

Lecture #13-14

Caries Prevention

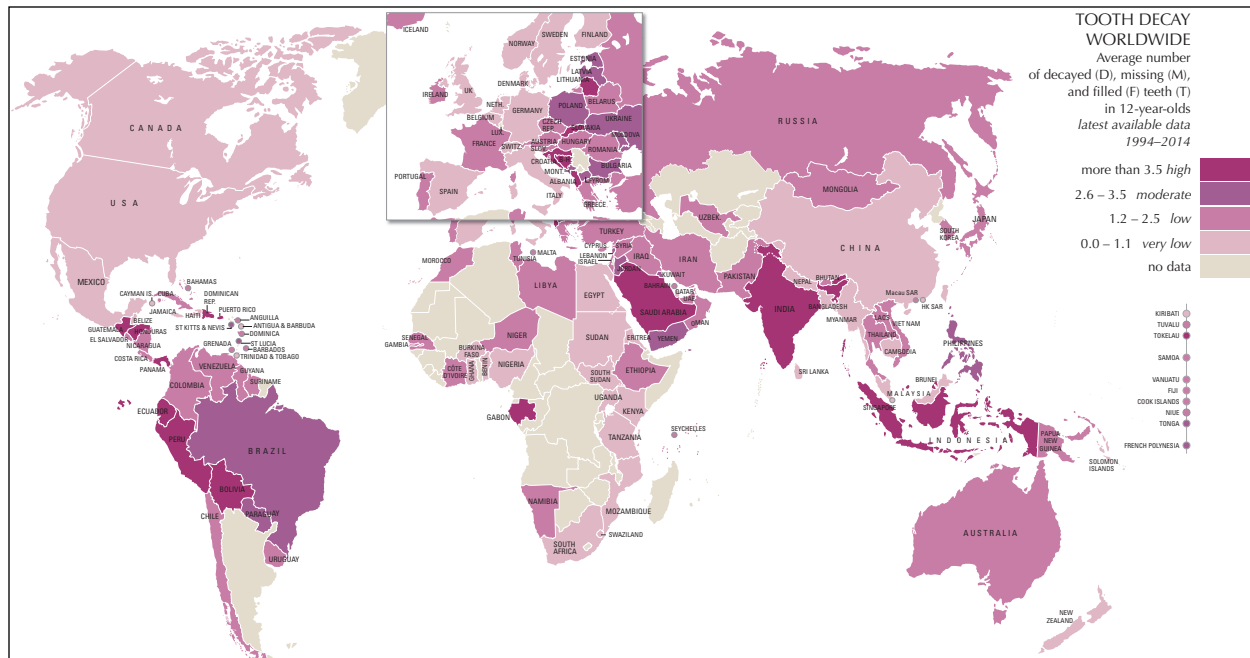
Prevention Lecture Objectives

Be Able To:

1. Explain how genetically-modified, less cariogenic *S. mutans* might someday be ‘painted’ onto children’s teeth to prevent colonization by more pathogenic strains. This is called Replacement Therapy.
2. Describe how Probiotic Therapies might someday impact caries development and treatment; and how probiotics are thought to work.
3. Describe how Vaccines might someday impact caries development and treatment. What antigens might be used in these vaccines?
4. Describe how STAMP (Specifically Targeted Anti-Microbial Peptides) might someday impact caries development and treatment. How do STAMPs work? Explain how lytic Phage Therapy could also work similar to STAMPs.
5. Describe how Replacement, Probiotics, Vaccines, STAMP, and Phage Therapy might someday impact other plaque-related disease treatments.
6. Explain the major problems associated with the four anti-caries treatments above.
7. Describe how Biofilm Interference, such as inhibiting biofilm formation or obstructing quorum sensing, might someday impact caries development and treatment.

Theme. Dental caries is considered the most common *chronic preventable disease* in the world, with a very high morbidity attached to it. Over 3 billion people are thought at any one time to be suffering from painful, untreated lesions. With the best treatment options either expensive restorations or permanent loss of the tooth by extraction, prevention of caries is certainly preferable.

Impact of caries. Dental caries is the most common chronic childhood disease, but it affects people of all ages throughout their lifetime. Current data show that untreated decay of permanent teeth has a global prevalence of over 40% for all ages combined and is the most prevalent condition out of the major diseases included in the Global Burden of Disease Study (the most authoritative estimation of global disease burden, which serves as a basis for health policy planning and resource allocation). <https://www.healthdata.org/gbd/2019>



Tooth Decay Worldwide. Average number of decayed (D), missing (M), and filled (F) teeth (T) in 12-year-olds; latest available data, 1994–2014

Untreated tooth decay frequently causes oral pain. Untreated tooth decay can also cause difficulties in eating and sleeping, may impact children's growth, and is a leading cause of absence from school and work.

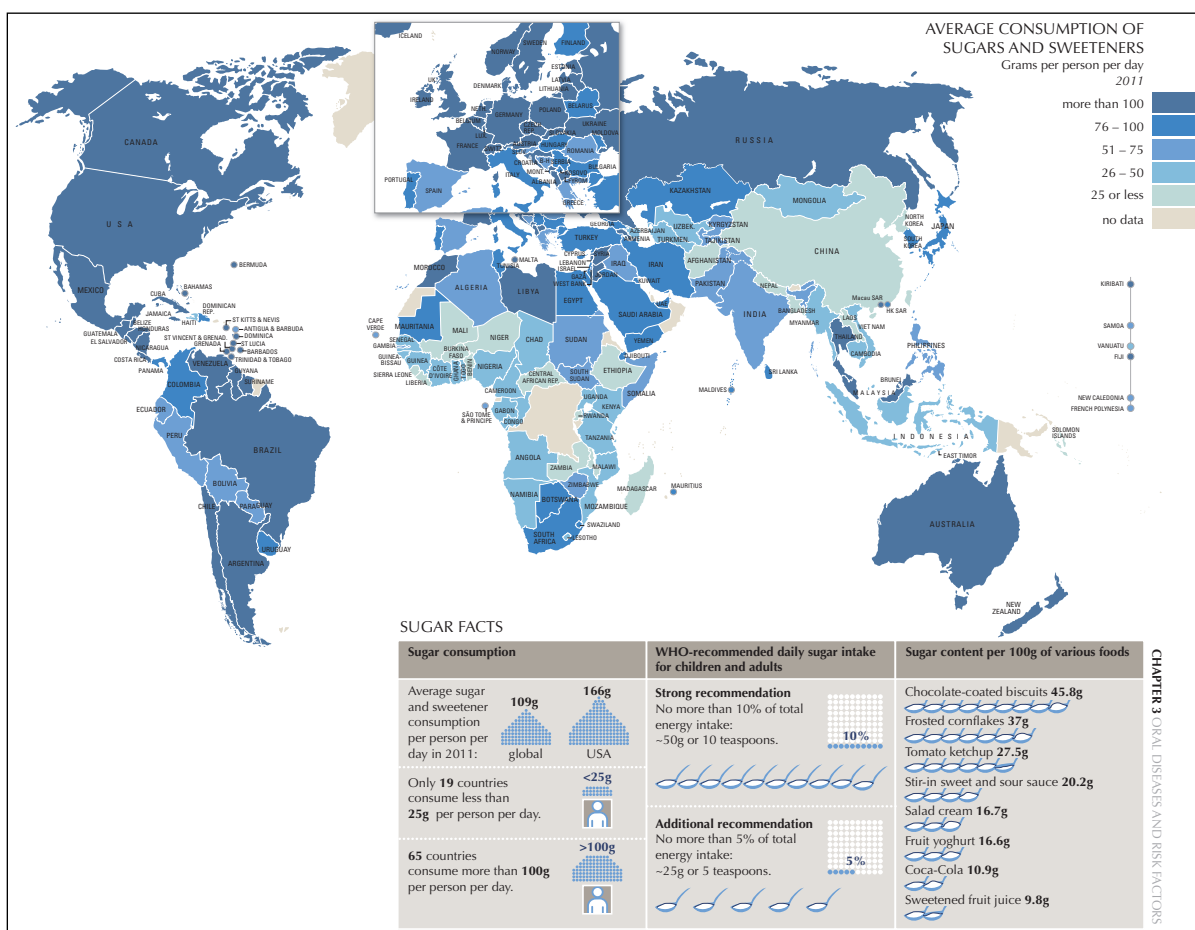
These are damning statistics and provide stark evidence of the neglect of dental caries, and constitutes a major global public health challenge.

Caries prevention classification: Primary, Secondary, and Tertiary. The goals of dentistry should be to promote and preserve oral health and restore it only when it is impaired, hence the key role of prevention – primary, secondary and tertiary.

Primary prevention aims at preventing caries before it occurs. It is most effectively done by preventing exposure to what causes the disease, by modifying unhealthy behaviors and by increasing resistance to the disease. **Secondary prevention** comes into play when caries has progressed to a stage which is clinically detectable (non-cavitated lesion or 'white spot'). It aims at reducing the impact of caries as early as possible by preventing further tooth destruction. It is accomplished through early detection and prompt intervention in order to reverse or arrest caries progression. **Tertiary prevention** applies in later stages of caries (cavitation) and it aims at lessening its impact by preventing further hard tissue destruction, pulpal involvement and tooth loss, and restoring function and aesthetics.

Caries Primary Prevention – Current. Obviously, the best caries prevention methods would fall under Primary Prevention. Therefore, primary prevention strategies mostly need to be directed at modifying or eliminating the major etiological factors driving the caries process (i.e., plaque biofilms, cariogenic substrates, time, and the tooth structure itself). Educating the public and patients on good oral health behaviors and thus empowering them, as much as possible, to be responsible for their own health is a major goal of primary prevention.

Besides patient education, public health prevention strategies might include reducing sugar consumption via increased taxation of sugary snacks, and limiting marketing of sugary snacks to children. Or perhaps, ‘leveling’ the distribution of oral health providers across the economic and social spectrums.



Sugar consumption is influenced by many biological, behavioral, social, cultural and environmental factors. Worldwide sugar consumption has tripled over the past 50 years, and this increase is expected to continue, particularly in emerging economies. To curb the growing epidemic of tooth decay and other sugar-linked diseases such as diabetes and obesity, WHO recommends limiting the daily consumption of free sugars to 5 percent or less of total energy. This is equal to 25 grams or 5 teaspoons of sugar per day per adult, even less for children!

Beyond the broad public health measures mentioned above are many caries prevention strategies. (More effective measures at the top of the list.)

Caries Prevention Strategies – Current

- Fluoride – highly effective in all forms
 - Water, salt, tablet, etc.
 - Professional applied (e.g., F-containing gels and varnishes)
 - Home oral hygiene (e.g., F-containing pastes, gels, and rinses)
- Sealants – highly effective when applied correctly
- Saliva Stimulation
 - Sugar-free gums
- Diet Modification – can be very effective, but hard to accomplish
 - Behavioral changes – very difficult for most
- Antimicrobials - Non-specific
 - Chlorhexidine
- Oral Hygiene – without fluoride, much less effective

Caries Primary Prevention – Future? There are many avenues of research looking for new ways to help in primary prevention of caries.

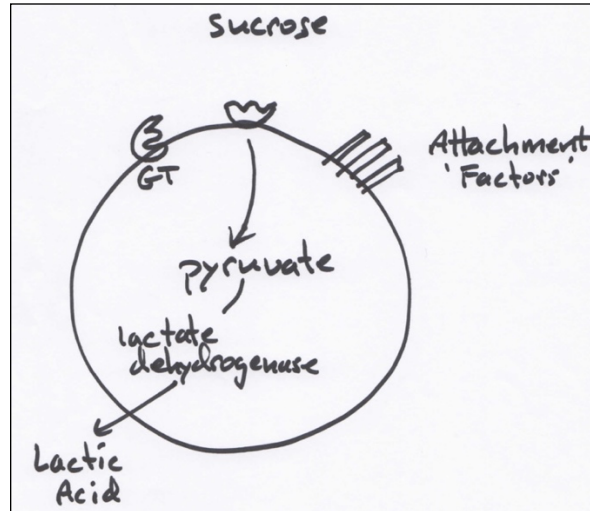
Some of the exciting possible prevention strategies ‘in the pipeline’ include:

Vaccines Target the most cariogenic bacteria, or keystone bacteria, such as *S. mutans*. Produce an effective vaccine using *S. mutans*, or more likely important structures on *S. mutans*, to induce a protective antibody defense against these microbes. This has been very effective in animal studies, but so far hasn’t translated into an effective human vaccine.

Q? What class of antibody would you like the vaccine to induce? How might a vaccine be designed to do this?

Replacement Genetically modified, ‘designer’ probiotics. Why try to remove the ‘weeds’, when you can design your own ‘less weedy, weeds’! The idea is to use what is known about a microbe’s virulence factors to make a genetically-modified, less pathogenic strain, which is competitive against the original more pathogenic wild-type strain. E.g., design a *S. mutans* that is no longer cariogenic, yet can compete for the same niches as the more pathogenic normal *S. mutans* strains.

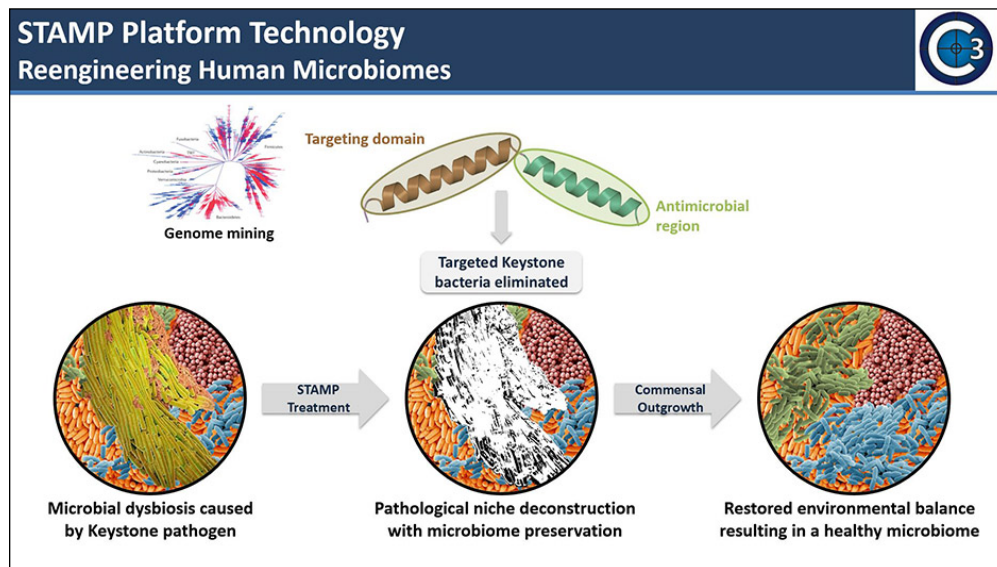
GMO’s are a hard sell in many communities. GMO germs would probably be even harder! Another way may be to search for naturally-occurring, less pathogenic strains. Being done now.



Both Vaccines and Replacement strategies take advantage of what has been learned about the major virulence factors of the major keystone bacteria of dental caries, such as *S. mutans*, to attempt to design strategies to modify the plaque biofilms and make it less cariogenic.

STAMP

Specifically Targeted Anti-Microbial Peptides - In vitro biofilms treated with *S. mutans* STAMP, resisted recolonization with wild-type *S. mutans*. Once established an ecosystem resists change! Early in vivo studies in humans are very promising. Implications well beyond caries prevention!



STAMP (specifically targeted anti-microbial peptides) is a very exciting new strategy to eliminate certain keystone cariogenic bacteria from dental plaque biofilms. Designer, specific 'weed killers!'

Phage Therapy No matter what bacteria, we will eventually identify bacteriophages, naturally occurring bacterial assassins, that can selectively kill bacteria more efficiently than antibiotics.

Probiotics Live microorganisms, which when consumed in adequate amounts, confer a health benefit on the host. This is ‘the wild west’ at this point. Marketing has really taken over this promising field. A glint of gold at the bottom of the pan, but many Ne’er-do-wells just trying to make a quick buck as well!

Probiotic mechanisms:

- Competitive exclusion of pathogens - By filling all the ‘seats’, less harmful microbes make it harder for pathogens to colonize area (competitive exclusion).
- Inhibit growth of pathogens - This can occur through a variety of ways, including:
 - Competing for nutrients
 - Releasing toxic substances such as acids, H_2O_2 , bacteriocins, etc.
- Optimize immune response - Through a wide variety of means, probiotics can bring the immune system into ‘balance.’
- Restore healthy flora after treatment - Treatments (antibiotics, dental treatments, etc.) often leave a lot of ‘empty seats’, which may allow an opening for more pathogenic microbes!



By filling in all of the ‘seats’, less harmful microbes make it harder for pathogens to effectively colonize an area (competitive exclusion). This is just one of the ways that probiotics are theorized to work. Probiotics are an attempt to optimize the oral ecology for health, and to lower the risk of pathology.