The role of diet in the etiology of dental caries is well established. A large number of carbohydrates, such as sugars and starch, are fermented by oral bacteria, but sucrose is usually the culprit.

A study from the UK showed a strong positive correlation between caries experience (DMF) and the amount of sucrose consumption over 50 years. At present, the relationship between sugar and caries seems to weaken.

A study done in 1994 demonstrated a linear relationship between caries experience (DMF) with sugar consumption from 90 nations. However, when industrialized nations were separately analyzed, the relationship was vague.

Also seen in the UK study, caries decrease more than the decrease in sugar consumption after 1985. One reason is the frequent use of fluoride, which has changed the impact of sugars.

**Sugars:** When talk about 'sugar', we usually refer to sucrose. Actually the terms 'sugars' includes all mono and disaccharides. Sugars are found naturally in foods (fruit, honey, milk), or added to foods during processing (white or brown sugar, corn syrup). Starches are digested by salivary amylase to oligosaccharides, which may be fermented by oral microflora.

Note that this group, polyols or sugar alcohols, is used as sugar substitute, for example in chewing gum. They are not fermentable, or ferment in very low amount, by oral bacteria. None of the high-intensity sweeteners is fermentable, so they are not promoting dental caries.
Questions: Myth or Fact

Honey is a natural product, you won’t get caries from it.

Potatoes are non-cariogenic.

Beer makes me drunk, but does not cause caries.

I put Splenda in my coffee, so I am safe from both calories and caries.

Cough syrup can cause tooth decay.

‘Baby bottle caries’ occurs when bedtime habits include lying with a bottle filled with milk.

Dietary factor: Not only the amount and type of sugars affect caries risk. Other important dietary factors are consistency, degree of retention, and content of ‘caries protective’ factors. There are also individual factors, such as eating pattern. The most important is intake frequency. The classic Vipeholm Study, is one of the most important contributions in the dental literature, although it is heavily criticized for the ethics issue. This study showed that the more frequently sugar is consumed, the greater the risk. Sugar consumed between meals and had ‘sticky’ consistency had much greater caries potential than when it was consumed during a meal.
Caries-protecting factors

'Sialogogue'
- Chewing gum stimulates saliva
- Increase the clearance of sugars and fermentable carbohydrates
- Buffering capacity

Polyphenols
- Tannins (cocoa, coffee, tea)
  - Interfere glucosyltransferase activity of MS → reduce plaque

Xylitol
- Sugar alcohol used in chewing gum
  - Stimulate salivary flow.
  - Antimicrobial action?
  - Clinical studies: Xylitol vs Sorbitol

Favoring remineralization
- Calcium, phosphate, protein: Cheese and dairy products

Caries-protecting factors:

'Sialogogue' means an agent that can stimulate secretion of saliva. Chewing gum stimulates saliva, increasing the clearance of sugars and other fermentable carbohydrates from teeth and the oral cavity, and increasing buffer capacity.

Polyphenols such as tannins found in cocoa, coffee, tea may reduce the cariogenic potential of foods by interfering with glucosyltransferase activity of MS which may reduce plaque formation.

Xylitol, a sugar alcohol used in chewing gum has anticariogenic effects related to antimicrobial action in addition to stimulation of salivary flow. But clinical studies are inconclusive if it is significantly better than the more common sorbitol.

Diet may favor remineralization when its content is high in calcium, phosphate, and protein. Cheese and dairy products are also shown to be anticariogenic.

Children and adolescents with low incidence of dental caries drank more milk.

Elderly people that eat cheese several times per week had a lower incidence of root caries.

Remineralization of enamel was observed when cheese and milk were used as between-meal snacks.

Dairy products, except sweetened yogurt, generally reduced the amount of dentin demineralization.

Is dental caries a transmittable, infectious disease?

There is a change in paradigm from a classic concept that dental caries is a transmittable, infectious disease. In most cases, it means exogenous specific microorganisms are transmitted from infected persons and that you get sick from it.

Dental caries is a multifactorial disease that results from an ecological shift in the tooth surface biofilm (dental plaque), leading to mineral imbalance between plaque fluid and tooth, hence net loss of tooth mineral.
Specific vs Non-specific vs Etiological plaque hypothesis

There are different schools of thought on the role of bacteria in the etiology of dental caries. Early belief viewed plaque as a pathogenic structure which had to be eliminated to prevent caries. Disease is the outcome of overall activity of the total plaque microflora. More plaque means the more disease. This non-specific plaque concept faded away because plaque in some sites is not disease-producing.

In the 50’s and 60’s there was evidence that hamsters developed caries when infected with Streptococcus mutans, and caries could be transmitted. This is the specific plaque hypothesis, dental caries is an infectious disease caused by specific bacteria. The most cariogenic group of bacteria is mutans streptococci (MS). Lactobacilli and A. viscosus are also important players.

Studies in humans found a strong correlation between MS and the initiation of demineralization. One example, 71% of carious fissures had more than 10% of MS count from total bacteria, whereas 70% of ‘caries-free’ fissures had no detectable MS. Patients undergoing radiation treatment and children with rampant caries had large increase in MS and lactobacilli in plaque and saliva.

This concept suggests the preventive and treatment strategies to eliminate specific infection. Antibiotics and immunization against specific strains (MS) resulted in a decrease in bacteria and the number of caries lesions in animal studies. This concept is not outdated. As you recall from the seminar, we discussed a paper about caries transmitted from mother to child, and research on caries immunity is still active. Is there a newer concept lately?

There is no doubt that MS is the main player in dental caries. But the association between MS and caries is not absolute. Relatively high proportion of MS may persist on tooth surfaces without evidence of demineralization, and it is quite often that caries develops in the absence of MS. So, bacteria other than MS also contribute to dental caries. For example, the metabolism of S. mutans can lower pH to 3.95-4.1. S. mitis, S. salivarius and S. anginosus lower pH to 4.05-4.5.

This does not go back to the non-specific approach. An alternative concept of Ecologic plaque hypothesis was proposed by Marsh in 1990’s, and has gained much attention since. This concept believes that MS and other microorganisms are part of the endogenous bacteria, resident of the oral cavity. They are present at sites without caries at lower levels where the stability in plaque composition is maintained (microbial homeostasis). Dental caries develops when change in local environment is large enough to shift the balance of the plaque microflora. Frequent sugar intake causes repeated conditions of low plaque pH and favors the growth of cariogenic species (MS and lactobacilli) which live well in acidic conditions. Host factors such as change in salivary flow can affect plaque homeostasis.
**Role of cariogenic microorganisms**

1. Produce acid rapidly from fermentable carbohydrate (Acidogenicity)
2. Survive and continue to produce acid at acidic pH (Aciduricity)
3. Produce extracellular polysaccharides from dietary sucrose to facilitate adherence to tooth surfaces and build-up of large bacterial deposits
4. Produce intracellular polysaccharides as storage components to prolong acid formation & acidic pH

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**Acidogenicity** is the ability of plaque bacteria to produce organic acids from fermentable carbohydrate. Bacteria in dental plaque derive their energy from glycolysis (or fermentation), an anaerobic catabolism of carbohydrates. By breaking down 1 molecule of glucose, they get 2 lactic acids and 2 ATPs. Cariogenic bacteria are usually 'homofermentative', they produce 90% or more of lactic acid as end products. Lactic acid is easier to dissociate than other acids. Heterofermentors produce a mixture of metabolites, including other organic acids like acetic, propionic, succinic, formic, and ethanol.

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**Aciduricity** is the ability of bacteria to live in a low pH environment. Dental caries is a consequence of successful adaptation by oral bacteria to survive and continue to produce acid at acidic pH. The aciduricity of cariogenic bacteria explains the ecological plaque hypothesis. In the beginning when the level of MS or lactobacilli still low, the acidic condition may be driven by other bacteria. Frequent consumption of fermentable carbohydrates gives advantage to those with the best acid adaptation. The adaptation and selection to acidic environment is important in the development of a cariogenic plaque.

Acid adaptation is mediated by maintaining intracellular pH in the optimal range by:

1. Low proton permeability of the cell membrane: cell wall thickening
2. Production of bases
3. Buffering capacity of the cytoplasm
4. Active transport of proton out of cell

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**How? Maintaining intracellular pH at optimum**

1. Low proton permeability of the cell membrane: cell wall thickening
2. Production of bases
3. Buffering capacity of the cytoplasm
4. Active transport of proton out of cell

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**Role of cariogenic bacteria**

Aciduricity = Ability of bacteria to live in a low pH environment

"Dental caries is a consequence of successful adaptation by oral bacteria to survive and continue to produce acid at acidic pH"

Ecologic plaque hypothesis:

- Beginning: Low level of MS or lactobacilli
- Other bacteria produce acid
- Frequent consumption of fermentable carbohydrate
- Best acid adaptation bacteria survive (MS & Lactobacilli)
- Increase level of MS & lactobacilli

**Acidogenicity**

Ability of bacteria to produce organic acids from fermentable carbohydrates

**Glycolysis (fermentation):**

- Anaerobic catabolism of carbohydrates
- Energy production

| Glucose | 2 lactic acids | + 2 ATPs |

**Homofermentative bacteria**

- Produce > 90% lactic acid

**Heterofermentative bacteria**

- Produce a mixture of metabolites:
  - Organic acids - acetic, propionic, succinic, formic
  - Ethanol

**Role of cariogenic bacteria**

- **Propionic**
- **Acetic**
- **Plaque Acids**
- **Formic**
- **Lactic**
- **Succinic**
Proton-translocating membrane ATPase drives protons out of a cell. The active transport process increases energy demand, which requires increased glycolytic activity, and more acid production. This sets off a cascade in which the plaque pH gets lower and lower.

Production of intra- and extracellular polysaccharides

Pathways of sucrose metabolized by cariogenic bacteria:
Sucrose is transported into cell and degraded to glucose and fructose by enzyme invertase.
1. The metabolites are used for production of energy through the glycolytic pathway, leading to lactic acid as the end product.
2. The metabolites are used in the synthesis of intracellular polysaccharides.
3. Outside the cell, sucrose is converted to extracellular polysaccharides by cell-bound and extracellular enzymes.

Intracellular polysaccharides (IPS) is a storage form of carbohydrate, glycogen-amylopectin type. This storage is used for energy and acid production (as by-product) when dietary carbohydrate is depleted. IPS is produced by most plaque bacteria during a period of excess nutrient. Up to 20% of sucrose consumed can be converted into IPS. Although IPS production is not unique to cariogenic bacteria, it can be a virulence factor because it contributes to acidogenicity and aciduricity.

Plaque of caries-prone individuals has higher proportion of bacteria that can synthesize intracellular polysaccharides. So they can produce acid for a long period after meals from the IPS storage (= Acidogenicity). The energy required to drive protons out of a cell that allow some bacteria to adapt to low pH environment (Aciduric) is also derived from IPS when dietary carbohydrate is depleted.

Extracellular polysaccharides (EPS): Before sucrose enters bacteria cells, a small percentage (<10%) is transformed into glucans and fructans that either diffuse into the surrounding plaque or remain associated with the bacteria cell. Glucans form a major component of the interbacterial matrix and constitute a barrier to the outward diffusion of acids formed in plaque. EPs may also serve as carbohydrate storage compounds. Fructans are degraded rapidly within a few hours, but glucans persist for longer periods.
S. mutans synthesized extracellular glucans and fructans from sucrose, but not from other common carbohydrates (including glucose). The enzymes responsible for the synthesis are glucosyltransferase and fructosyltransferase. The energy used in the process is derived from the disaccharide bond of sucrose, which explains why sucrose is the essential substrate. These polymers enable the bacteria to accumulate on the surface. As shown in the SEM picture. Only S. mutans grew in sucrose had amorphous material covering the colony which permit them to accumulate. Glucosyltransferase is one of the virulent factors of S.mutans. It also functions as glucan-binding ligand on the surface of S. mutans. The interaction of these ligands with glucans promotes the adherence and accumulation of S. mutans on the tooth surface.

One of the key characters that contribute to the dynamic of the carious process is the fluctuation of plaque pH. When plaque pH drops from acids produced by bacterial glycolysis, it is followed by a period of alkalinization that neutralizes the acids. This alkalinization is a result of acid diffusion out from the biofilm, buffering capacity, and bacterial metabolism that generates alkali.

Sources for plaque alkali are: ureolysis, Strickland reaction, and arginine deiminase system and deaminase/decarboxylase as minor reaction.

Ureolysis: A small amount of urea is found in saliva. Bacterial ureases produced by S. salivarius, Actinomyces naeslundii and oral haemophili hydrolyze urea to ammonia and CO2.

Strickland reaction involves the oxidation-reduction of amino acids by peptostreptococci in dental plaque. Peptostreptococci oxidize proline in amino acids and reduce protons in plaque.

Arginine catabolism is a major source of ammonia in plaque. Arginine is from the diet or from the degradation of salivary proteins or crevicular fluid. S. gordonii, S. rattus and S. sanguis catabolize arginine to ammonia and CO2 with arginine deiminase. These bacteria are desirable in terms of having plaque with low cariogenic potential.

The understanding of alkali production can lead to novel anticaries strategies. For example, replacement therapy to replace cariogenic bacteria with the 'good' bacteria, or genetically engineer bacteria to produce more base.
Methods to modify plaque acidity/cariogenicity

1. Stimulate salivary flow
   - chewing gum
2. Increasing plaque pH
   - bicarbonate ('baking soda')
   - ammonium salts
3. Disrupt plaque
   - mechanical (?)
   - enzyme
   - plant extracts
4. Antimicrobial agent
   - chlorhexidine
   - xylitol
   - fluoride, stannous
5. Caries vaccine
6. Modify microflora
   - reduce lactate producer
   - increase lactate user (Veillonella)
   - increase base producer

Methods to modify plaque acidity/cariogenicity

Some methods are practical, some are theoretical:

1. Stimulation of salivary flow washes away and buffers plaque acids. One easy way to stimulate salivary flow is chewing gum.
2. There are agents that act directly on plaque acids to increase pH. These includes bicarbonate ('baking soda') added in toothpaste, and ammonium salts.

3. Plaque can be disrupted by physical or chemical means. Brushing and flossing disperse plaque. Some enzymes have been proposed to disrupt plaque by lysing the matrix or modify plaque diffusion character. Several plant extracts have antiplaque and/or antibacterial properties by affecting plaque biomass or affect acid production and acid tolerance of cariogenic bacteria.

4. Antibacterial agents reduce acid production, like fluoride, stannous, xylitol, and chlorhexidine.

5. Caries vaccine.


Recommended references