NUTRITION, DIABETES & THE MICROBIOME

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Webinar key messages summarised for you.

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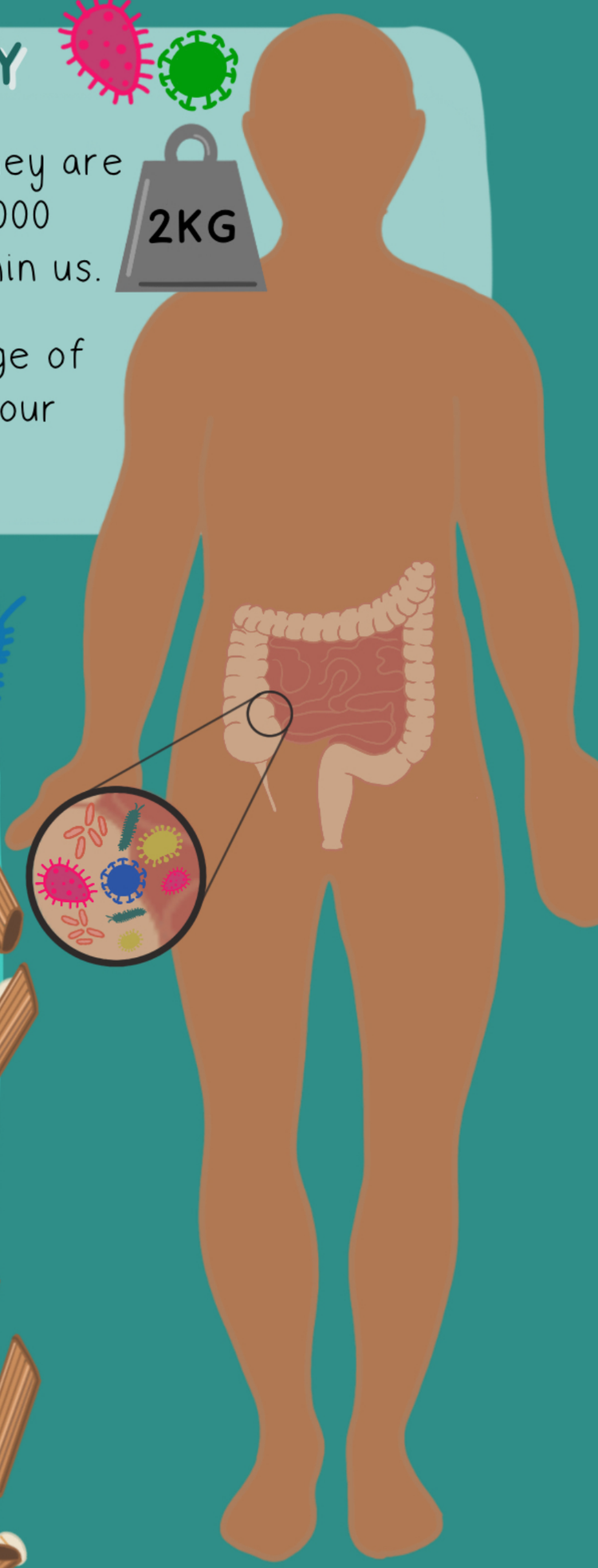
MICROBIOTA IN HEALTH & DISEASE

BACTERIA IN THE HUMAN BODY

In our bodies, we have 10^{14} microbial cells (that's about 2kg!) and they are found mostly in the gut. In an average person there will be ~1,000 different types of bacteria and 1,200 different viruses living within us.

Our unique mix of gut microbiota is largely set from around the age of 3 years but there is still an opportunity for this to shift through our behaviours and with disease, such as type 2 diabetes.



THE MICROBIOTA AND NUTRITION

Potentially the biggest role that our gut bacteria plays in our bodies is as a salvage mechanism during digestion.

When we consume non-digestible dietary components, bacterial fermentation enables us to utilise some of the energy and metabolites for our benefit. It's estimated that this process contributes to around 5% of our energy needs!

OTHER IMPORTANT ROLES OF OUR GUT BACTERIA ARE:

- Maintaining intestinal integrity, which helps to protect our body from harmful toxins.
- Bacterial synthesis of vitamins, such as K (& B12 in animals).
- Normal part of enterohepatic circulation of bile acids, which is important for fat metabolism.

WHAT ROLE DOES OUR GUT BACTERIA PLAY IN DIABETES?

DIET & THE GUT

Diet is fundamental to the gut microbiota, but often ignored in research on diabetes and the gut.

What we eat can have direct implications on metabolism and health. Food can also impact the composition and activity of the microbiota–which may also indirectly impact our health, such as diabetes risk.

We need to look at how diet quality and quantity impacts the composition of the microbiota, and how this affects functionality because that is what is important.

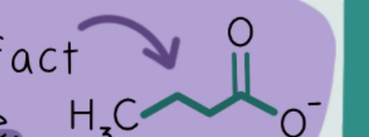
A RECENT REVIEW LOOKING AT 42 STUDIES, PRIMARILY IN T2DM, FOUND:

High levels of *Bifidobacterium* (seen as a probiotic species) was associated with a reduced incidence of diabetes.

High levels of *Lactobacillus* (also seen as a probiotic species) was associated with higher incidences of diabetes in some cases, although it was more unpredictable.

Species traditionally not seen as beneficial, such as *Roseburia* and *Faecalibacterium* were also consistently found to be associated with lower incidences of diabetes.

This may be due to the fact they produce Butyrate.



We also see differences on the microbiota in those who are on treatment for their diabetes e.g., Metformin and those who are not.

THERE ARE TWO IMPORTANT FACTORS TO CONSIDER:

SHORT CHAIN FATTY ACIDS: metabolites produced within us by the gut bacteria.

LIPOPOLYSACCHARIDES: components of the outer membrane of some bacteria, which potentially influences metabolism.

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BACTERIAL METABOLITES - SHORT CHAIN FATTY ACIDS

PRODUCTION OF METABOLITES

Bacteria in the gut utilise non-digestible dietary components as a food source, which produces metabolites.

As our food moves through the gut, bacteria will prioritise carbohydrates before eventually utilising energy from dietary proteins.

Transit time in the large intestine can be anything between 5–72 hours. The longer the digestion time the more likely it is that carbohydrates will be completely depleted and bacteria need to use protein.

CARBOHYDRATE METABOLITES OFFER MORE BENEFITS

Fermentation of carbohydrates, including dietary fibre, produces short chain fatty acids (SCFA) such as acetate, butyrate and propionate, which are thought to be beneficial.

Fermentation of protein produces less beneficial substrates such as branch chain fatty acids, ammonia, phenol and p-cresol.

HOW ARE SCFA BENEFICIAL FOR METABOLIC HEALTH?

Increased SCFA in the blood

=

More insulin sensitive adipocytes (fat cells)

=

Increased glucose uptake into fat

=

Reduced fatty acids released from fat tissue

=

Fat is stored in adipose tissue, which reduces fat stores the liver, kidneys and muscle.

- Increased glucose clearance
- Increased insulin sensitivity
- Decreased diabetes risk

BACTERIAL FRAGMENTS - LIPOPOLYSACCHARIDES

DOES DIABETES ACTUALLY BEGIN IN THE GUT WITH BACTERIAL FRAGMENTS?

Animal model showing how bacterial fragments such as lipopolysaccharides (LPS) may increase diabetes risk.

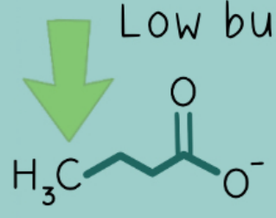
NUTRITIONAL & GENETIC OBESITY

High fat, high sugar diets

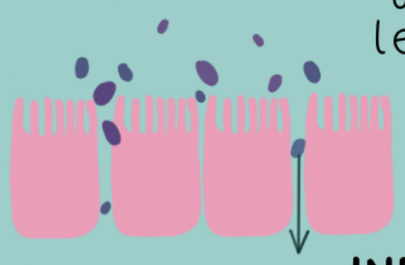
CHANGES IN GUT MICROBIOTA

Reduction of carbohydrate fermentation and an increase in gram-negative bacteria

Low butyrate concentration and increase of the intestinal burden of LPS



Disruption to the gut barrier, increasing the permeability of the gut wall and leading to LPS leaking into the periphery



INFLAMMATORY RESPONSE

Linked to insulin resistance and diabetes

LPS LEVELS IN HUMAN DIABETES

Since this model was developed, human studies have consistently found that people with diabetes do have elevated LPS levels.

People with **T2DM** have

66%

LPS in the blood

People with **T1DM** have

236%

LPS in the blood compared to healthy controls.

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WHAT ROLE CAN DIET PLAY?

PLANT VS ANIMAL-BASED DIETS

Research suggests that diet can rapidly change our microbiota composition and SCFA levels. One study examined the differences between a 100% plant-based diet vs 100% animal-based diet.

PLANT-BASED DIET	ANIMAL-BASED DIET
Increased fibre	No fibre
Lower fat	Higher fat
Lower in protein	Higher in protein

The differences in the macronutrient composition of each diet resulted in interesting findings after just 2 days:

- Compared to the control, the animal-based diet resulted in a significant reduction in the diversity of gut bacteria.
- In the animal-based diet there was a drop in SCFA and a significant increase in BCFA, which is the result of protein fermentation.

THE INTERPLAY BETWEEN CARBOHYDRATE, FAT AND PROTEIN

Butyrate is a key metabolite for maintaining the integrity of the gut.

Increased protein can actively deregulate butyrate production.

High fat, high sugar diet can change the gut bacteria and also impact on the LPS burden aka how much gram-negative bacteria you have and the permeability of the gut wall.

Carbohydrates or prebiotics can have a positive effect by:

1. Up-regulating butyrate.
2. Reducing the amount of gram-negative bacteria, therefore reduce the LPS burden within the gut.

There is still no dietary recommendations for prebiotics but research suggests that in order to get a reasonable effect on glycaemia in T2DM intakes of 10g/day for 6-8 weeks are necessary.

WHAT ABOUT FIBRE?

Research from meta-analysis shows that increasing fibre to the recommended 30g/day can reduce the risk of developing diabetes and most importantly reduce all-cause mortality in diabetes.