

# An Insight into Caries Vaccine

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## ABSTRACT

Dental Caries is a microbiologic disease that depends on various factors like host, agent and environment. The Colonization of *S. mutans* occurs in the oral cavity at the age of 2-3 years. This period is known as Window of Infectivity. Different preventive approaches have been laid for the prevention of Dental Caries, among which Caries Vaccine is the one which has caught researchers' attention at present. Immunization can be both active or passive. The targets of vaccine are proteinous substances that are present on bacterial surface, enzymes. Immunity is achieved by concentration of immune response on suspected functional areas of targeted components by using synthetic peptides and recombinant DNA Technology. Application on human depend on the successful animal trials.

**KEYWORDS:** Vaccine, *Mutans Streptococci*, Immunoglobulin, Recombinant DNA Technology

## INTRODUCTION

Dental Caries which is considered as a major public health problem, is caused by interaction between host, diet, environmental factors and time.<sup>1</sup> Numerous studies have been conducted on determining the etiology of Caries. He was Clarke who isolated *streptococcus mutans*.<sup>2</sup> In 2002 complete genomic sequence of *S.mutans* was reported.<sup>3</sup> Various microorganisms harboring in the oral cavity are responsible for dental caries and periodontal disease such as Mutans group of streptococci, which includes *S.Sobrinus* and *S.mutans*, that are considered as the chief etiological agent of dental caries.<sup>4-6</sup> Developing of vaccine for this oral disease has been a major task for many researchers since many years and many studies have been conducted to develop an effective vaccine for preventing the occurrence of Dental Caries.<sup>7</sup> Caries Vaccination is a programmed and planned 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.<sup>8</sup>

In late 1969, the modern era of vaccination began with intravenous immunization experiments conducted by William Bowen on animals like irus monkeys.<sup>9</sup> Studies conducted on the natural history of oral streptococcal acquisition in infants showed that children between 19-31 months often face colonization of mutans streptococci in oral cavity under factors like diet, environment and time factors during eruption of teeth. This period is known as Window of Infectivity.<sup>10</sup> So, there exists a window of vaccine opportunity between 12<sup>th</sup> and 18<sup>th</sup> months. According to DNA probe technology, low level of *S.mutans* are found in oral cavity during the first year of life.<sup>11</sup>

With age, maternal dose of a child varies which leads to variation in MS (*Mutans Streptococci*) level. Children

exposed to modest maternal challenge have approximately 50% bacterial colonization and children exposed to high maternal levels have approximately 90% colonization. When high maternal MS levels are combined with exposure to dietary sucrose, initial dental colonization with MS occurs at a younger age (Figure 1).

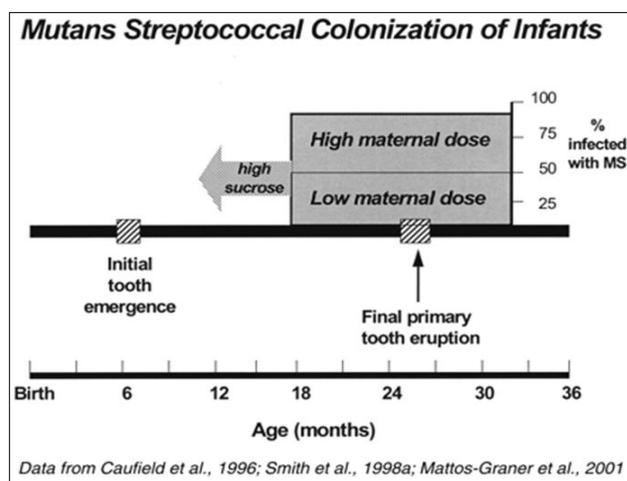


Figure 1. Mutans streptococcal (MS) colonization of humans in the first three years of life. The percentage of children colonized with mutans streptococci is indicated on the ordinate.

## VACCINE-IMMUNE RESPONSE

### 1--Streptococcal pathogenesis:

Colonization of streptococcal bacteria occurs by binding of its pre-existing receptors within biofilms. It occurs when bacterial protein attaches to dental pellicle.<sup>12</sup>

### 2--Host defense system:

Among the various immunoglobins, IgA is the one which is present in maximum in saliva and provides specific immune defence.<sup>13</sup> The immunoglobulins acts as a specific agglutinin, that interact with bacterial surface

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receptors. The lymphoid tissue synthesizes T and B cells that interact with saliva and thus aid in modulation of IgA, IgG, IgH through induction of Cd4 and Cd8.<sup>14</sup> The immune response and immunological memory form the basics of vaccination and revaccination.<sup>15,16</sup>

**3--Antigenic components of S.mutans as Activators Of Immune Response:** S.mutans has various antigenic components like Adhesins, Glucosyltransferases, and Glucan binding proteins against which immune responses are produced (Figure 2).<sup>17</sup>

**a) Adhesins:** These are principle antigenic components of S.mutans that are identified as antigen I/II, Pac or Pi. The antibody which are directed to AgI/II molecule, block adherence of S.mutans of saliva coated over hydroxyapatite.<sup>18,19</sup>

**b) GTF(Glucosyl transferase):** It is an enzyme which plays role in cleaving the bond between glucose and fructose in sucrose. The activated glucose is then added to glucan polymer which produce more targeted immune response.

**c) GBP(Glucan Binding Protein):** These proteins are present on surface of mutans Streptococci and act as a receptor cell for glucan mediated aggregation.

**d) Dextranases:** It is an enzyme produced by S.mutans. When used as antigen, it prevents colonization of organisms in early dental plaque.<sup>20</sup>

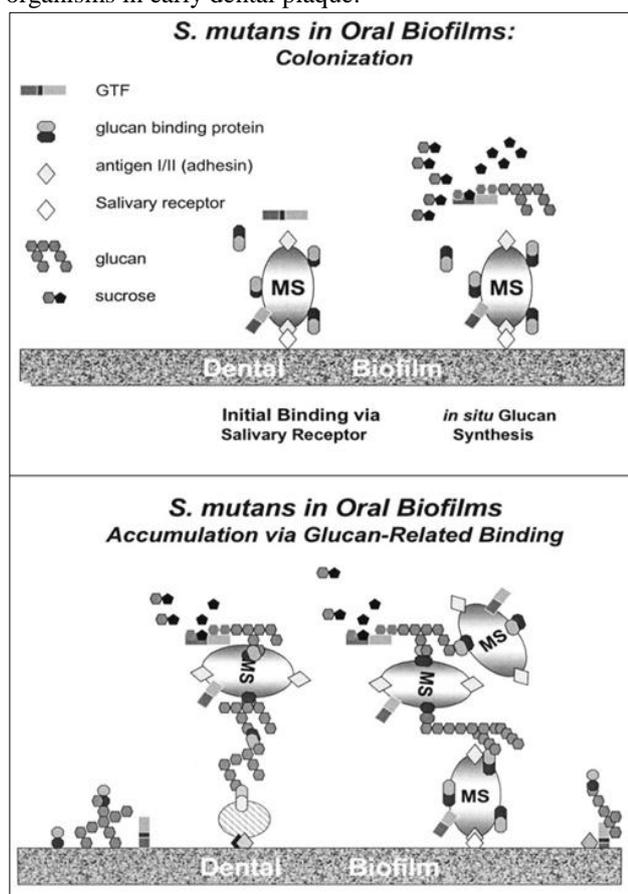


Figure 2: Molecular Pathogenesis of Mutans streptococci

Further immunity can be achieved by concentration of immune response on suspected functional elements by

either using synthetic peptide or recombinant DNA technology.<sup>17</sup>

There are various other approaches in which lactobacillus flora is programmed against caries and they prevent binding of S.mutans to enamel.<sup>21</sup> Besides this, Phage therapy is also used for controlling oral bacterial load.<sup>22</sup>

## ROUTES OF IMMUNIZATION

There are different routes of administration of Vaccine: They are as follows:

### 1) Active immunization:

- Mucosal route.
- Systemic route (subcutaneous).
- Active-gingivo salivary route.

#### a) Common Mucosal route:

This route is most common and is used for induction of salivary IgA.<sup>23</sup> 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
- ❖ **Tonsillar route-** ability of tonsillar application to induce immune response.
- ❖ **Minor salivary gland-** lips, cheeks, soft palate act as potential routes

#### b) Systemic Route of Immunization:

By subcutaneous administration of S.mutans antibodies which find their way to oral cavity.

**c) Activo-Gingivo Salivary Route:** Gingival crevicular Fluid is also used as a vaccine route associated with increased levels of IgA and IgG.<sup>24</sup>

### 2) Passive Immunization:

Passive immunity can be obtained by external supplementation of antibodies through bovine milk, mouth washes, dentifrices, egg yolk antibodies, transgenic plants.<sup>25,26</sup>

In active immunization, there is induction of salivary antibodies production and memory formation, so more of clinical trials should be performed to determine its efficacy on larger group of population and its safety. However in passive immunization due to pre-formed exogenous antibodies, there is advantage of evading risks.<sup>1</sup>

## DELIVERY SYSTEMS AND ADJUVANTS

Alone antigen was poorly immunogenic so there are modifications of antigen preparations with adjuvant or using other delivery systems to improve immunogenicity.<sup>27</sup> 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.<sup>28</sup>

**\*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.<sup>29</sup>

## RISKS OF USE OF CARIES

*S.mutans* vaccine when introduced in crude may not only react against specific antigen but also cross-react against heart tissues, which is most common in rheumatic fever patients. So vaccine should be pure enough with removal of specifically epitope on AgI/II due to which it causes heart reactivity.<sup>30</sup>

## RECENT ADVANCES

p1025, a protein, is a vaccine that has been recently developed that outwit *S.mutans* by showing no vacant sites on tooth for its attachment. It has also been found that, p1025 mimics bacterium protein, occupying all docking sites .

## PUBLIC HEALTH ASPECTS

Epidemiology of Dental Caries is a major concern for developing countries. The limited resources available in these countries add to their disadvantage. Hence, Dental Caries vaccine if developed would save money, time of the majority of population.<sup>7,30</sup>

## CONCLUSION

Procedure of Active and Passive Immunization to work against pathogenesis of *S.mutans* in oral cavity holds promise. In order to make it feasible on human, more of clinical trials are required primarily on experimental animals. The main aim of vaccine should be long term prevention from dental caries, as the disease is gradual developing process. The vaccine should be safe and effective. Caries vaccine if successful tested on humans could be a valuable immunomodulator as compared to other caries preventive measures.<sup>31</sup>

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