

Take home messages on the microbiome

The MB is the fastest growing area of research and research funding. It will dominate biomedical research for years to come and will reveal how complex human biology really is. It will also change how we use drugs and how we relate to our food. It will change how we do research on human subjects and how we interpret new findings. It will not be possible to give a full appreciation of the MB in a short amount of time.

1. The human body has a very close relationship with bacteria and other microbes.
 - 600 species on the skin
 - 800 species in the mouth
 - 10,000 species in the large intestine
 - few if any in the stomach, but maybe one (*H. pylori*)
2. All animals and plants probably have mutualisms with microbes.
 - termites can't digest wood well and use microbes in their stomach
 - cows and ruminants don't digest grass at all, but bacteria ferment the materials
 - all nutrients come from products made by the bacteria
3. Evolutionarily, if env. stress results in death, then adaptations are changes that reduce stress. If a mutualism reduces stress, then the mutualism is an adaptation. Forming a mutualism with bacteria is probably much easier than forming one through random mutation. Therefore, we should expect that beneficial bacteria are common.
4. Why do we tolerate so many bacteria in our bodies? Is it because we just can't keep them out? Or is it not accidental and the presence of the bacteria (some) is beneficial in some way? We eat plants. The only way to digest plants is to have bacteria. So, our ability to eat many kinds of plants is probably because of our mutualisms with bacteria.
5. About 80 years ago, human society went through a great transformation. Technology provided us with very important changes to health and lifestyle all at the same time.
 - Artificial pesticides were introduced in 1947 with DDT
 - *Quickly became ubiquitous and we assumed no harm to humans.
 - Artificial fertilizers were introduced at the same time from WWII weapons plants
 - *Agricultural production exploded and changed in scope and volume
 - Antibiotics were introduced in 1945 and became ubiquitous
 - *Miracle drugs were everywhere and used indiscriminately
 - Meat production became a factory process
 - *Took advantage of pesticides, fertilizers and drugs all at once.
6. From ~1900, the US has transitioned from a culture dominated by early death and infectious disease. Vaccines changed that and by 1945, we became an age-dominated society. Causes of death went from pneumonia, flu, and TB to heart disease, cardio-vascular, and cancer and average age at death from the 40s to the 80s. However, we have a very long-standing dislike of bacteria and we believe that good bacteria (mostly) are dead bacteria.

7. In the past 50+ years, we have seen the emergence of new and novel forms of disease and they do not afflict only the elderly. They are now epidemic in the US and elsewhere and they include: autism, obesity, diabetes, asthma, allergies, ADHD, lupus, rheumatoid arthritis, colitis, coeliac disease/gluten sensitivity, irritable bowel syndrome, multiple sclerosis, Alzheimer's disease, Parkinson's disease, ALS, psoriasis. Many of these are autoimmune diseases. Is this a coincidence? Very unlikely.

8. We evolved in an environment that did not include artificial chemicals and drugs. We have always used drugs, but they were compounds found in plants. All early medicine was plant-based. As we have developed technologically, we have removed ourselves from close contact with the environment and plant-based compounds and we now rely on artificial chemicals or chemicals that have been divorced from their plant context.

9. Remember plant ecology: all of the flavors and smells, all of the alkaloids, phenols, and terpenes were adaptations to herbivory. Those compounds kill insects, bacteria, fungi, and deter large animals from eating the plants. Those same compounds are what we find tasty and medicinally useful, and form the basis of our regional and cultural cuisines. This is not random. Those compounds have benefits for humans and those benefits are related to the toxicity of the chemicals.

10. When we eat plants, we are eating for nutrition and we are eating for health. When we do not eat plants, we do not get those benefits. The new normal is to substitute artificial and purified substances for the natural and complex substances. We assume that the most active chemical in a plant is the important one, but we ignore the context of that chemical. The result is an unbalanced response in term of the bodies biochemistry.

11. If we assume that the presence of 30 trillion bacteria of about 1000 species in our colon is NOT accidental and is not a random assemblage, then we have to assume that there are benefits to having the microbiome.

- Your MB is similar to the people you live with, not very similar to other people.
- Your MB is highly dynamic and resilient. It can recover from damage.
- Your MB is highly responsive to the food you eat and the chemicals you consume.
- Your MB is badly damaged by antibiotics, perhaps irreversibly

12. The presence of the MB creates your immune system and keeps it strong. In part because the body is constantly on alert because of the bacteria. However, some bacteria act as part of the immune system and destroy pathogens. This occurs mostly in the lining of the colon.

13. The heavy use of antibiotics seems to lead to autoimmune and developmental diseases and conditions. Antibiotics are used on people and used to make all of our meat.

14. We have no idea what the interactions might be between the MB and pesticides, drugs, plant foods, chronic exposure, low quality food, hormonal responses, genetics, trauma. We do not know how eating animals that were raised on antibiotics can affect the eater. We do know that germ-free mice develop differently and do not have an immune system. And we know that when they are introduced to a microbiome they develop an immune system.

15. How do we get the microbiome? When a baby is born, it is bathed in fluids from the mother's birth canal and the fluid is full of beneficial bacteria. Some get in the mouth and move to the gut and they are the first to arrive. Mother's milk is full of beneficial bacteria which also move to the gut. The baby also gets bacteria from mother's digestive system by facing backwards at birth. In other words, the mother provides the first part of the microbiome and it appears to be essential for the baby to begin developing a mature digestive system. Babies born by C-section and those fed baby formula do not get the same initial bacteria and their bacteria never quite match those that are born and fed naturally. They also may have more health issues later in life.

17. The MB develops in complexity as solid food is eaten and by age 3, it is about the same as an adult MB. However, nearly all children receive regular doses of antibiotics and these drugs are lethal to bacteria in the entire body regardless of their activity. All antibiotics given for "infection" are broad-spectrum and are intended to kill as many bacteria as possible. It is estimated that every American child has received 17 courses of antibiotics by age 20.

18. There is evidence that once you have taken antibiotics, your MB never fully recovers. Serial use of AB results in a depleted MB and is closely linked to development of health issues, especially in the digestive system. The lining of the large intestine is covered with protective bacteria. When they are killed, pathogens can get through to the lining and the interior. These cause inflammation and prevent the immune responses that normally would occur here. They may also eventually result in cancers.

19. The recovery from antibiotics is credited to the appendix which is a refuge for bacteria. Previously it was considered useless and even dangerous because of the bacteria. As of 2018, it is highly recommended that the appendix NOT be removed unless necessary. This is the source for bacteria to recolonize the gut after trauma like antibiotics.

20. When the gut is way out of balance and not able to recover quickly, other non-beneficial bacteria can take over. One example is *Clostridium difficile* (*C. diff.*). It causes cramping, diarrhea, loss of appetite and weight. The usual treatment is a series of antibiotics (which probably caused the problem) and the usual response is no cure.

21. However, there is one cure that has >90% success: fecal transplant. That is, recolonizing the gut with the MB from a healthy person. There is a high demand for fecal donors and one very big problem: finding a healthy MB is unlikely in people that have taken antibiotics in recent years.

22. For a healthy microbiome, we must eat plant material (cellulose) and of different kinds. Each kind of bacteria feeds on different parts and kinds of plant cellulose, so we need a diversity of plants to help maintain a diversity of bacteria. Chemicals that kill bacteria also kill our microbiome.

23. Your microbiome is full of bacteria, but exposure to your own bacteria **will not** make you sick. However, other people's microbiome has other types of bacteria and might make you sick.

The people you live with share their microbiome with you and you with them, and your microbiomes will become more and more similar, and less and less dangerous.

24. Children share microbiomes and this is one way they add more bacteria to their microbiomes. Teachers and those working with children are exposed to the microbiomes of many children and the families of those children. This often results in sicknesses among new teachers, but eventually the teachers' immune systems are strengthened because their microbiomes become more diverse.

25. The microbiome inside us depends on the microbiomes outside of us for diversity and for information about the world. The movement of bacteria into our microbiome is the movement of information and possibly of beneficial mutualists. The more depleted our external microbiome is, the less new information we get about the outside world. The more antibiotic resistant bacteria there are in the world, the more dangerous it becomes for us also.

26. The fact that we have a microbiome that depends on us for food, but that we depend on for our health, means that we are not truly individuals, but small mobile ecosystems. When we eat, we must eat for our bodies (protein, fats, carbs), but we must also eat for the microbiome (fresh plant materials). We should worry less about our calories because they are super-abundant and worry more about the quality of foods we are giving the microbiome. In some ways, carb/fat/protein quality is not particularly important; the quality of plant materials for the microbiome is critically important.

27. The importance of the MB is poorly understood and how directly and indirectly it affects human health will take decades to figure out. That also means that the damage we have done to the MB with our artificial environment will haunt us for at least 2-3 generations unless each person begins to take control of their diet and health and becomes as educated as possible about the MB.

28. Caveats

- We must think of ourselves as an ecosystem. We don't eat for a person, but for our MB.
- The MB is likely responding to our environment, not just to individual factors.
- The health of our environment affects the health of the MB.
- The MB is bacteria and can adapt to almost anything.
- It is in the best interest of the MB to keep you alive. It is in your best interest to keep the MB as diverse as possible.