THE ORAL MICROBIOME
AND ITS ROLE IN HEALTH
LEARNING OBJECTIVES

In this module, you will learn about

- Evolution of the human microbiome and how it has changed through time
- The importance of the microbiome in human health
- Role of saliva in maintaining a balanced oral microbiome
- Consequences of dysbiosis
AGENDA

THE MICROBIOME

• The human microbiome
• The oral microbiome

DYSBIOSIS

• Contributing factors
• Consequences of dysbiosis

EFFECTS OF ZENDIUM

• Three relevant clinical studies on the microbiome and gingival health
THE MICROBIOME
THE HUMAN HOLOBIONT

The human body is colonised by a diverse community of commensal, symbiotic and pathogenic microorganisms and their genetic material, collectively known as the **microbiome**\(^1\)

Together with our microbiome, we form a single entity known as the **holobiont**\(^2\)

The ratio of microbial:human cells in the holobiont is **at least 1:1**\(^3\)
HUMANS AND MICROORGANISMS HAVE CO-EVOLVED

The **co-evolution** between microorganisms (blue lines) and their respective hosts (green lines) over a period of 1.5 billion years has resulted in **mutual adaptation** and **functional integration**¹
Resident microbes have been performing metabolic functions in animals for at least 500 million years\textsuperscript{1}

Throughout human evolution, our environment has continually shaped the composition of our oral and gut microbiomes

**Historical periods of oral/gut microbiome evolution\textsuperscript{2,3}**

- **Neolithic Period**
  - ~ 10,000 BC
  - Advent of fire
  - Introduction of agriculture

- **Industrial Revolution**
  - ~1850
  - Industrially processed flour and sugar

- **Modern Age**
  - ~1900
  - Antibiotics
  - Oral care regimens
A BALANCED MICROBIOME IS ESSENTIAL FOR HEALTH

The microbiome contributes to critical metabolic, physiological and immunological functions\(^1\text{–}^4\)

- Maintains a healthy digestive tract
- Confers resistance to colonisation by pathogens
- Regulates the cardiovascular system
- Supports host defence functions
- Has anti-inflammatory properties
- Provides additional metabolic potential
- Has antioxidant activity
The composition of our microbiome shows great diversity and is highly variable within and between people\textsuperscript{1}

Different body sites support distinct microbial communities according to the biological and physical properties of each location/habitat\textsuperscript{1}

**Some human microbiome habitats\textsuperscript{2}**

- Oral cavity
  - (second-most diverse human microbiome)
- Gastrointestinal tract
  - (most diverse human microbiome)
- Airways
- Skin
- Urogenital tract
THE ORAL HABITAT

The mouth has distinct habitats that form a heterogeneous ecological system\(^1,2\)

The warm, moist environment suits the growth of many microorganisms and offers host-derived nutrients\(^3\)

Non-shedding surfaces of teeth provide unique opportunities for biofilm formation\(^4\)
To date, >700 prokaryote species have been identified that colonise the oral cavity\(^1\)

**Oral species detected in the oral cavity (n = 700)\(^1\)**

- Validly named species
- Unnamed, but cultivated
- Uncultivated phylotypes

Data from a recent study\(^2\)

**Number of taxa found in 9 oral sites of 26 individuals:**

557

**Mean number of taxa found in each individual:**

296
ACQUISITION OF THE ORAL MICROBIOME

Birth
- Microbes are transmitted from mother to child during birth\(^1\)
- Delivery method (natural vs Caesarean) influences the diversity of the child’s oral microbiome\(^2\)

\(~3\) months
- The method of feeding also has an effect, with 3-month-old breast-fed infants showing a higher colonisation with oral lactobacilli than formula-fed infants\(^3\)

\(~3\) years
- Eruption of teeth provides new surfaces for microbial colonisation and constitutes a major ecological event in the mouth of a child\(^4\)
- By the age of 3, the oral microbiome of children is already complex, and becomes increasingly so with age\(^5\)

\(~6\) years
- Replacement of the primary teeth with an adult dentition again significantly alters the oral microbial habitat\(^6\)
SALIVA MAINTAINS A BALANCED ORAL MICROBIOME

1. Proteins in saliva bind microorganisms for rapid clearance by flushing (swallowing, chewing, speaking), preventing colonisation of teeth/soft tissues.

2. Salivary components provide complex nutrients for microorganisms, enabling the development of a balanced microbiome.

3. Some salivary components have natural antimicrobial action.

Microorganisms colonise the pellicle by attaching to receptor proteins.

Salivary proteins cover the tooth and epithelial surfaces in the form of a protective pellicle.
DYSBIOSIS:
The Oral Microbiome in Disease
HOW DOES PLAQUE LEAD TO DENTAL DISEASE?

**Specific plaque hypothesis (1970s):**
only a few species are pathogenic;
targeting these with antibiotics could cure or prevent disease

**Non-specific plaque hypothesis (19th century):**
dental infections are caused by non-specific over-growth of all bacteria in dental plaque

**Updated non-specific plaque hypothesis (1980s):**
any microbial colonisation of sufficient quantity in the gingival crevice causes at least gingivitis

**Ecological plaque hypothesis (1990s):**
substantial changes in a local environment can alter the competitiveness of plaque bacteria, leading to the enrichment of organisms most suited to the new environment

**Evolution of the plaque hypothesis**
A DISTURBANCE IN THE BALANCE OF THE ECOSYSTEM LEADS TO DYSBIOSIS AND DISEASE

The complex equilibrium between resident species in the oral cavity is responsible for the maintenance of a healthy state (symbiosis) or a state associated with disease (dysbiosis)\(^1,2\)

**Healthy**
- Stable and balanced community of microbiota, and relatively low levels of potential pathogens

**Disease**
- The diversity and relative proportions of species within the microbiota are disturbed\(^1\)

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**Oral microbiome**
- Diverse bacteria in symbiotic relationship with host
- Potentially cariogenic/periodontopathic bacteria
INTRINSIC AND EXTRINSIC FACTORS CAN TRIGGER A SHIFT TOWARDS DYSBIOSIS

The composition of the healthy oral microbiome is remarkably stable; however, changes in physiological or lifestyle factors can lead to dysbiosis and disease. 

Healthy
Stable and balanced community of microbiota and relatively low levels of potential pathogens. 

Disease
The diversity and relative proportions of species within the microbiota are disturbed.
DYSBIOSIS: LINKED TO CARIES AND GINGIVITIS

Healthy

Frequent sugar
Reduced saliva
Acidic pH\textsuperscript{1,2}

Selects for organisms that produce acids themselves and/or are more tolerant of an acidic environment\textsuperscript{1,2}

Caries

Inflammation
Increased gingival crevicular fluid\textsuperscript{3}

If biofilm is not removed, selected anaerobes are suited to the low oxygen levels\textsuperscript{3}

Healthy

Gingivitis
ORAL DYSBIOSIS CAN HAVE SYSTEMIC CONSEQUENCES

Co-evolution to a harmonious co-existence only works as long as microbes remain in their natural habitat and are not disseminated to other body sites, where they can cause a number of diseases\(^1\)\(^-\)\(^3\)

- Arthritis
- Heart disease and stroke
- Adverse pregnancy outcomes
- Diabetes
  *Bi-directional relationship with periodontitis*
- Meningitis and brain abscess
- Irritable bowel syndrome and bowel cancer
- Respiratory diseases
- Alzheimer’s Disease*
  *New association*
CLINICAL GOAL: MAINTAINING A BALANCED ORAL MICROBIOME

Preventative measures that can help to maintain a healthy symbiotic state:

- Educating patients on appropriate lifestyle choices
- Effective plaque control techniques to preserve dental biofilms at levels compatible with oral health

Measures that can be followed to re-establish symbiosis:

- Avoidance of indiscriminate use of antibiotics
- Continued education on oral hygiene and lifestyle strategies to promote symbiosis
ZENDIUM: A TOOTHPASTE INSPIRED BY SALIVA
BOOSTING NATURAL SALIVARY DEFENCES WITH ENZYMES AND PROTEINS

The Zendium active systems

<table>
<thead>
<tr>
<th>Triple Enzyme System&lt;sup&gt;1,2&lt;/sup&gt;</th>
<th>Role</th>
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<tbody>
<tr>
<td>Amyloglucosidase</td>
<td>Produces glucose from polyglucans</td>
</tr>
<tr>
<td>Glucose oxidase</td>
<td>Oxidises glucose to gluconate and <strong>hydrogen peroxide</strong></td>
</tr>
<tr>
<td>Lactoperoxidase</td>
<td>Catalyses the oxidation of thiocyanate to <strong>hypothiocyanite</strong> by hydrogen peroxide</td>
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<tr>
<th>Protein System&lt;sup&gt;1,3,4&lt;/sup&gt;</th>
<th>Role</th>
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</thead>
<tbody>
<tr>
<td>Lysozyme</td>
<td>Interrupts bacterial cell wall formation, and helps inhibit bacterial glucose metabolism</td>
</tr>
<tr>
<td>Lactoferrin</td>
<td>Inhibits growth of iron-dependent bacteria and microbial adhesion</td>
</tr>
<tr>
<td>Colostrum as a source of immunoglobulin</td>
<td>In saliva helps to provide resistance against infection</td>
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- 1450ppm sodium fluoride
- Natural enzymes and proteins