Dental Insights — What is the oral microbiome, and how does it change during disease?

1. How do we get our oral microbiome?

What is the microbiome?
All life forms appeared in the presence of bacteria. We have to live together with them. Humans have 37% of the same genome as bacteria.
There are both beneficial, neutral and pathogenic bacteria.
Microbiome = Microbiota + Theatre of Activity.
The Human Microbiome Project: A healthy person has a human genome 23.000 genes and human microbiome 1 mio+ genes.

How do we aquire our individual microbiome?
Aquiring normal human microbiome happens:
1. Pre-natal exposure
2. Exposure during birth
3. Post-natal exposure

Aagard et al 2014 study found microbes in healthy placentas, and out of all the body's microbes the placenta's microbes were most similar to microbes on the tongue and the tonsils.

Pregnant women offer suffer from pregnancy gingivitis, which opens their blood vessels and allows oral bacteria to enter the bloodstream. The placenta organ is very active during pregnancy and will attract the mobile microbes.

The placenta is a barrier to protect the fetus from infection with microbes, and this way it can mitigate communication between fetal cells and maternal cells. Lymphatic cells are going away and coming back from the placenta, and maybe this way it will create antigenic presenting of the maternal cells to the fetal cells. Maybe this way the placenta will create the newborn baby's immune system will know which microbes are good bacteria from the mother, and which are bad foreign bacteria (regonizing a "friend" from a "foe").

Many studies have found microorganisms in the placenta, including oral taxa.
Mishra et al 2021 found bacteria in all 2. trimester fetal organs and the fetal memory T-cells already had information from these bacteria.

Post-natal babies get their microbiome from breastfeeding, from their siblings, from the mother (fx sharing the pacifier), from the environment and from food.

Breastfeeding allows microbes (mostly bifidobacteria) from the mom's gut to migrate to the breast, where they are released in the breastmilk during the first weeks of lactating. Babies need those bacteria to break down the oligosaccharides in the breastmilk.

When does our microbiome change to a more pathologic state?
Exposure to healthy bacteria is not enough, we have to provide the right conditions to make them stay.

Unfortunately, we are doing many wrong things to lose the diversity of our microbiome, fx fast processed food, physical inactivity, antiseptic mouthwash and soap, medicine creating antibiotic resistance and killing the beneficial microbiome.

We should treat our microbiome with care, because it does many important functions for us. During different life stages, the oral microbiome and ecosystem will change (fx no teeth, teeth, braces, dentures etc.). The oral microbiome have to be resiliant to withstand different stressors.

NO2 (nitric oxide) dilates our blood vessels (important for normal blood pressure). To get NO2 we have to eat healthy foods to produce NO2. However, we need oral bacteria to break down nitrate to create nitrite to produce nitric oxide. The oral bacteria breaks down nitrate, after it has been swalloed to the stomach, gone through the intestines, gone into our blood stream, back into the salivary glands, and hours later oral bacteria can reduce nitrate into nitrite.

Senkus and Crowe-White 2020: Antibacterial mouthrinse influence the enterosalivary pathway and blood pressure by reducing the concentrations of salivary and plasma nitrite, and thereby rises blood pressure.

The human is a ”holobiont”, we need to think ”one health” and a holistic approach.
The oral microbiome can be either in a saccharolytic state (breaking down sugars, early dysbiosis for caries), neutral (eubiosis), or proteolytic state (breaking down proteins, early dysbiosis for periodontitis).
A healthy oral ecosystem: a balance between all its components.

2. Stability of the oral microbiome in health and disease

David, L.A. et al 2015. The oral microbiome within an individual is very stable compared to the gut. Fx living abroad or having diarrhea very much affects the gut microbiome composition, but not the salivary microbiome. The gut microbiome is very flexible and is significantly influenced by the diet. Diet has very little effect on the oral microbiome, unless the person excessively and frequently eats refined carbohydrates. Gastric tube diet administration does not influence the oral microbiome composition.

Saliva is the primary nutrional source for supragingival bacteria, while gingival crevicular fluid is important nutrional source for the subgingival organisms in disease.
Salivary mucins are a major nutrition source for oral bacteria. Salivary mucins are complex structures with a very high molecular weight, and are heavily glycosylated (90%), which restricts access to the protein core. Bacteria need many different ”breaking down tools”, enzymes, to break down a salivary mucin. The bacteria in the microbial community work together and act cooperatively to break down the complex salivary mucin.

They are dependent on each other to carry out different tasks in the oral microbiome. It doesn’t matter which bacteria carrys out a certain function, as long as the function itself is carried out.
Study ”The evolution and changing ecology of the African hominid oral microbiome”: We have a core oral microbiome that has been stable during the last 40 mio years in our evolution, and that we share with several monkey species.

During disease the environment changes significantly.
Inflammation brings a rich source of readily digestible proteins (no glycosylation) and micronutrients such as iron/heme, as well as a range of innate and aqcuired immune defence systems: AMPs, complement, serum immunoglobulins. A different set of microbial cooperative funtions will be needed.

The oral microbiome has health-associated species (core species), and periodontal disease associated species.

Periodontal disease creates and is created by a significant activity shift and change microbial community composition.

Is the microbiology driving the disease, or is the disease driving the microbiology? BOTH!
Many experimental studies cannot be done in humans, but are done in mice instead. The mouse oral microbiome has been established.

Mice that are challenged with P. gingivalis periodontal disease develops long term bone loss compared to the control group. Periodontal disease changes the metabolism dramatically.
When the oral microbiome with P. gingivalis is transferred from the diseased mouse to the germ-free mouse, the germ-free mouse develops the disease too!

3. The "good guys" in the oral microbiome: are there health-associated species?

Oral Microbiome Lab and Fisabio Foundation.

The best biomarkers for gum disease is still Socransky's red bacteria complex:
* P. gingivalis
* T. forsythia
* T. denticola

In healthy gum pockets there are under 1% pathogenic bacteria. But as pocket depth increases, the healthy bacteria disappear, and the pathogenic bacteria increase dramatically. Pathogenic bacteria only increase when the ecosystem becomes dysbiotic.

Prebiotics can help shift the ecosystem back towards a healthy balance.
Healthy gums consists mostly of aerobe/facultative aerobe bacteria.
Brushing teeth and tongue favors the oxygen-loving aerobe bacteria species.
Nitrate-reducing bacteria decrease in periodontitis.
Individuals with gum disease have a chronic deficit in available nitrate-oxide, which can impact our systemic health.

Non-surgical periodontal therapy modifies the subgingival microbiome.
Nitrate-nitrite-nitric oxide pathway: fx drink beetroot juice, and 1 hour later NO2 can be measured in saliva = good nitrate reclycing.

Antiseptic mouthwash kills oral bacteria and creates poor NO2 reclycing.
Rothia bacteria have enzymes that reduce nitrate to nitrite and nitric oxide.
Stric anaerobe bacteria are very sensitive to nitric oxide and may die from it.

Nitrate is present in green leafy vegetables, beet root, broccoli etc. After ingestion nitrate peaks i saliva after ½-4 hours, and nitrite peaks in saliva after 5-9 hours. After 9 hours nitrate and nitrite is used up by the oral bacteria, and ammonia has been created from the nitrate and nitrite.
Ammonia buffers the pH, which lowers the risk of having cavities.

Health-associated subgingival bacteria has potential benefits:
1) Anti-microbial (production of bacteriocins and nitric oxide)

2) Anti-plaque (inhibition of key architect species, fx Fusobacterium, and production of signals that induce cell detachment)
3) Anti-inflammatory (probiotic S. dentisani, Rothia, Bifidobacteria)
4) Inhibition of gingipains (S. gordonii, S. dentisani etc.)

There is both health-associated bacteria AND health-inducing/health-promoting bacteria in the oral microbiome.

Good resources
The evidence for placental microbiome and its composition in healthy pregnancies: a systematic review, 2022
Mishra et al 2021
Aagard et al 2014
Senkus and Crowe-White 2020
Oral Microbiome Lab and Fisabio Foundation
David, L.A. et al 2015

Top 3 Dental Insights — Key Take Aways

1. How do we aquire our individual microbiome?
Aquiring normal human microbiome happens:
1. Pre-natal exposure: microorganisms from the pregnant mother are found in the placenta.
2. Exposure during birth
3. Post-natal exposure: babies get exposure to microorganisms from breastfeeding, siblings, mother, environment, and food.

2. When does our microbiome change to a more pathologic state?
Wrong things to lose the diversity of our microbiome: fx fast processed food, physical inactivity, antiseptic mouthwash and soap, medicine creating antibiotic resistance and killing the beneficial microbiome.

The oral microbiome can be either in:
- A saccharolytic state (breaking down sugars, early dysbiosis for caries)
- Neutral (eubiosis)
- Proteolytic state (breaking down proteins, early dysbiosis for periodontitis)

3. How does our diet affect our microbiome?
We need oral bacteria to break down nitrate to create nitrite to produce nitric oxide. NO2 (nitric oxide) dilates our blood vessels (important for normal blood pressure).

Diet has very little effect on the oral microbiome, unless the person excessively and frequently eats refined carbohydrates.

Under normal circumstances, salivary mucins are a major nutrition source for oral bacteria. The bacteria in the microbial community work together and act cooperatively to break down the complex salivary mucin. However, during inflammation the environment changes significantly. Inflammation brings a rich source of fx readily digestible proteins and micronutrients such as iron/heme. A different set of microbial cooperative funtions will be needed.

In healthy gum pockets there are under 1% pathogenic bacteria. But as pocket depth increases, the healthy bacteria disappear, and the pathogenic bacteria increase dramatically. Pathogenic bacteria only increase when the ecosystem becomes dysbiotic. The microbiology is driving the disease, AND is the disease driving the microbiology. When the oral microbiome with P. gingivalis is transferred from a diseased mouse to a germ-free mouse, the germ-free mouse develops periodontal disease and bone loss, too!

Sources

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That was Dental Insights. Thank you for being here. ❤

Dental love, Anne Mette