Dental caries is one of the common microbiologic and multifactorial diseases; it depends on factors such as host, agent and numerous environmental factors. Generally caries develop in between the age of 2nd and 3rd years in children during tooth eruption when colonization of S.mutans get started in oral cavity. This period is named as “Window of Infectivity”. Different preventive techniques have been developed against dental caries, out of which caries vaccine is one. Immunization can either be active (mucousal, systemic, activogingivo salivary) or passive (bovine milk, mouth washes, transgenic plants etc). Vaccine targets are various proteinous substances present on bacterial surface, enzymes and glucan binding proteins and therefore the protection is gained by salivary antibodies stimulation which can inhabit sucrose dependent and sucrose independent accumulation on tooth surface. Furthermore achievement of immunity is by concentration of immune response on suspected functional areas of targeted components by use of synthetic peptides and recombinant DNA technology acting as immunomodulators or vaccine deliverers. Use in humans depends on success of clinical trials in animals.

**Keywords:** Anti Caries DNA Vaccine, Dental caries vaccine, Mutans streptococci, Mucosal immunization.

### Introduction

Greater studies have been made in understanding the dental caries etiology. In the last century Clarke isolated *Streptococcus mutans*. In 2002 complete genomic sequence of *S.mutans* was reported. Indigenous microorganisms present in oral cavity are responsible for dental caries and periodontal disease. Mutans streptococci including *S.sobrinus* and *S.mutans* are considered to be the main cause and etiological agent of dental caries. Dental caries is considered to be the major public health problem resulting by interaction b/w host, its intake diet and micro flora present on tooth surface influenced by time factor. Many studies have been conducted in order to develop an effective vaccine for prevention of dental caries. “A Caries Vaccination is programmed approach to pre immunized and protect caries prone people mainly children by using proteins present on oral flora bacterial surfaces mainly Streptococcus mutans (antigens ) themselves for inducing human body to produce antibodies against these antigens naturally.”

### History

Modern era regarding vaccine theory began in late 1969 with intravenous immunization experiments on animals like rhesus monkeys by William Bowen. Natural history study of oral streptococcal acquisition in infants revealed that there is colonization of mutans streptococci in children b/w the age of 2nd and 3rd year of life under named circumstances of diet and other challenges during teeth eruption referred as “WINDOW OF INFECTIVITY”. So window of vaccine opportunity exist b/w 12th and 18th months. DNA probe technology suggests that during first year of life in caries prone patient low level of *S.mutans* is found in oral cavity.

### Discussion

**NATURAL IMMUNE SYSTEM:**

1. Streptococcal pathogenesis

In oral cavity colonization is by binding of agent’s pre-existing receptors within biofilms. Initial attachment to tooth occur by bacterial protein with dental pellicle.

![Mutans Streptococcal Colonization of Infants](image_url)

**Figure 1.** Mutans streptococcal (MS) colonization of humans in the first three years of life. The percentage of children colonized with mutans streptococci is indicated on the ordinate. Percentages reflect children under modest maternal challenge (approximately 50% colonized) or children exposed to high maternal levels (approximately 90% colonized). If high maternal MS levels (dose) are combined with significant exposure to dietary sucrose, initial dental colonization with MS occurs at a younger age.

Because dental caries fulfil the criteria of infectious diseases so its prevention is needed.

2. Host defense system

Majority of immunoglobulin concentration in saliva is of IgA. IgA provide specific immune defense. However, saliva also contain other immunoglobulin from gingival sulcular fluid. These immunoglobulin acts as a specific agglutinin interacting with bacterial surface receptors. There is direct production of saliva by Gut Associated Lymphoid tissue (GALT), In lymphoid tissue, T and B cells
are synthesized, the interaction of cells with saliva play part in modulation of IgA, IgG, IgH by induction of Cd4 and Cd8.\textsuperscript{13} "the immune response and immunological memory are the basics of vaccination and revaccination".\textsuperscript{16,17}

3—Antigenic components of S.mutans as Activators of Immune Response:
Various antigenic components against which immune responses are produced are Adhesins, Glucosyltranferases, and Glucan binding proteins.\textsuperscript{18}

a) Adhesins form two principle human pathogens of S.mutans (variously identified are antigen I/II, Pac or Pi). The antibody which are directed to AgI/II molecule block adherence of S.mutans of saliva coated hydroxyappitite.\textsuperscript{19,20}

b) GTF An enzyme cleaving the bond b/w glucose and fructose in sucrose and then the activated glucose is added to glucan polymer which produces more targeted immune response.

c) GBP These proteins are present on surface of mutans Streptococcal and act as a receptor cell for glucan mediated aggregation. GbpB has been shown to induce protective immune response among its three types.\textsuperscript{21}

d) Dextranases An enzyme produced by S.mutans when used as antigen prevent colonization of organisms in early dental plaque.\textsuperscript{22}

Further achievements of immunity are by concentration of immune response on suspected functional elements of these components by either using synthetic peptide or recombinant DNA translating complete functional domains.\textsuperscript{18,19}

Another approach along with case of other microorganisms is BASF in which lactobacillus flora is programmed against caries and they prevent binding of S.mutans to enamel.\textsuperscript{21}
Phage therapy is also used for controlling oral bacterial load.\textsuperscript{23}

ROUTES OF IMMUNIZATION

1) Active immunization:
   a) Mucosal route.
   b) Systemic route (subcutaneous).
   c) Active-gingivo salivary route.

   a) Common Mucosal Immune route:

   There is an administered chimeric proteins by research which enhance mucosal immune responses to single virulence determinants alone.\textsuperscript{24} This route is most common and is used for induction of salivary IgA.\textsuperscript{25} Other route methods with mucosal immunity are: -

   Oral route through oral feeding of vaccine

   Intranasal for GTF activation, used for sites in closer anatomical relation to oral cavity

2) Passive Immunization

   External supplementation of antibodies can be through bovine milk, mouth washes, dentifrices, egg yolk antibodies, transgenic plants. (The first plant derived vaccine from Genetically Modified Plant)\textsuperscript{7,25,27}

   Hence in active immunization there is induction of salivary antibodies production and memory formation but in order to establish efficacy and safety requires commitment in performing human trails. However in passive immunization due to preformed exogenous antibodies there is advantage of evading risks.\textsuperscript{6}
Delivery Systems and Adjuvants (Immunomodulators): -

Alone antigen was poorly immunogenic so there are modifications of antigen preparations with adjuvant or using other delivery systems to improve immunogenicity. Sources and different vectors used to deliver vaccine are:

**Synthetic peptide:** derived from GTF enzyme and deliver vaccine to saliva. They induce their response by IgG and T-cell proliferation in humans.

**Coupling of protein with cholera toxin B Subunit** protein is Ag I/II, it is powerful immunoadjuvant and suppress S.mutans colonization.

**Coupling of protein with salmonella** attenuated mutant vectors such as Salmonella, which contain plasmids expressing recombinant peptides, can target the vaccine to appropriate inductive lymphoid tissue for mucosal responses.33

**Microcapsules, macrocapsules (Polylactide-co-glycolide)** because of ability of slow degradation and controllable releasing rate they are used as local delivery system e.g. PLGA(poly lactide -co-glycolide)

**Liposomes** phospholipids membrane vesicles, and facilitates M-cell uptake and delivery of antigen to active antibody producing areas of lymphoid tissue.7, 23, 29,30,31,32

Risks of Use of Caries Vaccine

Introduction of crude form of S.mutans vaccine induce antibodies production that not only react against those specific antigens but also against heart tissues usually in rheumatic fever patient they are heart cross reactive. So vaccine should be pure enough with removal of specifically epitope on Ags/II due to which it causes heart reactivity.33

Public Health Aspects

Developing countries without water fluoridation system, poor access to dental health education are in great need of vaccine. An effective safe and readily available vaccine may not only help to fight against pain but save billions of money spend on restorative treatment.7, 1, 34

Conclusion

Active and Passive Immunization strategies to work against pathogenesis of S.mutans in oral cavity hold promise. However to make it practical in humans it depends on clinical findings and their results outcome in animals. Main goal concerned with their use in humans is that it should be safe and as caries is gradual developing process so the vaccine administered should also be long-lasting and effective and should have increasing impact in high risk population. Thus, a successful vaccination of dental caries could be a valuable immunomodulator as compared to other caries preventive measures.7,1,34

References


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