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MEDICINE,
NURSING &
HEALTH SCIENCES

Manipulating the composition of the gut microbiota in diabetes: what is the evidence?

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GROUP OF EIGHT AUSTRALIA

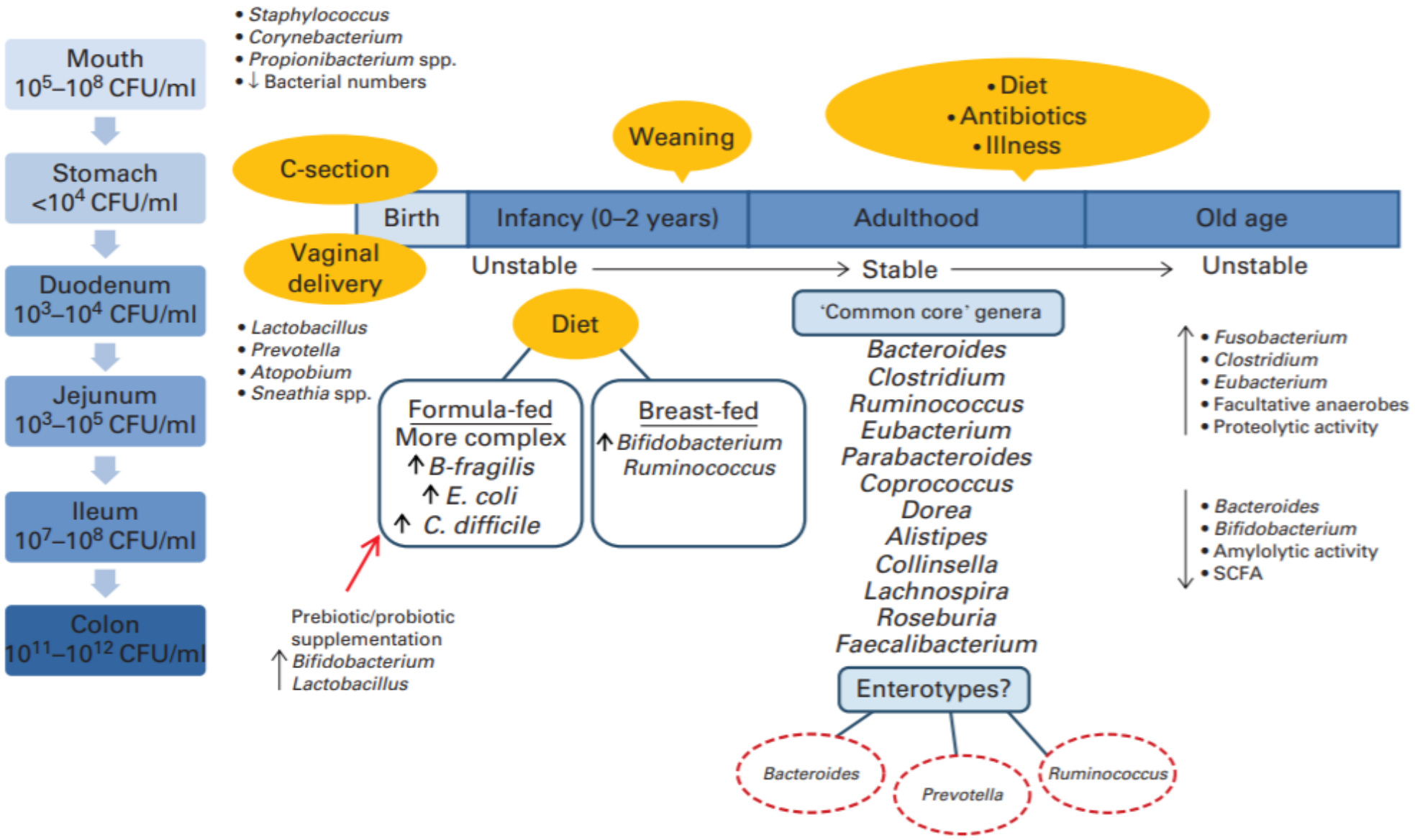
What we will cover:

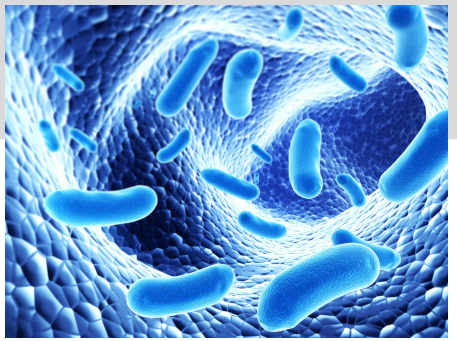
- Gut microbial changes across the lifespan

- Can we beneficially alter the gut microbiota to prevent or improve diabetes management?

- Probiotics
- Prebiotics
- Faecal microbial transplant
- Metformin, artificial sweeteners
- Practical dietary advice for gut health

Gut microbiota across the lifespan





Live micro-organisms that, when administered in adequate amounts, provide a health benefit to the host

Box 1 | Consensus panel recommendations for the scope of probiotics

- Retain the FAO/WHO definition[1] for probiotics, with a minor grammatical correction as "live microorganisms that, when administered in adequate amounts, confer a health benefit on the host"; inconsistences between the Expert Consultation[1] and the FAO/WHO Guidelines[2] were clarified
- Include in the framework for definition of probiotics microbial species that have been shown in properly controlled studies to confer benefits to health
- Any specific claim beyond "contains probiotics" must be further substantiated
- Keep live cultures, traditionally associated with fermented foods and for which there is no evidence of a health benefit, outside the probiotic framework
- Keep undefined, faecal microbiota transplants outside the probiotic framework
- New commensals and consortia comprising defined strains from human samples, with adequate evidence of safety and efficacy, are 'probiotics'

Abbreviation: FAO, Food and Agriculture Organization of the United Nations.

Hill, C. *et al. Nat. Rev. Gastroenterol. Hepatol.* 11, 506–514 (2014)

Probiotics

- 0.1 – 5% will survive the passage through the gastrointestinal tract
- No impact on microbial diversity in the gut, in healthy adults
- 4 weeks after you stop taking them, they are gone
- Biological effects of probiotics are strain specific
- Until a bacterial species (or strain) has been isolated, characterised and a credible case presented for its health effects, it cannot be called a ‘probiotic’.

Kristensen *et al. Genome Med* 2016; 14:82

Probiotic supplements

Fermented foods – not technically probiotics

Yoghurt

Sauerkraut

Kombucha

Kimchi

Benefits of Probiotics

Immunological benefits:

- Activates local macrophages to increase cytokine production (stimulate macrophages to produce cytokines).
- Stimulate antibody production by the host.
- Induce response to food antigens.

Non-immunological benefits:

- Metabolism of dietary fibres, resulting in the bacterial production of fermentation by-products such as SCFAs (acetate, butyrate, propionate).
- Compete for nutrients with pathogens.
- Reduce the local pH to create an unfavourable environment for pathogens.
- Produce bacteriocins to inhibit pathogens (toxins which destroy opportunistic bacteria).
- Scavenge superoxide radicals (some bacteria bind to toxins and the host excretes them instead of absorbing them).
- Stimulate mucin production (a gel that protects the lining of the gut).
- Enhance intestinal barrier function and intestinal cell repair.

Evidence of effectiveness: probiotics

- Convincing evidence for use in:
  - Acute viral diarrhoeal disease
  - Antibiotic associated diarrhea
- Developing evidence for a role in:
  - Necrotising enterocolitis (only in infants with birth weight <1500g, but not widely used due to safety concerns)
  - *Helicobacter pylori* infection (used prior to and during standard eradication therapy to improve rate of eradication and reduce side effects)
  - Prevention of Clostridium difficile-associated diarrhea in adults and children (Goldenberg, *Cochrane Database Sys Rev* 2017)
  - Inflammatory bowel disease (No effect on Crohn's Disease, but VSL#3 may help induce remission in Ulcerative Colitis) (Ghouri, *Clin Exp Gastro* 2014)

Probiotics in obesity and diabetes: the evidence

Latest systematic review exploring the effect of probiotics on obesity and diabetes-related outcomes summarised 105 RCTs involving 6826 participants:

- In overweight individuals, probiotics resulted in a weight loss of 0.94 kg (1.2%), which is below the clinically meaningful weight loss threshold of 2-5%.
- In obese individuals, probiotics had no significant effect on body weight.
- In people with T2DM, probiotics significantly reduced fasting blood glucose, fasting insulin, HbA1c and insulin resistance (HOMA-IR)

HOWEVER…

- These results were heavily influenced by the 38% of trials that were conducted in Iran and published within the last 6 years. Exclusion of the Iranian trials from the analysis rendered the effect of probiotics on T2DM non-significant.
- Authors of this review recommend that the positive effects of probiotics on people with T2DM cannot be generalised to those living outside of Iran.

Koutnikova H, *et al*. *BMJ Open* 2019;9:e017995.

Probiotics for the prevention or management of GDM in pregnant women: the evidence

- Some RCTs (n=6) have shown reductions in insulin resistance (HOMA-IR) or fasting insulin concentrations in pregnant women and women with GDM consuming probiotic supplements (5 of these 6 trials were conducted in Iran).

- However, trials investigating fasting BGL following probiotic supplementation during pregnancy are contradictory (out of 11 trials in total: 6 trials found no reduction in FBG, 5 trials - including 3 conducted in Iran found significant reductions in FBG).

- While an improvement in insulin sensitivity may result in reduced insulin requirements in women with GDM, this has not yet been explored - all of the trials conducted so far have excluded women requiring treatment with insulin or metformin.

- All studies have provided women with a probiotic cocktail containing a variety of different bacterial species, making it impossible to identify the specific bacterial species or strain associated with insulin-sensitising effects.

Han et al. *Ann Transl Med* 2019;7(5):99; Taylor et al. *Nutrients* 2017; 9(5).

Probiotics for the prevention of GDM in pregnant women with overweight/obesity: Australian context

Diabetes Care. 2019 Mar;42(3):364-371. doi: 10.2337/dc18-2248. Epub 2019 Jan 18.

Probiotics for the Prevention of Gestational Diabetes Mellitus in Overweight and Obese Women: Findings From the SPRING Double-Blind Randomized Controlled Trial.

Callaway LK[1,2], McIntyre HD[2,3], Barrett HL[2,3], Foxcroft K[4], Tremellen A[3], Lingwood BE[2], Tobin JM[5], Wilkinson S[3,6], Kothari A[7], Morrison M[8], O'Rourke P[9], Pelecanos A[9], Dekker Nitert M[10].

Author information

Abstract

OBJECTIVE: Given the role of gut microbiota in regulating metabolism, probiotics administered during pregnancy might prevent gestational diabetes mellitus (GDM). This question has not previously been studied in high-risk overweight and obese pregnant women. We aimed to determine whether probiotics (*Lactobacillus rhamnosus* and *Bifidobacterium animalis* subspecies *lactis*) administered from the second trimester in overweight and obese women prevent GDM as assessed by an oral glucose tolerance test (OGTT) at 28 weeks' gestation. Secondary outcomes included maternal and neonatal complications, maternal blood pressure and BMI, and infant body composition.

RESEARCH DESIGN AND METHODS: This was a double-blind randomized controlled trial of probiotic versus placebo in overweight and obese pregnant women in Brisbane, Australia.

RESULTS: The study was completed in 411 women. GDM occurred in 12.3% (25 of 204) in the placebo arm and 18.4% (38 of 207) in the probiotics arm ($P = 0.10$). At OGTT, mean fasting glucose was higher in women randomized to probiotics (79.3 mg/dL) compared with placebo (77.5 mg/dL) ($P = 0.049$). One- and two-hour glucose measures were similar. Preeclampsia occurred in 9.2% of women randomized to probiotics compared with 4.9% in the placebo arm ($P = 0.09$). Excessive weight gain occurred in 32.5% of women in the probiotics arm (55 of 169) compared with 46% in the placebo arm (81 of 176) ($P = 0.01$). Rates of small for gestational age (<10th percentile) were 2.4% in the probiotics arm (5 of 205) and 6.5% in the placebo arm (13 of 199) ($P = 0.042$). There were no differences in other secondary outcomes.

CONCLUSIONS: The probiotics used in this study did not prevent GDM in overweight and obese pregnant women.

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Prebiotics: definition

A substrate that is selectively utilised by host micro-organisms, providing a health benefit to the host

Box 1 | Main conclusions of the consensus panel regarding prebiotics

- The definition of a prebiotic has been modified to 'a substrate that is selectively utilized by host microorganisms conferring a health benefit'
- Although most current prebiotics are administered orally, they can also be administered directly to other microbially colonized body sites, such as the vaginal tract and skin
- Health effects of prebiotics are evolving but currently include benefits to the gastrointestinal tract (for example, inhibition of pathogens, immune stimulation), cardiometabolism (for example, reduction in blood lipid levels, effects upon insulin resistance), mental health (for example, metabolites that influence brain function, energy and cognition) and bone (for example, mineral bioavailability), among others
- We acknowledge that definitive proof of causality is difficult to provide. However, a human or animal study showing a change in heath markers or symptoms after a specific influence on the microbial population (that is, a blinded placebo-controlled trial with appropriate exclusion and/or inclusion criteria) then it is reasonable to assume that the two are causally related
- Currently established prebiotics are carbohydrate-based, but other substances such as polyphenols and polyunsaturated fatty acids converted to respective conjugated fatty acids might fit the updated definition assuming convincing weight of evidence in the target host
- The beneficial effect(s) of a prebiotic on health must be confirmed in the target animal for its intended use and mediated through the microbiota

Gibson et al. The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of prebiotics. NATURE REVIEWS **GASTROENTEROLOGY & HEPATOLOGY Vol 14, 2017**

Criteria for Prebiotics:

- Must not be hydrolysed or absorbed in the upper gastrointestinal tract
- Must be a substrate for growth or activity of one or a limited number of beneficial colonic bacteria
- Must therefore be able to alter the colonic microbiome towards a healthier composition and
- Must be able to induce luminal or systemic effects which are beneficial to the host.

Gibson GR & Roberfroid MB (1995) Dietary modulation of the human colonic microbiota: introducing the concept of prebiotics. J Nutr 125, 1401–1412.

Prebiotics

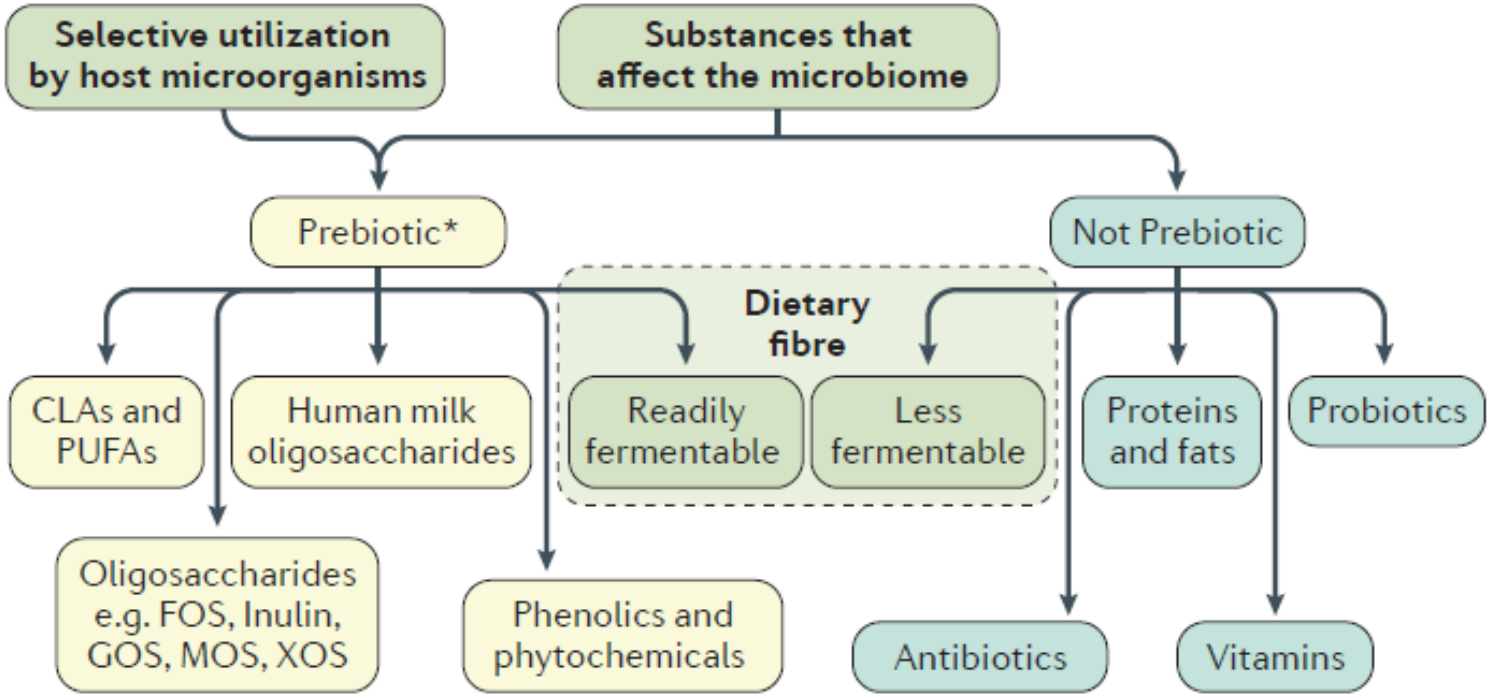


Figure 1 | **Distinguishing what is considered a prebiotic with the proposed definition.** Prebiotics must be selectively utilized and have adequate evidence of health benefit for the target host. Dietary prebiotics must not be degraded by the target host enzymes. *The figure shows candidate as well as accepted prebiotics in that levels of evidence currently vary, with FOS and GOS being the most researched prebiotics.CLA, conjugated linoleic acid; PUFA, polyunsaturated fatty acid; FOS, fructooligosaccharides; GOS, galactooligosaccharides; MOS, mannanoligosaccharide; XOS, xylooligosaccharide.

Gibson et al. The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of prebiotics. Nat. Revs. **GASTROENTEROLOGY & HEPATOLOGY Vol 14, 2017**

Food sources of prebiotics

- Beta-glucan
  - barley, oats
- Fructo-oligosaccharides (FOS) and inulin
  - onions, Jerusalem artichoke, asparagus, bananas, leek, chicory

- Galacto-oligosaccharides (GOS)
  - legumes
- Arabinoxylans
  - cereal grains, psyllium husk, pangola grass, bamboo shoots, corn hulls
- Xylo-oligosaccharides (XOS)
  - fruit, vegetables, milk, honey

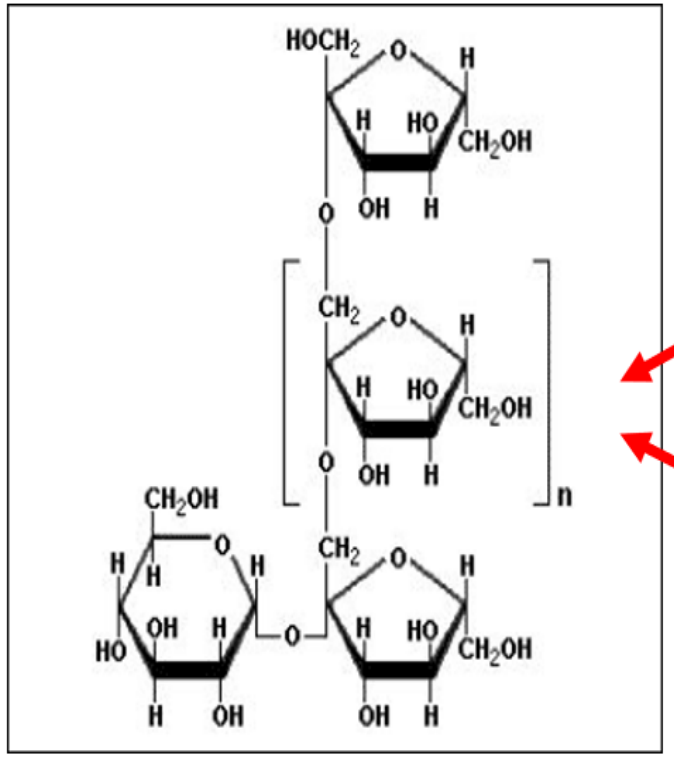
Food sources of prebiotics

Chicory root

Food	Prebiotic Fiber Content by Weight
Raw chicory root	64%
Raw Jerusalem Artichoke	31%
Raw Dandelion Greens	24%
Raw Garlic	17%
Raw Leek	11%
Raw Onion	8%
Cooked Onion	5%
Raw Asparagus	5%
Raw Wheat Bran	5%
Whole Wheat Flour, cooked	5%
Raw Banana	1%

Jerusalem artichoke

Inulin-type fructans: structure



Inulin
(n > 10 fructose units)

Fructo-oligosaccharides (FOS)/Oligofructose

(n < 10 fructose units)

Chicory root powder

“Synergy 1”:
Inulin-enriched FOS

Benefits of prebiotics

Butyrate is the primary fuel for colonocytes

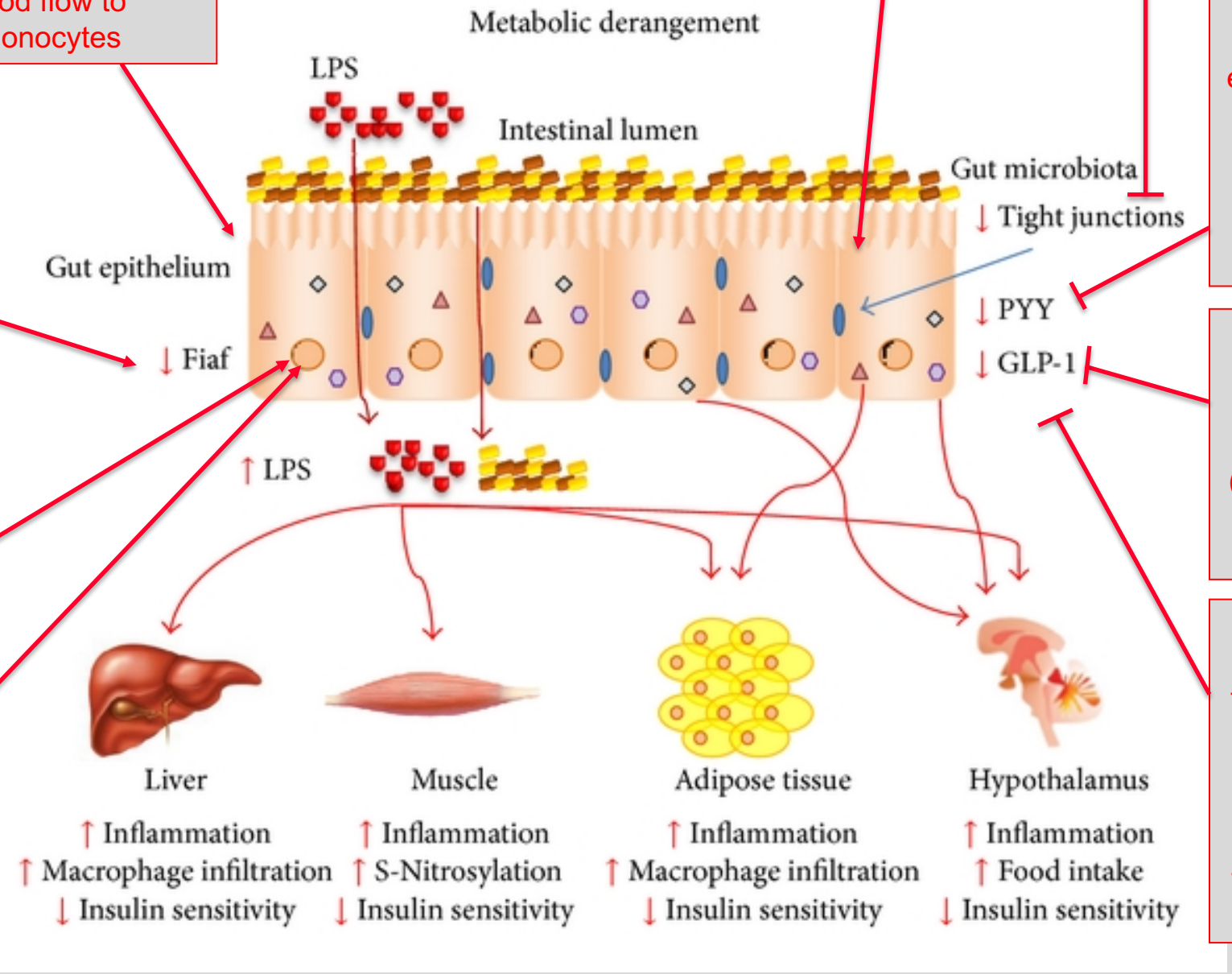
Butyrate promotes transcription of tight junction proteins (eg. occludin)

Acetate increases blood flow to colonocytes

The intestinal microbiota suppresses the expression of fasting-induced adipose factor (Fiaf), an intestinal epithelial cell-derived circulating inhibitor of lipoprotein lipase (LPL). Increased LPL activity results in reduced fat storage

Butyrate upregulates the expression of mucin-associated genes

Butyrate reduces inflammation in colonic epithelial cells by increasing PPARγ gene expression



SCFA binding to GPR41 increases the intestinal expression of Peptide YY, a hormone that slows intestinal transit time and inhibits production of the appetite-stimulating hormone, grehlin

SCFA binding to GPR43 increases the production of incretin hormone glucagon-like peptide 1 (GLP-1), which increases insulin sensitivity and reduces appetite

Gut microbiota are also involved in the transformation of primary bile acids into secondary bile acids, which are capable of binding to the GPR19. GPR19 induces the intestinal secretion of GLP-1

Adapted from Tilg et al, *BMJ* 2015

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Prebiotics in diabetes: the evidence

Systematic review of 27 RCTs exploring the effect of dietary prebiotic (and substances with prebiotic properties) consumption on blood glucose management in adults with type 2 diabetes:

- Country of study origin (Iran: 10, Canada: 3, Taiwan: 3, UK: 3, France: 2, the Netherlands: 1, Mexico: 1, Brazil: 1, Greece: 1, Australia: 1, India: 1). Length of intervention: 4 days – 12 weeks.
- Prebiotics (or products with prebiotic properties) investigated: Resistant Starch: 7, beta-glucan: 2, GOS: 1, XOS: 1, FOS-enriched inulin: 4, FOS: 2, inulin: 3, MOS (konjac glucomannan): 2, guar gum: 2, arabinoxylan: 1, flax seed gum: 1, inulin + butyrate: 1.
- "During the analysis phase, it became evident that several of the publications presented information from the same participant population but reported outcomes separately. Seven publications appear to have used the same sample population registered under the clinical trial number IRCT201110293253N4. Two additional publications also appeared to use the same sample population registered under IRCT201203103565N4".
- Reported effects on HbA1c, FBG, HOMA-IR, lipid levels and body weight were contradictory.
- No significant changes in any outcomes: 7 trials; reduction in HbA1c: 8 trials; reduction in FBG: 10 trials, reduction in HOMA-IR: 3 trials; reduction in Diastolic BP: 4 trials; reduction in LDL-cholesterol: 8 trials; reduction in body weight: 6 trials.

Colantonio *et al. J Acad Nutr Diet* 2019, in press

Polyphenols

Table 7 Effects of polyphenols on gut microbiota

	Bifidobacteria	*Lactobacilli*	*Bacteroides*	*Clostridia*	*Salmonella typhimurium*	*Staphylococcus aureus*
Polyphenols	↑	↑	↓	↓	↓	↓

Singh *et al. J Transl Med* 2017;15:73

- Dietary polyphenols (which include catechins, flavonols, flavones, anthocyanins, proanthocyanidins and phenolic acids) are actively studied for their antioxidant properties.
- Common foods rich in polyphenol content include fruits, seeds, vegetables, tea, cocoa products, and wine.

- Consumption of cocoa-derived polyphenols has been associated with significant increases in plasma HDL and significant reductions in plasma triacylglycerol and C-reactive protein concentrations.

Tzounis *et al. Am J Clin Nutr* 2011;93:62–72.

Resistant Starch: potential prebiotic

Resistant Starch (RS) is starch that escapes digestion in the human small intestine, but undergoes bacterial fermentation in the large intestine.

Categories of Resistant Starch:

RS Type	Description	Examples
RS1	Physically inaccessible	Coarsely milled grains/seeds, legumes
RS2	Ungelatinised starch	Raw potato, unripe banana High-amylose maize starch
RS3	Retrograded starch	Cooked, cooled foods (potatoes, pasta, rice), Corn Flakes
RS4	Chemically modified starch	Cross-linked starch and octenyl succinate starch
RS5	Amylose-lipid complex	Stearic acid-complexed high-amylose starch

Resistant starch

nutrients

MDPI

Review

Metabolic Effects of Resistant Starch Type 2: A Systematic Literature Review and Meta-Analysis of Randomized Controlled Trials

Matthew Snelson [1], Jessica Jong [2], Deanna Manolas [2], Smonda Kok [2], Audrey Louise [2], Romi Stern [2] and Nicole J. Kellow [2,*]

Resistant starch

Received: 17 June 2019; Accepted: 5 August 2019; Published: 8 August 2019

Abstract: Published evidence exploring the effects of dietary resistant starch (RS) on human cardiometabolic health is inconsistent. This review aimed to investigate the effect of dietary RS type 2 (RS2) supplementation on body weight, satiety ratings, fasting plasma glucose, glycated hemoglobin (HbA1c), insulin resistance and lipid levels in healthy individuals and those with overweight/obesity, the metabolic syndrome (MetS), prediabetes or type 2 diabetes mellitus (T2DM). Five electronic databases were searched for randomized controlled trials (RCTs) published in English between 1982 and 2018, with trials eligible for inclusion if they reported RCTs involving humans where at least one group consumed ≥ 8 g of RS2 per day and measured body weight, satiety, glucose and/or lipid metabolic outcomes. Twenty-two RCTs involving 670 participants were included. Meta-analyses indicated that RS2 supplementation significantly reduced serum triacylglycerol concentrations (mean difference (MD) = −0.10 mmol/L; 95% CI −0.19, −0.01, $P = 0.03$) in healthy individuals ($n = 269$) and reduced body weight (MD = −1.29 kg; 95% CI −2.40, −0.17, $P = 0.02$) in people with T2DM ($n = 90$). However, these outcomes were heavily influenced by positive results from a small number of individual studies which contradicted the conclusions of the majority of trials. RS2 had no effects on any other metabolic outcomes. All studies ranged from 1–12 weeks in duration and contained small sample sizes (10–60 participants), and most had an unclear risk of bias. Short-term RS2 supplementation in humans is of limited cardiometabolic benefit.

Keywords: resistant starch; dietary fiber; obesity; metabolic syndrome; type 2 diabetes; metabolic health; systematic review

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Next generation probiotics:

- Synbiotics: Combination of probiotics and prebiotics
- Postbiotics: soluble factors (products or metabolic byproducts) secreted by live bacteria (or released after bacterial lysis) with physiological benefits to the host, e.g. SCFAs, bacteriocins, enzymes, peptides, cell surface proteins, vitamins.
- Paraprobiotics: inactivated (non-viable) microbial cells, which when administered in sufficient amounts, confer a health benefit to the host, e.g. pasteurised *Akkermansia mucinophila.*

Dietary patterns and gut microbiota in metabolic disorders: the evidence

Dietary patterns associated with a **more** favourable gut microbial profile in humans	Dietary patterns associated with a **less** favourable gut microbial profile in humans
Mediterranean diet	Western diet
Low fat, high carbohydrate diet	High protein/low carbohydrate diet
Vegetarian diet	100% animal product-based diet
High resistant starch diet (only in responders)	High saturated fat diet
High fibre/low fat diet	
Macrobiotic diet (plant-based, very low fat)	
High carbohydrate (regardless of GI)	

Santos-Marcos, et al. *J Nutr Biochem* 2019; 70: 1–27

Faecal microbial transplant (FMT)

How to Safely do a Fecal Transplant at Home - DIY Instructions

thepowerofpoop.com/epatients/fecal-transplant-instructions/

DISCLAIMER: These "**Fecal Transplant** At Home – DIY **Instructions**" are based on the experiences of one person, the anecdotal reports of others and questions most frequently asked by e-Patients. They are not medical advice. FMT is still considered an experimental procedure without known future consequences. Please ...

Donor Pathology Tests · How to find a Fecal Transplant ... · DIY Fecal Transplant

The Rise of the Do-It-Yourself Fecal Transplant - WebMD

https://www.webmd.com › Digestive Disorders › News

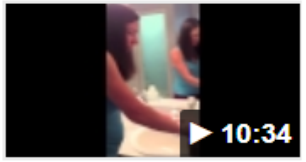
Dec 9, 2015 - A growing number of people have flocked to blogs and social media sites like YouTube and Facebook to share advice and techniques for at-home **fecal transplants**. WebMD has the details.

How to Perform a Fecal Transplant - The Healthy Home Economist

https://www.thehealthyhomeeconomist.com/how-to-perform-a-fecal-transplant-at-home/

Below are written **instructions** as well as a how-to video of a Mother who has used at home **fecal transplants** to help eliminate her daughter's debilitating gut problems and get her off strong medications. She demonstrates exactly **how to do** an at home **fecal transplant** using a simple, low cost enema bottle available over the ...

FECAL TRANSPLANT (FMT) - YouTube



https://www.youtube.com/watch?v=xLIndT7fuGo

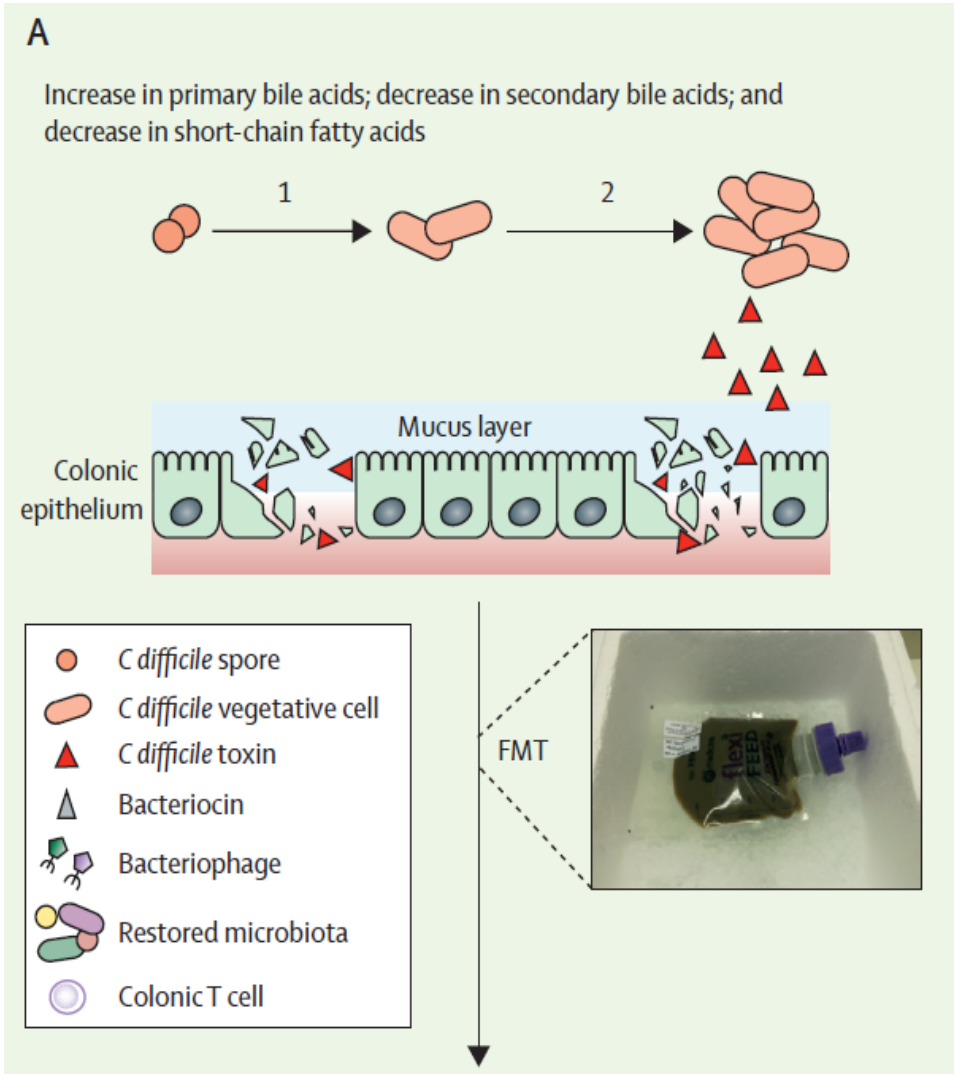
May 13, 2013 - Uploaded by HomeFMT

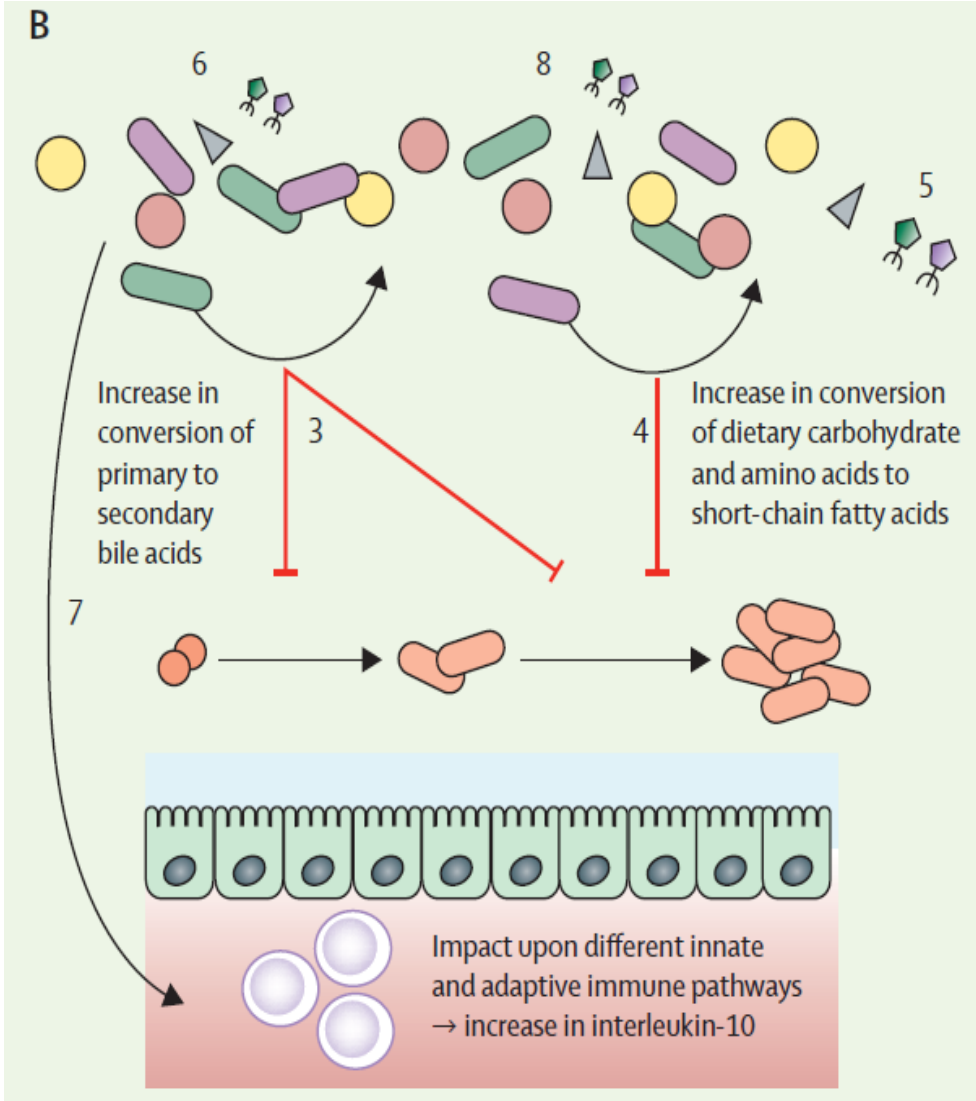
turn point you want to be able to hold the enema in person as possible. I dump out the solution that comes in ...

- Currently only approved for use in patients with antibiotic-resistant *Clostridioides difficile* infection (formerly named *Clostridium difficile*).
- One FMT is sufficient to induce complete remission in 80-90% of cases of antibiotic resistant *C.difficile.* Quraishi et al. *Aliment Pharmacol Ther* 2017; 46: 479–93.
- Stool donation is obtained from either a healthy relative of the patient, or a stool bank.
- The donor is screened using a detailed health questionnaire and blood test. The donated stool is screened for the presence of known toxins. Frozen and fresh stool donations have similar efficacy.
- FMT delivery methods include upper endoscopy, nasoenteric tubes, or freeze-dried and packaged into capsules for upper gastrointestinal tract transplant delivery, and colonoscopy, flexible sigmoidoscopy, or enema for lower gastrointestinal tract transplant delivery.

Allegretti et al. *Lancet* 2019; 394: 420–31.

FMT: proposed mechanism of efficacy





Allegretti et al. *Lancet* 2019; 394: 420–31.

FMT in obesity & metabolic syndrome: the evidence

- A small RCT (n=18) involving FMT from healthy donors to males with metabolic syndrome resulted in a temporary improvement in peripheral (muscle) but not hepatic insulin sensitivity, increased intestinal microbial diversity and increased levels of butyrate-producing bacteria in the recipients (Vrieze et al, Gastroenterology 2012)

- A larger RCT (n=38) involving FMT from healthy lean donors to males with metabolic syndrome. At week 6 post-transplant, insulin sensitivity was significantly increased in the intervention group, but the effect had disappeared by week 18. (Kootte et al. *Cell Metab* 2017)

- Not all participants showed improvements in insulin sensitivity. Participant response was dependent on the individual's gut microbial composition at baseline, and unknown unique characteristics of specific donors.

- An RCT (n=22) involving FMT from a single lean donor to participants with obesity (but not metabolic syndrome). Over 12 weeks of follow-up, no changes in body weight or GLP-1 concentrations were seen, although the intervention group showed changes in gut microbiota composition that resembled the donor. (Allegretti et al. *Clin Gastroenterol Hepatol* 2019)

Metformin:

- Some of the therapeutic effects of Metformin are mediated by changes in the gut microbiota:

- ↑ butyrate and propionate-producing species
- ↑ *Akkermansia mucinophila*
- ↑ *Lactobacillus* species
- ↑ *Escherichia* species (thought to influence GI side effects)
- ↓ *Bacteroides fragilis*

- Alpha-glucosidase inhibitors (Acarbose):

- ↑ Bifidobacterium & Lactobacillus

Forslund K, et al (2015) Disentangling type 2 diabetes and metformin treatment signatures in the human gut microbiota. *Nature* 528: 262–266

Artificial sweeteners:

- Artificial sweeteners are generally considered safe, have no effect on blood glucose levels and can result in a small reduction in energy intake for people with diabetes who are overweight and are trying to control BGLs.
- Article published in *Nature* in 2014, showed artificial sweeteners resulted in adverse changes to the composition of the gut microbiota (mainly presenting results in mice) and impaired glucose homeostasis. The findings of this original study have now been confirmed by some more recent studies (still in mice).
- The American Diabetes Association still says artificial sweeteners can be used by people with diabetes. Context is also important: for a person with T2DM who is consuming 2.25L bottle of Coke/day, switching to the diet version is an improvement.
- People without diabetes do not need to use artificial sweeteners. The kilojoule reduction achieved by using them is quite small, so they should instead be encouraged to get accustomed to having less sugar in their diet if they want to lose weight, rather than using artificial sweeteners.

Suez et al. *Nature* (2014); Bian et al. *PLoS One* (2017)

Obstet Gynecol. 2017 Nov;130(5):e274-e278. doi: 10.1097/AOG.0000000000002402.

Committee Opinion No. 725: Vaginal Seeding.

Committee on Obstetric Practice.

Collaborators (2)

Wharton KR, Birsner ML.

Abstract

Vaginal seeding refers to the practice of inoculating a cotton gauze or a cotton swab with vaginal fluids to transfer the vaginal flora to the mouth, nose, or skin of a newborn infant. The intended purpose of vaginal seeding is to transfer maternal vaginal bacteria to the newborn. As the increase in the frequency of asthma, atopic disease, and immune disorders mirrors the increase in the rate of cesarean delivery, the theory of vaginal seeding is to allow for proper colonization of the fetal gut and, therefore, reduce the subsequent risk of asthma, atopic disease, and immune disorders. At this time, vaginal seeding should not be performed outside the context of an institutional review board-approved research protocol until adequate data regarding the safety and benefit of the process become available.

PMID: 29064974 DOI: 10.1097/AOG.0000000000002402

[Indexed for MEDLINE]

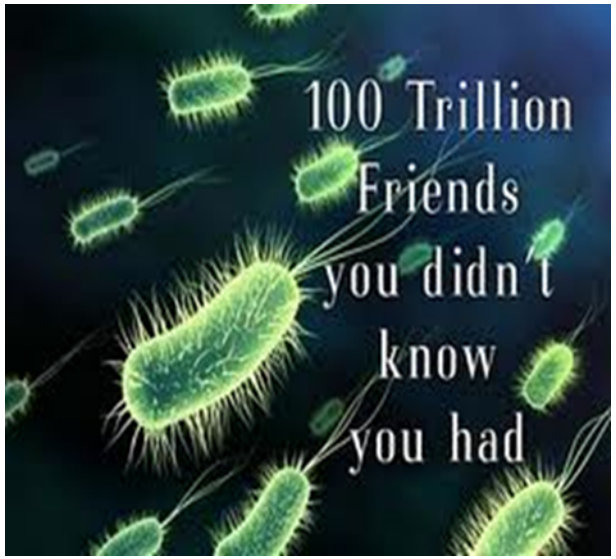
Future research required:

- Who else lives in the gut and what are they doing? Strain-level resolution required.
- Optimal composition of probiotics (individualised based on genotype?)
- Suitability of faecal microbial transplants in cardiometabolic disorders (what are the unique characteristics of super-donors?)
- Postbiotics: SCFA supplements?
- Ideal prebiotic or synbiotic intake with minimal side effects?
- Gut microbial composition in indigenous people and response to consumption of traditional bush foods versus highly processed food?

Practical dietary advice:

- Normal vaginal birth (where possible). “Vaginal seeding” after C-section not recommended.
- Encourage and support breastfeeding where possible
- Avoid unnecessary use of antibiotics under the age of 2 years (or use antibiotics which do not alter gut microbiota)
- Encourage consumption of a variety of dietary fibre sources (including prebiotics, resistant starch) from wholegrain breads & cereals, fruits & vegetables
- Encourage consumption of polyphenol sources (fruit, vegetables, nuts, tea, coffee, wine)
- Reduce consumption of high saturated fat, highly processed diets
- Encourage daily physical activity and adequate sleep quality.

Thank you for listening



VSL#3:

- a mixture of lactobacilli and bifidobacteria (*Bifidobacterium infantis*, *Bifidobacterium breve*, *Bifidobacterium longum*, *Lactobacillus plantarum*, *Lactobacillus casei*, *Lactobacillus delbrueckii* ssp. *Bulgaricus*, and *Lactobacillus acidophilus*)