THE CARB-APPROPRIATE REVIEW

THE GUT ISSUE: PART 1

A MONTHLY RESEARCH REVIEW BY

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In association with The Holistic Performance Institute

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ABOUT CLIFF

Dr Cliff Harvey is an author, clinician, and researcher. He was one of the first clinical nutritionists to begin working with ketogenic and low-carb diets, way back in the 1990s and is also considered a pioneer in the area of mind-body integrative healthcare.

Cliff's early post-graduate work was in mind-body healthcare, while his master's research focussed on the use of medium-chain triglycerides to mitigate 'keto-flu' and encourage faster induction of nutritional ketosis.

His doctoral thesis continued to investigate keto-flu and ketogenesis, and the effects of different types of low-carbohydrate diets along with the individualisation of dietary prescription and how 'carbohydrate tolerance' varies from person-to-person.

He is a former world champion strength athlete, submission grappler, and author of several best-selling books, including *The Carbohydrate Appropriate Diet*, *Carb-Appropriate 101*, *Time Rich Cash Optional* and *The Credo.*

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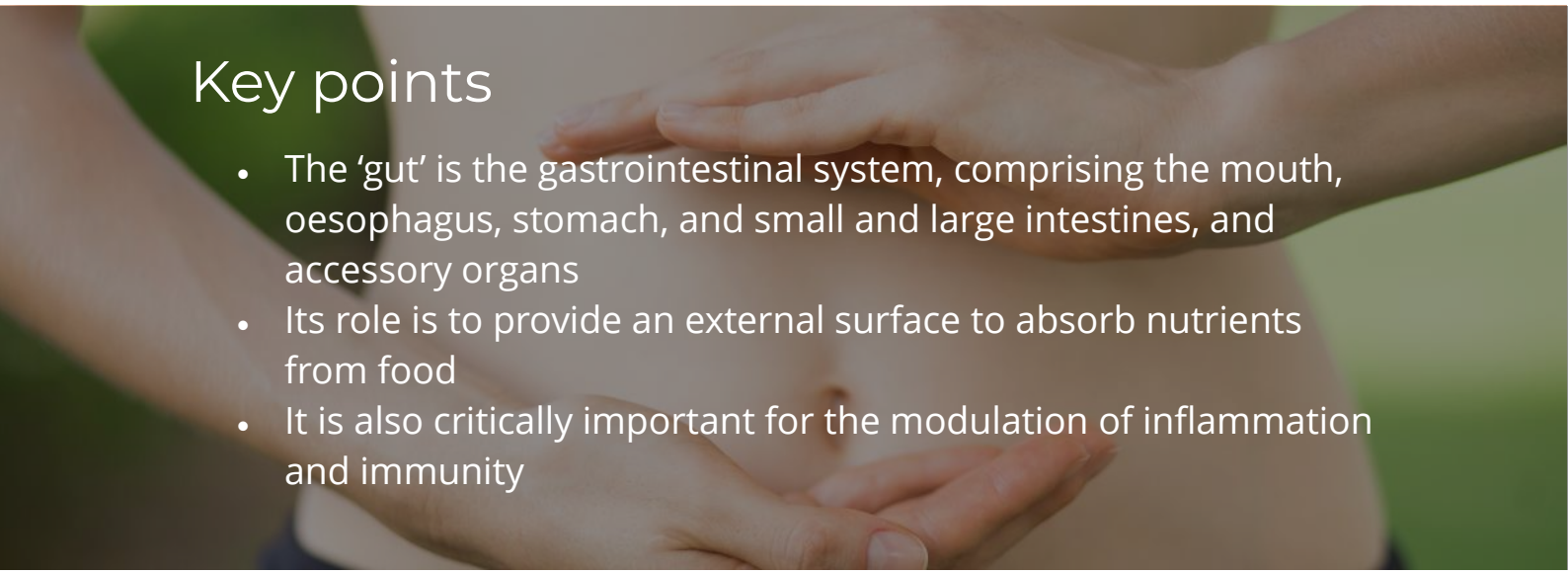
THIS MONTH

INTRO TO GUT HEALTH



Key points

- The 'gut' is the gastrointestinal system, comprising the mouth, oesophagus, stomach, and small and large intestines, and accessory organs
- Its role is to provide an external surface to absorb nutrients from food
- It is also critically important for the modulation of inflammation and immunity

When people talk about the 'gut', they're referring to the gastrointestinal system, also known as the digestive system or digestive tract. This system includes the mouth, oesophagus, stomach, and the small and large intestine. It also includes the accessory organs which aid digestion by helping to break down larger particles of food into absorbable particles (i.e. the tongue, salivary glands, pancreas, liver, and gallbladder). Having a healthy digestive system allows us to absorb nutrients optimally and helps to reduce inflammation, support immunity, and even plays a role in helping us to feel better mentally.

Why is gut health important?

Because it's exposed to the external environment, the digestive system is an external organ by which we absorb the nutrients that make up the body's structures, chemical messengers, and fuels. Because it's exposed to the outside environment, it is also a potential site of infection from pathogens (disease-causing microbes) and pollutants in food and water and so, is part of our innate defences against disease and disorder that has an important relationship with the immune system of the body.

Is gut health just another fad?

Because the role of the gut is so important for both nourishment and immunity, 'gut health' couldn't be called a fad. Having a healthy gut is an essential

component of wellbeing. However, there can be dubious claims made about supplements and diets for gut health that aren't backed by strong evidence.

What is the microbiome?

The microbiome is the community of microbes found in the body. Technically, microbiome refers to collective genomes of these microbes with *microbiota* used to describe the communities of microbes but in general use, these terms are used synonymously. Usually, the microbiome in common usage refers to the community of bacteria in the gut but it also includes other microbes like fungi, protozoa, and viruses and there is distinct microbiota of the skin, oral cavity, and other surfaces.

> The microbiome is the community of microbes found in the body

What are probiotics?

Probiotics are microbes (usually bacteria) that can be taken as a supplement to help improve the balance of the microbiome.

What are prebiotics?

Prebiotics are the fuels that feed (beneficial) microbes in the gut. Usually, these are fibres and resistant starches that feed particular bacteria.

Intro to the effects of the gut on health

Gut health and the microbiome play an important role in our overall health. Poor gut health caused by disturbances to the balance of 'good' and 'bad' microbes in the gut can affect both nourishment and growth *and* metabolic conditions like obesity and type 2 diabetes.[1]

Nourishment

The key role of the gastrointestinal tract is to absorb nutrients from food. So, having a gut that functions correctly (that can also keep out any 'nasties') and absorb nutrients from food is essential to achieving optimal health. The microbiome also contains bacteria that produce nutrients, like short-chain fatty acids which feed cells of the digestive wall, other bacteria, and can be taken up into the body to use as fuel. These and other chemicals produced by bacteria in the gut also act as messengers that provide a 'metabolic interaction' between the host (you) and the microbiota and digestive environment.[2]

Chemicals produced by bacteria provide a 'metabolic interaction' between the host and the microbiota

Inflammation and immunity

Far more than just being an organ to absorb nutrition, the gut is essential for the regulation of systemic inflammation, and plays a role in inflammatory conditions like psoriasis.[3] Interestingly, in people with inflammatory conditions there is typically a reduced diversity and abundance of bacteria in the gut,[4-6] and reduced diversity and abundance of bacteria in the gut is also associated with increased inflammation.[7]

Obesity is also an inflammatory condition because excessive amounts of fat tissue result in increased inflammation causing 'adipokines' which are cellular messengers produced in fat cells.

Obesity and metabolic diseases cause low-grade inflammation that is a co-factor for the development of other diseases, especially cardiovascular disease. In a review studies on cardiovascular disease and the microbiome it was found that lower bacterial diversity in the gut is associated with higher white blood cell counts (indicative of inflammation), and higher c-reactive protein (a key measure of systemic inflammation).[7]

Obesity and metabolic diseases cause low-grade inflammation that is a co-factor for the development of other diseases

Relative increases or decreases of certain bacteria types is also associated with changes in inflammatory markers, although the results of studies thus far are incomplete and with some conflicting results and there have not been any long term studies of the impacts of changes in these bacteria, chronic inflammation, and outcomes.

Unsure or conflicting results: Total bacterial number and total gene count.

Dysbiosis also occurs in people with autoimmune conditions. This is thought to be because of a combination of genetic susceptibility to the diseases, environmental factors, *and* the microbiota.[6]

Additional points

- Inflammation and the gut have a bi-directional relationship
- Inflammatory conditions are associated with dysbiosis

  Probiotics might offer a therapeutic option for inflammation and inflammatory conditions

THE GUT-BRAIN CONNECTION AND HEALTH

Key points

- The gut and both its barrier and inflammation-regulating functions affect the brain and mental health
- 'States' of mental health also affect the gut (esp. motility) and the microbiota
- Comorbidities exist between mental health challenges like depression and bipolar disorder and IBS, IBDs, and other gut disorders
- Many psychiatric illnesses are characterised by differing microbiome signatures
- Probiotics, prebiotics and other gut interventions may be of use in psychiatric treatment

The gut and brain are linked, and this has led some to call the gut 'the second brain' as it helps to play a role in the regulation of the central nervous system. While once, mental health challenges were considered to be restricted to structural or functional (i.e. neurotransmitter imbalances) problems within the brain, it is now known that systemic health, inflammation, and gut-health play a role in the health of the brain, nervous system, and the psyche of an individual.[8] The gut-brain axis (more importantly, the effect of the microbiome on the entire body) has been implicated in mental health and it is now clear that there is an intimate connection between psychiatry and gastrointestinal health.

The gut and depression

Recent research provides a strong indication that depression is both an inflammatory disease and that there is communication between the gut and the brain and nervous system, and that this is related to depression and other mental health challenges. Reviews of the research shows associations between disturbed gut microbiota and psychiatric illness in humans, and animal research has shown that when the faecal microbiome from animals showing depressive signs is

transplanted into non-depressed subjects, they develop depressive symptoms. Animal research also suggests a role for probiotics as antidepressants and a negative effect from antibiotics.

Several probiotics in particular have shown promise:

- *L. rhamnosus* – reduced stress response
- Combination *B. bifidum W23, B. lactis W52, L. acidophilus W37, L. brevis W63, L. casei W56, L. salivarius, W24, Lactococcus Lactis W19, and Lc. Lactis W58* – reduces depressive-like behaviour
- *L. helveticus* – resilience to depressive symptoms

However, other studies have shown no benefit from supplementing bacteria known to be reduced in subjects with depression and a 2020 meta-analysis showed no clear effect of either prebiotic or probiotic supplements on depression.[9]

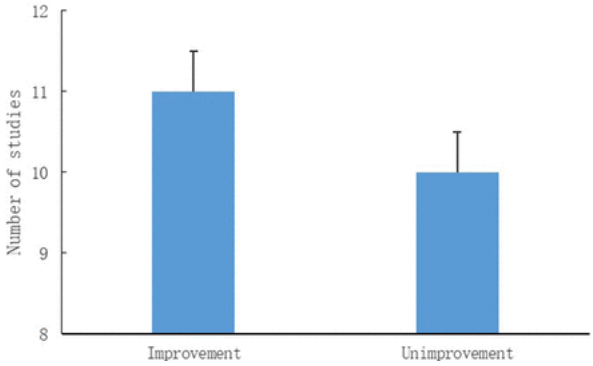
Most reported studies though have demonstrated some correlation between the gut microbiota and depression,[10] and it is worth remembering that the interplay between genes, diet, lifestyle, environment, microbiota, and mental health is a complex one that begs for further research, and that the effects of supplementation on particular illnesses is likely to be dependent on the species-disease interaction.

Most studies have demonstrated some correlation between the gut microbiota and depression

Gut-health and anxiety

Recent research now suggests that the microbiome plays a role in regulating mood, anxiety, and stress.

In a review of 21 studies[i] (extracted from a search yielding 3334 articles), 11 studies showed a positive effect on anxiety symptoms by regulating intestinal microbiota (by supplementation or dietary interventions). Interestingly, non-probiotic (dietary interventions) appear to be more effective for regulating the microbiome and reducing anxiety.[11]

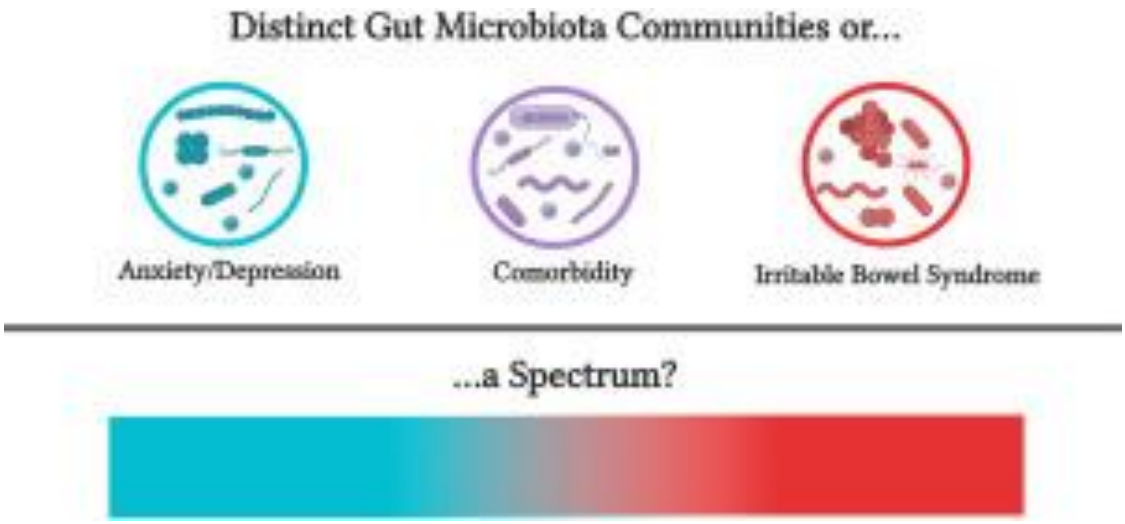


[i] *n* = 1503

Non-probiotic interventions appear to be more effective for regulating the microbiome and reducing anxiety

The gut, IBS and anxiety

Anxiety and depression, and irritable bowel syndrome (IBS) are common, and around 40-90% of those with anxiety share these conditions. In a review of 17 human and animal trials indicated that people with IBS and anxiety had lower diversity of bacteria and higher abundance of Proteobacteria, *Prevotella, Bacteroides* and lower levels of *Lachnospiraceae* relative to healthy controls.[12]



Are there differences in microbiota in depression vs bipolar disorder?

Depression and bipolar disorder may show differing microbiota.[13] In both depression and bipolar disorder, increased numbers of F*irmicutes* and *Actinobacteria* and decreased *Bacteroidetes* have been found, and at the genus level, *Bacteroides*, *Clostridium*, *Bifidobacterium*, *Oscillibacter* and *Streptococcus* were increased compared to controls.

Between people with depression and bipolar disorder, depressive patients had greater abundance of *Prevotellaceae* including *Prevotella* denticola F0289, *Prevotella intermedia* 17, *Prevotella ruminicola*, and *Prevotella intermedia*. While in the bipolar patients, *Fusobacteriaceae, Escherichia blattae DSM 4481* and *Klebsiella oxytoca* were significantly increased, whereas the *Bifidobacterium longum* subsp. Infantis ATCC 15697 = JCM 1222 was

decreased compared with the depression group.[14]

Gut health and bipolar disorder

Many conditions related to gut-health are co-morbid with bipolar disorder, including inflammation, irritable bowel disease and antibiotic induced mania.[15] People with bipolar disorder also have a greater incidence of gastrointestinal illnesses and inflammatory bowel diseases which are linked to microbiome status.[16] The microbiota of people with bipolar disorder and schizophrenia also differ from controls and GI inflammation is known to be increased in both conditions.[17, 18]

In particular, *Flavonifractor* has been associated with having a newly diagnosed bipolar disorder (and also with smoking).[18]

> Many conditions related to gut-health are co-morbid with bipolar disorder

People with bipolar disorder may also have reduced bacterial diversity in the microbiome, lower *Faecalbacetrium (*as a proportion of total bacteria),[19] and a greater abundance of *Clostridiaceae* among bipolar type 1 subjects and *Collinsella* among bipolar type 2 subjects.[20]

There was a lower *Bifidobacteria*-to-*Enterobacteriaceae* ratio (which represents microbial colonization resistance) than control subjects.

> There was a lower *Bifidobacteria* to *Enterobacteriacea* ratio in people with bipolar disorder

Treatment with the drug quetiapine increased the levels of *Eubacterium rectale*, *Bifidobacteria*, and B/E ratio.[21] Greater representation of *Faecalibacterium* in people with bipolar disorder is associated with better self-reported health outcomes (including for sleep, mood, and anxiety).[19]

There may also be interactions between specific microbiota and metabolites, causing increased oxidative stress and nitric oxide production in bipolar disorder,[22] possibly also related to increased gut permeability (leaky gut) related to poor gut health.[23]

Studies also suggest increased intestinal inflammation and permeability, which may be among the principal mechanisms by which microbial dysbiosis impacts systemic physiological functioning and mental health.[24]

GUT HEALTH & SLEEP

Key points

- There is a bi-directional relationship between sleep and the gut
- Lack of sleep affects the motility of the gut which is likely to affect gut health
- Lack of sleep influences the microbiota and the microbiota influence circadian rhythms and length and quality of sleep
- The effects of short-term restriction or extension on sleep in humans are unclear though

It has been suggested that sleep and circadian rhythm dysfunctions affect the microbiome, contributing to an inflammatory state and metabolic diseases.[25, 26] It is thought that metabolites from the gut microbiome (compounds produced by bacteria) help to influence circadian rhythm and help to regulate sleep, metabolism, and body composition and these end products of bacterial species are also able to induce fatigue. Furthermore, probiotic supplementation has been found to improve subjective sleep quality.[27]

However, the relationship between sleep and gut health is likely to be bidirectional. Microbiome diversity is correlated with sleep efficiency and abstract thinking, while several genera including *Lachnospiraceae*, *Corynebacterium*, and *Blautia* are correlated with poorer sleep measures.[28]

Microbiome diversity is correlated with sleep efficiency and abstract thinking

Sleep quality is also associated with faster cognitive functions and tests results for this (the Stroop test) are related to *Verrucomicrobia* and *Lentisphaerae*.[29]

Good self-reported sleep quality is positively associated with microbial diversity, Firmicutes to Bacteroidetes ratio, and butyrate-producing bacteria (such as *Blautia* and *Ruminococcus*), while poor self-reported sleep quality was positively associated with the genus *Prevotella*.[30]

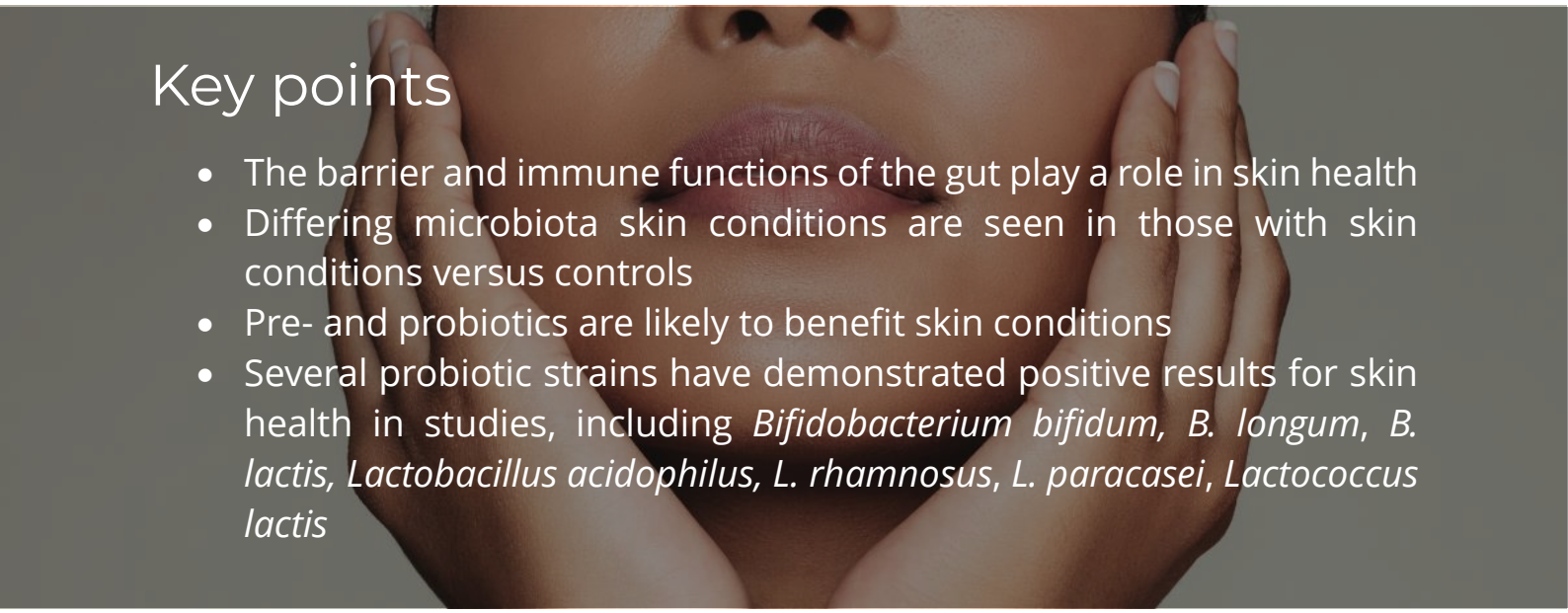
Disturbed sleep is known to worsen eating behaviours and thus may play a further role in the disturbance to the microbiota seen

with poor sleep. Animal and human research have shown that disturbed sleep increases ad libitum food intake and changes the microbiota. This increases highly fermentative *Lachnospiraceae* and *Ruminococcaceae* while decreasing *Lactobacillaceae* families. In mice, this leads to inflammation, insulin resistance, and is associated with colonic epithelium disruption. These results have been confirmed through inoculation of germ-free mice with microbiota from sleep disturbed subjects.[31] Antibiotics (which reduce bacteria number and diversity) have also been shown to reduce sleep in mice.[32] Research in people with IBS also suggests that gut dysfunction affects sleep.[33]

Short term sleep restriction over several days has not been shown to overly influence gut microbiota in either rats or humans

However, short term sleep restriction over several days has not been shown to overly influence gut microbiota in either rats or humans.[34] Similarly, sleep extension has not been demonstrated to influence the overall gut composition, but better quality sleep was related to a higher abundance of the phyla *Tenericutes*.[35] Finally, in a study of young, active adults (18-35 yrs.) no significant relationship between habitual sleep duration and microbiota diversity was observed.[36]

THE GUT, & SKIN HEALTH



Key points

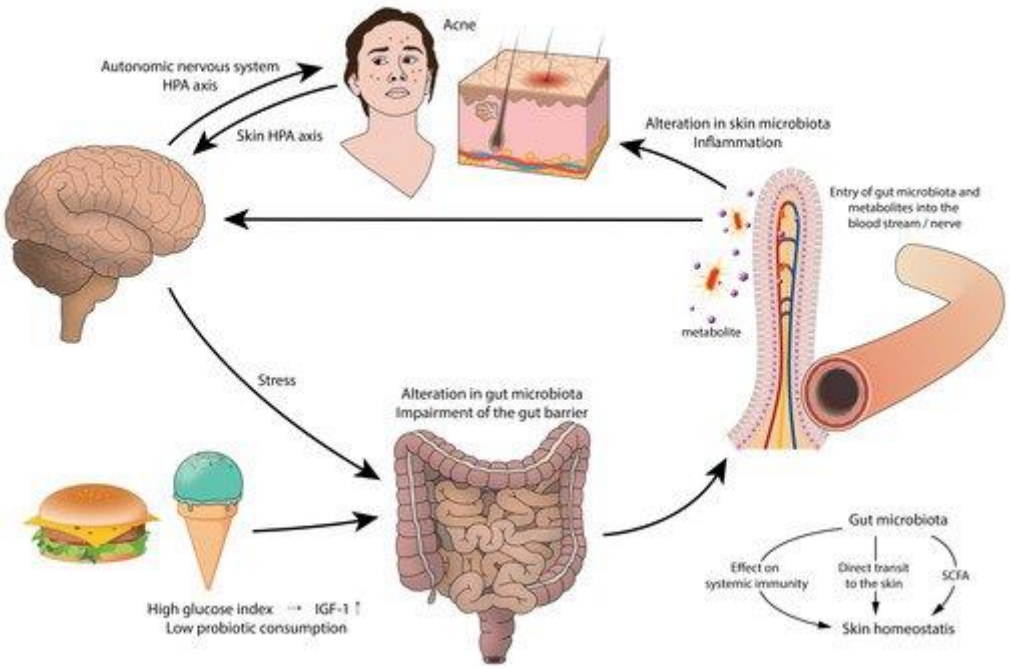
- The barrier and immune functions of the gut play a role in skin health
- Differing microbiota skin conditions are seen in those with skin conditions versus controls
- Pre- and probiotics are likely to benefit skin conditions
- Several probiotic strains have demonstrated positive results for skin health in studies, including *Bifidobacterium bifidum, B. longum*, *B. lactis, Lactobacillus acidophilus, L. rhamnosus*, *L. paracasei*, *Lactococcus lactis*

The connection between gut and skin health has been known for some time. Many conditions of the skin such as psoriasis and eczema result from a combination of factors which include allergy and inflammation and so, both the barrier *and* immune functions of the gut are important for skin health.

Gut health and acne

Acne is an inflammatory skin condition and for nearly a century the link between the gut, brain, and skin has been suggested.[37] More recent research has demonstrated that the microbiome of the skin plays an important role in acne and the skin microbiomes of people with and without acne differ.[38]

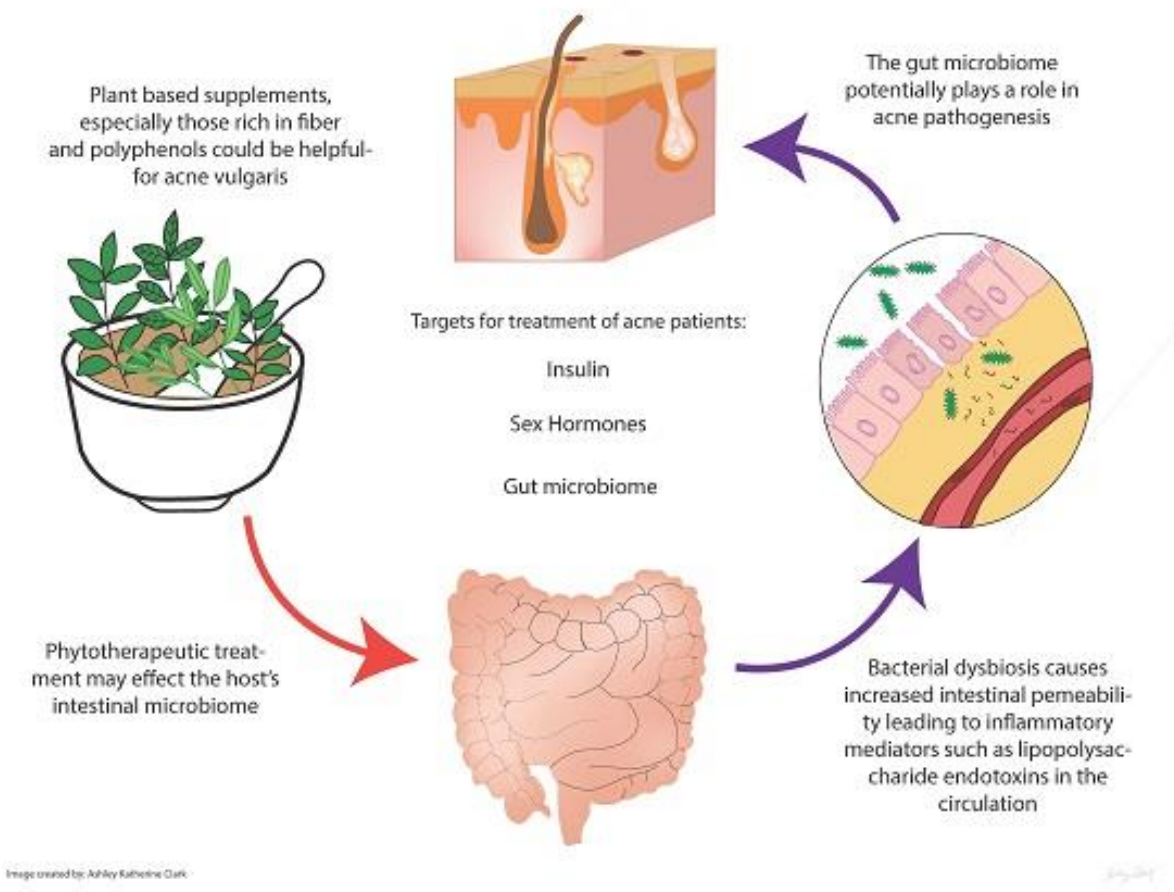
The gut microbiome is also important for this condition, due to the roles of the gut as a barrier and immune modulator, and also due to the effects of emotions and stress on motility in the gut and resultant effects on the microbiome, which further affects immunity and inflammation and increases intestinal permeability, contributing to skin inflammation.[38]



Case-control studies have shown differences in the microbiomes of people with and without acne. Particularly, Actinobacteria was decreased and Proteobacteria (8.35% in increased in acne patients while *Bifidobacterium, Butyricicoccus*, *Coprobacillus, Lactobacillus,* and *Allobaculum* were all decreased.[39]

Case-control studies have shown differences in the microbiomes of people with and without acne

Changes in diet had typically been considered to have little effect on acne but clinical experience suggests otherwise. It is now suggested that diets that reduce inflammation and support a healthy microbiome, including those based on natural, unrefined foods and with plenty of gut-supporting fibre and resistant starch, be considered for acne.[40]



https://www.mdpi.com/1422-0067/18/5/1070

In a randomised open-label study, antibiotic treatment and treatment with a probiotic were comparable for reducing acne over 12 weeks (a combination antibiotic and probiotic resulted in the greatest reductions).

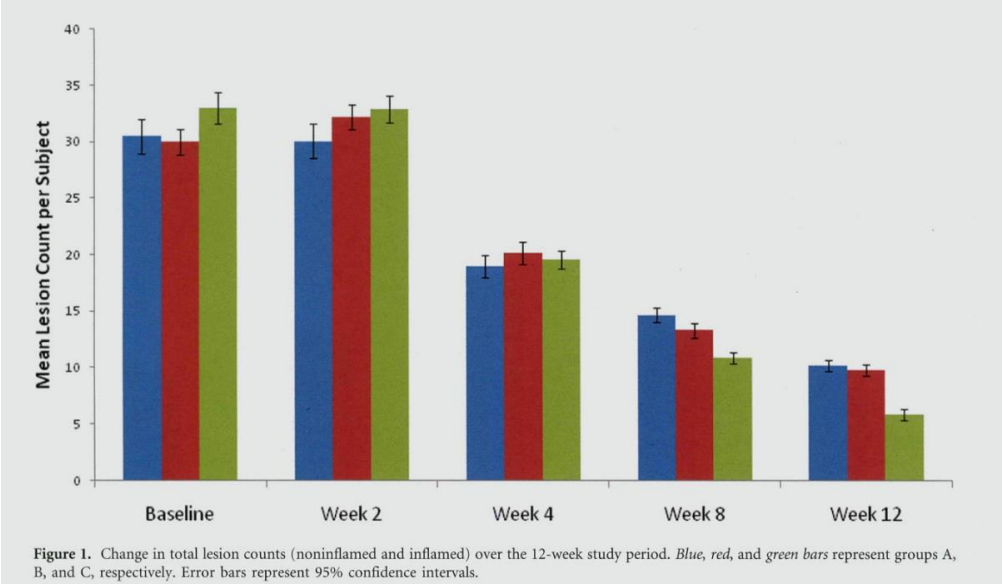


Figure 1. Change in total lesion counts (noninflamed and inflamed) over the 12-week study period. *Blue*, *red*, and *green bars* represent groups A, B, and C, respectively. Error bars represent 95% confidence intervals.

Gut health and eczema

Eczema is a common inflammatory condition of the skin affecting around 1 in 10 people at some point in their lives. It has several subtypes:

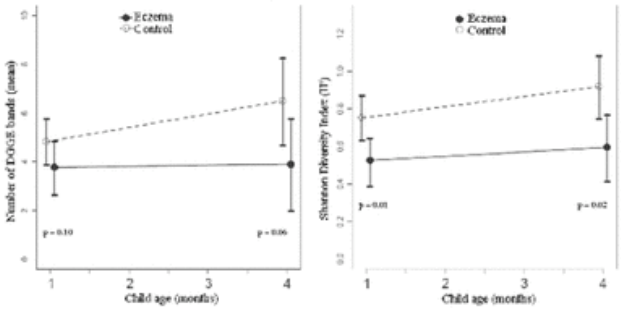
- Systemic immune or allergy-related: Atopic dermatitis, dyshidrotic eczema, nummular eczema (also known as discoid eczema)
- Contact allergen related: Contact dermatitis, seborrheic dermatitis (caused by a combination of genetics, hormones, and microbes on the skin)
- Related to trauma (possibly also allergen or immune activity): Neurodermatitis (also known as lichen simplex chronicus)
- Related to metabolic dysfunction (along with co-factors of genetics and immune/inflammatory status): Stasis dermatitis (when poor circulation to the legs causes the veins to swell and leak fluid, causing swelling and skin redness and itch—mostly in older people).

https://nationaleczema.org/research/eczema-facts/

Increasing research is demonstrating a link between the gut microbiome and eczema.[41] A significant proportion of children who develop food sensitivities go on to develop food allergies and eczema, and these anomalous immune responses are thought to be linked to the gut-immune axis of the body.[42]

At 1-16 weeks of age, there is lower bacterial diversity in children with atopic and allergic eczema,43-45 and children without eczema have been shown to have up to 56% greater microbial diversity in the intestinal microbiome than those diagnosed with eczema.[46, 47]

In other research, at 6 months of age, healthy children had 3-fold greater amounts of Bacteroidetes, while microbiota of children suffering from eczema had increased abundance of the *Clostridium* clusters IV and XIVa, which are typically more abundant in adults.[48]



Children with eczema had increased abundance of the *Clostridium* clusters typically more abundant in adults

Additionally, lower numbers of *Ruminococcaceae*, *Bifidobacterium*, *Megasphaera*, *Haemophilus*, *Streptococcus* and *Lactobacillus* species, and higher levels of *Escherichia/Shigella*, *Veillonella*, *Faecalibacterium*, *Lachnospiraceae incertae sedis* and *Clostridia*, *Enterobacteriaceae*, *Bacteroidaceae*, *Clostridiaceae*,

Deinococcaceae and E. coli are associated with eczema in children and the sensitisation to allergies, and asthma.[49-55]

Reduced abundance of *Ruminococcaceae* and *Enterobacteriaceae* seen in children with eczema (at 1-4 weeks of age) has been associated with increased inflammation (Il-6 and TNF- α).

Mothers whose infants developed IgE-associated eczema had lower α-diversity of Bacteroidetes (although this was not seen later in their infants). At 1 year, α-diversity of Actinobacteria was lower in infants with IgE-associated eczema compared with controls.[56]

However, differing species within the same genus could result in quite different outcomes. For example, in children up to 1-year-old, the presence of *B. catenulatum* at 3 months was associated with a higher risk of developing eczema, [ii] infants colonised with *B. breve* up to 3 months had a reduced risk of developing eczema, [iii] and the presence of *B. breve* at 3 months was associated with a lower risk of atopic sensitization at 12 months.

B. breve colonization patterns were influenced by maternal allergic status, household pets and the number of siblings.[57] Additionally, breast-fed infants are more likely to harbour *Bifidobacterium*

[ii] OR $_{adj}$ = 4.5; 95% CI : 1.56–13.05, p_{adj} = 0.005

[iii] (OR $_{adj}$ = 0.15; 95% CI : 0.05–0.44, p_{adj} = 0.00001)

bifidum [iv] , while *Bifidobacterium pseudocatenulatum* was detected more commonly in faeces of non–breast-fed childre [v] and children with eczema, but there were no significant associations between clinical measurements and detection of *B pseudocatenulatum*.[58]

Several species, such as *Faecalibacterium prausnitzii* and *Ruminococcus gnavus*, that are known to be associated with atopy or inflammation, were found to be significantly enriched in infants with eczema. Higher abundance of *Akkermansia muciniphila* in eczematous infants might reduce the integrity of intestinal barrier function and therefore increase the risk of developing eczema. On the other hand, *Bacteroides fragilis* and *Streptococcus salivarius*, which are known for their anti-inflammatory properties, were less abundant in infants with eczema. The observed differences in genera and species between cases and controls in this study may provide insight into the link between the microbiome and eczema risk.[54]

A role for 'superantigens'?

Certain bacteria carrying 'superantigens' might also promote the later development of allergic sensitisation and eczema. For example, while the early gut colonisation by *Staphylococcus aureus* was not related to subsequent eczema development, the *S. aureus* strains that were found to colonize those infants who developed atopic eczema were less likely to carry the gene encoding a 'superantigen' (SE lM) and the gene for elastin-binding protein compared with strains that were isolated from infants who had not developed atopic eczema by 18 months of age.[59]

Metabolites

Reduced short-chain fatty acids produced by gut bacteria along with succinate, phenylalanine and alanine, and higher glucose, galactose, lactate, and lactose have been found in faecal samples of children who later developed eczema. Supplementation of multispecies probiotics induces higher levels of lactate and short-chain fatty acids, and lower levels of lactose and succinate (compared to placebo) and this might explain some of the protective roles for probiotics on the development of eczema.[60]

Probiotics for eczema

There is some debate about the role that probiotics might play in eczema. Overall, systematic reviews of the literature suggest around a 26% reduction in risk for eczema with probiotic supplementation,[61] and current evidence supports the use of *Lactobacillus* strains for the prevention of eczema. Prebiotics have also been shown beneficial for primary prevention of eczema

[iv] (odds ratio, 5.19; 95% CI, 1.47-18.36; *P* = .01).

[v] (odds ratio, 5.6; 95% CI, 1.3-24.3; *P* = .02) eczema, 26%; no eczema, 4%; *P* = .04

in formula-fed infants with prolonged use greater than 6 months.[62] However, results differ between probiotic species.

In a randomised, double-blind, placebo-controlled trial, 112 pregnant women with a family history of allergic diseases received a once-daily supplement, either a mixture of *Bifidobacterium bifidum* BGN4, *B. lactis* AD011, and *Lactobacillus acidophilus* AD031, or placebo, starting 4-8 weeks before delivery and continuing 6 months post-delivery. The prevalence of eczema at 1 year in the probiotic group was significantly lower than in the placebo group (18.2% vs. 40.0%) and the cumulative incidence of eczema during the first 12 months was reduced significantly in probiotic group (36.4% vs. 62.9%). However, there was no significant difference in allergies between the groups.[63]

The probiotic *Lactobacallus rhamnosus* (HN001) might also reduce eczema risk. In an analysis of faecal samples from 650 infants, *L. rhamnosus* HN001, and *Bifidobacterium animalis lactis* HN019 supplementation resulted in a 50% reduced eczema risk in the HN001 probiotic group compared to placebo.[64]

In a double-blind, placebo-controlled study of 241 mother-infant pairs, mothers with allergic disease and atopic sensitization were randomly assigned to receive *Lactobacillus rhamnosus* LPR and *Bifidobacterium longum* BL999, *L. paracasei* ST11 and *B. longum* BL999, or placebo, beginning 2 months before delivery and during the first 2 months of breast-feeding. The risk of developing eczema during the first 24 months of life was significantly reduced in infants of mothers receiving probiotics[vi].[65]

In a double-blind, randomized, placebo-controlled trial, a mixture of the probiotics *Bifidobacterium bifidum, B. lactis,* and *Lactococcus lactis* (Ecologic® Panda) was administered prenatally and during the first 12 months after the birth of both the mother and child. This resulted in significantly lower rates of eczema at 3 months and lower cumulative eczema over 2 years, along with greater colonisation by Lc. lactis.[66]

Lactobacillus rhamnosus GG (LGG; 10 billion CFU per day) and 225 mg of inulin supplementation did not appear to reduce the incidence of eczema, asthma, or rhinitis in infants between 0 and 2 years of age.[67]

Similarly, a trial of *Bifidobacterium longum* and *Lactobacillus rhamnosus* supplemented cow's milk formula did not affect eczema or allergen sensitization in the first year of life in Asian infants at risk of allergic disease.[68]

[vi] LPR+BL999 (odds ratio [OR], 0.17; 95% CI, 0.08-0.35; $P < .001$) and ST11+BL999 (OR, 0.16; 95% CI, 0.08-0.35; $P < .001$).

Prebiotics

The faecal microbiota of formula-fed children supplemented prebiotic fibre is closer to that of breastfed children than infants receiving standard formula.[69]

Other gut-factors that influence the microbiome and eczema:

- Whether the birth is premature or full-term
- Mode of delivery: Caesarean vs vaginal birth
- Type of feeding: Formula vs breast-fed
- Antibiotic use in childhood
- Older siblings (those without older siblings have similar microbiome to caesarean)[70]

Full-term vaginal birth allows for the greatest transference of microbiota to the baby during birth. Breast milk also contains indigestible carbohydrates that encourage the population of the infants gut with health-promoting bacteria,[71, 72] and also contains bacteria transported to the mammary glands via the enteromammary pathway. Attempts have been made to mimic this pre- and probiotic activity of breast milk. Prebiotic supplementation added to formula increases the number of bifidobacteria to a level comparable to breastmilk and reduces the pathogenic bacteria *Clostridium dificile.*[73] Inulin (a prebiotic fibre) has demonstrated efficacy in increasing bifidobacteria in the gut.[74]

Prebiotic supplementation added to formula increases the number of bifidobacteria to a level comparable to breastmilk

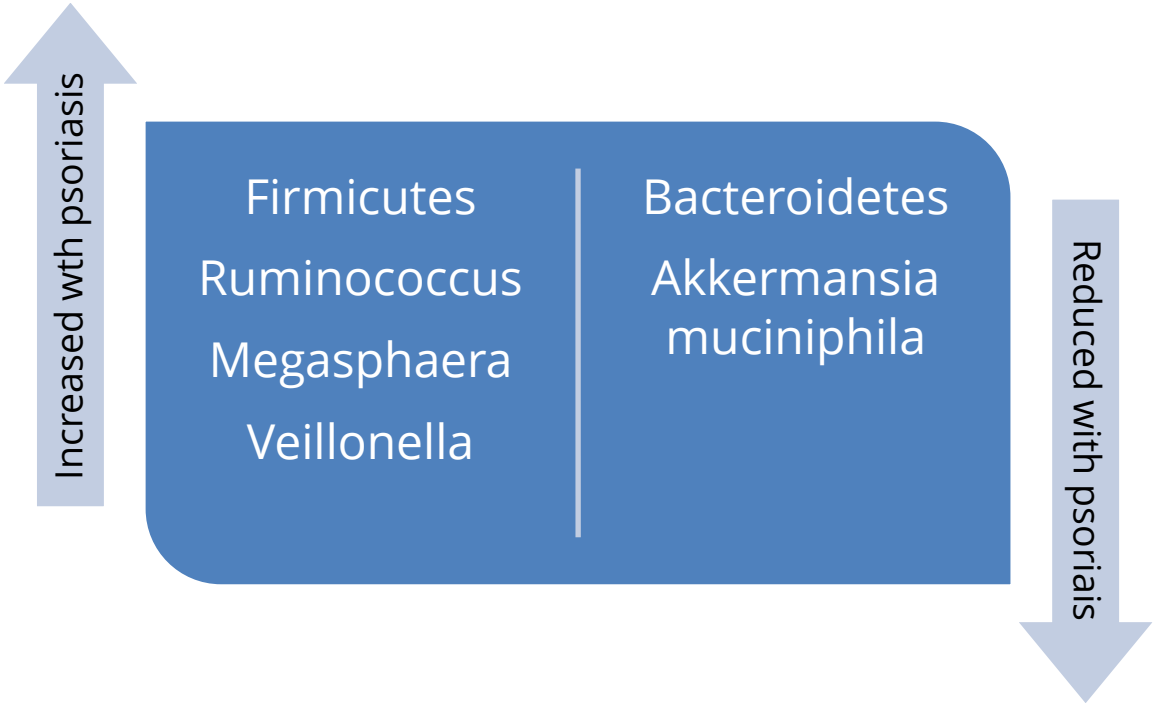
Gut health and psoriasis

The gut-skin axis is be related to the immune-inflammatory cascade. There is, for example, an increased prevalence of psoriasis and psoriatic arthritis with inflammatory bowel disease.[75] The gut microbiota of patients with psoriasis also shows reduced diversity,[76] and a distinct 'signature' compared to controls.[77] There is an increased abundance of *Firmicutes* and decreased *Bacteroidetes* with *Ruminococcus* and *Megasphaera* (phylum *Firmicutes*) the top-two genera abundant in psoriasis,[78] while *veillonella* in faecal microbiota showed a positive relationship with hs-CRP in blood.[79]

The abundance of *Akkermansia muciniphila* was also significantly reduced in patients with psoriasis and this bacteria is believed to have an important function in the pathogenesis of inflammation, inflammatory bowel diseases and obesity.[80]

In a case study, a 36-year-old male with plaque psoriasis and irritable bowel syndrome was given 2 faecal microbiota transplants 5 weeks apart. Following the

second treatment, his IBS was completely resolved with no adverse reactions observed.[81]



Probiotics likely to be of benefit to the skin

- Bifidobacterium bifidum
- B. longum
- B. lactis
- Lactobacillus acidophilus
- L. rhamnosus
- L. paracasei
- Lactococcus lactis

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