Microbiological & Immunological Aspects of Dental caries

Hong-Sen Chen. DDS. MS. Ph.D
Introduction and overview
<table>
<thead>
<tr>
<th>CELL TYPE</th>
<th>NORMAL</th>
<th>DISEASED</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>pocket depth</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2mm</td>
<td>7mm</td>
</tr>
<tr>
<td>COCCI</td>
<td>74</td>
<td>22</td>
</tr>
<tr>
<td>RODS</td>
<td>16</td>
<td>18</td>
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<tr>
<td>FILAMENTS</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>FUSIFORMS</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>MOTILE</td>
<td>0.3</td>
<td>13</td>
</tr>
<tr>
<td>SPIROCHETES</td>
<td>2</td>
<td>38</td>
</tr>
<tr>
<td>MOTILE/NON-MOTILE</td>
<td>1/49</td>
<td>1/1</td>
</tr>
</tbody>
</table>

*LISTGARTEN AND HELLDÉN*
*J. CLIN. PERIODONT, 1978*

Fig. 6-24. Percentage distribution of plaque flora in health and periodontal disease using darkfield microscopy. (Courtesy of Listgarten and Helldén.*)
1. 雙球菌 (diplococci)
2. 鏈球菌 (streptococci)
3. 葡萄球菌 (staphylococci)
4. 桿菌 (bacilli)
5. 球桿菌 (coccobacilli)
6. 棍狀桿菌 (fusiform bacilli)
7. 絲狀桿菌 (filamentous bacillary forms)
8. 孢菌 (vibrios)
9. 螺菌 (spirilla)
10. 四聯球菌 (tetrads)
Types of Caries

- Pit and Fissure
- Smooth Surface
- Root Surface
- Recurrent Caries
ETIOLOGICAL FACTORS IN DENTAL CARIES

- Plaque micro-organisms
- Teeth
- Diet (sugar)
- Time

No Caries

Caries
The theory

- Acidogenic theory
- Proteolytic theory
- Acidogenic - proteolytic theory
- Proteolysis – chelation theory
The infectious nature of dental caries in experimental animals
Germ-free animals

Normal bacterial flora

Sugars

Caries

No bacteria

Sugars

No Caries

Animals kept together leads to cross contamination by oral bacteria

Figure 2: Diagram summarising results of studies on caries and bacteria
Figure. Suggested anatomical pathways for maternal transmission of oral microbes or their tissue-derived inflammatory mediators during pregnancy.
New born (2 days)

- 98% facultative *streptococci*, *lactobacilli*
- Few anaerobic organisms
- Few G (+), yeasts
- *Vaginal lactobacilli*
- *Air–borne bacteria*
- *Other microorganisms*
- Food, Water, Air dust,
- Dirt, Parents, Medical personnel
TABLE 2. CHANGES IN THE ORAL FLORA ASSOCIATED WITH THE ERUPTION OF TEETH

<table>
<thead>
<tr>
<th>Organism</th>
<th>Before Eruption</th>
<th>After Eruption</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Sreptococcus salivarius</em></td>
<td>usually present</td>
<td>usually present</td>
</tr>
<tr>
<td><em>Sreptococcus sanguis</em></td>
<td>usually absent</td>
<td>usually present</td>
</tr>
<tr>
<td><em>Sreptococcus mutans</em></td>
<td>usually absent</td>
<td>usually present</td>
</tr>
<tr>
<td><em>Actinomyces sp.</em></td>
<td>usually absent</td>
<td>usually present</td>
</tr>
<tr>
<td><em>Bacteroides sp.</em></td>
<td>usually absent</td>
<td>usually present</td>
</tr>
<tr>
<td><em>Fusobacterium sp.</em></td>
<td>usually absent</td>
<td>usually present</td>
</tr>
<tr>
<td><em>Lactobacillus sp.</em></td>
<td>usually present</td>
<td>usually present (low numbers)</td>
</tr>
<tr>
<td><em>Veillonella sp.</em></td>
<td>usually present</td>
<td>usually present</td>
</tr>
</tbody>
</table>
Initial reports of *mutans streptococci*
Clark (1924)
G(+)，chain – forming cells
Fitzgerald and Keyes (1968) *Mutans Streptococci* began to appear in literature
S. Mutans are the main bacteria cause of caries
(Emission and Krasse 1985)
(Loesche 1986)
<table>
<thead>
<tr>
<th>Caries Type</th>
<th>Organisms Isolated</th>
<th>Possible Significance in Caries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pit and fissure</td>
<td><em>Streptococcus mutans</em></td>
<td>Highly significant</td>
</tr>
<tr>
<td></td>
<td><em>Streptococcus sanguis</em></td>
<td>Slight significance</td>
</tr>
<tr>
<td></td>
<td><em>Streptococcus mitis</em></td>
<td>No significance</td>
</tr>
<tr>
<td></td>
<td><em>Lactobacillus sp.</em></td>
<td>Highly significant</td>
</tr>
<tr>
<td></td>
<td><em>Actinomyces sp.</em></td>
<td>May be significant</td>
</tr>
<tr>
<td>Smooth-surface</td>
<td><em>Streptococcus mutans</em></td>
<td>Highly significant</td>
</tr>
<tr>
<td></td>
<td><em>Streptococcus salivarius</em></td>
<td>Little significance</td>
</tr>
<tr>
<td>Dentinal caries</td>
<td><em>Lactobacillus sp.</em></td>
<td>Highly significant</td>
</tr>
<tr>
<td></td>
<td><em>Actinomyces viscosus</em></td>
<td>Significant</td>
</tr>
<tr>
<td></td>
<td><em>Actinomyces naeslundii</em></td>
<td>Highly significant</td>
</tr>
<tr>
<td></td>
<td><em>Streptococcus mutans</em></td>
<td>May be significant</td>
</tr>
<tr>
<td></td>
<td>Filamentous rods</td>
<td>Significant</td>
</tr>
<tr>
<td>Root caries</td>
<td><em>Actinomyces viscosus</em></td>
<td>Highly significant</td>
</tr>
<tr>
<td></td>
<td><em>Actinomyces naeslundii</em></td>
<td>Highly significant</td>
</tr>
<tr>
<td></td>
<td><em>Streptococcus mutans</em></td>
<td>Some significance</td>
</tr>
<tr>
<td></td>
<td><em>Streptococcus sanguis</em></td>
<td>Significance unclear</td>
</tr>
<tr>
<td></td>
<td><em>Streptococcus salivarius</em></td>
<td>No clear significance</td>
</tr>
<tr>
<td></td>
<td>Filamentous rods</td>
<td>Highly significant</td>
</tr>
</tbody>
</table>
Physiology of cariogenic bacteria
Extracellular and cell – surface polymers synthesis

- Glucans (glucose homopolymers) – dextran
- Fructans (fructose homopolymers) – levan
Sucrose $\xrightarrow{\text{GTF}}$ Glucan
$\text{(G-O-G)}_{n+1} + \text{Fructose}$

Glucosyl transferase

Sucrose $\xrightarrow{\text{FTF}}$ Fructan
$\text{(F-O-F)}_{n+1} + \text{Glucose}$

Fructosyl transferase
Sucrose $\xrightarrow{\text{GTF}}$ glucose + fructose

Glucose $\xrightarrow{\text{GTF-S}}$ water-soluble glucans

Glucose $\xrightarrow{\text{GTF-I}}$ water-insoluble glucans
Glucans

- Water – soluble
- Alkali – soluble

→ plaque
Fructans

* Water – soluble  →  plaque
Degradation of glucans & fructans

* $\text{H}_2\text{O} + \text{Fructan} \rightarrow \text{Fructanase} \rightarrow \text{nFructose}$

* $\text{H}_2\text{O} + \text{Glucans} \rightarrow \text{Dextranase} \rightarrow \text{nGlucose}$
Intercellular metabolism and polymer formation
(Lactic acidogenic theory)
The synthesis of intercellular polysaccharide (IPS$_s$) is not sucrose – dependant any fermentable carbohydrate can serve
**Extracellular polysaccharides** glucans, fructans

**Intracellular polysaccharides** glycogen
Glycolysis

- Acid production
- IPS synthesis
Fig. 22-21. The synthetic and degradative pathway for intracellular glycogen in *S. mutans*. 
Virulence (Cariogenicity) determinants of the *mutans streptoccci*

* Water-insoluble glucan synthesis
* Intercellular polysaccharide synthesis
* Acid tolerance
* Lactic acidogenicity
* Endo dextronase
Molecular pathogenesis

- Initial attachment
- Accumulation
- Acid formation and cavitation
Molecular pathogenesis

- Initial attachment pellicle binding protein
Specifical binds glucan (glucan binding protein)
Accumulation

- Glucosyltransferase (GTF) → glucans
  - GTF-S (water-soluble glucans)
  - GTF-I (water-insoluble glucans)
- Glucan binding protein (a mutans receptor)
Acid formation and cavitation

- Lactic acid
Cariogenic features of *mutans streptococci*

1. Binding to and colonization of teeth
2. Accumulation on tooth surfaces and participation in the formation of dental plaques.
3. Production of acid at high rate.
4. Tolerance of high concentrations of sugar, high ionic strength, and highly acidic conditions.
Cariogenic features of *mutans streptococci*

5. Association with dental caries in humans.
6. Causation of dental caries in animals.
7. Transmissible in animals and apparently in man.
8. Reduction or elimination of *mutans streptococci* will result in reduction or elimination of dental caries.
Monitoring the cariogenic flora in clinical practice and research

- Sampling
- Transporting
- Diluting
- Plating
Oral streptococci

* S. sanguis
* S. mutans
* S. salivarius
* S. mitis
S. mutans

- Mitis salivarius agar (MS)
- MSB (20% sucrose + 0.2 u/ml bacitracin)
- G(+) , cushion – shaped , frosted glass
## Taxonomy of *mutans* streptococci

<table>
<thead>
<tr>
<th>Species</th>
<th>Bratthall / perch serotype</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>S. cricetus</em></td>
<td>a</td>
</tr>
<tr>
<td><em>S. rattus</em></td>
<td>b</td>
</tr>
<tr>
<td><em>S. mutans</em></td>
<td>c.e.f.</td>
</tr>
<tr>
<td><em>S. sobrinus</em></td>
<td>d.g.SL</td>
</tr>
<tr>
<td>Serotype</td>
<td>Total Number</td>
</tr>
<tr>
<td>----------</td>
<td>--------------</td>
</tr>
<tr>
<td>a</td>
<td>0</td>
</tr>
<tr>
<td>b</td>
<td>1</td>
</tr>
<tr>
<td>c</td>
<td>184</td>
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<tr>
<td>d</td>
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<tr>
<td>e</td>
<td>22</td>
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<tr>
<td>f</td>
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<tr>
<td>g</td>
<td>1</td>
</tr>
<tr>
<td>Nontypeable</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>231</td>
</tr>
</tbody>
</table>
Oral lactobacilli

- Bunting (1925) *Bacillus acidophilus*
- G(+), non – spore forming rods
- Rogosa agar
<table>
<thead>
<tr>
<th>Homofermentative</th>
<th>Heterofermentative</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>L. casei</em></td>
<td><em>L. fermentum</em></td>
</tr>
<tr>
<td><em>L. acidophilus</em></td>
<td><em>L. brevis</em></td>
</tr>
<tr>
<td><em>L. plantarum</em></td>
<td><em>L. buchneri</em></td>
</tr>
<tr>
<td><em>L. salivarius</em></td>
<td><em>L. cellobiosus</em></td>
</tr>
</tbody>
</table>
Oral actinomyces

* G(+) non – spore forming rod and filaments (NAC – 20 , CFAT)
<table>
<thead>
<tr>
<th>Anaerobic</th>
<th>Facultative Anaerobic</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>A. bovis</em></td>
<td><em>A. viscosus</em></td>
</tr>
<tr>
<td><em>A. israelii</em></td>
<td><em>A. naeslundii</em></td>
</tr>
<tr>
<td></td>
<td><em>A. odontolyticus</em></td>
</tr>
</tbody>
</table>
Immunological aspects of dental caries
Immunological protection

* Intravenous
* Intraductal
* Subcutaneous
* Submucosal
The immune response to streptococcal antigens

- Thymus-derived T cell
- Bone-marrow derived B cell
COMPONENTS OF ORAL IMMUNITY

Blood → crevicular fluid

Salivary gland → Salivary secretion

IgG, IgM, IgA
Proteins
Complement
Enzymes
Electrolytes
Polymorphs
B lymphocytes
T lymphocytes
Macrophages

Secretory IgA
Proteins
Enzymes
Electrolytes
Polymorphs

Whole saliva

Secretory IgA
IgG, IgA
Proteins
Enzymes
Electrolytes
Polymorphs
Serum antibody and disease

- Caries-free: greater serum antibody inhibits GTF
- Caries-prone: less serum antibody
Effect of antibody to glucosyltransferase

* GTF-I
* GTF-S
Dental caries and the mucosal immune system

- Salivary antibody (IgA)
- Gingival crevicular (IgG)
Individuals with immunologic deficiency

* IgA deficiency --- dental caries elevated

* IgM compensatory --- less dental caries
Role of antibody in dental caries

- IgA antibody makes up less than 1% of the total IgA
S. mutans (serotype c, e, and f)

S. sobrinus (serotype d, g, and h)
Salivary antibody and disease

* Salivary antibody level depends on the rate of salivary flow
METHODS OF PREVENTING DENTAL CARIES

- Reduce carbohydrate in saliva, e.g. by dietary change or artificial sweeteners

• Increase tooth resistance to acid attack, e.g. by fluoride

• Reduce tooth susceptibility, e.g. by fissure sealants

• Reduce or eliminate cariogenic micro-organisms, e.g. by antimicrobial agents
Sugar substitutes and caries

- Sorbitol
- Mannitol
- Xylitol
- Penitol
Saliva

The function of saliva are:

1. Lubrication
2. Cleansing
3. Digestion
4. Antiacid
5. Antibacterial
Fluoride effect on cariogenic bacteria
Conclusion

- It is clear that caries is a complex disease whose etiology involves multiple interactions at the molecular level and thus whose prevention will require an understanding of the entire process at this level.
References

Curriculum Vitae

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