associated with obese people compared to underweight individuals. Lean individuals tend to have higher amounts of microbes belonging to the *Bacteriodetes* family while obese subjects and those suffering from metabolic syndrome are home to more members from the *Firmicutes* family. Although the specific species of these two microbial families responsible for the lean and obese traits have yet be catalogued, it is clear that obesity is characterized with increased levels of toxins like lipopolysaccharide (LPS) in the blood. Symptoms associated with weight gain and decreased sensitivity to insulin have been attributed to the presence of microbial toxins. Hence, modulating the nature of the gut microbiome and restoring the proper microbiota have to be included as part of the strategy dedicated to combating these disorders.

The food we eat is a major instigator of the establishment and fluctuation of the microbiome we possess. In fact, the adage we are what we eat applies aptly to the microbiota that constitute our body. One can even add that our physiological processes are the way they are because of the microbes we own. These invisible partners that accompany us throughout our live-journey are part of the elaborate communities responsible for our well-being. However, this is not a permanent relationship as it is susceptible to evolution and disruption by what we eat. This intimate relationship that we have forged with our invisible partners and all of our other bodily organs faces lots of twists and turns as we navigate through our lifelong journey. In the case of our microbial ecosystem these changes are non-stop as it is extremely prone to the vagaries of what we put in the mouth. And this is a daily activity that is most relentless and continual and commences the day we are born and ceased only upon our death.

Indeed it is important to remember that every component of body is in constant flux, we are never exactly with the same body parts that we are born with. These are evolving every second. For instance, we get a new skeletal system every 40 years and this happens on an ongoing basis day by day. Otherwise you will be soft like jelly one day and then wake up the next morning with a brand new skeleton. Thus, depending on our eating habits, we may be saddled with a microbial ecosystem that can promote or impede our wellness in the same way we have toned body if we exercise or we are stuck with a flabby belly if we are a potato couch.

A fat-rich diet together with a combo of a sugary drink is sure a concoction to upset the fine balance of our invisible organ. Such a nutritional habit is responsible for the non-alcoholic fatty acid disease (NAFLD) and cardiovascular complications. These greasy foods are known to promote the proliferation of some bacteria and arrest the growth of others. The establishment of this unbalanced ecosystem is a perfect brewing ground for the genesis of liver and heart diseases. These oil-laden nutrients contain copious amounts of choline, a chemical responsible for the yellow colour in the egg yolk. It plays an important role in the development of the brain in children. However, its excessive consumption via the food we intake specifically in adults can be problematic and the unwelcomed microbial residents aggravate our overindulgence in these choline-containing goodies. In reality our gut microbiota transform this into a product known as trimethylamine (TMA). This diversion of choline into TMA prevents the body from making some good lipids and subsequently leads to the accumulation of the bad lipid known as triglycerides. Remember the number 200 associated with triglycerides in the blood of adults. This magic number if higher is a relatively precise predictor of potential coronary abnormalities. These triglycerides have nowhere to go but to accumulate in the liver where they become the precursor of fatty acid disease. This is not all that can come out of this greasy food, it can become worst.

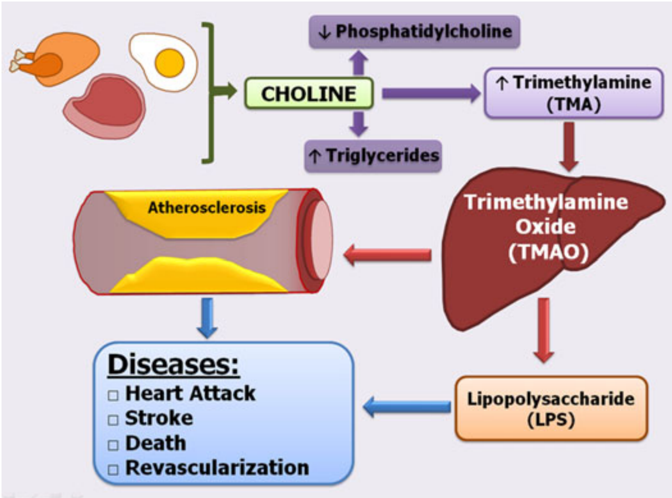


Fig. 3.9 Fatty liver and coronary diseases. (the microbial activity triggers the production of triglycerides and trimethylamine oxide)

If you harbour microbes that can metabolize TMA i.e. process it into the oxygenated variety known as trimethylamine oxide (TMAO), this can spell danger for your heart. The benign TMA falls prey to microbial manipulation in our gut that renders this relatively innocuous agent into a toxin with devastating impact on our well-being. TMAO is an important tell-tale sign of cardiovascular diseases. There are other intestinally derived toxins fuelled by microbial activities that can cause havoc to the normal functioning of our body. Sulphate derivatives of aromatic chemicals originating from microbial intervention in the intestine can be a major burden on the kidney and may lead to renal abnormalities. Controlling the microbes that are in the business of transforming harmless chemicals into noxious ones is critical strategy that need to be pursued in order not to succumb to the microbial imbalance promoted by fatty foods (Fig. 3.9).

3.8 What Mood Changes Have to Do with Gut-Dwelling Microbes

Even though we may not be completely aware there is an important communication corridor between the gut and the brain that is nourished by numerous signals emanating from the microbial activities in the intestine. The gut-brain axis relies on the messengers and/or their precursors generated by the microbes we harbour. They produce short-chain fatty acid (SCFA) like butyrate and neurotransmitters like γ-aminobutyric acid (GABA), dopamine and serotonin. Whenever you have a rewarding feeling due to some activity like eating that you are engaged in, blame

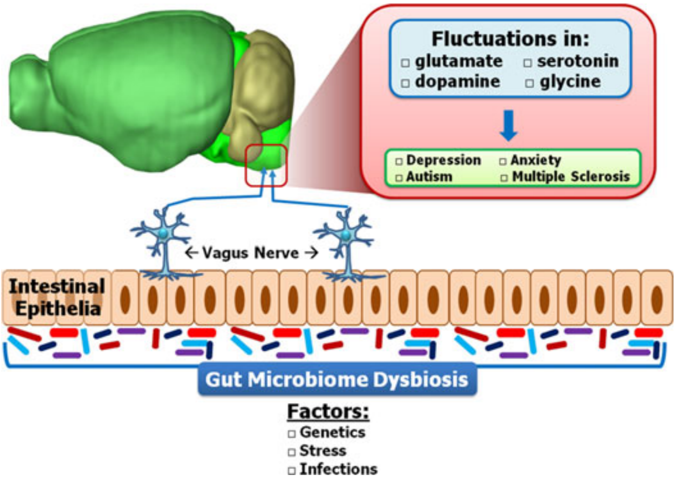


Fig. 3.10 Dysbiosis, abnormal metabolite production and neurological disorders

it on dopamine. These instruction-laden chemicals that are also produced by other organs in our body are central to numerous tasks executed by the brain and can stir our behaviour in one direction or the other depending on the concentration of a specific neurotransmitter. Hence, factors that modulate the flux of the microbial communities and their propensity to dish out these neuro-active commanders have tremendous influence on our health and well-being. For instance the lack of microbial diversity associated with ageing impedes the ability of the body to generate SCFA such as acetate, propionate and butyrate that supply the brain cells with energy. The loss and/or the rationing of the nutrients fuelling the brain result in a reduction of cognitive and memory power. This attribute is a common characteristic reminiscent of ageing. Hence, the propensity of people in retirement homes not to remember or retain mundane facts (Fig. 3.10).

The microbiome definitely has its imprint on the functioning of the brain, a feature that has yet to be fully deciphered. For instance, the amino-acid tryptophan is the precursor of numerous neurotransmitters that dictate a variety of our behavioural responses that are usually tailored to the stimuli we receive. This is an essential nutrient that humans cannot make with their own traditional organs and have to acquire it from the food we eat. However, depending on our microbial communities we can easily have ample supply as numerous gut microbes are capable of synthesizing this nutrient; but with caveat that the amounts of tryptophan we have access to need to be modulated if our response is to be commensurate to its presence or its derivatives. Any abnormal variation of this commodity in our body can become a harbinger of neurological complications. A shift in microbial communities induced by a myriad of factors can create havoc with blood tryptophan levels. This can then results in depression, mood swings and neurological ailments like Parkinson's or Alzheimer's diseases. Keeping a careful watch on our microbial partners and their ability to generate these brain responsive signals will lead to better health outcomes (Box 3.5).

Box 3.5 Microbial Communications with the Brain and Neurological Disorders

The ability of the microbiome to produce a variety of neuroactive chemicals makes the invisible organ a potent modulator of human behavior and an instigator of neurological diseases. For instance, Parkinson's disease is an incurable adult neurodegenerative disorder characterized by abnormal movements due to defective motor control. Dopamine production is impeded and there is an increased formation of aggregated neurotoxic protein known as α-synuclein. These two biochemical manifestations may be shaped by the nature of the microbial residents by limiting precursors of dopamine and activating the immune system with the release of pro-inflammatory chemicals like LPS. The gut microbiome in Parkinson's patients is usually characterized by a decrease in *Prevotella* spp and an increase in *Enterobacteria* spp. A diminution of mucin synthesis increases intestinal permeability and leads to an acute dysbiosis that contributes to the abdominal discomfort, bloating and premature satiety reported in these patients. Autism spectrum disorders (ASD) are another set of neurological perturbations leading to social and behavioural impairments including repetitive behaviours and non-standard communications. Here again, the microbiome may be a contributing factor. A decrease in *Veillonella* spp coupled with a rise in *Clostridium* spp and *Campylobacter* spp have been reported. Microbial products like p-cresol has been observed in elevated amounts in autistic children and 4-ethyl sulfate (4-EPS) has been shown to trigger anxiety like behavior. This microbial link is prompting the search of probiotics (e.g. *Bifidobacterium fragilis*) that may help in curing these diseases.

3.9 Microbiome and the Cancer Connection

Cancer is a multi-factorial disease that is a major global concern. Almost everyone knows of someone who has been affected by this disease. Numerous governments have recognized this disease as a national priority and have decided to provide all the support necessary to fight cancer. Although life-style, genetic disposition and environmental factors are important contributors to the spread of this disease, it is becoming amply clear that our microbial landscape and cancer proliferation are interconnected. It is being increasing recognized that the microbiome plays a key role in preventing and promoting cancer. The gut microbial ecology provides an important cover against invading pathogens that contribute to the onset of tumour formation. However, a shift in microbial communities induced by diet and pollution creates a favourable environment for opportunistic microbes to thrive and neutralise the protection offered by the finely tuned original microbial guards. The invading microbes produce virulence elements responsible for unimpeded cellular growth, a key feature of all cancers. They also put in motion processes that result in the instability of the DNA and furthering the progress of cancerous cells. Understanding the communal work of the intestinal microbes is pivotal if this problem is to be tackled. Indeed it has been shown that Africans from rural areas exhibit lower risk of colon and rectal cancers due to the increased abundance of the microbes known as *Bacteroides* spp. These are avid producers of short-chain fatty acid like butyrate, an important energy-producer and a promoter of cellular growth. This is a critical signaling molecule that can goad the body to synthesize sentinels that stop cancer cells on their tract.

On the other hand, the group of individuals whose colon is home to higher amounts of *Prevotella* spp tend to have higher levels of bile acid and lower amounts of butyrate. This switch in colonic microbial ecology is suspected to be responsible for the colorectal cancers (Fig. 3.11). The *Prevotella*-rich individuals are programmed to secrete bile acids in the feces. These compounds are known to promote the proliferation of cancerous cells. The interplay between these two microbial communities and their ability to produce these metabolites afforded wellness to one group and colorectal cancer to the other. Hence, the promotion and nurturing of functional microbial communities and limiting the presence of unregulated microbial ecosystem in the gut are pivotal to maintaining our well-being. This invisible organ has to be tended in the same manner like any other visible organ; one cannot expect to have working lungs supplying the furthest nooks in the body with oxygen if one indulges in smoking or toiling in occupation

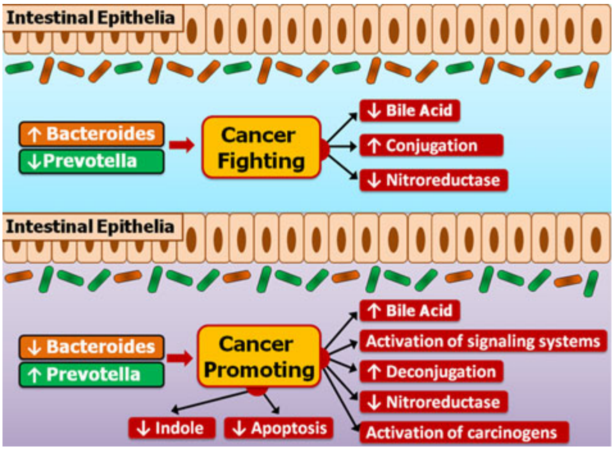


Fig. 3.11 Colorectal cancer triggered by microbial imbalance in the colon. (Decrease in detoxification and increase in cancerogenic metabolites and enzymes)

with toxic air. This cardinal rule also applies to the microbiome even if its anatomical features do not readily pop out to our eyes. Otherwise we run the risk of turning this organ that we almost never see but hear rumblings of once in a while into a cancer-causing entity. The critical attributes of these microbes need to be tapped as cancer preventers and fighters.

3.10 The Road to Our Well-being: The Microbiome Way

The microbiome is an essential component of humans if not of all multicellular organisms. This invisible component of the body that quite often makes itself heard with a rumbling sound is involved in a variety of biological tasks that are essential for the proper functioning of any human. Although these microbes residing in and on us have their genetic information they are bound by the communal existence they have adopted. The role and behaviour of each member are dictated by the host and other members of the collectivity. This harmony and synchronicity of purpose force everyone to comply with the rules set-up during the establishment of the community. However, these communities evolve in relation to the host and the changing landscape they have to deal with. They accompany us from the very beginning when we are developing till death. It is becoming more apparent that these microbes contribute to our development and eventually mould us the way we are both anatomically and physiologically. They have a say virtually in all aspects of our life and prod us as we go about our daily living. From providing essential nutrients like vitamin K that we are dependent on but incapable to make on our own to protecting us against opportunistic organisms and helping heal our wounds, these microbes partake in a myriad of tasks just as visible organs do. However, their constituents and interactions like all other organs in the body are modulated to large extent by the changes in environment, food, stress, and hormonal fluctuations we are subjected to.

The invisibility of this organ and its dispersed anatomy have contributed to the relegation of the microbiome to a low esteem in the hierarchy of our body parts. But this view is being discarded at a rapid pace as intriguing information about its role is being revealed. Its intimate link to our existence was only visualized very recently. What you cannot see, you cannot appreciate. This dictum fits perfectly the microbiome. The advent of next generation sequencing (NGS) coupled with bioinformatics tools is laying bare the indispensability of the microbial communities roaming within and on us to our very existence. Our life will not be the same without our intricate network of microbial communities. Hence, understanding how this invisible communal habitat is constituted, how it evolves and how the various partners communicate amongst themselves is crucial for our being. The host will not exist without the microbiome. It is as crucial as the heart and any other body part. This mission is as critical as our desire to unravel the workings of the brain or to venture in the outer galaxy. Its systematic functional identification will be akin to the discovery of a new organ as in occurred in the

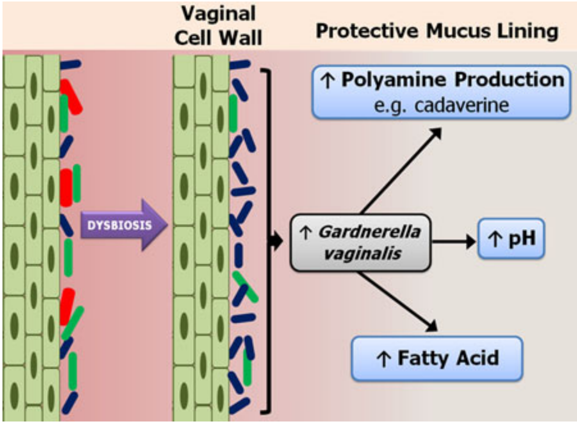


Fig. 3.12 Microbial proliferation and Vaginosis. (increased pH and polyamine smell are common markers of this disease)

sixteenth century when human was first beginning to comprehend the workings of various body parts. Just imagine the excitement when the Italian surgeon, Realdo Columbo identified how the four valves of the heart permitted the flow of blood in only one direction i.e. from the right ventricle to lungs and back to the left ventricle and on to the aorta. We are on the brink of tantalizing discovery on a part of our body that has long been ignored due to the lack of proper tools to decipher the microbial communities. It is indeed more exciting as this invisible organ has at least 1,000 times more genes than our own visible body. The microbiota we possess must play an important role in our development and we are physically and physiologically the way we are because of them. We would be entirely different if it was not for the microbiome and this holds true to most if not all organisms wandering on this planet and most probably beyond.

The proper functioning of this community with multiple partners depends on the finely tuned relationship among all the constituents. Every member operates in a mode that is beneficial to this cooperative life-style where interdependence is the modus operandi. However, this harmony can be perturbed by a variety interfering influences and can result in a multitude of ailments. The intrusion of opportunistic organisms fuelled by a change in the ecosystem gives rise to dysfunctional communities that are the precursors of debilitating diseases like cancers, IBS, and vaginosis. The latter is a disease arising from the uncontrolled proliferation of microbes such as *Gardnernella vaginalis*, *Veillonella spp*, and *Bacteriodes spp*. that promotes an increase in pH, fatty acids and polyamines (Fig. 3.12). Cadaverine, a polyamine secreted during this dysbiosis is the cause of the malodor characteristic of the disease. Once the fine balance involving the constituents and the signals that are responsible for a proper microbial community is uncovered, we will be in a better position to predict what makes us tick and what ails us. This knowledge is just now beginning to emerge and ignoring this important aspect of our body will be to our peril; it would be akin to not wanting to know how the brain functions (Fig. 3.12; Fig. 3.13).

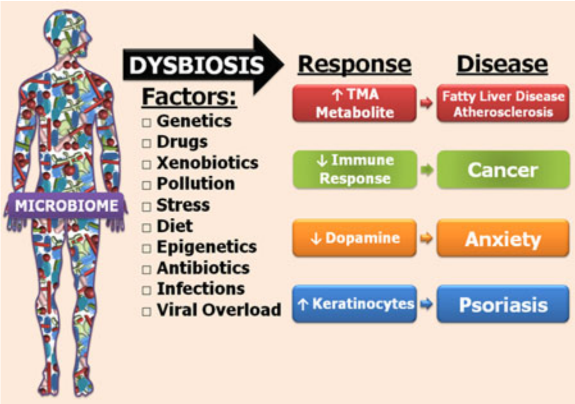


Fig. 3.13 Summary of dysbiosis: causes and diseases

3.11 Probiotics, Prebiotics and Synbiotics: The Nurturing of the Microbiome

The microbial communities that constitute our microbiome are dependent on a myriad of factors such as the genes we inherit, our mother's milk, the environment we live in, our hobbies, the seasonal changes we are subjected to, the food we eat, the life-style we lead and the medications we take. Despite the ability of our microbiota to respond and adjust to these situations, the invisible organ can be influenced by either taking in select beneficial microbes with known functional attributes or by consuming foods and plant products that promote the proliferation of specific microorganisms. This microbiome-rearing strategy is akin to feeding our brain with the books we read or the educational programs we watch or the games we play. Remember some eager mothers keen on giving their children a head-start in life, read to them or play music even when babies are in the womb. To promote a healthy life-style, seniors are being encouraged to partake in neuron-stimulating games on a regular basis. This brain exercise has becoming a common place in residences for the elderly. Thus probiotics, prebiotics and synbiotics can be utilized to guide the microbiome to perform optimally and ameliorate our well-being (Fig. 3.14).

Probiotics are live microbes administered as foods or even in capsules that confer health benefits on the body. Microbial cultures have been consumed by humans since the dawn of civilization. Mongolian women sprayed fermented milk on horsemen and their horses in belief that this provided strength and health on the recipients, while in some civilizations fermented milk was utilized to treat a variety of ailments. Dahi, a fermented milk is widely consumed in the Indian Sub-Continent and is known to impart numerous healthy outcomes. However, the first clinic trials on the health claims of these bacteria-rich fermented foods were not performed until the twentieth century. Eli Metchnikoff who obtained a Nobel laureate in medicine was first to correlate the longevity of some Bulgarian citizens

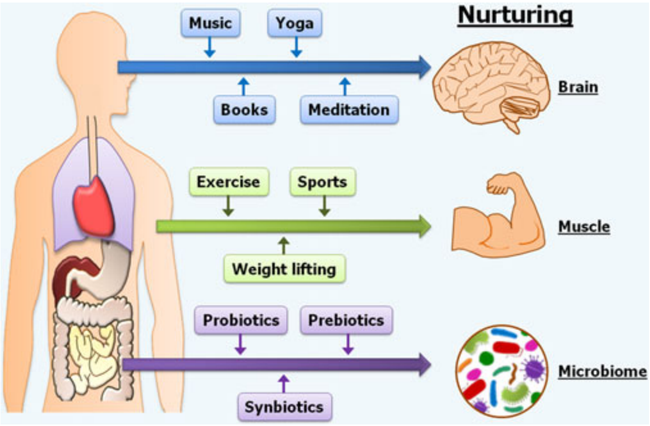


Fig. 3.14 Nurturing of the microbiome, the brain and the muscle. (activities and nutrients involved in fortifying these organs)

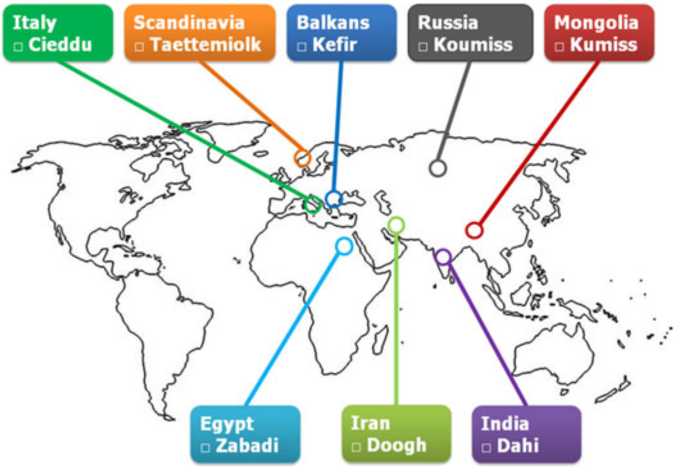


Fig. 3.15 Consumption of probiotic-rich foods around the globe

to the prolific consumption of fermented milk that was rich in *Lactobacillus bulgaricus* and *Streptococcus thermophilus*. In 1930, the Japanese scientist Shirota isolated microbes with probiotic properties from healthy human subjects. These were later utilized in the development of milk products that were commercialized as Yakult. Subsequently, a French pediatrician reported the lack of Bifidobacteria in stool of infants suffering from diarrhea. In 1965 the term probiotics was coined by Lilly and Stillwell to describe products that stimulate the growth of microorganisms beneficial to the body. It was in 1984 the first probiotic species, *Lactobacillus acidophilus* was introduced followed subsequently by *Bifidobacterium* spp. Their use in food products is widespread. The significance of probiotics in fortifying the immune system has officially been recognized by the World Health Organization (WHO). Currently a wide variety of micro-organisms such as *E. coli, Propionobacterium, Enterococcus, Streptococcus, Leucomostoc*, and *Bacillus cereus* are being consumed in order to regulate and adjust the body's microbiome (Fig. 3.15, Box 3.6).

Box 3.6 Probiotics: Occurrence and Uses Worldwide

Humans have been consuming microbe-laden foods unknowingly since the dawn of civilization. Fermented milk, vegetables, meat and fish were and are a regular part of the daily diet for most people around the globe. Recently probiotics enriched foods like yogurt, yakult, kefir, dahi and cheese have become a regular repertoire of natural products that nutritionists are eager to extoll the health virtues of. *Lactobacillus* spp, *Bifidobacterium* spp and *Bacillus* spp. are the more prominent probiotics even though other microbes are being added to this list. They are also being used in non-consumable items like oral care gel and anti-ageing serum. Their ability to produce acid, enzymes, SCFA, immune responsive factors and to help establish functional microbial flora have made these probiotics excellent candidates to cure a variety of diseases that are provoked by dysbiosis. While *E.coli Nissle* provides relief to patients suffering from ulcerative colitis, a disease like vaginitis can be remedied with *Lactobacillus rhamnosus* GG. Irritable bowel syndrome victims can find comfort with the intake of *Bifidobacterium animalis* and *Lactobacillus acidophilus*. The role lactic-acid microbes like *Bifidobacterium breve* has been recognized in diminishing high blood pressure due to their ability to produce vitamin D, anti-hypertensive factors and interrupting cholesterol absorption. Although influence of probiotics in promoting wellness and as therapeutic agents aimed at numerous illnesses are becoming more prominent, their usage will become universal once the dosage and the intake frequency of these microbial supplements have been properly evaluated.

3.12 How Probiotics Work

Probiotics not only help the body to fine-tune the microbiome, they can also perform some very specific functions. Depending on the probiotics, these microbes act as a barrier and prevent colonization by opportunistic bacteria. They do so by re-enforcing the protective function of the gut mucosa and by generating signals that arrest the invasion by infectious organisms. They produce antibiotics, antioxidants and improve the body's immune system. Probiotics are also known for their ability to synthesize SCFA and vitamins, ingredients essential for numerous metabolic activities. They secrete enzymes that help in digestion and in the elimination of wastes. A good probiotic should be able to impart health benefits to the host and be bestowed with no pathogenic properties. Its presence in the microbial community should enhance some biological functions and/or curtail any negative influence on an individual's well-being. These can preferably be taken orally and must survive the harsh environment of the digestive system, especially the stomach where the pH can be unforgiving. The low pH of the stomach can be avoided if the probiotics are mixed with food such as milk, dietary fibres and yogurt. They can be designed to generate specific biomolecules that can be of benefit to the host. For example, lactose-intolerant individuals can consume probiotics with the ability to synthesize lactase or galactosidase that helps in metabolizing the milk sugar, lactose.

Probiotics have virtues almost like stem cells. Stem cells i.e. cells that have not yet made up their mind what they will become or which organ they will develop into can be utilized as a therapy to fortify ailing components of the body. For instance, they can be injected in the cornea or the liver with the proper commands that enable them to mature into corneal or hepatic cells that become part of the rejuvenated organs with optimal biological functions. Probiotics act in a similar manner in regard to our microbial communities. They can be consumed with the aim of enhancing a specific function like in the case of a select targeted fortification that is desired in the body. Individuals suffering from the inability to digest milk are readily relieved of their aversion to milk or milk products by the consumption of *Lactobacillus*. This microbe secretes lactase, an enzyme that can clip the milk sugar lactose into glucose and galactose which are then utilized by the body. Probiotics such as *Aspergillus oryzae* found in fermented foods like soy sauce, and sake secretes amylase and lipases that help in the digestion of starchy and oily meals. In instances where the microbiome has been infiltrated by opportunistic microorganisms that prevent the invisible organ from performing its regular task, an intake of the probiotics can shift the microbial balance toward a more fruitful one for the body. One case in point is the colonization of the dental space by *Streptococcus*, a microbe responsible for carving cavities on the tooth. Food enriched with various species of *Lactobacillus* can rectify this situation by creating an unfavourable situation for the invading bacteria to survive.

Among other various biological weapons they have in their armoury, *Lactobacillus* group of probiotics can generate an acidic environment. This situation is known to impede the growth of the occupying bacteria and arrest their assault on the teeth. Unlike the stem cells that are mainly involved in regenerating desired tissue or organ, probiotics can tilt the balance of a non-functional microbiome towards a functional one by quashing undesirable elements in the community. They can also be engaged in a targeted task designed to thwart a discomfort an individual is experiencing as in the case of intolerance to lactose or abnormal movement of the digestive system. World-wide people have been consuming fermented products laden with probiotics. These foods have evolved through centuries and each region has its own speciality of delicacies full of microbes. These probiotics have become part of the culinary culture and it will not be surprising if we learn that our palates have evolved accordingly. Yogurt, a diary product supplemented with microbes *Lactobacillus, Bifidobacteria* and *Lactococcus* is part of the grocery shelves in almost all countries. In India dahi, a fermented milk product

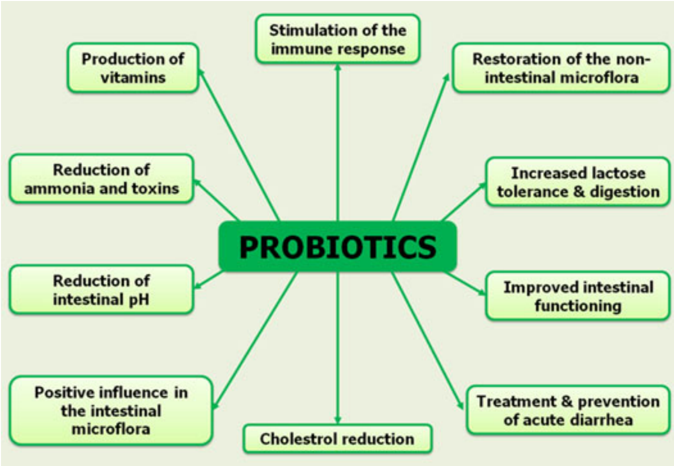


Fig. 3.16 Functions of probiotics in human health

rich in *Lactococcus lactis* and *Lactobacillus acidophilus* is taken with nearly all foods and its curative powers are readily touted. In the Caucus region, kefir with its bountiful of *Lactobacillus, Lactococcus*, *Leuconostoc* and *Bifidobacteria* is a daily staple. This is derived from goat's milk and contains yellowish grains resembling cauliflower. These grains are in fact polysaccharide capsules full of probiotics. In Japan the miso soup prepared from barley, rice, beans and rye is king while in Africa Uji the probiotics charged maize or sorghum or millet is widely cherished. Although not currently available probiotics with the ability to metabolize ethanol or cure obesity will be a welcome help to those individuals who are susceptible to adverse reaction upon intake of alcoholic drinks or have difficulty controlling their body mass index (Fig. 3.16).

3.13 How Probiotics Helps Adjust Our Microbial Community

The mouth is literally a continuation of our external environment and is being constantly challenged by the microbes we are exposed to in our surroundings. Even under this threat, the soft and hard components of the mouth harbour a good number of microbial communities that allow them to fulfill various essential tasks. The change in the chemical milieu in the mouth triggered by the intake of foods provides a fertile landscape for foreign organisms to set foot, proliferate and disturb the working microbial harmony. This happens at the onset of dental cavities when *Streptococcus* rapidly colonizes the tooth. In this instance, a probiotic like *Lactobacillus rhamnosus* can spring in action and create an acidic environment by the secretion of lactic acid. Its ability to produce antimicrobial factors administers another debilitating punch thwarting the *Streptococcus*-driven assault. This probiotic also helps train the immune system to fend the noxious microbe.

Bile, a product that is produced in the liver has been shown to be involved in a variety of tasks that make the body ticks. Its acid derivatives are emerging as important signals that allow us to control our weight, regulate the level of cholesterol in the blood and determine how much fat we are going to store. The key enzyme that facilitates this formation of the bile-derived acids is bile salt hydrolase. A number of probiotics like *Lactobacillus, Bifidobacteria, Bacteriodes and Enterococcus* spp is known to secrete this enzyme. These probiotics can be designed to produce this enzyme that will be an excellent tool to control weight gain. This role of probiotics is akin to the use of lactase-producing *Lactobacillus*. Intake of food enriched with *Lactobacillu*s is a common therapy given in order to easy the misery of people suffering from the aversion to milk. In fact, lactase derived from probiotics is the most popular form of therapy for this ailment. Nearly 90–100% adults in East Asia cease to produce lactase as they reach adulthood. Although it is totally natural not to have lactase after the weaning years, the omnipresence of dairy products significantly raises the importance of this enzyme beyond our childhood. Hence, the remedy provided by *Lactobacillus*-supplemented foods or capsules is a boon to the adult population world-wide who wants to partake in their dairy-laden delicacies. The curing of enzyme deficient diseases or conditions with the aid of probiotics will become a common practice as our understanding of the microbiome becomes clearer (Fig. 3.17).

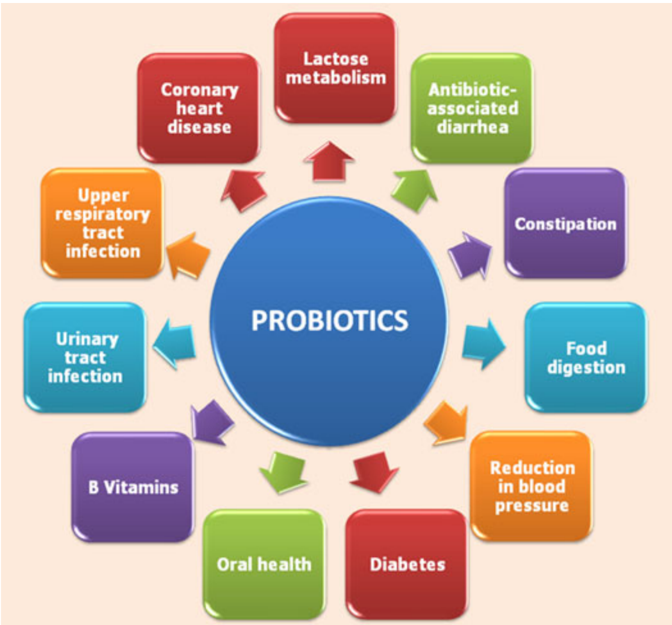


Fig. 3.17 Probiotics: the natural cure for diseases

In diabetic patients a microorganism referred to as *Akkermansia muciniphilia* that shelters in the mucus in the intestine can be an excellent candidate to promote carbohydrate metabolism. These microbes constitute 3–5% of the gut microflora and are known to stimulate glucagon – like peptide (GLP), an important modulator of blood sugar. Glucagon and insulin are the sugar police in the blood. Glucagon becomes active at night during asleep. This is when the blood sugar is low. The sugar sentinel ensures that we wake up healthy by maintaining the right sugar balance. Insulin on other the hand, protects against high blood sugar. For instance, when you indulge in a big bar of chocolate, it preserves the proper blood sugar and directs the extra to be stored. Hence, people with a hardy dose of *A. muciniphilia* are less insulin resistance, a major contributing factor to obesity. The abundance of these microbes decreases with age and the intake of high fat diet. The magic of *A.muciniphilia* is in the production copious amount of mucin, a slimy lining for intestine that promotes a diverse microbial ecosystem and fends off opportunistic microbes. Hence, the population of this blood-sugar balancing microbe can achieved by either taking it as a probiotic or by consuming nutritional fertilizer like fibers aimed at stimulating its proliferation. *Bifidobacteria* is another group of microorganisms that dissuade infectious microbes to colonize the gut by blocking the anchoring sites and stimulating the immune system. It is not surprising that they constitute almost 80% of the cultivable microbes in the stool of infants as opposed to the meagre 20% found in adults. They contribute to the defense power in babies as they are vulnerable at this tender age (Fig. 3.18a).

a

Microbial Markers	Diseases
Helicobacter pylori	Gastric ulcers
Propionibacterium acnes	Acne, eczema, allergy
Pseudomonas aeruginosa	Cystic fibrosis
Porphyromonas gingivalis	Gum disease
Enterobacterium spp.	Crohn's disease
Dialister spp.	Spondyloarthritis
Campylobacter spp.	Neurological diseases
Fusobacterium spp.	Appendicitis
Lactobacillus spp.	Vaginosis
E.coli	Colorectal cancer

Fig. 3.18a Microbes as biomarkers for diseases

3.14 Microbes at the Rescue of the Most Vulnerable: Infants and Seniors

Infants especially those who are born premature can also suffer from damaged intestinal tissues that begin to die. This disease known as necrotizing enterocolitis is characterized by bloating and swollen abdomen responds favourably to probiotics. Use of the probiotic *Lactobacillus* is quite effective in mitigating this disease. On the other hand, the intervention with a concoction of *Bifidobacterium, Propionobacterium* and *Lactobacillus* significantly reduces the risk of allergy in infants delivered by C-section. In fact these C-section babies are devoid of the microbes that mothers impart on them if they are not born naturally. Recent studies involving the sprucing the babies with the mums' microbiota are showing positive results. This kind of probiotic treatment where someone else or one's own microbe is used as probiotics to rectify aberrant biological activities is becoming more prevalent. Transfer of microbes from fecal matter, ear wax, skin and other body parts is gaining medical traction and are being implemented in health centers world-wide. Microbial transplant undoubtedly impart numerous health benefits (Fig. 3.18b; 3.18c).

Elderly individuals are another segment of the population who can benefit tremendously from the enrichment of their microbiome with probiotics. Ageing is characterized with a sharp decline in microbial diversity and density. This phenomenon is the leading cause of the decrease of metabolic activities and in some cases of physiological abnormalities observed in seniors. The lower abundance of *Bifidobacteria* coupled with the increased presence of *Enterobacteriaceae* is a common predictor of the ageing process and such a shift in microbial population is responsible for the diminished production of enzymes and essential vitamins like vitamin B that are critical in maintaining a constant supply of energy in the

b

Therapy: Microbes Suggested	Target Diseases
Lactobacillus; Bifidobacteria	Diarrhea
Lactobacillus salivarius	Gastric ulcers
E. coli 83972	Urinary tract infection
Salmonella typhimurium	Pancreatic cancers
Streptococcus salivarius	Halitosis
Staphylococcus epidermidis	Atopic dermatitis
Akkermansia muciniphila	Obesity
E.coli Nissle 1917	Ulcerative colitis

Fig. 3.18b Microbial therapy: Microbes to cure diseases

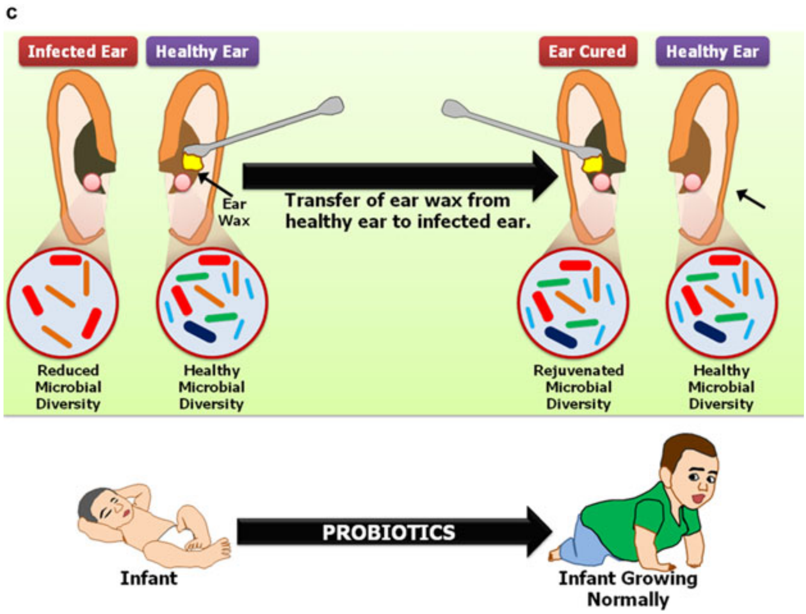


Fig. 3.18c Ear wax transplant and infant needs probiotics to develop

body. There is also a build-up of toxic products as the proper microbial communities involved in their decomposition are severely hampered. This situation is analogous to someone not going to the toilet on regular basis. The build-up of noxious elements in the colon can be the cause of a variety of ailments including head aches and digestive discomfort. The advanced age of centenarians is attributed to a diversity of microbial populations that are a hallmark of all individuals living beyond the ripe of age 100 years. The mission of these microbes may be compared to the role stem cells play in rejuvenating the organs and extending their functional life span (Fig 3.19). In this instance the diversity of the microbes observed in centenarians may be allowing these microbiota to supplement some of the functions their visible organs cannot perform or to generate chemical ingredients triggering the proper physiological responses from these ageing organs. Hence, harnessing the power of probiotics in reconfiguring the dysfunctional microbiome characterized by the ageing process can be an important game-changer in the life-style of seniors. This will be critical in seniors who are usually on microbiome-distressing medications. That is why it should not come as a surprise if elderly individuals take more time to heal and are invaded at a rapid rate by opportunistic bacteria. In fact microbial infection is a major concern when elderly patients are admitted to health facilities. They may be in for a hip replacement but unfortunately they run a higher risk of being contaminated by hospital dwelling-microbes. The prevalence of hard to eliminate microbes like *Clostridium difficile* in elderly patients is a problem world-wide. And often infectious outbreaks occur in these places. Unbalanced nutrition and erratic eating habits

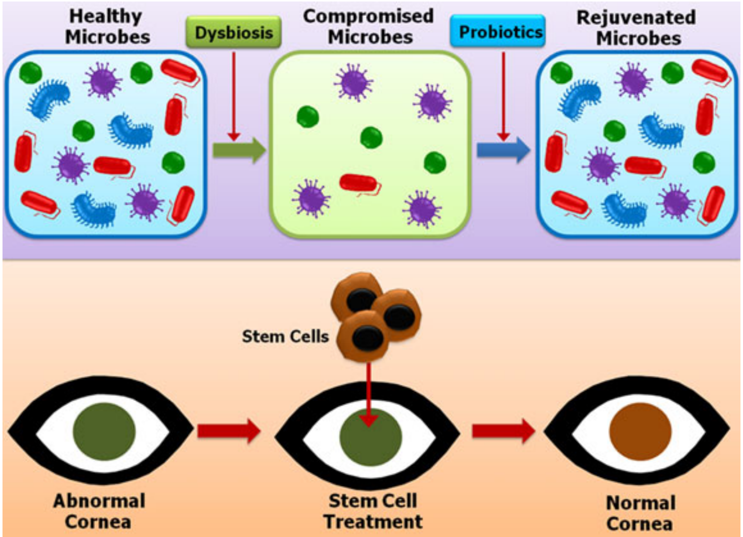


Fig. 3.19 Some probiotics are like stem cells and help in the rejuvenation of the microbiome. Stem cells in corneal treatment.

induced by reduced sensation in the olfactory and taste systems add to the dilemma facing seniors. These conditions create a nutritional environment deficient in essential nutrients like calcium and vitamins that further exacerbate the microbial ecosystem. Intake of the probiotic *Bifidobacterium longum* stimulates the proliferation of other *Bifidobacterium* spp. Administration of *Lactobacillus acidophilus* is known to increase the synthesis of antioxidants like glutathione and oxidant bursting enzymes like catalase. While the regular consumption of *Bifidobacterium animalis* helps reduce the time food transits in the gut, the probiotics *Lactobacillus rhamnonu*s and a *Propionibacterium* spp contribute to the improved defecation frequency. Hence the implementation of a nutritional regime rich in probiotics will go a long way in easing the discomfort and some of the ailments that are associated with old age.

3.15 Probiotics: The Disease Fighters

Evidence-based research is revealing how probiotics can help reverse ailments caused by the disruption of the microbial communities in our body. Irritable bowel syndrome (IBS) is one such disease where a perturbation in microbial population is the main cause of the disease. This shift in the ecosystem of the microbiota is punctuated by a loss in immune tolerance and a rise in inflammatory response. To mitigate this situation and to remedy this ailment, the administration of probiotics like *E.coli Nissle* has been relatively more effective than the use of antibiotics.

In this instance, the probiotics appear to deliver a three-pronged attack on the invasive and crafty microbes. They improve the fence lining the intestine, they out-compete the bad bacteria and they secrete molecular soldiers like hydrogen peroxide and lactate that stop invaders right on their tract. The significance of probiotics as therapeutic agents is only now beginning to be appreciated and is slowly challenging the aggressive use of antibiotics in treating these conditions. Unfortunately, antibiotic-based remedies tend to seriously interfere with the workings of our microbiome as their action against toxic microbes also eliminates some of our trusted invisible partners. The uncontrolled proliferation of the stomach residing *Helicobacter pylori* is a cause of concern as it is a risk factor for gastroduodenal ulcers and lymphomas. The intake of probiotics such as *Lactobacillus* and *Streptococcus thermophilus* has been demonstrated to correct this imbalance. The ability of these probiotics to secrete SCFA like acetate and butyrate is known to be a key factor in impeding the march of the over-reactive *H. pylori*. Wound healing and cancer prevention are other two activities that probiotics are also involved in. *Lactobacillus acidophilus* that is an excellent candidate with the power to heal injuries is known to arrest the colonization driven by the scheming *Pseudomonas aeruginosa*. The acidic environment nurtured by the *Lactobacillus* renders the ability to conquer the tear on the skin almost impossible. The propensity of probiotics to bind to mutagenic compounds and inhibit the production of carcinogens by opportunistic pathogens is central for their anti-tumour activity. The lactic acid producing bacteria such as *Lactobacillus acidophilus, Bifidobacterium bifidum* and *Streptococcus lactis* are routinely being recommended for the prevention of cancers. Some select tumours like in colorectal cancers are being treated with the aid of these life-microbial concoctions. Hence it comes as no surprise that the use of probiotics as a prevention of diseases and a therapy against some specific disorders is on the rise. The commercial value of this industry is into hundreds of billions of dollars, a figure that is further expected to increase as probiotics are safe and well-tolerated in children, premature infants and in the general population as a whole. Furthermore, unlike pharmaceutical products, probiotics are very easily administered mostly as components of foods and the lingering effects of these chemicals are quickly becoming a relic of the past.

3.16 Prebiotics: The Microbiome Fertilizers

The microbiome can also be nurtured and programmed with the assistance of prebiotics. These are natural products that foster an environment propelling the proliferation of some desirable microbes. In the same manner as we are always eager to give our visible organs a boost when they are not working well or when they are sluggish, we can revitalize our invisible organ. Our more traditional visible organs can be invigorated by taking supplements like vitamins or minerals that provide ammunition to various metabolic activities in the muscle, brain, heart or liver. For instance, athletes take creatine, a product responsible for energy stabilization to

Fig. 3.20 Prebiotics: the microbiome fertilizers

Prebiotic Active Ingredient	FOOD
Arabinogalactan	carrots, tomatoes
Pectin Oligosaccharides	apples, pears
Fructooligosaccharides	asparagus, bananas
Galactooligosaccharides	lentils, chickpeas
Xylooligosaccharides	oats, barley
Beta-glucan	mushrooms, seaweeds
Polyphenols	blueberries, prunes
Milk oligosaccharides	milk

improve their performance. Creatine and creatine kinase duo enables us to engage in physical activities quickly and fast. Without the intervention of this dynamic couple, daily chores will happen in a relatively sluggish manner. Individuals with excess body mass consume carnitine with the hope of inducing the various body parts in burning fats. Well, the constituents of the invisible organ can be strengthened with the intake of prebiotics.

These are like fertilizers that create the proper environment for the desired microbial ecosystem to flourish. They tilt the microbial community in a manner favouring some specific tasks to be performed. For instance, a prebiotic promoting the growth of lactase-secreting microbes will help lactose intolerant people while a prebiotic inhibiting the competitors of vitamin K-producing bacteria will be of immense assistance to patients having difficulty with blood coagulation. Prebiotics are excellent nutritional supplements involved in modulating and adjusting the microbiome that can undergo disruption due to ageing, infection, climate change and a sleuth of other factors one may be subjected to as one goes through one's daily activities (Fig. 3.20).

What are these magical prebiotics? They are usually plant derived fibers and complex carbohydrates contained in milk that help promote the growth of specific microbial ecology in our body especially in our digestive system. They are mostly resistant to digestion by the enzymes produced by the gut. They are metabolized only by our invisible organ and/or promote proper microbial communities that impart health benefits to the host. The production of short-chain fatty acids (SCFA-acetate, butyrate) in response to the intake of prebiotics can contribute to the energy budget of the muscle, can regulate cholesterol biosynthesis and can provide fuel to the colon. Stimulation of calcium absorption, reduction in infections and repression of allergic symptoms are some of the other activities prebiotic intake is known confer on the host. These physiological processes are of course a major boon to our well-being as these are like lubricants oiling our body machines. The prebiotics prime the microbiome and this invisible organ is reflective of the prebiotics consumed. As a toned muscle system is indicative of the time spent at the gymnasium, specificity and diversity of the invisible organ is a tell-tale sign of our dietary fiber-eating habit (Fig. 3.21).

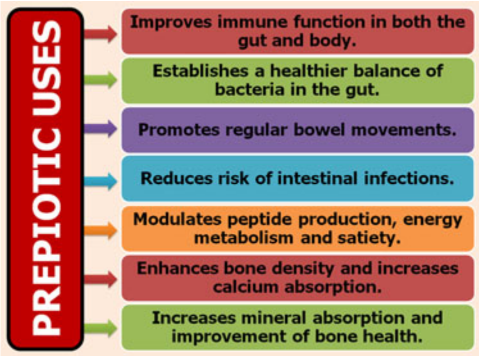


Fig. 3.21 Prebiotics and their health impact

3.17 Prebiotics in Everyday Foods

Prebiotics or dietary fibers have been part of human nutrition since the dawn of civilization. In 450 BC Hippocrates had noted the laxative attribute of coarse wheat compared to the refined variety. In the 1920s Kellogg sang the praise of bran as a nutrient that increased stool weight, prevented diseases and acted as a laxative. All health gurus extoll the praise of the nutritional quality of fiber-rich foods. After a relative quiet epoch in the health benefits of the dietary fibers, their involvement in mitigating ailments like obesity, cardiovascular disorders and diabetes were widely revived in the 1970s and has now become a staple of balanced nutrition. The main prebiotics are the galacto-oligosaccharides (GOS) obtained from milk, inulin associated-fructo-sugar (FOS) found in chicory roots and xylooligosaccharides (XOS) present in plant products like palm oil and corn plants. They also occur naturally in milk, asparagus, garlic, onion, leeks, wheat, oats and soya beans. They are soluble, resistant to the acidic environment in the stomach, fermentable and stimulate growth or the activity of intestinal microbes responsible for the well-being of the host. Prebiotics tend to be relatively selective to microorganisms like *Bifidobacteria* and *Bacteroides*. They are converted into simpler derivatives before they reach the colon. Here they act as an anchor for the establishment of a unique ecosystem that is aimed at aiding the host in accomplishing a variety of tasks. They generate energy that fuels the muscles and the colon. They are also involved in repressing allergic symptoms. The reduction of infection and promoting the proliferation of good microbes like *Akkermansia* are some other positive features prebiotics contribute to. They are also known to decrease glucose absorption, activate cholesterol excretion, and promote laxation.

One of the most intriguing influence of prebiotics in dictating our microbial ecosystem and promoting our well-being has been observed in infants just immediately after birth. Babies who are fed their mothers' milk have much better health outcomes than those fed formulated milk. They are less susceptible to allergic reactions and kids nourished by natural milk tend to be less prone to asthma. The GOS, a natural ingredient in the mother's milk cannot be digested by the babies' developing guts. They are designed to promote the growth of microbes that are crucial for a variety of tasks at this critical juncture in their lives. One can safely conclude that mother-nature is making these goodies not for the babies but for the microbes feeding on them. In fact, the presence of a unique ingredient known as sialic acid in the milk of some Malawian mothers result in well-nourished infants as opposed to infants who are fed by mothers without this magical tonic in the milk. This prebiotic is responsible for the growth of a unique set of microbes that generates simple sugars utilized by infants for their development. Even from such an early stage of human life, the body is programmed to depend on these invisible partners. It is not surprising to learn that various milk products are being formulated with oligosaccaharides in an effort to generate increased microbial population in growing infants.

The elderly can also benefit from the intake of prebiotics as their microbiota tend to undergo a drastic change and there is a significant reduction in the diversity and abundance of the microbial ecosystem as age progresses. The fructo-oligosaccharide (FOS)-based prebiotics have an excellent bifidogenic activity while resistant starch like sprouted legumes improves bowel movement by promoting the growth of *Lactobaccilli* and *Bifidobacteria*. These microbial fertilizers can be given to relieve seniors of constipation, a condition quite acute in this segment of the population. Prebiotics not only promote a healthy life, their intake can be tailored to remedy a number of ailments that are due to dysbiosis i.e the perturbation of microbiota in the body. Their ability to nurture a select group of bacteria that possess a range of tools to combat the opportunistic invisible invaders can be put to good use.

Obesity is a disease that is characterized by low grade inflammation and is punctuated by a decrease in the diversity of gut microbiome, a situation resulting in the ineffective harvesting of calories from what we eat. The inadequate energy extraction from food intake automatically triggers the hunger hormone, ghrelin which stimulates the desire to eat more food. This vicious circle causes the body to gain weight. The utilization of FOS prebiotics like inulin-laced pasta decreases the bacterial LPS, suppresses the hunger signal, promotes satiety and increases microbial diversity events aimed at countering obesity. A prebiotics is an effective means in controlling weight gain. Cardiovascular diseases do also respond well to prebiotics therapy. Water soluble fibers such as pectin found in fruits and guar gum from guar beans are known to decrease the bad cholesterol (LDL low density lipoprotein) without affecting the good cholesterol (HDL high density lipoprotein). They also help lower the blood pressure. The positive influence of these prebiotics on the functioning of the heart has been widely documented and accepted as a means of averting cardiovascular diseases. Mitigating constipation and prompting proper bowel mobility are the gold standard treatment fuelled by the intake of prebiotics. Cereal fibers like wheat bran are religiously utilized to counter any abnormality associated with fecal bulking. Prebiotics can also be a potent remedy against cancers. Enhanced micronutrient absorption and stimulation of microbes with cancer fighting enzymes like glutathione transferase are some of the mechanisms that these nutritional elements confer to the body. The ability of prebiotics to enrich the diversity of the microbiome is central to its curative power (Fig. 3.22; Fig. 3.23; Fig. 3.24).

Fig. 3.22 Prebiotics: Anthocyanins against obesity

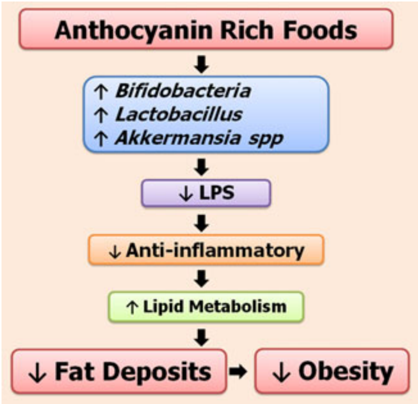


Fig. 3.23 Prebiotics and their molecular interactions

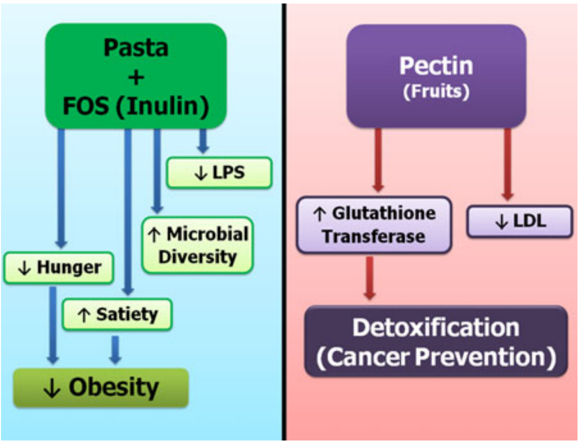
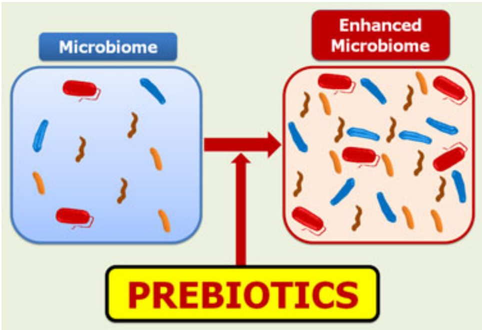


Fig. 3.24 Prebiotics therapy



Prebiotics is almost like a dietary manure that transforms the microbial landscape in the gut. A similar strategy is utilized to help the visible body parts if something goes amiss. During anemia when the level of hemoglobin is low, iron sulfate pills enables the blood system to stimulate the production of this oxygen carrier. In the case of keratoconus, an eye condition where the cornea loses its focusing power, the surgical administration of vitamin B2 allows the eye to function normally. In this instance, the infusion of vitamin B2 promotes the cross-linking of collagen, a biological event that fortifies the cornea and enables it to contribute to visual sensation. The same can be said of lipoic acid and calcium supplements. The former helps fortify the workings of the brain while the latter enable the proper functioning of the skeletal system. As these ingredients assist the target organs optimize their biological roles, the intake of prebiotics provides a proper nutritional environment for the right microbial ecosystem to flourish in order to maximize the output of the invisible organ in promoting a healthy body. However, this is a non-invasive exercise and usually corresponds to an accompaniment of the food we consume unlike the surgical intervention needed to feed the cornea with vitamin B2. Hence, prebiotics are natural fertilizers for the microbiome and can remedy the microbial perturbations that the body has to often undergo due to age, environmental change or intake of medications.

3.18 Synbiotics: A Probiotic and Prebiotic Concoction

One can also utilize a two-pronged approach comprising probiotics and prebiotics to regulate an unbalanced microbial landscape. This is termed as synbiotic and can be equated to a multi-drug regime to cure a disease. A combination of these two stimulators can have a more vigorous impact on the invisible organ and can provide a very effective therapy against ailments mediated by uncontrolled proliferation of some opportunistic microbes. The blending of live microbes and the microbial fertilizers that enable them to thrive is a very powerful tool to goad the constituents of the invisible organ in executing a dedicated task. For instance, muscle wasting and inflammation that characterize cancer cachexia has been shown to be mitigated with a concoction of a synbiotic consisting of *Lactobacillus reuteri* and inulin-based fructans (FOS). The intake of this synbiotic reduces the population of *Enterobacteriacae*, replenishes the *Lactobacillus* colonies and prolongs the life of the patients. The therapeutic value of the FOS and *lactobacilli* taken together in combatting hemorrhage triggered by bacterial infection has also been recognized. In this instance, a sharp decrease in *E.coli* counts coupled with an increase in the population of *Lactobacillus* spp contribute to bringing relief to these patients. Quite often a cocktail of drugs is prescribed to combat a viral infection; this can be equated to synbiotic therapy. The AIDS virus, can only be eliminated from the blood system of infected individuals by the use of anti-proteases and medications inhibiting the replication of the viral genetic code. Hence, this double punch aimed at aiding the microbiome naturally is of immense benefit to the body.

3.19 Conclusion

The human body is made of cells that are in constant flux due a variety of factors including wear and tear as age progresses. These can be repaired or rejuvenated with the aid of medical intervention. One can seek the help of a cosmetic surgeon to remove ageing spots or modify the shape of the nose. In case of the microbiome, any perturbations (dysbiosis) that the invisible organ experiences can be modulated by the programmed intake of probiotics and prebiotics. Hence, the microbiome behaves in manner that is comparable to the organs composed of visible cells. It is clear that the body is made up of visible and invisible cells. Most visible cells assemble as various organs we can see; there are few exceptions like the blood system where the cells are mobile and interact directly and indirectly with all the organs. Just like dysbiosis that robs the microbiome of its natural functions, the organs can also be subjected to a number of challenges over body's life span. The inherent repair machinery cannot remedy the situations the organs are facing in a timely manner, intervention in form of medication or surgery is needed to bring them back as contributing members of the body. For example if some oily clutters are impeding the flow of blood, the arteries are unclogged by surgical procedure. If organs of the body are insulted by overuse of some products or by accidental intake of toxic compounds, antidotes are utilized to bring back these anatomical structures in tip-top shape. For instance, fomepizole can give reprieve to a liver challenged by alcohol abuse while high levels of cholesterol in the blood that contribute to plaque build-up in the arteries can be rectified by statin family of cholesterol-busters (Fig. 3.25).

In the same manner any disturbance in the microbial communities constituting the microbiome can be adjusted with the intake of probiotics, prebiotics or

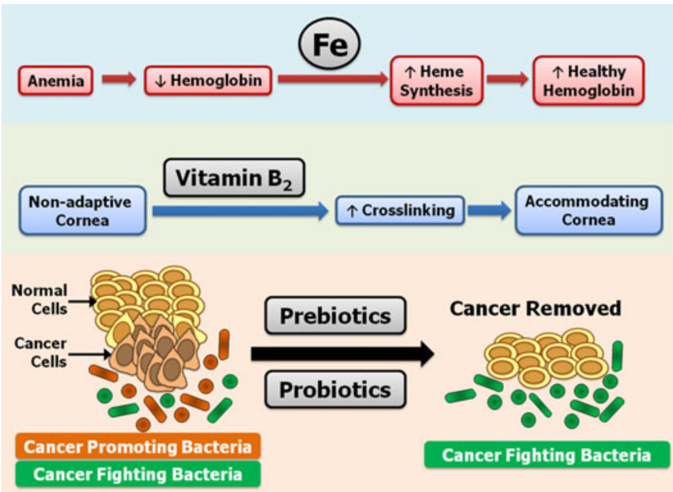


Fig. 3.25 Rejuvenation of visible and invisible organs

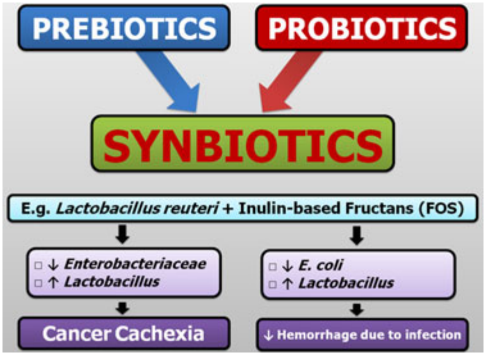


Fig. 3.26 Probiotics and prebiotics to counter dysbiosis and diseases

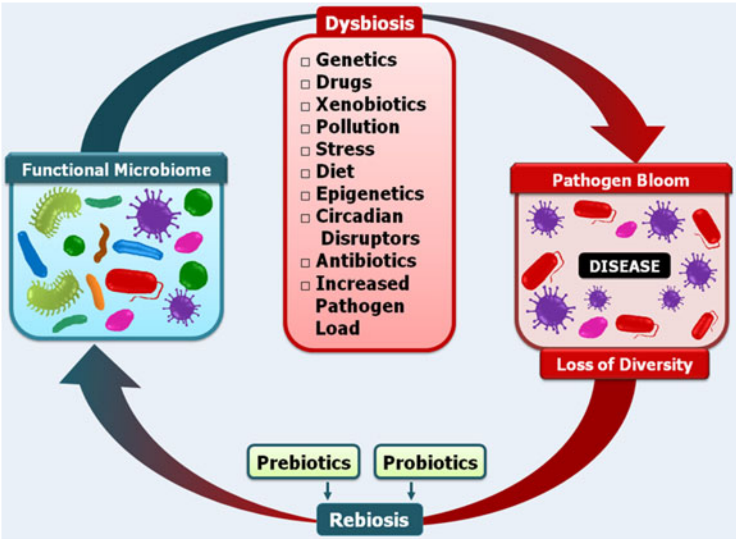


Fig. 3.27 Link between dysbiosis, probiotics and prebiotics

synbiotics. These ‘therapies’ are akin to the medications, the surgery, antidotes or stem cells that are deployed to tweak the visible organs in an effort to bring them to a normal working condition (Fig. 3.26). The fact that the microbiome is invisible and its molecular operation is still not fully understood compared its visible counterparts like the liver should not preclude it from being an important component of the cellular collectivity responsible for the body’s well-being. The microbial system spans a wide surface area within and on the body just like the blood system as it imparts extremely valuable functions. This microbial ecosystem is to some extent responsible for the human anatomy and makes it work the way it does. Understanding how the invisible organ operates, how the harmony amongst its cells are disrupted and how the fine-balance is reconstituted with the aid of probiotics and prebiotics are essential if we are to understand the intimate details about ourselves. Ignoring these invisible collaborators is like disregarding the majority our own cellular components. Hence, dysbiosis and rebiosis propelled by the infusion of live seeds (probiotics) and the fertilizers (prebiotics) will go a long way toward promoting wellness and will bestow upon us a healthy life (Fig. 3.27).

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