# The role of nutrition in gut health

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# The intestinal microbiota

- Homeostasis of the intestinal microbiota, often referred to as eubiosis, fosters interactions between the gut microbiome and the host that promote effective innate and adaptive immunity, including pathogen recognition, self-tolerance, and identification of beneficial commensals.
- A well-balanced intestinal microbiome is also responsible for harvesting energy from food sources, producing short chain fatty acids (SCFAs) from indigestible carbohydrates, and synthesizing vitamins and amino acids for maintenance of gut barrier function.
- Dysbiosis can affect any of these critical processes and increase an individual's risk of developing chronic diseases, for example, obesity and other metabolic comorbidities

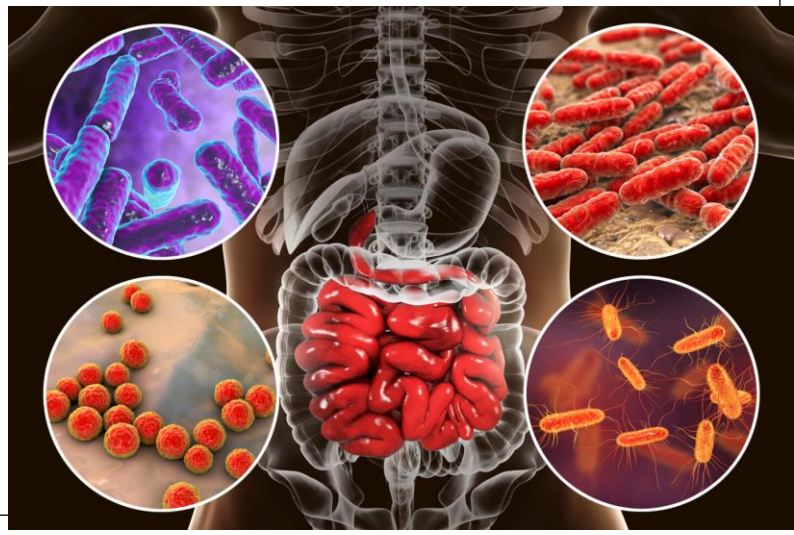
# The intestinal microbiota

- Dysbiosis: result from an unhealthy diet composed mainly of commercial formula and foods high in fat and low in fiber.
- Shifts in bacterial abundance, decreased microbial diversity, increased inflammatory mediators, and increased intestinal permeability are consequences of this type of diet and subsequently increase an individual's risk for a host of gastrointestinal pathologies



# The intestinal microbiota

- Diet is recognized as one of the key, modifiable environmental factors and may account for 20% and 50% of microbial structural variations in humans and mice, respectively.
- Recent population-based studies demonstrate that effects of diet on the gut microbiome and long-term health outcomes may dominate over host genetic.



# MICROBIOME IN PREGNANCY AND EARLY NUTRITIONAL PROGRAMMING OF THE NEWBORN

- Environmental factors, primarily diet, along with prepregnancy body mass index (BMI) and maternal weight gain during pregnancy, may significantly influence offspring's gut microbiome and increase their risk of obesity and metabolic syndrome as children and adults.
- The microbiome of pregnant women was evaluated during the first and second trimester in overweight women (BMI >30) and compared with normal weight individuals (BMI <25).
- Overweight pregnant women had significantly higher levels of Bacteroides and Staphylococcus compared with controls.
- Other studies of microbiota shifts during pregnancy in obese women versus controls found a decrease in Bifidobacterium, findings similar to those in nonpregnant obese individuals.

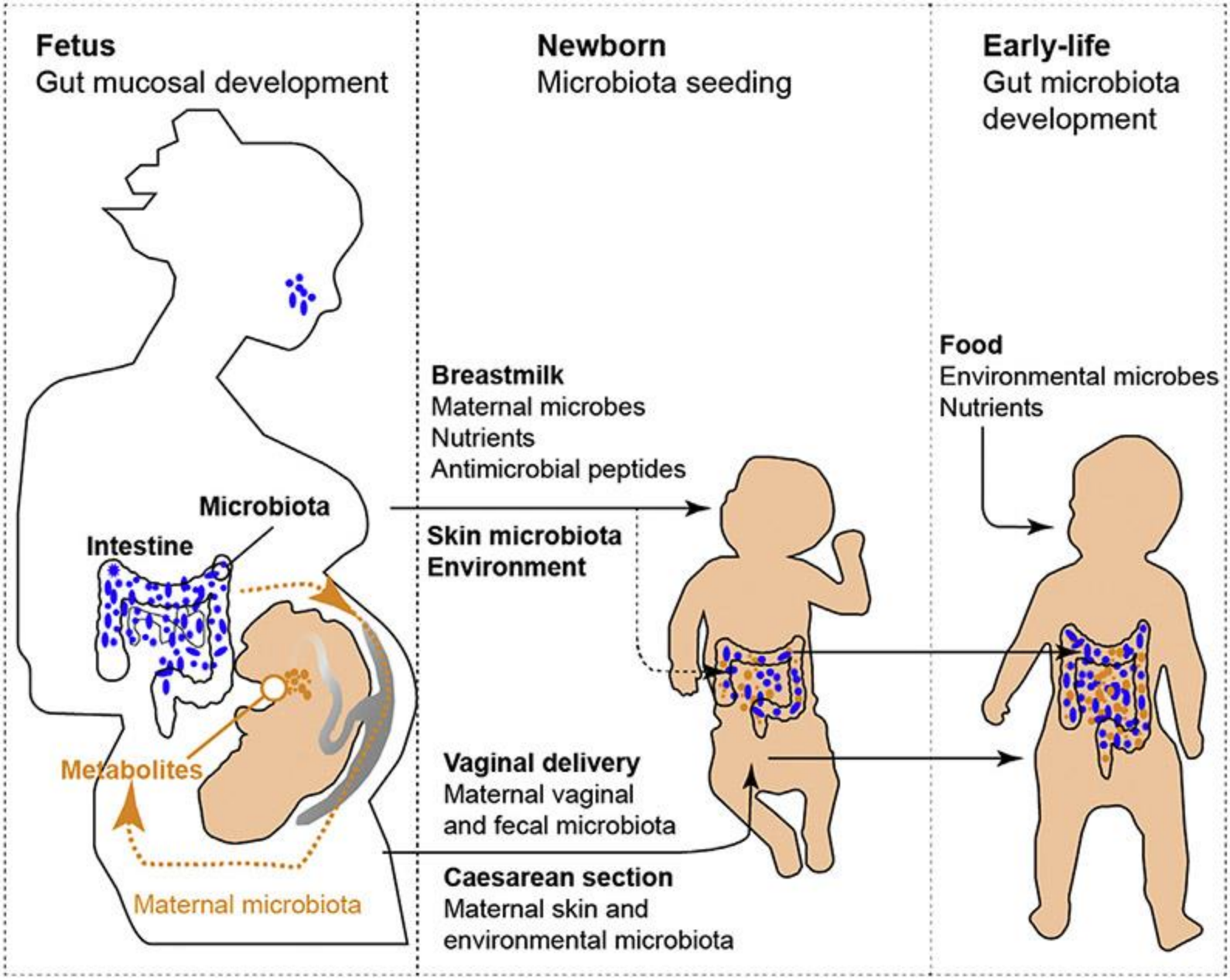
# MICROBIOME IN PREGNANCY AND EARLY NUTRITIONAL PROGRAMMING OF THE NEWBORN

- Dietary intake is most influential on microbial colonization during the first 2 to 3 years of life when the dynamic and nascent gut microbiome is in its early stages of assembly.
- As an infant's diet expands from breast milk or formula to solid foods, α-diversity (bacterial diversity in one specific region of the body) increases and β-diversity (regional differences in bacterial composition in different parts of the body), which is initially highest at birth, gradually decreases.
- However, as the gut microbiome stabilizes in adulthood, individuals separate into clusters or "enterotypes," which are classified based on proportions of major taxa.

# NEWBORN MICROBIOME AND NECROTIZING ENTEROCOLITIS

- Breast milk is rich in nondigestible oligosaccharides that serve as prebiotics to promote the growth of beneficial bacteria, including Lactobacillus acidophilus, Bacteroides fragilis, and Bifidobacterium infantis.
- Although newborns are also rapidly colonized by a variety of environmental factors (eg, maternal oral and skin flora, household, or hospital organism), the most important environmental factor, much like with adults, is diet whether it be breast milk or formula.
- Necrotizing enterocolitis: One of the only dietary strategies that has proven preventative for necrotizing enterocolitis is the use of breast milk

- Environmental factors, including medications, malnutrition, and infections, which can cause large shifts in bacterial composition and the relative abundance of some taxonomic groups.
- The microbiome during pregnancy is dynamic, with shifts in both composition and bacterial load unique to each trimester.


Fetus
Gut mucosal development
Newborn
Microbiota seeding
Early-life
Gut microbiota development
Microbiota
Intestine
Metabolites
Maternal microbiota
Breastmilk
Maternal microbes
Nutrients
Antimicrobial peptides
Skin microbiota
Environment
Vaginal delivery
Maternal vaginal
and fecal microbiota
Caesarean section
Maternal skin and
environmental microbiota
Food
Environmental microbes
Nutrients

# *H. pylori* and Nutrition

- In addition to host or strain genetic differences, environmental factors, such as **host diet**, are emerging as important components of the ecology within the gastric environment.
- It is likely that the gastric environment is highly influenced by host nutrient intake.
- Epidemiological studies have revealed that dietary habits such as high intake of green tea, fruits, or vegetables are protective against gastric cancer risk.

# *H. pylori* and Nutrition

- Conversely, case-controlled and cohort studies reveal that high intake of red meat and/or processed meat (which are high in transition metals) and preserved foods (pickled, dried, smoked, or salted) which are often high in salt is associated with increased risk of noncardia gastric cancer.
- It is hypothesized that carotenoids, folate, vitamin C, and phytochemicals from fruits and vegetables have a protective role against carcinogenesis.
- Conversely, salt and the availability of some transition metals can alter H. pylori virulence and accelerate carcinogenesis

# MICROBIOTA OF GASTRIC PATHOLOGIES: ESOPHAGEAL ADENOCARCINOMA, BARRETT'S ESOPHAGUS, AND GASTROESOPHAGEAL REFLUX

- Cross-talk between one's diet and gastric and esophageal microbiomes
- Patients with GERD and BE have lower esophageal tract microbiomes that are high in gram negative organisms, including Proteobacteria, Fusobacteria, and Spirochaetes.
- High-fiber and low-fat diets support a gut microbiome robust with commensals that stimulate normal metabolism, nutrient and vitamin absorption, and elimination of pathogenic bacteria and toxins.
- Conversely, diets rich in fat and processed foods (simple sugars, animal proteins) are associated with chronic inflammation of the esophagus and a dysbiosis that contributes to BE.

# MICROBIOTA OF GASTRIC PATHOLOGIES: ESOPHAGEAL ADENOCARCINOMA, BARRETT'S ESOPHAGUS, AND GASTROESOPHAGEAL REFLUX

- Individuals in rural areas, who are more likely to have balanced diets with adequate fiber intake, have microbiomes that assist with the digestion of fiber-rich foods and polysaccharides.
- People in urban areas, who are more likely to consume diets high in fat and processed foods, have a gut microbiota with increased levels of Bacteroidetes

# MICROBIOTA, DIETARY TRIGGERS, AND THE PATHOGENESIS OF CELIAC DISEASE

- Treatment of this disease more complex than simple adherence to a gluten free diet.
- Recent studies are evaluating the role of prebiotics, probiotics, and fermentable oligosaccharides, disaccharides, monosaccharides and, polyols (FODMAP) as potential therapies for CD.
- In CD patients, it is suspected that levels of Bifidobacteria and Lactobacilli are decreased, and probiotics that target these strains might be beneficial.

# INFLAMMATORY BOWEL DISEASES

- A Western diet, characterized by excessive consumption of refined sugars, salt, and saturated fat, low consumption of dietary fiber, and limited food diversity, is associated with an increased risk of IBD.
- Such a diet promotes the production of bacterial metabolites with adverse effects on the gut microbiota and the intestinal immune system.
- Breast milk: considered to be protective against IBD.
- Commercial formula use and Western diets, more frequently consumed by urban populations and developed countries with easy access to ultraprocessed foods, are also associated with decreased intestinal bacterial diversity.

# MICROBIOME AND DIETARY ASSOCIATIONS WITH COLORECTAL CANCER

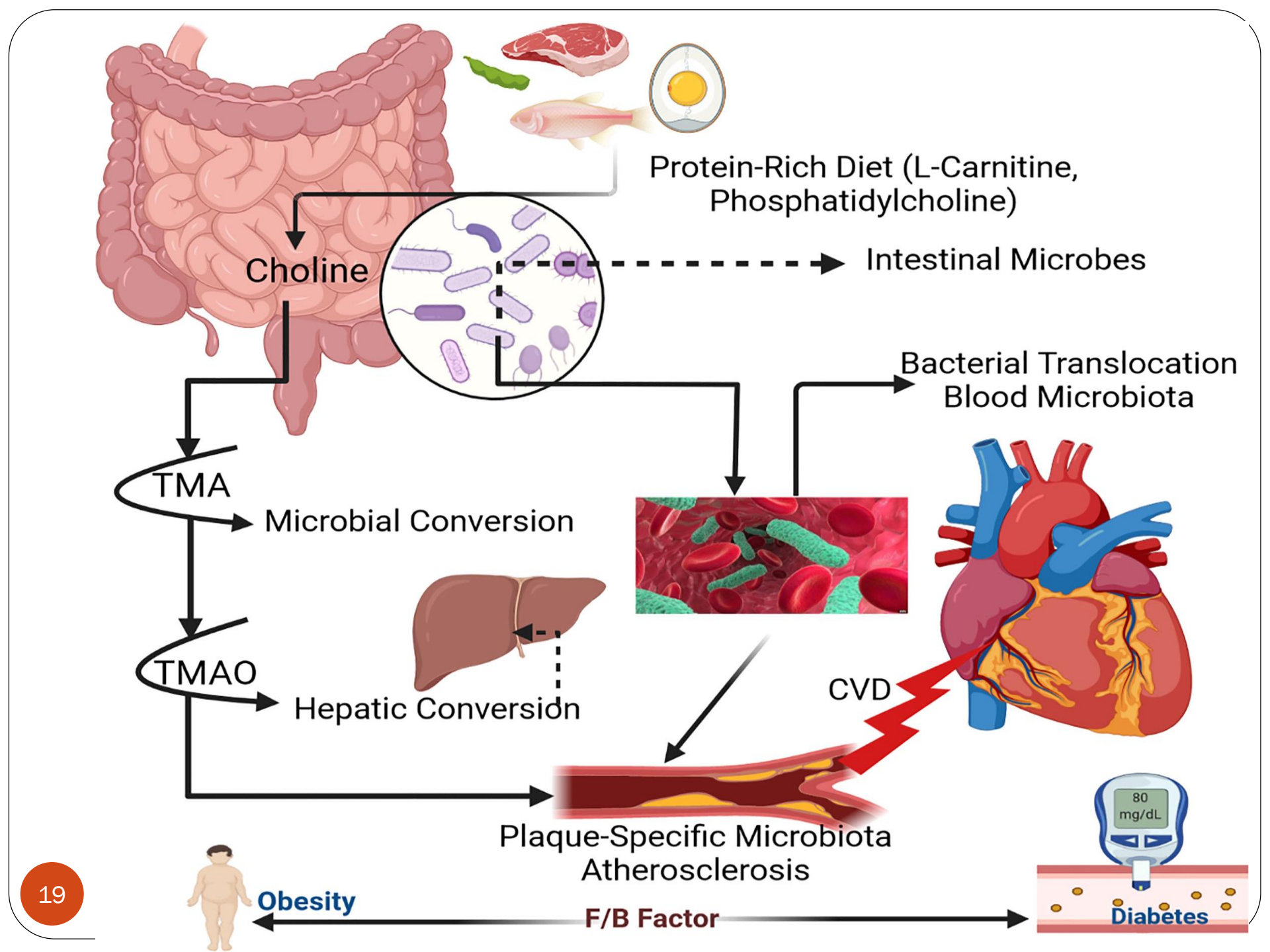
- CRC, the third most common cancer and the leading cause of cancer deaths in the United States among men and women is strongly influenced by dietary risk factors that affect the intestinal microbiome.
- In fact, up to 60% of CRC cases are attributable to modifiable risk factors, including BMI, physical activity, and diet.

# MICROBIOME AND DIETARY ASSOCIATIONS WITH COLORECTAL CANCER

- No linear association was found between fiber intake and CRC risk in a meta-analysis of 21 prospective studies in the United
- Conversely, data from the European Prospective Investigation into Cancer and Nutrition have consistently demonstrated an association between fiber intake and a decreased risk of CRC.
- Differences in the findings between these 2 populations are hypothesized to be due to the dietary sources of fiber, which in the United States is typically whole grains and in Europe is mainly fruits and vegetables.

# MICROBIOME AND DIETARY ASSOCIATIONS WITH COLORECTAL CANCER

- Red and processed meats may also be implicated in the pathogenesis of CRC.
- Specifically, the high content of choline and carnitine in red meat can serve as precursors for the production of trimethylamine and trimethylamine N-oxide (TMAO) by the gut microbiota now with pathologic enrichment of gram-negative organisms including Prevotella, Bacteroides, and bacteria from the Teneriticutes and Deferribacteres phyla.

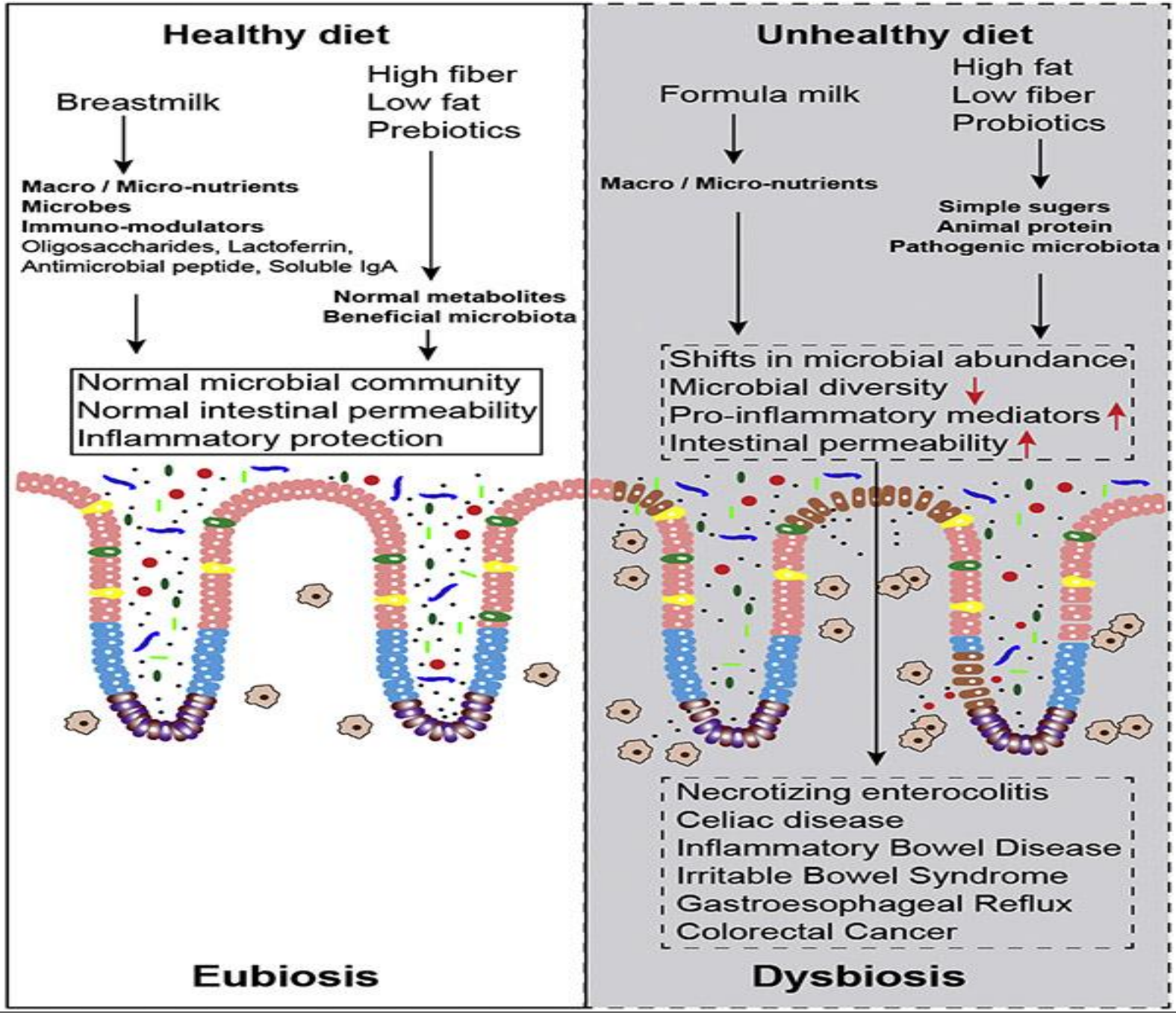

Protein-Rich Diet (L-Carnitine, Phosphatidylcholine)
Choline
Intestinal Microbes
Bacterial Translocation
Blood Microbiota
TMA
Microbial Conversion
TMAO
Hepatic Conversion
CVD
Plaque-Specific Microbiota
Atherosclerosis
Obesity
F/B Factor
80 mg/dL
Diabetes

# MICROBIOME AND DIETARY ASSOCIATIONS WITH COLORECTAL CANCER

- Another mechanism through which processed, red meat may increase CRC risk is by the bacterial production of hydrogen sulfide from inorganic sulfur, routinely used as a preservative for red meats.
- Bacteria driving these hydrogen sulfide–producing pathways, which are known to be increased in metabolomic analyses of fecal samples from CRC patients, include gram-negative
- These shifts in bacteria-driven hydrogen sulfide activity trigger oversuppression of effector T cells, without which tumorigenic activity proceeds unopposed.

# MICROBIOME AND DIETARY ASSOCIATIONS WITH COLORECTAL CANCER

- Interestingly, patients with **breast cancer** have similar alterations in their gut microbiome, including enrichment of Clostridia, Enterobacterium, Bacteroides, and E coli
- The dysbiosis also affected mammary tissue homeostasis with an increased presence of macrophage-derived inflammatory cytokines.
- Western diets are identified as a risk factor for developing breast cancer.
- Plant-based Mediterranean diets, which include soluble fibers and lignans, found in whole grains, soy, fruits, and vegetables, may decrease the risk of breast cancer.


Healthy diet
Breastmilk
High fiber
Low fat
Prebiotics
Macro / Micro-nutrients
Microbes
Immuno-modulators
Oligosaccharides, Lactoferrin,
Antimicrobial peptide, Soluble IgA
Normal metabolites
Beneficial microbiota
Normal microbial community
Normal intestinal permeability
Inflammatory protection
Eubiosis
Unhealthy diet
Formula milk
High fat
Low fiber
Probiotics
Macro / Micro-nutrients
Simple sugers
Animal protein
Pathogenic microbiota
Shifts in microbial abundance
Microbial diversity
Pro-inflammatory mediators
Intestinal permeability
Necrotizing enterocolitis
Celiac disease
Inflammatory Bowel Disease
Irritable Bowel Syndrome
Gastroesophageal Reflux
Colorectal Cancer
Dysbiosis

# ROLE OF DIET AND MICRONUTRIENTS IN MICROBIOME AND DISEASE PREVENTION

- **Vitamin D:** is one of the micronutrients recently identified to have a major impact on chronic intestinal inflammation, including IBD.
- Novel studies in intestinal epithelial vitamin D receptor knockout mice demonstrated exaggerated intestinal colitis owing to activation of the nuclear factor-κB pathway and shifts in the gut microbiome toward increased E coli and decreased Lactobacillus and butyrate-producing bacteria.

# ROLE OF DIET AND MICRONUTRIENTS IN MICROBIOME AND DISEASE PREVENTION

- In one study, children with infectious diarrhea, who were also found to be vitamin A deficient, had a decrease in butyrate-producing bacteria, an increase in opportunistic pathogens (Enterococcus), and an overall decreased bacterial diversity.
- It was suggested that vitamin A deficiency induces colonic inflammation.
- Colitis is amplified by deficiency of vitamin A and ameliorated by supplementation of the vitamin A.
- In another study, it was suggested that the apricot or β-carotene treatment may protect the impairment of oxidative stress and ameliorate MTX-induced intestine damage at biochemical and histological levels

# ROLE OF DIET AND MICRONUTRIENTS IN MICROBIOME AND DISEASE PREVENTION

- Vitamin E, a well-recognized antioxidant, may have an anti-inflammatory role in the gut microbiome by scavenging for excess free radicals and protecting against mucosal immune damage.

- Furthermore, it was suggested that the α-tocopherol, ascorbic acid, and β-carotene, when given concurrently, have primarily antioxidant effects on lipids under stress

# ROLE OF DIET AND MICRONUTRIENTS IN MICROBIOME AND DISEASE PREVENTION

- Vitamin C, which is exclusively obtained from dietary sources, has antioxidant properties similar to vitamin E and may support the gut microbiota by increasing intestinal populations of Lactobacillus and Bifidobacterium populations while decreasing E coli.
- Zinc supplementation may promote growth of beneficial bacteria and limit replication of pathogenic organisms.

# sweeteners

- High-intensity sweeteners are commonly used as sugar alternatives, being many times sweeter than sugar with minimal calories.
- Some animal studies have shown that these sugar substitutes may have negative effects on the gut microbiota.
- Sucralose, aspartame, and saccharin have been shown to disrupt the balance and diversity of gut microbiota.



# Dietary Polyphenols on Human Gut Microbiota

- Polyphenols' interaction in several metabolic pathways resulted in the release of metabolites which have shown a positive effect on the gut microbiota by promoting the growth of useful bacteria.
- The gut microbes can transform the polyphenols into bioactive metabolites influencing the intestinal ecology
- In intestinal microbial colonization, the polyphenols promoted the growth of Gram-positive bacteria compared to Gram-negative bacteria

# Dietary Polyphenols on Human Gut Microbiota

- Polyphenols are the secondary plant metabolites abundantly from the food sources such as tea, coffee, cocoa, spices, several fruits and vegetables.
- Of those sources, fruits and vegetables constitute the highest content of polyphenols.
- The group of flavonoids is classified under six sub classes, i.e., flavanols, flavones, isoflavones, flavonols, flavanones and anthocyanidins.
- Tea polyphenols: Tea catechins
- Resveratrol : a significant increase in the growth of Bifidobacterium spp.

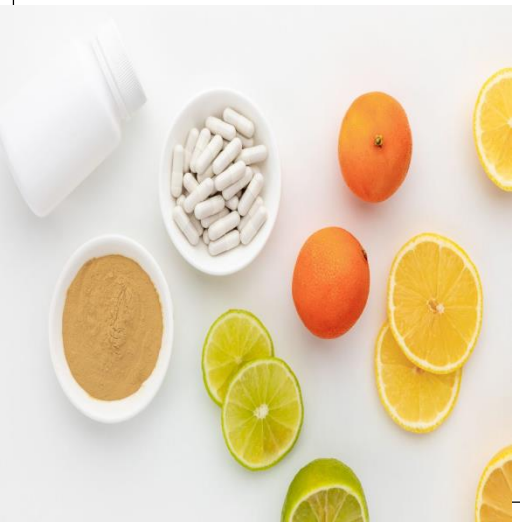
# Dietary Polyphenols on Human Gut Microbiota

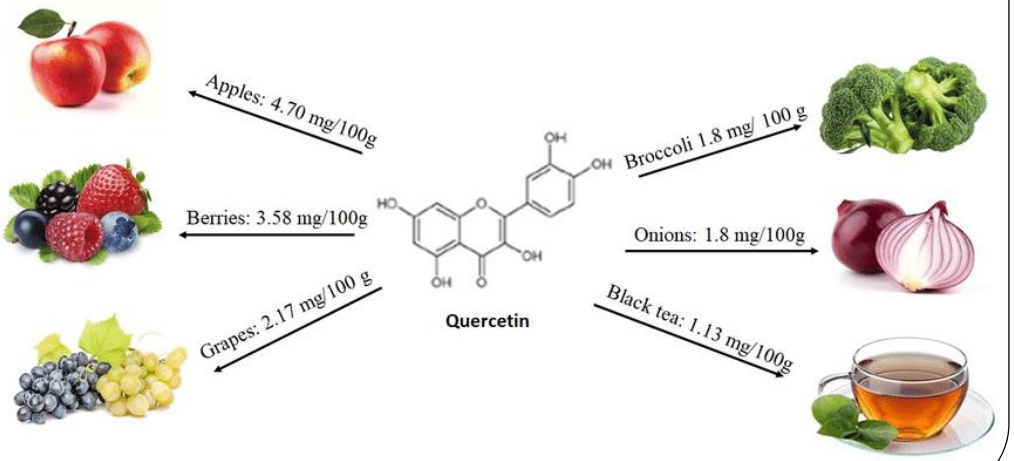
- The dietary intake of pomegranate juice extract (urolithin) : Anti-Inflammatory Effects on Human Colon Fibroblasts
- From the experimental results, the authors observed that quercetin had the highest inhibitory potential against human gut bacteria compared to other flavonoids such as naringenin, hesperidin, rutin and catechii-inflammatory activity.
- Quercetin (i.e., concentration ranging from 62.5–250 µg/mL) on the gut microbiota, the in vitro study results showed a decrease in E. coli, Staphylococcus and Salmonella.



# Dietary Polyphenols on Human Gut Microbiota

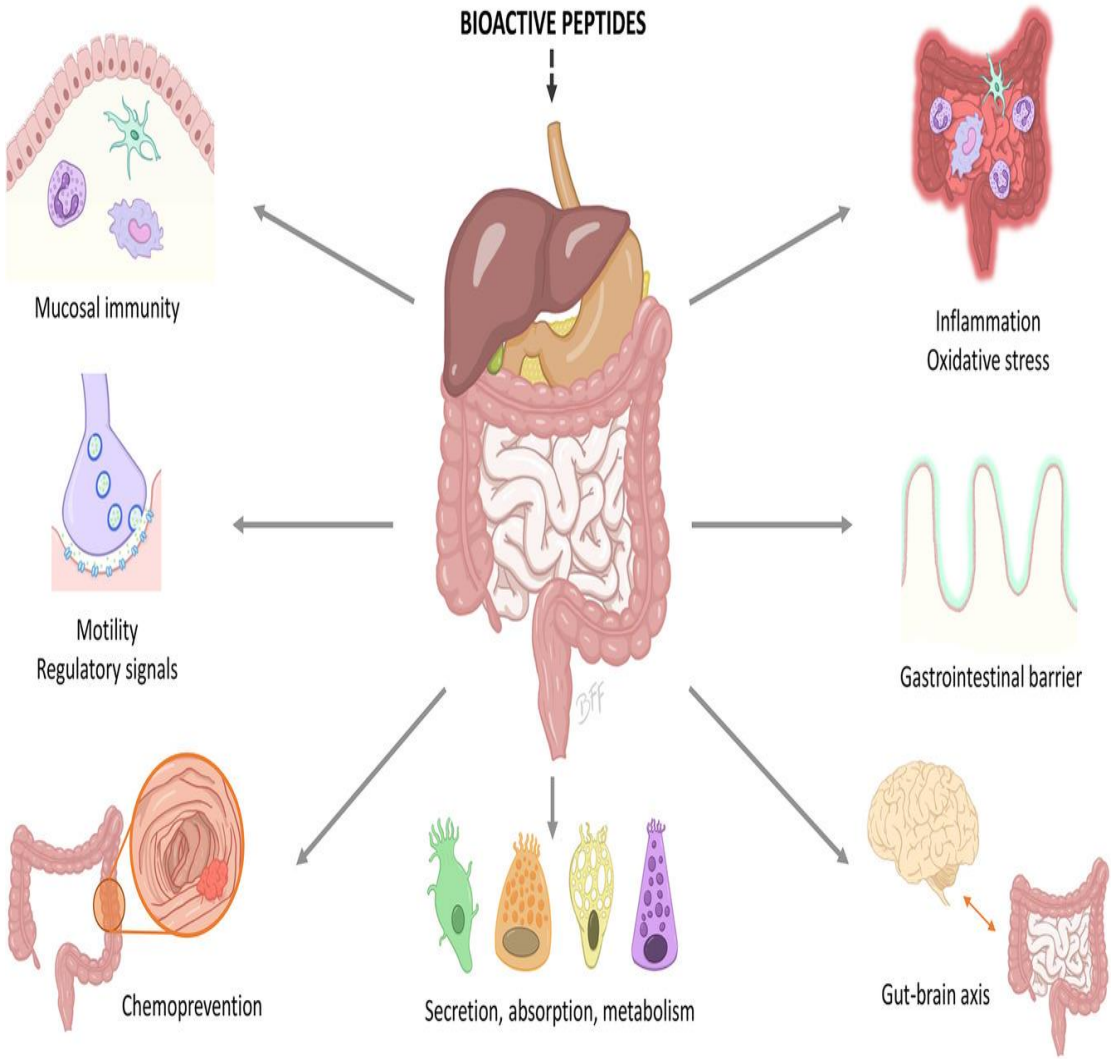
- The polyphenolic compound querectin is degraded by Bacteroides
- Hesperetine (a rutinoside containing aglycon), is poorly degraded by the colonic microbiota.
- This aglycon has an inhibitory activity against Staphylococcus aureus and H. pylori





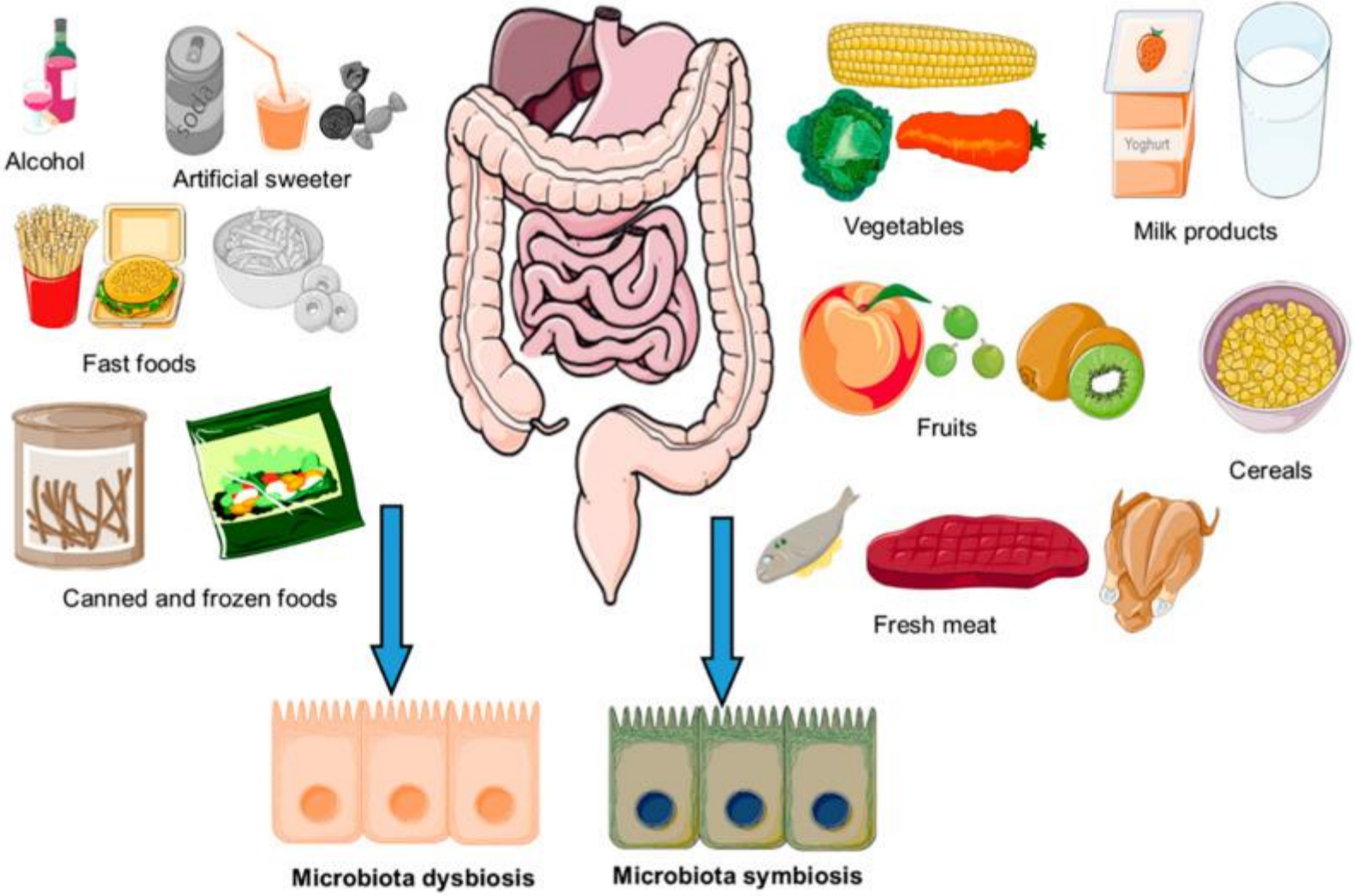
# Protein

- **Bioactive peptides** modulate the composition of gut microbiota, which in turn might affect host gut and immune system.
- The differences in gut metabolites within individuals was linked with level of amino acids amongst individual.
- The consumption of hydrolyzed proteins significantly reduced gut microbiota dysbiosis.



# Omega-3 PUFAs Could Affect Gut Microbiota:

- **Omega-3 PUFAs** affect the gut microbiome in three main ways:
- (1) modulating the type and abundance of gut microbes
- (2) altering the levels of proinflammatory mediators, such as endotoxins (lipopolysaccharides) and IL17
- (3) regulating the levels of short-chain fatty acids or short-chain fatty acid salts


Alcohol
Soda
Artificial sweeter
Fast foods
Canned and frozen foods
Vegetables
Yoghurt
Milk products
Fruits
Cereals
Fresh meat
Microbiota dysbiosis
Microbiota symbiosis

# KEY POINTS

- Diet is a key extrinsic factor that impacts the gut microbiome, particularly during the dynamic colonization process that occurs in the first several years of life.
- An imbalance in the complex gut ecosystem referred to as a dysbiosis can have short- and long-term effects on immune system development and impart life-long health complications on an individual in intestine and extraintestine (eg, breast).
- New research suggests effects of microbiome on the central nervous system. The "gut-brain-microbiome axis" may have a significant role on brain development and the pathogenesis of neuropsychiatric disorders.
- Poor macronutrient and micronutrient intake contribute to a dysbiosis.
- However, supplementation with specific prebiotics and probiotics might modulate the microbiome and restore host homeostasis.