Introduction

Our modern day problem, essentially deficiencies or under exposure to dirt and animals, and overuse of antibiotics and C-section births, are creating imbalanced microbiotas and immune systems, leading to a host of autoimmune and inflammatory conditions [1,2].

The ancestral perspective is that not living like our hunter-gatherer ancestors has created an imbalance in our microbiota and thus our immune systems. And one of the items you often hear cited is that hunter-gatherers don’t have autoimmune or inflammatory conditions [3].

Briefly, the proposed solution, to enhance diversity of our microbiota, is to eat a lot of fiber and prebiotics, test and track our microbiota, be less hygienic, get more time in nature and exposure to dirt, soil, and animals [4]. However, this proposed solution is not without side effects. Too much fiber and prebiotics will make some people have more severe symptoms. Children who experience periodic exposures to animals may experience increased allergy. Episodic trips might not be enough to replicate the ancestral environment. Some research studies indicate that children who only go to a farm occasionally actually see inflammatory and allergic conditions worsen. Children might need a constant saturation of bacteria and fungi and not e.g. at age 6 one strong exposure from going to a farm, which might give the child’s immune system an offensive attack leading to a defensive response. Studies indicate that we have a limited window around age 3 through which our microbiota and thus our immune systems can form [5,6]. If individual did not evolve or form in a certain society, but have contact with that society later, e.g. around 30 years of age with hunter-gatherer diet or lifestyle, individual may have a harmful response.

Pitfalls of the Proposed Solution, Examples

Those with less than ideal gastrointestinal immune regulation may attack the resident microbiota or have difficulty regulating their microbiota and thus do better with a minimally fermentative diet with less fiber and prebiotics. Irritable bowel syndrome (IBS) and inflammatory bowel diseases (IBD: ulcerative colitis (UC) and Crohn's disease (CD)), are examples of these conditions [7].

Further, antibiotics (abx), administered earlier in life, increase the incidence of allergy and autoimmune diseases [8]. However, abx can also induce remission of inflammatory bowel disease and improve symptoms in adult IBS [9–12], and early administration of probiotics and prebiotics have greater protective effect [13]. For example in type I diabetes, administration of probiotics before 27 days was protective but after 27 days had no protective effect [14].

Hunter-gatherer Microbiota and Diet

Many studies of diet and microbiota of modern day hunter-gatherers represent only equatorial populations e.g. study of equatorial coprolites (fossilized stool remains) [15].
When populations farther away from the equator are studied, carbohydrate intake decreases, and protein and fat intake increases [16–19]. Study concluded that 73% of worldwide hunter-gatherer societies derived more than 50% of their substrates from animal foods [20]. This indicates that equatorial African diet may not increase quality and length of life in other populations than equatorial, and most hunter-gatherers do not eat diet high in carbohydrates and fiber. Especially, in IBS or IBD patients, high-prebiotic diet increases inflammatory bacteria and disease activity. Main objective of diet of these patients is to reduce symptoms, inflammation and control blood sugar, and then in healthy environment, feed healthy microbiota and starve symptom promoting microbiota. The whole ecosystem might not recalibrate itself with abundant prebiotics and fiber.

**Better Solutions**

Randomized controlled trial (RCT) of CD patients investigated high-FODMAP (Fermentable, Oligo-, Di-, Mono-saccharides and Polyols) and low-FODMAP diets. FODMAPs are mainly high prebiotic foods, mostly vegetables, some fruits [21]. Symptoms, in high-FODMAP diet crossover trial period, doubled in severity but relative abundance was higher for an anti-inflammatory bacterium, *Akkermansia muciniphila* [22]. This points to that, based on this study and my clinical experience, increasing anti-inflammatory bacteria with prebiotics might not have a clinical benefit to a patient [23].

**How Do We Assess if We Have a Problem in the Gut? Testing**

We have in clinic reliable tests for screening small intestinal bacterial overgrowth (SIBO), candida, ulcers or IBD. However, assays of phylogenetic maps of microbiota are in academic research, not in clinical use. Studies have shown that microbiota oscillates from month to month and even diurnally within the day [24–26]. Secondly, definition of healthy microbiota is not yet specified. *Methanobrevibacter smithii* has a very high colonization density in Africans. Study implies that *M. smithii* helps Africans probably thrive on the food supply they have access to [27]. However, in SIBO patients, this archaea causes constipation, bloating and may cause weight gain, high blood sugar, and high cholesterol in societies not living in equatorial Africa [28,29]. Another hunter-gatherer bacterium *Prevotella copri* 18205, depending on the person, can worsen rheumatoid arthritis or improve blood sugar [30].

Further, commercial microbiota assays study only colonic luminal microbiota. Small intestine, absent in assays, represents over 50% of gastrointestinal (GI) tract, 90% of caloric absorption, and is the main area that programs immune system with the largest density of immune cells [31,32]. Next, in randomized intervention, women with obesity were treated with prebiotics. Study reported an improvement in blood sugar but no change in weight. They also tracked microbiota. However, the blood sugar improvements did not correlate with changes in the microbiota [33]. This study infers that microbiota tests are important, and clinician’s participation in gathering data is needed but clinical utility is still in future.

**How to Create a Healthy Environment for a Healthy Microbiota**
Clinicians aim is to optimize the patient's environment for healthy microbiota. I start with diet and lifestyle. Microbiota supports, in a form of dietary supplements, are added for symptom relief and faster recovery to optimal health for the individual. A microbiota reset with herbal anti-microbials, antibiotics, or liquid elemental or semi-elemental diets are used based on symptom severity. The aim is to have more flexibility in the diet by gradually increasing FODMAPs and decreasing supplements. Final step would be considering to add in some supplemental fiber, prebiotics, or resistant starch without causing side effects.

Specifically, the diets used for gastrointestinal conditions like IBS, IBD, GERD, and reflux are low carbohydrate, moderate-to-low carbohydrate paleo, autoimmune paleo and low FODMAP and/or Specific Carbohydrate Diet. In addition, these diets have been shown with highest quality and clinically relevant research methods to work better than the more traditional higher-carbohydrate, higher-fiber diets for metabolic conditions like diabetes, heart disease [34–42] (Figure).

Figure. The evidence pyramid shows the least clinically relevant at the bottom and the most clinically relevant at the top [43].

Expanding lifestyle modifications for increasing microbiota diversity, recommendation is to connect with nature like walking in a forest or by the sea. Other examples are using hand washing instead of dishwashing machine, less abx for children, managing stress, sleep on a natural circadian rhythm, and the appropriate amount of exercise.

Fiber in colorectal cancer prevention
The overall impact of supplemental fiber, including resistant starch, on colorectal cancer risk appears to be minimal at best. Most of the data show no positive impact [44–49].

Some studies of dietary fiber show benefit but an equal number of studies show no effect in systematic reviews or meta-analyses including thousands or tens of thousands of people [50–66].

Conclusion

The evidence points to optimal health at broadest diet tolerated by the individual. Diet may be somewhere between low and high carbohydrate and fiber spectrum and can change overtime. Both low and high carbohydrate and fiber diets are associated with increasing health and quality of life of individual. Future research will be conducted to test the hypotheses that wide variety of diverse diets can be a basis for health promoting microbiota in healthy host.

Disclosure

No conflict of interest.

References


