# Periodontal Vaccine

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## Abstract :

*Vaccination is a process that induces specific immune resistance to a bacterial or viral infection and Periodontal disease though is multifactorial the complexity of the periodontopathic bacteria might be a problem in determination of Antigens. Till date no preventive modality exists for periodontal disease and treatment rendered is palliative. The search for periodontal vaccine revolves around the antigenic factors of the periodontal pathogens. The objective of periodontal vaccine is to identify the antigens involved in the destructive process of periodontitis against which antibodies would be evoked to exert protection. It also aims to induce mucosal antibody response with little or moderate doses of vaccine. Thus availability of periodontal vaccine would not only prevent and modulate periodontal disease but also enhance the quality of life for whom periodontal treatment cannot be easily obtained.*

**Key Words:** *vaccine, immunity, antibody, antigen, Porphyromonas gingivalis, periodontitis.*

## Introduction

It was like a dream come true when for the first time vaccine were invented. The formulation of the novel hypothesis requires fantasy and creativity. Marvelously said by **Einstein's** "all our knowledge remains fallible", i.e. science will never grow by merely by multiplying the data and observations but only by desiring and struggling to make our dreams come true like **Edward Jenner**.

## Review of literature

### VACCINES:

The term vaccine was coined by **Pasteur**. Vaccines which had been the dream long back but now has been made a reality by the efforts of **Edward Jenner** who invented the 1st successful vaccination against smallpox started in 1796. The vaccine term is derived from Latin word which means 'a suspension of attenuated or killed microorganism administered for prevention, amelioration or treatment of infectious disease. [1], [2]

Vaccine is an immuno - biological substance designed to produce specific protection against a given disease .It stimulates the production of protective antibody and other immune mechanisms .Vaccine may be prepared from live attenuated or killed organisms ,extracted cellular fractions ,toxoids or combination of these .Most recent preparations are subunit vaccines and recombinant vaccine .For the first three decades of twentieth century, vaccines were commonly employed in attempts to control bacterial infections .[3], [4]

Three types of periodontal vaccine were employed for the control of periodontal diseases . These vaccines were prepared from: [5]

1) Pure cultures of streptococci and other organisms

2) Autogenous vaccines

3) Stock vaccines like van cott's, goldenberg's etc

### VACCINATION

It is the development of immunity or resistance to infection, after secondary response that is adequate to

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consider the individual to be immune to a subsequent infection. [6]

## IMMUNIZATION

Immunization is of 2 types- [7]

1) Active Immunization &

2) Passive Immunization

## ACTIVE IMMUNIZATION

Active immunity is induced by exposure to a foreign antigen. This activates lymphocytes to produce antibodies against the antigen. The immune system of the host plays an active role in responding to the antigen. Whole -cell formalin-killed P. gingivalis has been used as the target antigen. [1] Active immunization confers specific immunity against infectious agents.

Results from active immunization studies were assessed using an experimental periodontitis model in M. fascicularis and detailed assessment of immunization impact with regard to immunological, microbiological, and clinical outcomes were summarized. The results from these studies demonstrated that the relationship between antibody titres and killing abilities, and protection against challenge with P. gingivalis infection in the nonhuman primate model was complex. [1] Evidence of a protective mechanism from a formalin-killed whole-cell P. gingivalis vaccine with SAF adjuvant could be found in the reported effect that vaccine-induced serum antibody titres to P. gingivalis resulted in a blockage of prostaglandin E2 (PGE2) response to LPS challenge. [8]

Furthermore, the whole-cell formalin- killed P. gingivalis (monkey strain 5083) in combination with an adjuvant results in a lower levels of PGE2 levels in gingival fluid in immunized M. fascicularis than in placebo immunized animals. The extent of alveolar bone loss was directly correlated to the levels of PGE2. [9] Decreased (PGE2) levels in GCF in immunized animals suggest a positive effect of the vaccine, as PGE2 is a major inflammatory mediator and is associated with bone loss. [1]

## PASSIVE IMMUNIZATION

Protective immunity can be obtained through passive immunization. This can be obtained by transfer of specific antibodies against the target bacteria (antigen). A passive immune response can be achieved by transfer of antibodies via serum, lymphocytes from immunized individuals, or monoclonal antibodies against specific pathogens. Transfer of maternal antibodies to the foetus is another example of passive immunization. The advantages of using antibody molecules to treat infectious diseases include their specificity and versatility. Passive immunization is short-lived and remains effective only as long as the injected antibody persists, host will not respond to the immunization. [1], [10]

## PERIODONTITIS

Two major form of periodontal disease are common in man and other animals, gingivitis and periodontitis. The infectious etiology of periodontitis is complex and no curative treatment modalities exist. Palliative therapy is available. A recent symposium suggested that periodontal diseases may have significant influences on the occurrence and severity of systemic conditions such as cardiovascular disease, diabetes mellitus etc.

The early colonizing bacteria on teeth and on gingival tissues include predominantly Neisseria, Streptococci, and Actinomyces species. Immunization against such bacteria with the objective of preventing colonization of later colonizing pathogens is currently unrealistic. The later phases of bacterial colonization occur in complex biofilm structures. Thus, different forms of diseases caused by specific single-type of infections and against which vaccines have been successfully developed, the etiology of periodontitis is a complex mixed infection that includes large numbers of different pathogenic organisms (i.e. **Socransky & Haffajee 2003**). The bacteria most frequently associated with periodontitis include *Porphyromonas gingivalis, Prevotella intermedia, Tanerella forsythia (forsythensis), Treponema denticola, Actinobacillus actinomycetemcomitans, and Fusobacterium spp.* (**Genco 1996**). Such bacteria and their by-products can elicit strong immune responses (**Socransky & Haffajee 1991**).Bacteria in biofilm structures can be protected from host immune responses and are dependent on environmental (passive response) and genetics (active response) factors. [1]

Changes and disconnection from biofilms occur via: [1], [11]

- Swarming dispersal in which individual bacteria are released
- Clumping dispersal in which aggregates of bacteria are released, or
- Surface disposal

**Vaccine candidate antigens of P. gingivalis**

P. gingivalis is a potential vaccine candidate because this pathogen carries several high potent antigens, an lippopolysaccharides, capsel, lipids, and outer membrane proteins. Whole cell formalin-killed P-gingivalis has been used as the target antigen. Different P.gingivalis antigens have been studied [1]

**Pathogenicity of P. gingivalis**

P. gingivalis, a gram-negative anaerobe, is involved in the pathogenesis of periodontal disease, found more frequently and as a higher population of the subgingival flora in patients with periodontitis. This microorganism easily survives in a hostile environment by successfully evading host antimicrobial defenses, utilizing variety of virulence factors like fimbriae, a polysaccharide capsule and lipopolysaccharide, hemagglutinin and hemolyzing activity, release of toxic products of metabolism, outer membrane vesicles and numerous enzymes.The fimbriae of this microorganism not only play a role in colonization of the microorganism but also activate cytokine production like lipopolysaccharide. The activation of host defense and induction of the inflammatory cytokines such as interleukin 1 and tumor necrotizing factor *a* play an important role.P. gingivalis has several cysteine proteases called as gingipains. Gingipains are classified into two types of groups based on substrate specificity- [1], [12]

1) Gingipains R

It has 2 types- RgpA and RgpB

2) Gingipain K (Kgp)

RgpA together with RgpB, account for all trypsin-like activity of P. gingivalis. Another aspect for the requirement of vaccine development for periodontal disease is as follows- efforts to prevent or arrest the progression of periodontitis have traditionally been directed in a major part toward removal and control of deposit of microorganism on the surface of teeth and elimination of infectious microorganisms. Treatment requires specialty care which is expensive and of limited availability. It can be painful and frequently unsuccessful, resulting in recurrence of or a contribution to the destructive process. More effective approaches for the prevention and control of periodontitis are needed. In searching for the appropriate antigen, it was found that a group of cell surface carbohydrates designated as K antigens, lipopolysaccharides, and various proteins including fimbriae, the 53-KDa and 67K-Da cell surface proteins, haemagglutinin and cysteine proteases referred to as gingipains. Gingipains have shown the highest potential for use as vaccine antigens. Gingipains are present in large quantities on the cell surface of P. gingivalis, and they can significantly contribute to the virulence exhibited by this species. The mature form of RgpA possesses both a catalytic domain and a hemagglutinin domain, while RgpB possesses only a catalytic domain. The hemagglutinin domain plays a role in the adherence of this microorganism to erythrocytes of this microorganism. Arginine-specific Gingipains (RgpA) and lysine specific gingipain (Kgp), enzymes produced by P. gingivalis, may be candidates for an anti-P. gingivalis vaccine. The gingipains (RgpA and Kgp) of P. gingivalis are potential candidates for a vaccine that could be used for prevention of P.gingivalis mediated periodontal disease. [1], [12]-[16]

## PROBIOTICS

Probiotics are live microorganisms administered in adequate amounts with beneficial health effects on the host. The Food and Agriculture Organization of the United Nations has defined Probiotics as ''live microorganisms administered in adequate amounts conferring beneficial health effect on the host''. Most probiotic products contain bacteria from the genera Lactobacillus or cell formalin-killed P. gingivalis has been used as the target antigen. [1]

## Conclusion

To sum it up following four points need to be revised: [1]

I) There is sufficient concurring evidence that serum antibodies against P. gingivalis antigens are induced by either infection or immunization.

II) There are non-human primate and murine study results with evidence of specific methods to induce an enduring antibody titre without recognizable systemic side-effects. The ambiguity in some study results may depend more on the study model (ligature-induced disease) than vaccine efficacy. High antibody titres appear to provide protection.

III) Immunization against P. gingivalis results in a reduction of the quantity of the target organism in animal models. P. gingivalis levels at infected periodontal sites are inversely correlated with antibody titres against the pathogen.

IV) Collaborative efforts are needed to ensure successful vaccine development against periodontitis.

Whereas most vaccine efforts are directed against infections caused by single viral or bacterial infectious agents, periodontitis is believed to have a complicated infectious pattern. Few vaccines based on a composition of antigens from different bacteria/viruses and linked to different infectious diseases have been tested or developed. [1] One example is the classical measles, mumps, and rubella virus vaccine combination, against three different diseases**.** [17] Vaccines studied in mice using conjugate multiple-antigen peptides against highly variable pathogens have been shown to elicit antibodies to a huge number of clinical isolates. [18] Thus, similar methods might be applicable to combined periodontal and caries vaccine trials. The current evidence collected from a large series of diverse and independent studies have clearly demonstrated that active immunization using vaccines against P. gingivalis will induce a significant humoral response across animal study models. If passive immunization studies are included, such evidence can also be gathered from human observational studies. [1]

Recent advances in mucosal immunology and the introduction of novel strategies for inducing mucosal immune responses now raise the possibility that effective and safe vaccines can be constructed.

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