Management of type 1 diabetes

The gut microbiome and type 1 diabetes risk: We are what we grow

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The gut microbiome is the term used to describe the bacterial ecosystem that lives within the human gut. We can carry up to 2 kg of bacteria within the bowel, and the total number of genes in the various species living within the gastrointestinal tract likely exceeds the number of human genes by at least two orders of magnitude. There is considerable variation between individuals in the composition of these bacteria. We could arguably consider each individual as a composite ecosystem of both human and bacteria. When viewed in these terms, it is perhaps not surprising that there is evidence of a relationship between the make-up of our bacterial flora and health or disease (Brenchley and Douek, 2012). The main focus, until recently, has been the relationship between the gut microbiota and obesity. Rodent studies suggest there are specific microbiota that may be more efficient at harvesting energy from the diet and so predispose to obesity. These can be transmitted between animals and are associated with weight gain. There is less evidence, however, that changing the intestinal flora is associated with weight loss.

Alkanani and colleagues present a study (summarised alongside) suggesting a link between alterations in intestinal bacterial composition and the risk of developing type 1 diabetes. The background to this paper is a number of studies showing a relationship between gut microbes and host immunity. These were mostly rodent studies. The Alkanani study differs as it had an observational design and was conducted in humans.

The authors use the term dysbiosis to describe changes in the intestinal microbe population that may contribute to disease – in this case type 1 diabetes. Stool samples were analysed from four cohorts: one group with new-onset type 1 diabetes, one group of autoantibody-positive individuals without diabetes, a group of first-degree relatives of individuals with type 1 diabetes (without autoantibodies) and a healthy control group.

The bacteria growing within the gut are diverse and the number of subjects studied was relatively small (20–35 in each group). As a consequence, the analysis is complicated and rather unclear. The authors describe differences in the bacterial makeup between seropositive and seronegative individuals and between healthy controls and the other groups. However, it is worth noting that these differences were only observed in a small number of what were multiple analyses. The idea is interesting but the authors have not yet proved their point. ■

Brenchley JM, Douek DC (2012) Microbial translocation across the GI tract. *Annu Rev Immunol* **30**: 149–73

Diabetes

Correlations between the gut microbiome and T1D susceptibility

Readability	✓
Applicability to practice	✓✓
WOW! Factor	✓✓✓

1 These authors used RNA sequencing from gut bacterial samples to evaluate whether the gut microbiome is associated with susceptibility to and progression of T1D.

2 They compared samples from 35 people with newly diagnosed T1D, 21 with islet cell autoantibodies but no T1D, 32 seronegative first-degree relatives of people with islet cell autoimmunity and 23 controls with no family history of autoimmunity.

3 After adjustment for age, gender, autoantibody presence and human leukocyte antigen genotype, compared with seronegative relatives, seropositive people were found to differ in the gut abundance of four bacterial taxa (the Bacteroidetes phylum, the RC9 gut group, *Prevotellaceae* spp and *Catenibacterium* spp).

4 Furthermore, people with autoantibodies, seronegative relatives and those with new-onset T1D had different levels of *Lactobacillus* spp and *Staphylococcus* spp compared with healthy controls.

5 There were trends toward increased *Bacteroides* spp and reduced *Prevotella* spp in seropositive subjects with multiple autoantibodies compared to those with just one.

6 The authors conclude that alterations in the composition of the intestinal microbiota are associated with T1D progression; however, it is not possible to conclude whether these changes cause progression or if they are a result, for example, of dietary changes that occur after diagnosis.

Alkanani AK, Hara N, Gottlieb PA et al (2015) Alterations in intestinal microbiota correlate with susceptibility to type 1 diabetes. *Diabetes* **64**: 3510–20

Diabet Med

Overdiagnosis of depression in people with T1D?

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! Factor	✓✓✓✓

1 These authors assessed 368 people with T1D using the eight-item Patient Health Questionnaire Depression Scale (PHQ-8), the T1D Distress Scale and a structured clinical interview to assess major depressive disorder (MDD). The PHQ-8 has a maximum score of 24, with higher scores indicating an increased likelihood of depression.

2 The prevalence of MDD according to PHQ-8 scores was 11.4%, 7.1% and 3.8% when cut-off scores of >10, >12 and >15, respectively, were used. Conversely, structured clinical interview according to Diagnostic and Statistical Manual-5 specifications revealed a true MDD prevalence of 3.5%. The prevalence of moderate or worse diabetes distress was 42.1%.

3 Depending on which PHQ-8 cut-offs were used, the rate of false-positive diagnoses ranged from 52% to 71%. Notably, a cut-off of >10, the most widely used cut-off for MDD on the PHQ-8, yielded the highest rate of false-positives.

4 Overall, 92–96% of participants who were classified as having MDD on the PHQ-8 had moderate diabetes distress or worse, as did 92% of those with an official diagnosis of MDD.

5 These findings suggest that the PHQ-8 should be used only as a screening instrument for MDD, not as a substitute for formal diagnosis.

6 The authors suggest that specific therapy to treat diabetes distress may be more appropriate in these individuals than treatment for affective disorders such as MDD.

Fisher L, Hessler DM, Polonsky WH et al (2015) Prevalence of depression in type 1 diabetes and the problem of over-diagnosis. *Diabet Med* 3 Oct [Epub ahead of print]

Diabet Med

Glycaemic behaviour while breastfeeding in women with T1D

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! Factor	✓✓

1 In this study, continuous glucose monitoring (CGM) was used to compare glycaemic variability and hypoglycaemia risk in eight breastfeeding and eight artificially feeding postpartum women with T1D.

2 Compared with the breastfeeding group, the high blood glucose index – a measure of hyperglycaemia risk based on the number and severity of high blood glucose levels on CGM – was higher in the formula-feeding group (mean, 16.3 vs. 9.5; P=0.02).

3 However, the low blood glucose index was similar between the groups, indicating equal risk of hypoglycaemia.

4 Breastfeeding induced a significant fall in blood glucose levels after suckling, but this did not result in hypoglycaemia in the majority of suckling episodes (85%).

5 A trend towards increased carbohydrate consumption (P=0.09) might explain the similar rates of hypoglycaemia in the two groups.

Achong N, McIntyre HD, Callaway L, Duncan EL (2015) Glycaemic behaviour during breastfeeding in women with type 1 diabetes. *Diabet Med* 19 Oct [Epub ahead of print]

Diabet Med

Dietary protein and postprandial blood glucose levels

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! Factor	✓✓✓

1 These authors measured postprandial blood glucose levels in 27 people with T1D who were given drinks with differing amounts of protein (0–100 g) or glucose (10–20 g), in a randomised order, over an 8-day period.

2 Protein loads of 12.5 g and 50 g did not result in significant postprandial glycaemic excursions compared with the control (water).

3 However, loads of 75 g and 100 g resulted in lower glycaemic excursions than controls (both water and glucose) in the short term (1–2 hours postprandially), but greater excursions between 1.5 and 5 hours.

4 These findings support adjusting insulin doses to account for protein-rich meals.

Paterson MA, Smart CE, Lopez PE et al (2015) Influence of dietary protein on postprandial blood glucose levels in individuals with type 1 diabetes mellitus using intensive insulin therapy. *Diabet Med* 26 Oct [Epub ahead of print]

N Engl J Med

Home use of an artificial pancreas

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! Factor	✓✓✓✓

1 In this pair of multicentre, crossover, randomised controlled studies conducted under free-living, at-home conditions, an artificial pancreas (AP) was compared with sensor-augmented pump therapy, each for a period of 12 weeks, in 33 adults and 25 children and adolescents.

2 In adults, day and night use of the AP increased the time spent in the target glycaemic range by 11% (P<0.001) and lowered mean HbA_{1c} by 3 mmol/mol (0.3%; P=0.02).

3 In children, night-time use of the AP increased the amount of time spent in the target range by 25% (P<0.001); however, mean HbA_{1c} was not significantly reduced.

4 Three severe hypoglycemic episodes occurred in the AP arm, all when the system was not in use.

Thabit H, Tauschmann M, Allen JM et al (2015) Home use of an artificial beta cell in type 1 diabetes. *N Engl J Med* **373**: 2129–40

> ***"The authors suggest that specific therapy to treat diabetes distress may be more appropriate in these individuals than treatment for affective disorders such as major depressive disorder."***