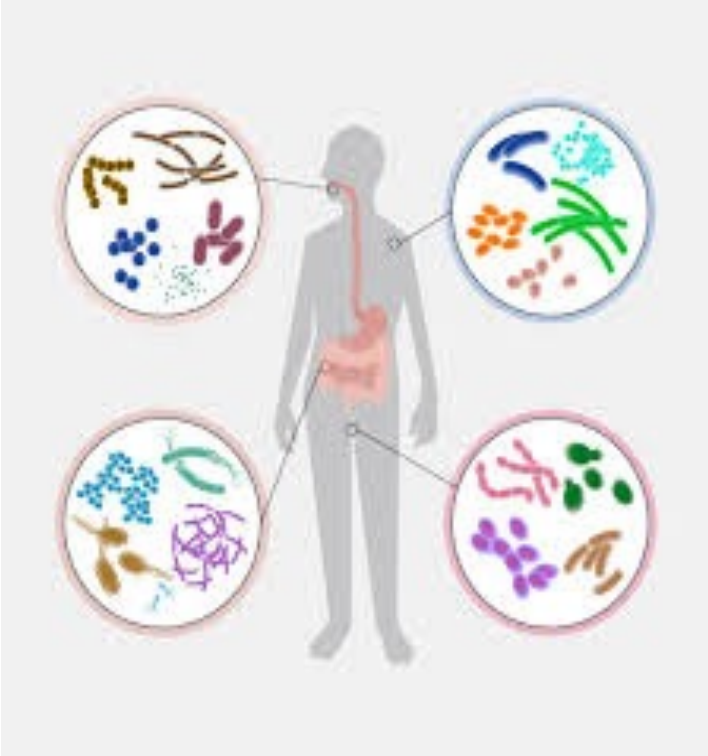
Portsmouth Hospitals University NHS Trust

Date:

The microbiome

Karen Lee



Microbiome

* What is the microbiome
* How the microbiome may affect health and wellbeing
* Practical diet and lifestyle tips to support our microbiomes

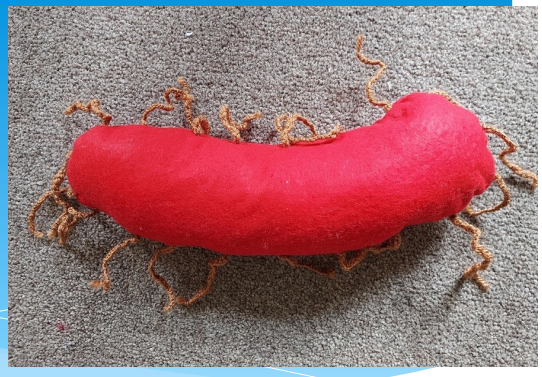
What is the Microbiome?

* Microbiome: the collection of all genomes of microbes (including bacteria, bacteriophage, fungi, protozoa, and viruses) in an ecosystem, particularly the collection living in and on the human body. There are roughly 40 trillion bacterial cells in the human body and only 30 trillion human cells.
* The human genome consists of about 23000 genes whereas our microbiome encodes over 3 million genes which produce thousands of metabolites
* Microbiota, in total, can weigh up to 2 kg.
* The gut is the main location of human microbiota

A look back through history…

* 1660s-1670s Antonie leeuwenhoek started studying microbes using his newly developed microscope
* 1840s discovery of gut associated microflora with the first observations of faecal bacteria
* 1850-1900 Founding work on host-microbe interactions , Louis Pasteur 1861 germ theory proved that bacteria caused individual diseases. Robert Koch developed the agar plate method to cultivate faecal bacteria and to analyse stools. Koch identified bacteria that Anthrax, TB and cholera
* 1900 – development of antibiotics- 1909 Salvarsan (a drug containing arsenic) was used to treat syphilis.
* 1928: Alexandra Flemming- development of Penicillium
* 1944 first cultured human associated anaerobes

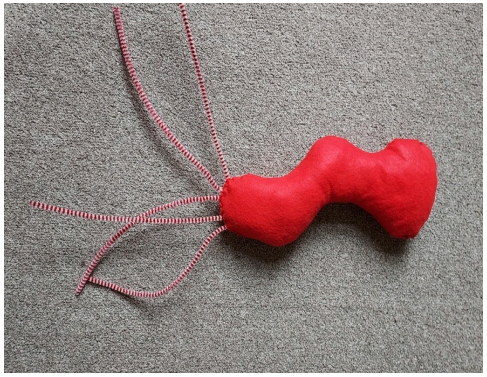
A look back through history



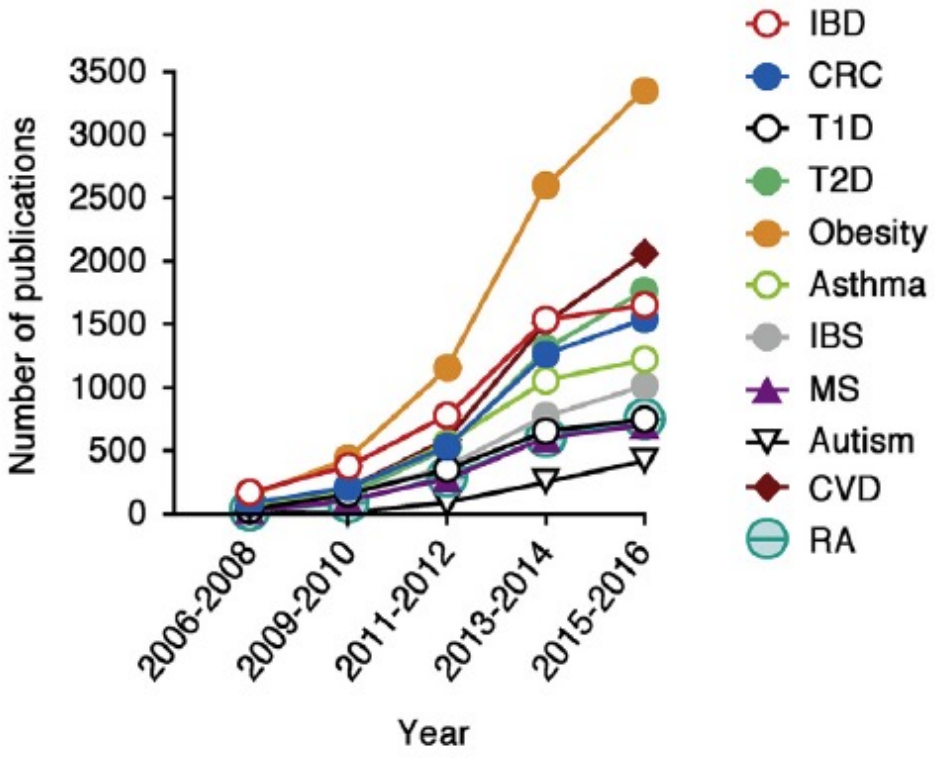
* 1958 study reported successful treatment of a bacterial infection using a faecal enema Faecal microbiota transplantation (FMT) is now widely recognized for helping with recurrent *Clostridium difficile* infections
* In 1965 use of germ-free animals began- mostly rice and rats (never on humans ! Except 1971- Texas boy in a bubble-David Vetter)
* Last 20-25 years Rapid development of next generation sequencing technology allowing culture-independent microbial analysis by reading DNA at high-speed distinguishing different bacteria by looking at 16S rRNA and checking for bacterial diversity using shotgun sequencing.

A look back through history…

* 2010 Dr Nina Salama and her colleagues demonstrated the ability of Helicobacter pylori to colonise the stomach
* American Gut Health project in collaboration with Twin research Kings College London 2018
* Metabolomics- used to detect and identify the small molecules used by the human microbiota and understand the role of these metabolites SCFAs, particularly acetate, butyrate, and propionate, are versatile signalling molecules by which bacteria can exert their effects on GI function also looking at how metabolites produced by the microbiota interact with the immune and enteric nervous systems.



Increasing Interest



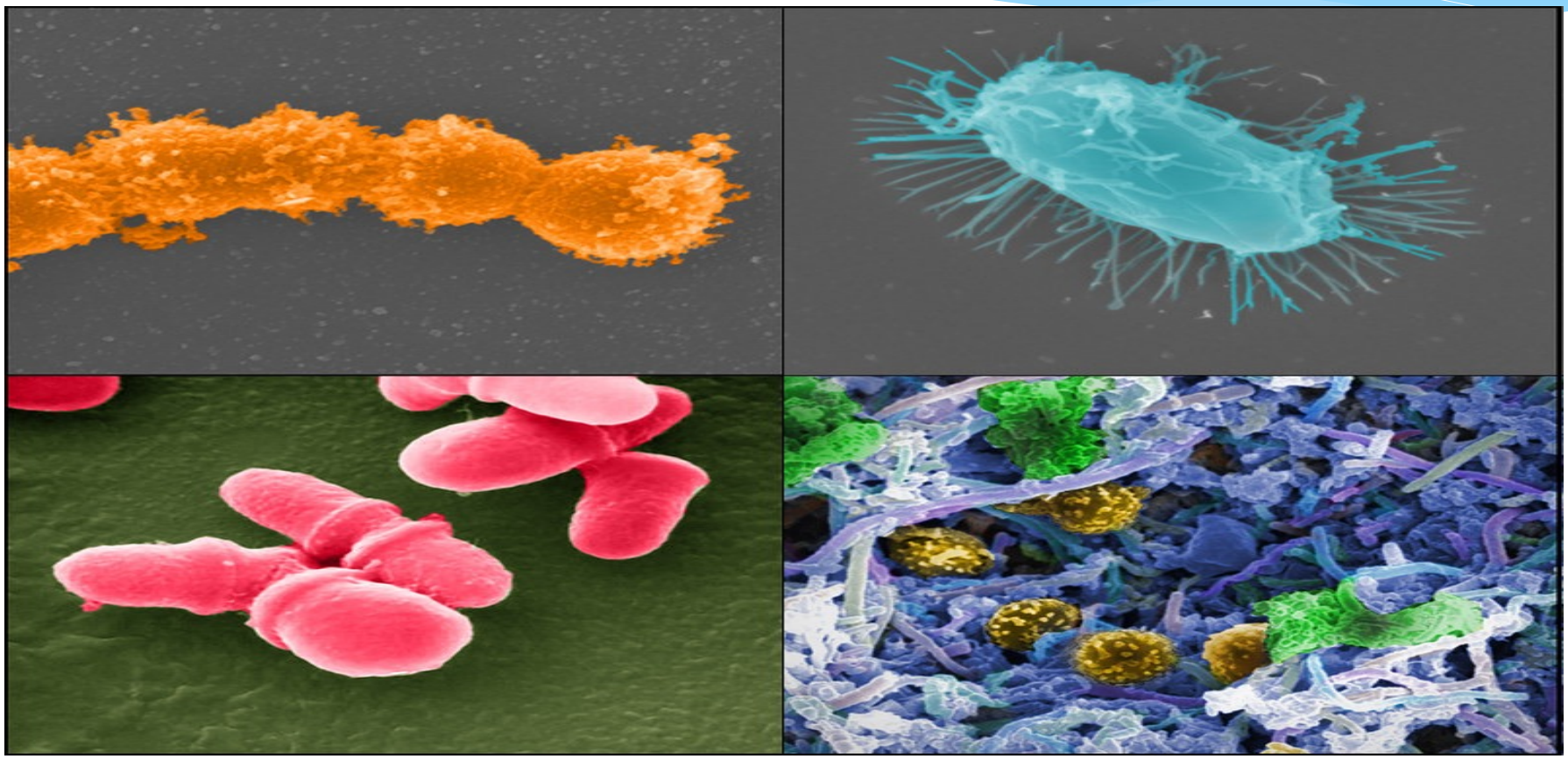
Butto. JACI 2017; 139: 1092.

Gut microbes

* Help the body to digest certain foods that the stomach and small intestine have not been able to digest
* Helps with the production of some vitamins such as Vitamin B and K
* Help us to combat aggressive attacks from other microorganisms by protecting the gut wall/ mucosa
* Helps to educate the immune system and produce substances called cytokines which activate immune cells in the brain to fight pathogens
* Produce neurotransmitters affecting our mood and behaviour
* Play an important role in promoting good digestion

Our Gut microbiome- Who's there?

* Bacteria make up 60% of our gut microflora.
* One third of our gut microbiota is common to most people, while two thirds are specific to each one of us.
* 10 trillion bacteria in the gut composed of at least 500 species. 99% of which come from 40 species divided into 4 big groups:
* Firmicutes, Bacteriodetes, Actinobacter and Proteobacteria.



Firmicutes

* Firmicutes 64% - name derived from the Latin words for thick skin. Rod shaped or round (coccus). predominant bacterial strains (including Lactobacillus) producing butyrate, vital for intestinal wall cell health and fibre digestion. Firmicutes/Bacteroidetes ratio influences overall health, linked with conditions like obesity. There are links between a western diet with high levels of fat and sugar with increased firmicutes
* Examples Faecalibacterium prausnitzi- produces SCFA, lower levels associated with Crohn's, obesity and depression.
* Lactobaccillus- mood enhancing can manipulate the opiod and cannabinoid receptors in the brain (like a shot of morphine)

Our Gut microbiome- Who's there?

* Bacteroidetes: Make up 23% of our gut bacteria
* Include Bacteroides – species of aerobic non spore forming bacteria
* Bacteroides: Found in the intestines, especially species bacteroides fragilis, aids in carbohydrate digestion, maintains energy balance, and regulates gut and systemic immune response, crucial for mucosal layer integrity.
* Other examples Prevatella Copri , commensal if too abundant linked to inflammatory arthritis

Our Gut microbiome- Who's there?

* Proteobacteria (8%)

  Actinobacter 3%
* Includes Bifidobacteria
* Beneficial for fermenting fiber, producing B vitamins, and lactic acid, aiding in maintaining gut balance and supporting immune function.

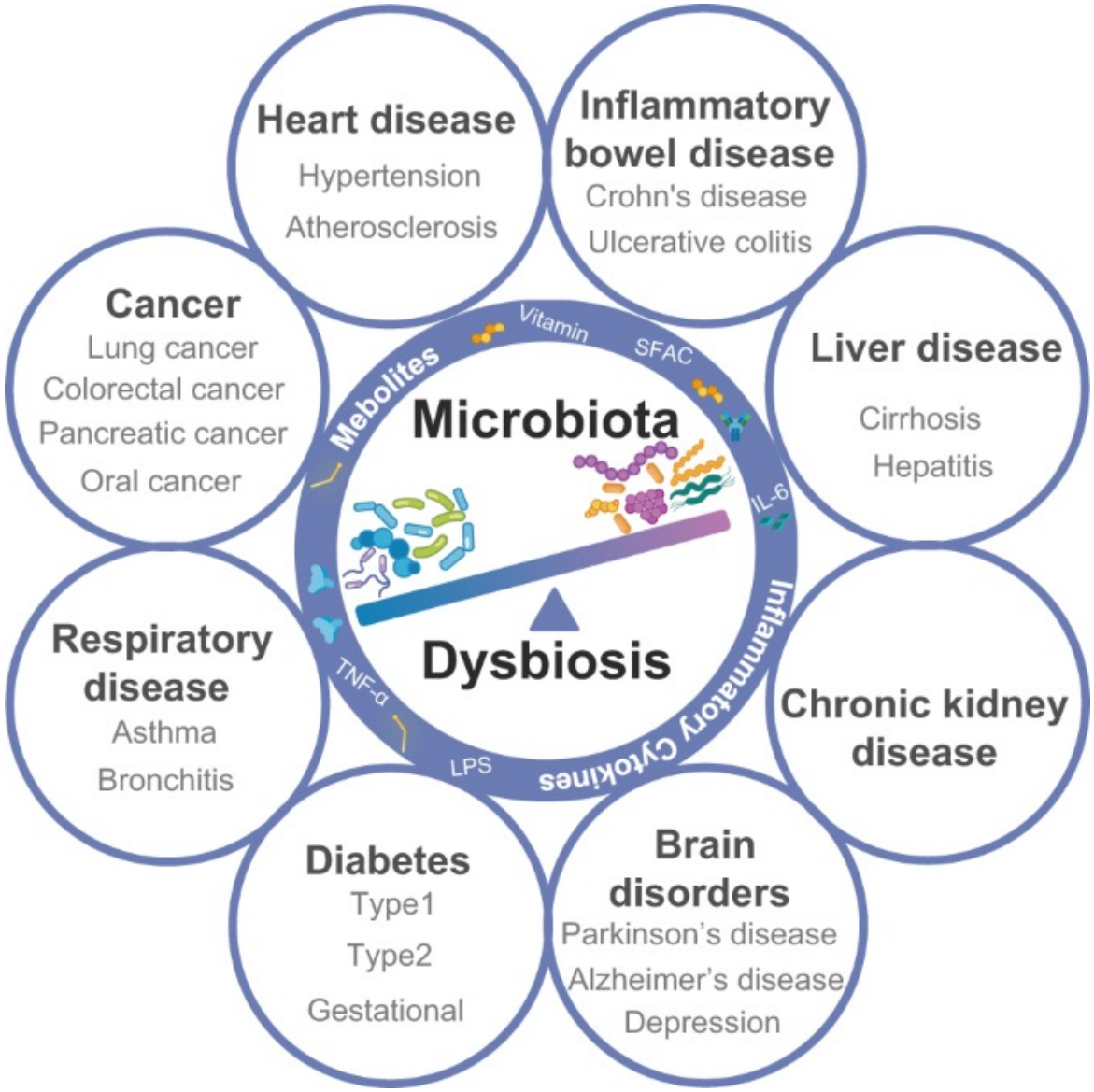
Our Gut microbiome- Who's there?

* Verrucomicrobiacae
* Akkermansia Muciniphilia-
* Thrives in the intestinal mucus layer, breaking down mucin, bolstering intestinal barrier integrity, and modulating insulin resistance, but imbalance may disrupt gut barrier and exacerbate inflammation.

Meet the gut microbes

* Pseudomonadaceae
* Pseudomonas

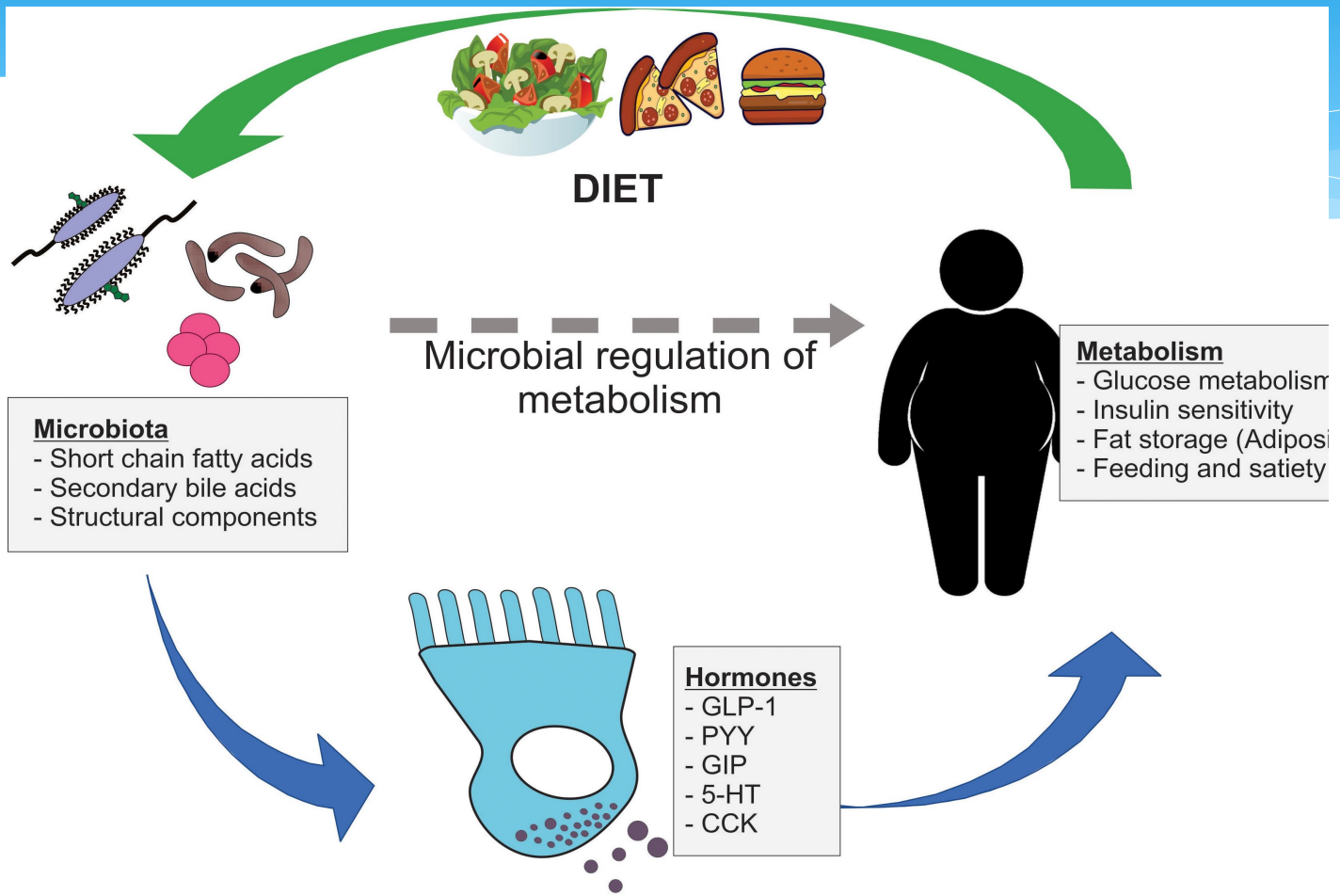
Escherichia coli (E. coli): While some strains cause gut infections, most synthesize essential vitamins like B12 and K and prevent harmful pathogen colonization.


Heart disease
Hypertension
Atherosclerosis
Inflammatory bowel disease
Crohn's disease
Ulcerative colitis
Cancer
Lung cancer
Colorectal cancer
Pancreatic cancer
Oral cancer
Liver disease
Cirrhosis
Hepatitis
Mebolites
Vitamin
SFAC
Microbiota
IL-6
Inflammatory Cytokines
TNF-α
LPS
Dysbiosis
Respiratory disease
Asthma
Bronchitis
Chronic kidney disease
Diabetes
Type1
Type2
Gestational
Brain disorders
Parkinson's disease
Alzheimer's disease
Depression

The gut microbiome and our weight

* Gut dysbiosis may contribute to weight gain by affecting the metabolism of fats and glucose
* Studies on identical twins have demonstrated that the gut microbiome plays a greater role than genetics when it comes to weight gain,
* Dysbiotic gut with a few domineering species of bacteria can mean that these bacteria feed into our cravings for certain types of food. People with more Prevotella compared to Bacteroides lost more weight in one study.
* Some bacteria may stimulate your gut cells to produce GLP-1 and PYY.
* Some parasites also affect weight:
* Presence of the Blastocystis parasite has been associated with healthier blood sugar responses after eating and lower body weight

Adapted from Gary Frost: Obesity and the microbiome



Gut problems

* The bloating, cramps and abdominal pain experienced by people with IBS may be affected by gut dysbiosis this is because microbes produce a lot of gas and other chemicals which contribute to discomfort
* Microbiota different in some patients with IBS lower diversity, lower Bacteroidetes higher firmicutes
* About 10% of IBS patients the symptoms can be traced back to an episode of infectious gastroenteritis
* Certain bifidobacterial and lactobacilli can help symptoms
* Proteobacteria levels were higher in the mucosa of IBS patients compared to healthy controls
* A recent study in healthy subjects and IBS patients found that the fungal species *Saccharomyces cerevisiae* and *Candida albicans*, which dominate the human mycobiome, were increased in IBS patients

Keeping our guts happy

* IBS patients have shown a 2-fold increase in the ratio of Firmicutes to Bacteroidetes
* IBD patients have shown greatly reduced diversity of Firmicutes (producers of anti-inflammatory SCFA)
* Increasing the fibre content of our diet can improve our gut symptoms in the long term but you may need to go low and slow. Inulin great for gut bacteria but fermentability means that if you have IBS it may initially increase pain due to increased gas

Controlling blood glucose

* Research suggests that an imbalanced gut microbiome can trigger inflammation in the body, leading to insulin resistance and impaired glucose metabolism. Certain types of gut bacteria produce compounds called lipopolysaccharides (LPS), which can trigger an inflammatory response in the body. When there is an overgrowth of these LPS-producing bacteria in the gut, it can lead to chronic inflammation and contribute to the development of insulin resistance and diabetes.
* Studies have shown that people with Type 2 diabetes have lower levels of butyrate producing bacteria . Unclear whether differences in the microbiome causes diabetes or whether the presence of diabetes causes differences in the microbiome. Coprococcal bacteria helped insulin sensitivity,Proteobacteria associated with insulin resistance.
* By adopting strategies such as consuming a fibre rich diet, incorporating probiotics and prebiotics can potentially modulate our gut microbiome and improve glucose regulation. A diverse microbiota can improve response to medications such as metformin

Managing our cholesterol

* Gut microbiome may help to promote good HDL cholesterol and reduce triglycerides
* One study on mice showed that if you transfer bacteria from a human with high cholesterol to a mouse, the mouse develops high cholesterol.
* Some species of gut bacteria can convert cholesterol to coprostanol which cannot be absorbed into the blood so is eliminated from the body example: Eubacterium coprostanoligenes
* Scientists have shown that some strains of bacteria add cholesterol to their membranes
* Certain unhealthy species in the gut microbiome may contribute to heart disease by producing trimethylamine N oxide (TMAO) TMAO is a chemical which contributes to heart attacks and strokes

Keeping us happy

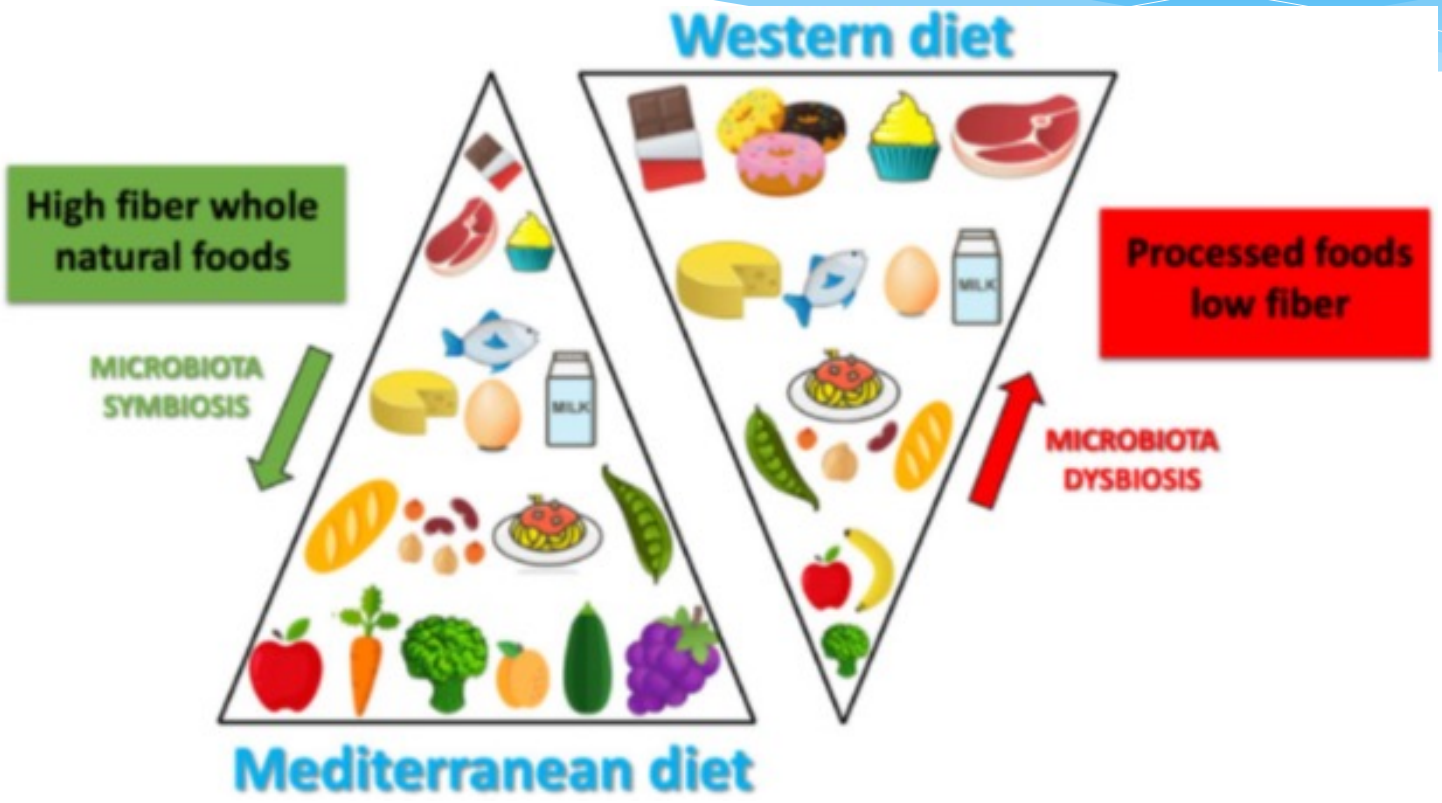
* Certain species of bacteria produce chemicals in the brain called neurotransmitters, e.g. serotonin is an antidepressant neurotransmitter that's mostly made in the gut
* The gut microbiome may affect brain health by controlling the messages that are sent to the brain through nerves
* Studies have shown that people with certain mental health conditions have different species of bacteria in their gut compared to healthy peopleCertain species of bacteria produce chemicals in the brain called neurotransmitters, e.g. serotonin is an antidepressant neurotransmitter that's mostly made in the gut
* Studies have transferred faecal matter from human patients with major depression to rats and noted that unlike the controls they became depressed too.

Factors affecting our microbiome

* Feeding methods (breast milk, formula milk and the introduction of solid food
* Genetics
* Gestational age and our delivery mode
* Aging
* Medication (antibiotics, acid suppressants , anti-diabetic drugs)
* Dietary habits and the way food is cooked
* Environment and lifestyle rural vs urban, exercise
* Weight gain

How to improve your gut microbiome

* Evidence that at any age you can improve your microbiota by adopting a Mediterranean –type diet and eating more fibre rich foods with less refined carbohydrates.
- More fruit and vegetables, wholegrain breads and cereals, nuts, pulses (peas, beans and lentils) and seeds. Less saturated fat from dairy and red meat sources. Less alcohol. More seafood especially oily fish.
* Why is a Mediterranean diet good for you?
- Healthier fats – from olive oils, nuts, oily fish – good for heart
- High in antioxidants – help with chronic low grade inflammation
- High in fibre – good for gut health and excretion of fat
- It's rich in B vitamins including folic acid.


Western diet
High fiber whole natural foods
Processed foods low fiber
MICROBIOTA SYMBIOSIS
MICROBIOTA DYSBIOSIS
MILK
MILK
Mediterranean diet

How to improve your gut microbiome

* Try eating a more plant-based diet, potentially aim for 30 plants a week, a more plant based diet helps to reduce levels of disease-causing bacteria such as E-coli as well as inflammation and cholesterol
* Eat a diverse range of foods: In particular legumes, beans and fruit with lots of fibre (promotes bifidobacteria)
* Eat prebiotic foods : prebiotics are a type of fibre that stimulates the growth of healthy bacteria prebiotic rich foods include artichokes bananas asparagus oats and apples
* Eat whole grains – wholegrain have lots of fibre and beneficial carbs like beta glucan which are digested by gut bacteria to benefit weight and risk of diabetes
* Eat foods high in polyphenols : these are plant compounds found in red wine green tea dark chocolate, olive oil and wholegrains they are broken down by the microbiome to stimulate healthy bacterial growth.

? Try a probiotic

- A probiotic supplement probiotics are live bacteria that can help to restore the gut to a healthy state after dysbiosis. They do this by reseeding it with healthy microbes. A probiotic is a ‘live organism which when administered in adequate amounts confers a health benefit to the host’.
- Shown to increase stool transit time in people who have constipation. Bifidobacterium lactis has had greatest effect.
- Different species/ strains have different effects. Probiotics need to be specific to a health condition
- Mushrooms, yeast, olives, fermented cabbage (sauerkraut, kimchi), vinegars, wines, fermented dairy (cheeses, kefir, buttermilk, sour cream, yogurt, cucumber pickles.

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Research Article

Evaluation of Commercial Probiotic Products

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* "Only **three out of the seven** products (43%) contained the claimed culture concentration or more."
* **None** of the multispecies products contained all the labeled probiotic bacteria.
* **Misidentification** of some species occurred.

Fredua-Agyeman M. , Parab S. & Gaisford S. (2016) "Evaluation of Commercial Probiotic Products", *British Journal of Pharmacy*. 1(1). doi: https://doi.org/10.5920/bjpharm.2016.11

How to improve your gut microbiome

* ? Try fermented food such as yoghurt , sauerkraut and kefir which contain gut healthy bacteria such as lactobacilli.
* Limit your intake of artificial sweeteners some evidence that artificial sweeteners like aspartame increase blood glucose buy stimulating the growth of unhealthy bacteria such as Enterobacteria
* Have less ultraprocessed foods e.g. those containing emulsifiers.
* Take antibiotics only when necessary: antibiotics kill many bad and good bacteria in the gut microbiome possibly contributing to weight gain and antibiotic resistance

Stress and a healthy lifestyle

* Stress has been shown to influence the integrity of the gut epithelium and to alter peristalsis, secretions, and mucin production
* Community living encourages bacterial diversity and an increased lifespan
* Having a household pet has been shown to increase levels of friendly Akkermansia.

Activity and sleep

* Activity could improve the Bacteroidetes-firmicutes ratio linked to obesity and gastrointestinal disorders.
* Useful resources: NHS Fitness studio: Fitness Studio exercise videos - NHS (www.nhs.uk)
- www.weareundefeatable.co.uk
* A diverse microbiome has been associated with improved sleeping patterns
- Sleep and Tiredness (NHS Live Well)
- How to Sleep Better (HelpGuide.org)