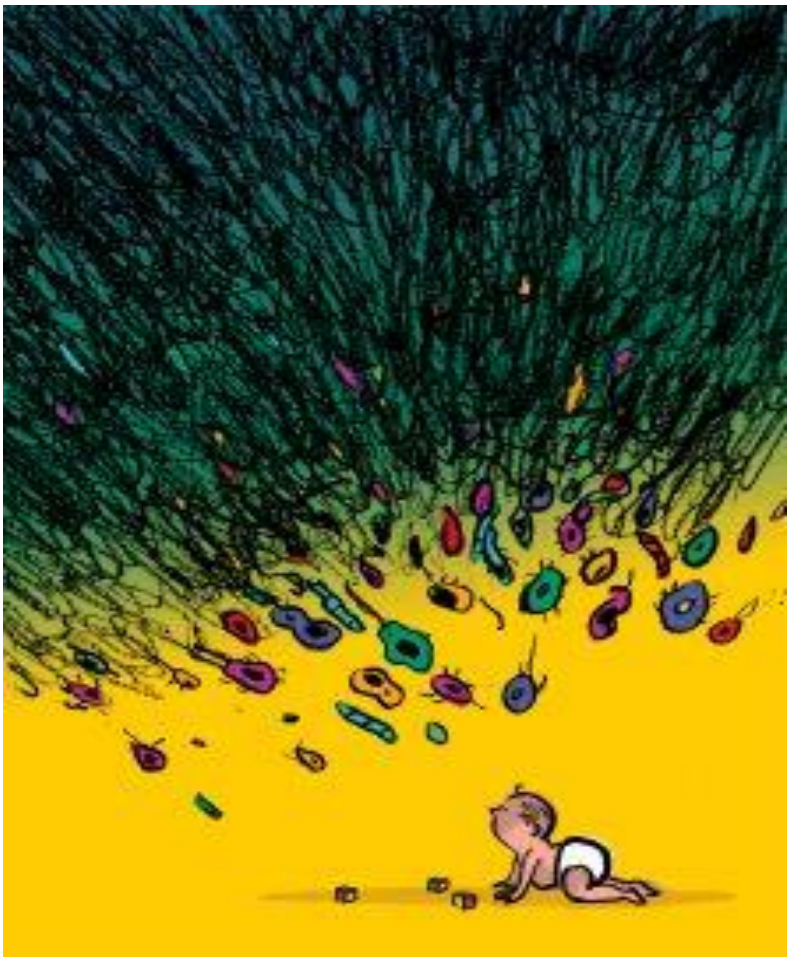
# Our early microbome

# Getting to Know You:
# Acquisition and Early Evolution of Our Microbiomes

## *Mum: where does my microbiome come from?*



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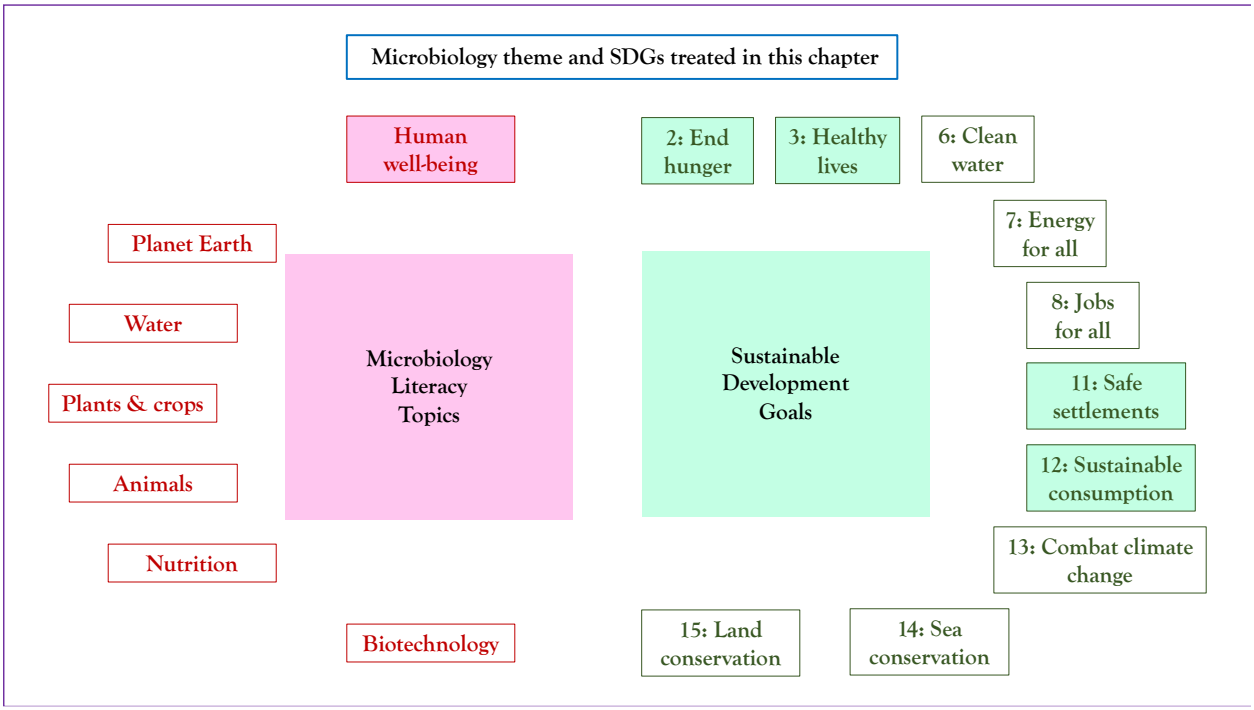
# Acquisition and Early Evolution of Our Microbiomes

## Storyline

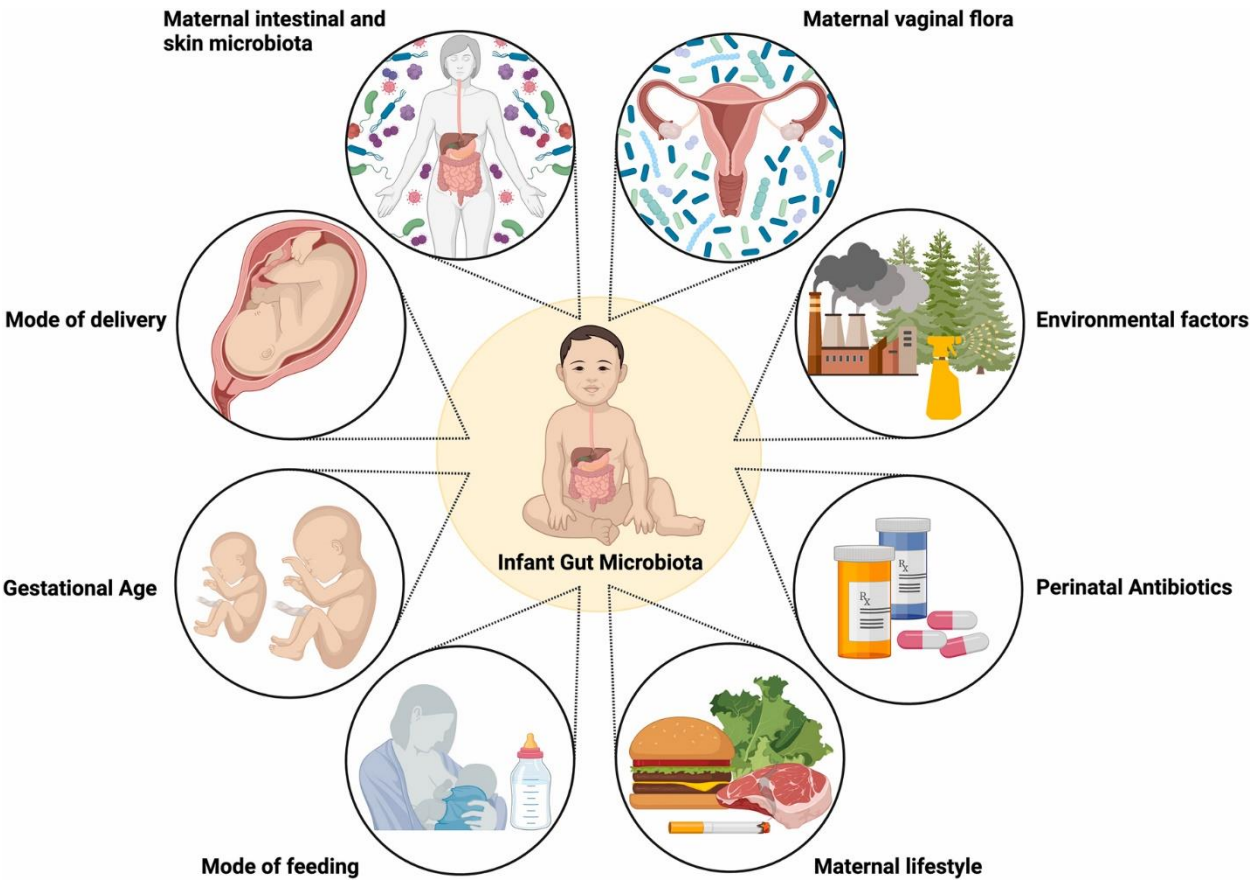
The microbiome is an essential part of all organisms, whether in the gut, mouth, or elsewhere in or on the body. Acquisition of the microbiome – establishment of bacteria, fungi, and other microorganisms in the microbial community – initially occurs immediately following birth. Prior to birth, the fetus – the unborn developing baby – grows in the womb, inside its mother's belly. The placenta, which keeps the baby safe and fed, is typically thought to be **sterile**, free of microbes. At birth, the newborn is exposed to the birth canal or, in a cesarean section, the mother's skin as well as the general environment - the hospital, the parents, and anything else it meets. These first contacts expose the newborn to diverse microbes that begin microbial colonization. Shortly after birth, the newborn is fed and may be given immunizations, both of which also expose the baby to colonizing microbes and microbial products that interact with the baby's developing immune system. As the baby grows, it comes into contact with more and more microbe-populated people, animals, environments, stimuli, and foods and, through all of these exposures, the body's microbiome begins to take shape. The composition of the infant microbiome is associated with **immune function** (how well our bodies fight off disease) and can affect future development and health outcomes.

## The Microbiology and Societal Context

*The microbiology:* microbiome; microbiome diversity; immune system development in infants. *Sustainability issues:* end hunger; healthy lives; environmental pollution.



## Acquisition and Early Evolution of Our Microbiomes: The Microbiology




Factors influencing the development of the infant microbiome and immune system. A variety of factors exert important influences on the neonatal microbiome including mode of delivery, mode of feeding, perinatal exposure to antibiotics, maternal genitourinary and intestinal microbiota, maternal skin microbiota, maternal comorbidities, and genetics. Created with BioRender.com. Hill et al. 2015 Journal of Laboratory Medicine (https://doi.org/10.1515/labmed-2021-0131). This work is licensed under the Creative Commons Attribution 4.0 International License.

1. ***Pre-pregnancy and infant microbiome acquisition.*** A woman's condition before she becomes pregnant can affect her own microbiome as well as her pregnancy outcome. Overweight women and those who suffer from inflammatory bowel disease (IBD) and other autoimmune conditions begin their pregnancies with a **dysbiotic** (unhealthy or imbalanced) microbiome. These conditions, and their associated microbial dysbiosis, can lead to pregnancy complications including excessive weight gain (cases of obesity). These conditions can also affect the early microbial community of the newborn. One study found that the reduced diversity of bacteria associated with IBD was mirrored in newborns.

2. ***Pregnancy and infant microbiome acquisition.*** A woman's microbiome, health, and eating behaviors during pregnancy can all affect both her and her future child's microbial community.

Some studies directly associated certain bacteria found in the mother's gut during pregnancy (or missing from it) with newborn health, allergy sensitivity, and overall development. Another study found significant differences in newborn microbiomes of mothers who ate different diets during pregnancy, even 18 months after birth.

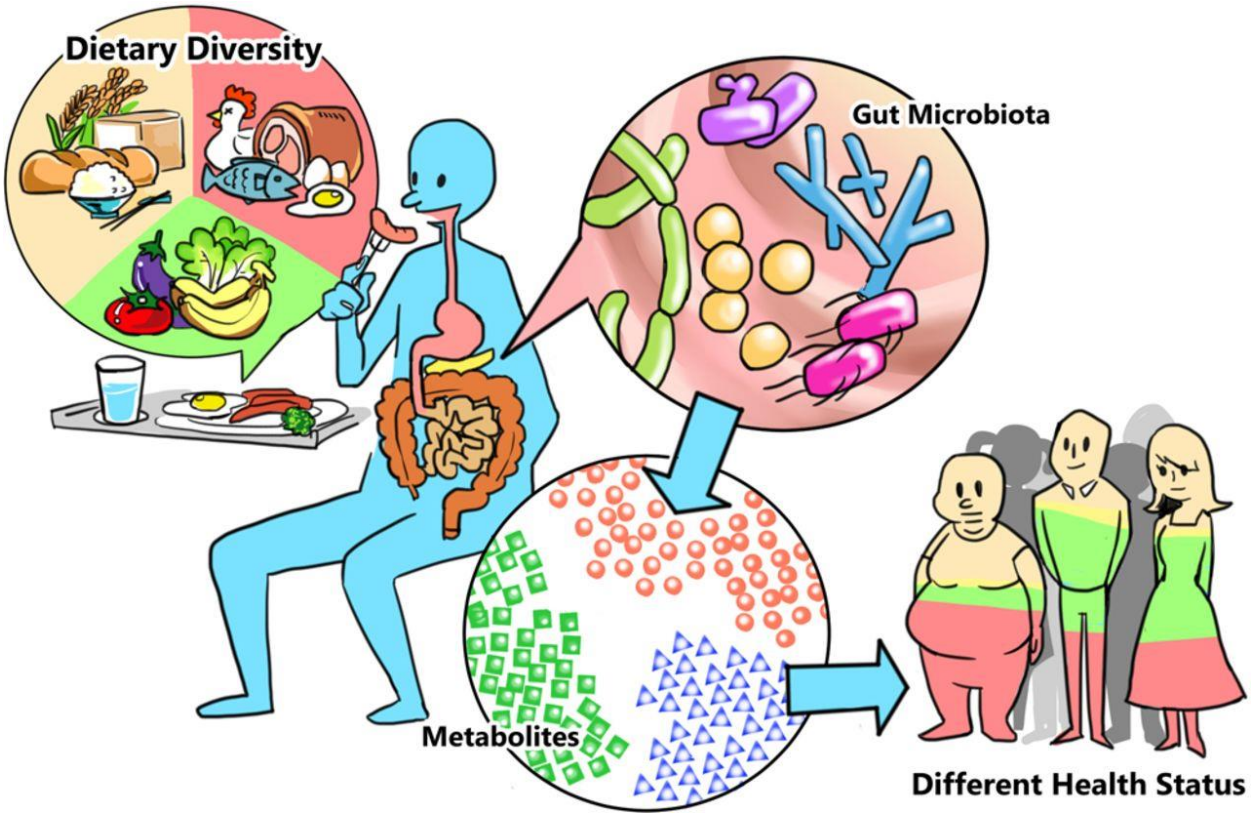
Further, pregnancy complications can also affect microbiome in newborns. For example, babies born to women who develop **gestational diabetes mellitus** (GDM, a form of glucose intolerance that develops for the first-time during pregnancy) have significantly different microbial communities, which are less **diverse** (have fewer unique bacteria) in their **meconium** (first bowel movement) compared to those of newborns whose mothers did not develop GDM. Additionally, women who do not suffer from excessive gestational weight gain passed significantly more 'leanness-associated microbes' to their offspring. This difference, though, may only persist for a short period after birth.

3. ***Birth and infant microbiome acquisition.*** A baby can enter the world – be delivered – vaginally or via cesarean section. Sometimes births are planned - induced or with a scheduled cesarean section - and sometimes they come as a surprise. Some require interventions, including antibiotics. Births can take place in hospitals, at home, at birthing centers, and even on the way to one of these places. Each of these factors not only affects the mother and her newborn directly, but also the colonization of the newborn's microbial community. There is also evidence that birth mode can have long-term health implications. In general, babies born vaginally have microbiome similar to those of their mothers' vaginal and rectal microbiome, whereas the microbiome of babies born via cesarean section are more similar to the hospital's environmental microbiome signature and their mother's skin microbiome. Effects of birth on the microbiome are present the first time a baby poops (in his **meconium**), in the weeks following his birth, and even later in life, when it reaches seven years old and beyond.

When a baby is born – near its due date or prematurely – also affects its microbiome. Premature babies ("preemies") often spend several weeks in a sterile neonatal unit, often inside incubators. They may be too small to breastfeed or drink from a bottle and may therefore be fed through a feeding tube. Their diets might also be different. Some preemies drink their mother's milk, some drink formula, and some drink pasteurized (sterilized) donor milk. All of these factors, taken together, reduce the numbers and types of bacteria to which preemies are exposed. Studies have also shown that even after preemies leave the neonatal care unit, it takes longer for their microbiomes to stabilize (Section 5, below).

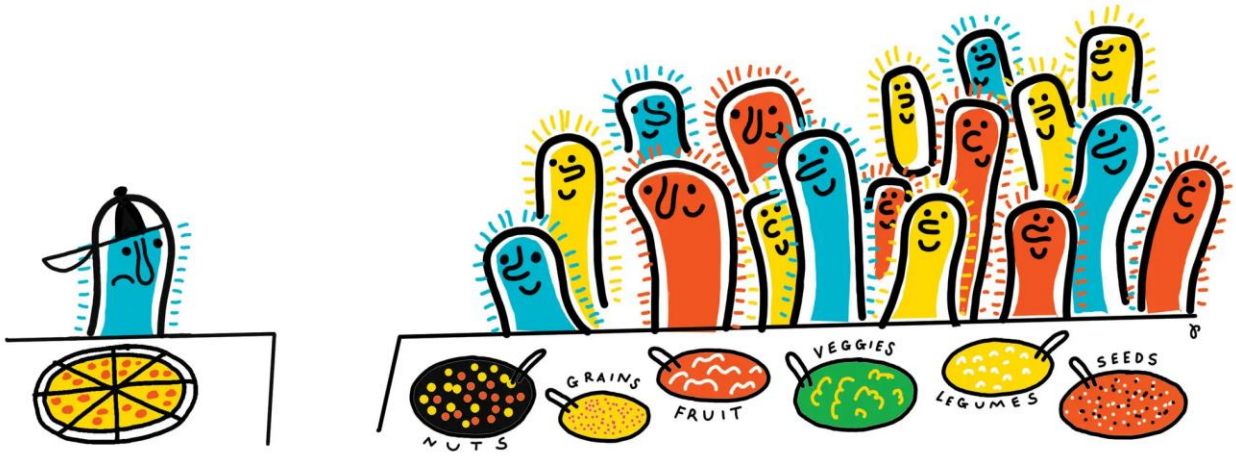
4. ***The first days of life and microbiome acquisition.*** In the first few days of life, the newborn is exposed to many new things. It is in a new environment, no longer protected by the placenta. It begins to eat (drink) - either breastmilk or formula. It may receive vaccines or other medical treatments. It is checked by doctors and hugged and kissed by loving parents, grandparents, aunts and uncles. Each of these interactions exposes it to different microbes, some of which will colonize the various surfaces of its body (mouth, gut, skin). For example, babies fed formula have microbiomes more similar to those of adults, whereas babies fed breast milk have unique microbial signatures. A number of studies have also demonstrated that there are long-term differences in both microbial communities and health outcomes among breastfed and formula-fed babies. Consequently, researchers are searching for potential formula additives that can be used to inoculate

formula-fed babies with health-associated bacteria linked with breastfeeding or encourage their colonization in the gut.




Lyu and Hsu 2018 mSystems (https://doi.org/10.1128/mSystems.00187-17). This work is licensed under the Creative Commons Attribution 4.0 International License.

5. ***The first years of life and microbiome acquisition.*** The microbial communities of infants and toddlers are constantly changing. Just like it takes babies time to settle into life outside of the womb (they cry a lot, eat at night, and sleep during the day), it takes the microbial community time to stabilize. In early life, a baby's gut microbiome is less diverse than that of its parents. Babies primarily drink milk or formula, and therefore they don't need the many different bacteria that break down complex diets. In babies, the microbiome is composed mainly of bacteria that can break down sugars found in milk. As a baby gets older and begins eating solid foods, the bacterial community in its gut changes, becoming more similar to that of adults. Newly incorporated microbial species can utilize carbohydrates, synthesize important **metabolites** (vitamins, antioxidants and other by-products of bacterial metabolism), and break down toxins and harmful substances consumed or produced by the body. Just as a toddler's diet becomes more similar to an adult's diet as it grows up, its microbial community also becomes more similar. In general, received wisdom is that a healthy microbiome is a diverse microbiome, so continual exposure to sources of healthy microbes in order to maintain diversity is desirable.




The diet we eat directly affects our microbiome. If we only eat a single food, here it's pizza, we will have less diversity than if we eat a balanced diet. A healthy diet results in a healthy microbiome. Image by Phil Marken, reproduced with permission.

## Relevance for Sustainable Development Goals and Grand Challenges

- **Goal 2. End hunger and malnutrition.** The foods we feed our newborns, infants, toddlers, and children have profound effects on their microbiome. Babies fed breast milk have significantly different microbial profiles from those fed formula, and the implications of these differences are not fully understood. Researchers are working hard to identify important bacteria associated with microbiomes from breastfed but not formula-fed infants, with the goal of developing supplements to formulas.

Furthermore, the nutritious content and compositions of foods fed to infants and toddlers can have lasting effects on their microbiome and health. **Fiber**-rich diets - those full of fruits and vegetables - provide food for important gut bacteria. When parents or caretakers cannot provide these foods to their children, often due to cost, important bacteria may be excluded from the microbial community with negative health impacts.

- **Goal 3. Improve health and reduce preventable disease and premature deaths.** The microbiome not only helps to break down the food we eat. It is also implicated in immune function, behavior, and overall well-being). If a newborn does not maintain a healthy, balanced microbiome, it may face negative health outcomes including obesity, food allergy, and susceptibility to infection and disease. In addition to poor diet, administration of antibiotics can suppress healthy bacteria, causing dysbiosis. Striking the balance between antibiotic administration, diet counseling, and probiotic consumption is important to ensure good gut health and good overall health.
- **Goal 11. Make cities inclusive, safe, resilient and sustainable.** Bacteria are incorporated into and add to the diversity of microbiomes through a number of pathways. While diet is central, exposure to soil, plants, animals, etc. is very relevant. Fresh air is also important and taking infants out of the home for walks and play is crucial, as indeed are the green spaces needed for this, particularly in urban settings.

- **Goal 12. Ensure sustainable consumption and production patterns.** In exploring their environments, babies instinctively put things in their mouths - keys, toys, and anything else they can get their hands on. As soon as they start to crawl, climb, and toddle, they begin eating sand, dirt and bugs and giving their cats and dogs kisses. While this is an important means of acquiring microbial diversity, it is also a route to ingest environmental pollutants. Exposure to harmful chemicals and materials at any age can have direct health implications, but for young children, the direct and indirect consequences can be even more serious. In addition to any direct toxic action such pollutants may have on the child, they can impact microbial communities and reduce their diversity. Air and environmental pollution exposure in early childhood have been found to affect both microbiome and health outcomes later in life. These findings highlight the importance of monitoring for pollutants where infants spend time and making sure they are not exposed.

## Potential Implications for Decisions

1. ***Personal***
    a. Maternal behavior during pregnancy: diet, medical interventions
    b. Type of birth: home vs hospital, vaginal vs planned cesarean, with or without antibiotics
    c. Vaccination schedule
    d. Exposure to other people, pets, environments in first days or weeks
    e. Food type: breast milk, formula, mix; introduction of solids
    f. Use of medicines or other medical interventions: in mother or infant

2. ***Community policies***
    a. Providing education and information campaigns on the topic of healthy microbiomes, including instructional videos on official websites
    b. Providing green spaces and play areas and ensuring that they are safe and clean
    c. Monitoring local air and water quality

3. ***National policies and recommendations***
    a. Type of birth: cost-benefit of vaginal delivery, induction, etc.
    b. Vaccination recommendations
    c. Newborn care recommendations
    d. Early-childhood diet recommendations
    e. Recommendations regarding antibiotic use under the age of two

## Pupil Participation

1. ***Class discussion of why it is important to have a "healthy" microbial community as an infant and how to foster one***
    a. Immediate health implications
    b. Future developmental implications
    c. Future health implications
    d. Diet considerations, medical interventions, environmental exposures

2. ***Pupil stakeholder awareness***
    a. How may inequality in food accessibility ("ending hunger") affect microbiome acquisition?
    b. How can inequality in living conditions ("healthy environments") affect microbiome acquisition?
    c. How do you balance short-term (e.g., acute sickness) and long-term (e.g. effects of antibiotics) health factors in decision regarding medical care ("healthy lives")?

## The Evidence Base, Further Reading and Teaching Aids

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## Glossary

**Colonization**: the action of establishment in a given habitat - here referring to establishment of bacteria, fungi, viruses, or other microbes in different body areas
**Diversity**: How unique the microbes in the microbiome are - how many unique microbes there are and how similar or different they are from one another
**Fiber**: parts of plants that we, humans, cannot digest, but which serve as important energy sources for many beneficial bacteria
**Gestational diabetes mellitus (GDM):** a form of glucose intolerance that develops for the first time during pregnancy

**Immune function**: the ability of the body to fight off diseases
**Meconium**: the first bowel movement(s) (poop) that a newborn passes
**Metabolites**: vitamins, antioxidants and other by-products of metabolism
**Sterile**: an area without live microbes