

**Tri-immuno-phasic periodontal therapy and Bone one session treatment: An enigmatic review**

<sup>1</sup>Dr.Sireesha K S, Periodontist, Tirupati -517501, Andhra Pradesh.

<sup>2</sup>Dr.Arati C Koregol, Professor, Department of Periodontics, PMNM Dental College & Hospital, Bagalkot-587101, Karnataka.

**Corresponding Author:** Dr. Sireesha K S, Periodontist, Tirupati -517501, Andhra Pradesh.

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**Abstract**

Periodontitis is considered to be the outcome of lowered immune response with the presence of periopathogenic bacteria. One of the researches in this field is Tri-immuno-phasic periodontal therapy (TIP). TIP allows practitioners to reach the depth of dentogingival unit and to destroy anaerobic bacteria which are aggressive pathogens that causes the degeneration of alveolar bone. It also penetrates the blood circulation and contributes to more systemic complications. To durably defeat anaerobic bacteria requires periodontal therapy that creates and maintains aerobic conditions. Healing in TIP occurs with the help of stem cells from the periodontal ligament. TIP therapy can thus help in regenerating the alveolar bone by improving the periodontal and oral health of the individual. Tri-immuno-phasic periodontal therapy has opened up new horizons in treatment of periodontal diseases by overcoming the disadvantages of traditional treatment modalities to heal back a new attachment. Early intervention and proper execution could save the patient

being subjected to unnecessary invasive, time consuming surgical procedures and thus improving the periodontal condition of the individual.

**Keywords:** Bacterial DNA testing, Bone one session treatment, New attachment, Non surgical therapy, Stem cells, Tri-immuno-phasic periodontal therapy.

**Introduction**

Inflammation, although acute or chronic is a result of response to various injuries or insults, including heat, chemical agents or bacterial infection. In chronic inflammation, there is activation of the adaptive immune response involving the cellular and non-cellular mechanisms of acquired immunity. Immune mechanisms play an important role in the resolution of inflammation and in the healing process, including repair and the regeneration of lost or damaged tissues. Thus, coordination between injured tissue innate immunity and acquired immunity is essential to maintain homeostasis. [1]

Periodontitis is a highly prevalent immuno-inflammatory disease in tooth supporting tissues including gingiva,

cementum, periodontal ligament and alveolar bone. Inflammation is induced by predominantly gram negative periodontopathic bacteria such as Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans, Treponema denticola and Tannerella forsythia. [2,3,4,5] The severity of the disease is determined by ecological interactions between the host and microbes. Periodontal diseases occur as infections mediated by the overgrowth of commensal organisms and immune mechanisms determining the ecological balance of commensal organisms need to change to preserve homeostasis owing to the rapid evolving capacity of mammalian hosts. [6]

Once periodontitis manifests, destruction of the periodontal tissue is caused by host periodontal enzymes. [3,7,8,9] Even there is considerable interindividual variation, periodontitis certainly results in loss of tooth supporting tissues. Ulceration of the pocket epithelium allows oral bacteria to enter the circulation. [10] This causes both transient bacteremia and formation of proinflammatory cytokines with possible systemic complications. [10,11] The progression of periodontitis is multifactorial including host response, genetics, general health, smoking habit, diet and other social determinants. [3]

Periodontist has the armory of traditional treatment modalities for periodontal diseases like non- surgical and surgical treatment. [12] Non -surgical includes scaling, root planing, local drug delivery, home oral hygiene practices and surgical includes periodontal flap therapy, gingivectomy. Newer and advanced techniques to combat oral microbiota have been developed which include probiotics, Ozone Therapy, Periodontal Vaccine, Microsurgery, Lasers, Waterlase, Stem cells, Tissue Engineering, Photodynamic Therapy [PDT], Gene therapy, RNA interference, Nanotechnology, Perioprotect, Use of newer molecules and therapeutic approaches to resolve inflammation Tri-immuno-phasic therapy [TIP],

Bone One Session Treatment [BOST]. [12,13] It was US periodontal therapist William Hoisington who masterminded a new technique called Tri-immuno-phasic Periodontal therapy [TIP] in treatment of periodontal disease which tackles this issue in an entirely new way. [14]

### **Methodology**

The search strategy involved in the present review included literature search by electronic and manual searches in English language. This was carried out through search of scientific databases like MEDLINE, EMBASE, PUBMED databases, preMEDLINE, Google scholar, Scopus, Web of science and textbook from 1985 to till date. The combination of keywords were used for search, which included TIP, BOST, DNA testing, Stem cell regeneration, Stretch flap, New attachment, Perioaid, Splinting, Nutrition, Antibiotics. All terms were used as full or with truncation to gather all the available literature. The search yielded 26 references.

The aim of this review was to discuss the principles, advantages and limitations of TIP and BOST in the field of periodontology with the future perspectives and to present new challenging indications of this modern technology for daily practices.

### **Tri-immuno-phasic periodontal therapy**

Tri-Immuno-Phasic periodontal therapy, otherwise known as TIP, allows practitioners to go under the gingiva and destroy anaerobic bacteria – aggressive periopathogens that not only cause degeneration of bone and gingiva but also penetrate the body’s circulation and contribute to more serious health complications such as heart disease, osteoporosis, premature birth and infertility. [14]

TIP therapy includes the following steps: Bone One Session Treatment, Controlling occlusal Forces, Oral Hygiene reinforcement with adjuvant modalities, Life Style modification, enhancing nutrition and Exercise.

This review provides an insight into integrating TIP and BOST as a part of routine periodontal therapy by exploring new horizons about various treatment modalities and suggesting how a damaged bone can regenerate and gain attachment healing.

Aggregatibacter [Aa] and Porphyromonas gingivalis [Pg] are those aggressive species of bacteria that cannot be controlled without the antibiotics. Identification of specific pathogenic bacteria causing inflammation will be laying the basis for successful treatment. This is achieved by using bacterial DNA test. Consumption of unnecessary antibiotics leads to drop in immune system. So with this bacterial DNA test, specific bacteria can be targeted by antibiotic therapy. If test shows presence of these bacteria, then definitive pharmacotherapy with appropriate antibiotics are added to treatment to accomplish complete healing. When invasive bacteria are present deep inside the tissue, on roots and bone, where the instrumentation can't reach, these antibiotics are needed to clear them out.

### **Bacteria DNA Testing**

Bacterial DNA testing is based on recognizing each strain of bacteria that has a specific fingerprint of genetic material to establish the specific species of bacteria that are present in the infection which helps in formulation of treatment plan. Compared to culturing the bacteria, Bacterial DNA testing offers much greater accuracy as well as reduced cost. It is a quick, safe, and a painless process.

47 pathogenic complexes have been identified in subjects with periodontitis. 10 different antibiotic regimens are selected according to their minimum inhibitory concentration [MIC] values and gingival crevicular fluid [GCF] concentrations might be required to specifically target various pathogen complexes. These antibiotic regimen includes 7 antibiotics [amoxicillin, amoxicillin/clavulanic acid, metronidazole, doxycycline,

tetracycline, clindamycin and ciprofloxacin] and 3 combination of the above mentioned antibiotics [metronidazole + amoxicillin, metronidazole + ciprofloxacin, metronidazole + amoxicillin / clavulanic acid].<sup>[15]</sup>

### **Method of performing bacterial DNA test-<sup>[14]</sup>**

Four tiny paper points are placed subgingivally for 15 seconds to collect periodontogenic bacteria. These anaerobic bacteria thrive in the biofilm that covers the roots below the attachment level. The paper points are then removed and further sent to the laboratory for analysis of specific pathogenic bacteria that is present.

### **Indications of bacterial DNA test:<sup>[14]</sup>**

- People with symptoms of gingival diseases
- Before Implant therapy
- Prior to orthodontic treatment
- For patients who have family history of Cardiovascular diseases, Diabetes, Arthritis, Respiratory infections, Gastrointestinal diseases, Alzheimer's, Aphthous ulcers as they are all linked to periodontogenic bacteria.

### **Bone One Session Treatment [BOST]-<sup>[16,17]</sup>**

The Bone One Session Treatment is a new generation non surgical aerobic treatment that aims at eliminating periodontal disease It is fast, non-invasive surgery and hence comfortable and reliable. The treatment is completed in 4-5 hours period. The use of custom heated beds by William Hoisington added comfort to the lengthy procedure. After B.O.S.T bone is able to heal and pockets fill with healthy tissue.

### **Procedure:<sup>[16,17]</sup>**

#### **Stretch Flap Technique**

Diseased tissue is spongier and loses its fibrous component and since there are elastic fibers it is possible to stretch the tissue to open the access into the deep pockets of upto 6-9mm and to the surface of bone without incisions.

Universal 4R-4L curette is inserted inside the gingival sulcus,  
 working end facing towards tooth surface  
 blunt non working end is facing the tissue surface

↓  
 On application of Slight pressure to gingival tissues

Removal of plaque and calculus and stretching of the gingival tissue till alveolar bone level

↓  
 Direction of curette changed to a circumferential motion starting at the corner  
 To mobilize the tissue and to avoid detachment of papilla thereby creating an Incisional flap

↓  
 As the tip of the curette advances,  
 Instrumentation of bone surface to remove attached granulation tissue and  
 Osteoplasty of the bone porosities will help to remove microorganism and toxins in the pockets  
 by encouraging fresh bleeding

**Advantages of Bost:** <sup>[16,17]</sup>

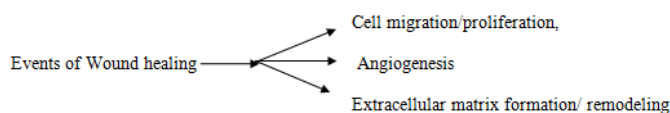
- Creating Personalized periodontal treatment by giving the body a chance to heal by itself.
- Creating aerobic environment by drainage of toxins and calculus subgingivally thereby reducing the number of aggressive periodontopathic bacteria
- Creating less discomfort by implementing non-invasive therapy and promoting long-term success.
- Chance of reinfection is reduced as the treatment is completed in single session.
- Helps improve aesthetics thereby improving oral health and general health.
- Helps to reduce burden on the immune system.

Table 1: Differentiating Bost From Traditional Scaling, Root Planning And Flap Surgery <sup>[18]</sup>

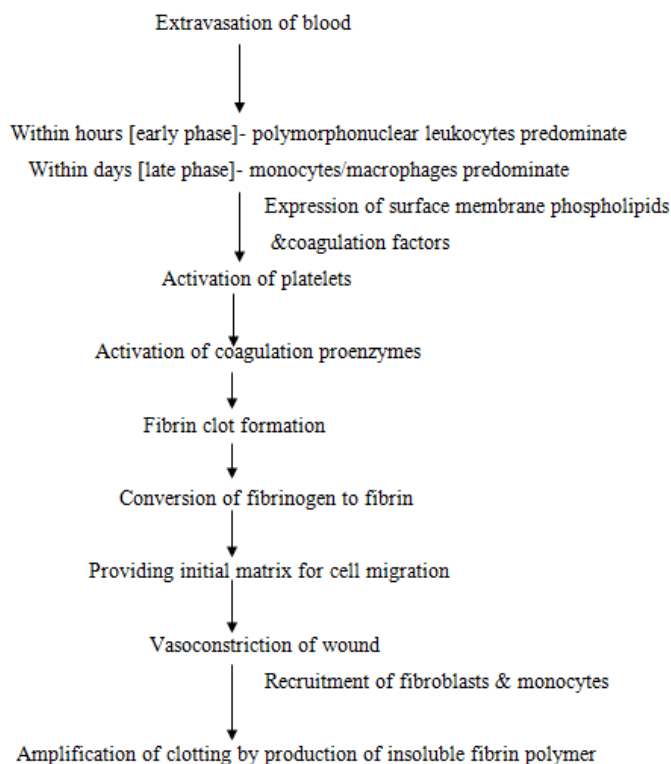
	Scaling and root planning	Flap surgery	Bone one session treatment [bost]
Incision	Not given	Given	Not given
Healing time	More	More	Less
Sutures	Not placed	Placed	Not placed
Bone necrosis	Does not occur	possible	Does not occur
Number of appointments	Single	Multiple [quadrant wise treatment, suture removal, follow up]	Single
Reinfection	May be present	Chances present	No chances
Healing process by	Fibrin clot formation	Fibrin clot formation	Stem cell proliferation and migration
Nature of treatment	Non-invasive	Invasive	Minimally invasive
Patient compliance	Compliant	Needs Motivation	Easily motivated
Instruments used	Curettes Suture material	Bard parker blades Periosteal elevator Curettes Scissors Suture material	Universal 4R-4L Curettes
Treatment duration	Less	Prolonged	Prolonged for 4-5 hours
Oral hygiene	Restarts the next day	Starts after the periodontal dressing is removed i.e., after 1 week.	Restarts the next day

In standard root planing technique, the effective penetration under the gingival tissue is limited to 4 or 5 millimeters into the periodontal pocket, after attachment from the gingiva to the roots has been lost, exposing the alveolar bone underneath. Normal root planing only accomplishes about 1/4 of the work that needs to be done to heal the bone and create conditions where the pocket can fill with healthy new attachment. As a result, root planing does not reach infected surface of the bone or deepest parts of the roots. The BOST treatment, on the other hand, reaches all the way down to infected bone and root, promoting aerobic conditions and complementing oral hygiene.

### Healing<sup>19</sup>



### Mechanism of wound healing in general



### Constraints in Wound Healing:<sup>[19]</sup>

1. Lack of stability in the fibrin clot formation which leads to the formation of a long junctional epithelium rather than a new connective tissue attachment and periodontal regeneration.
2. Position, rigidity and mineralized avascular nature of the root surface, as well as the confined spaces between teeth and tensile forces acting on the wound margins is challenging the flap adaption.
3. Physiologic masticatory and induced forces that may jeopardize early events of periodontal wound healing.
4. Maintained wound closure for primary intention healing depends on the strategy and materials used for suturing.

### Evolution and Mechanism of Woundhealing in Tip

Since the periodontal diseases are now recognized as eco-genetic diseases, it is essential to consider not only host-microbial interactions but also impact of gene polymorphisms, host immunoinflammatory responses, local and systemic environmental factors and various medications on the gingival and periodontal connective tissue structure and function in both health and disease. These new approaches offer interesting alternatives to existing therapies for the repair and regeneration of the periodontium.<sup>[20]</sup>

Friedenstein and colleagues first isolated mesenchymal stem cells in adult bone marrow aspirates by their capacity to form clonogenic clusters and potential to undergo extensive proliferation in vitro and to differentiate into different stromal cell lineages.<sup>[21]</sup> Periodontal ligament comprises of a pool of many cells, including cementoblasts, osteoblasts, fibroblasts, myofibroblasts, endothelial cells, nerve cells and epithelial cells. The identification of putative mesenchymal stem cell populations within the periodontium has raised interest in its potential use in stem cell based therapies in treatment of periodontal disease.<sup>[20]</sup>

Melcher proposed the concept of stem cells residing in periodontal tissues which ultimately were derived from a single population of ancestral cells or stem cells. [22] Periodontal regeneration includes morphogenesis, cytodifferentiation, extracellular matrix production and mineralization, which support the concept of periodontal ligament stem cells [PdlSCs] playing a major role in maintaining tissue homeostasis, thus serving as a source of renewable progenitor cells generating cementoblasts, osteoblasts and fibroblasts throughout adult life. Mesenchymal stem cells could be activated in the event of periodontal injury leading to terminal differentiation and tissue repair or regeneration. Mesenchymal stem cells in contrast to embryonic stem cells show lack of telomerase

expression, which would normally be maintaining the telomere lengths and chromosomal stability during cellular division. This may be important for prolonging cellular senescence by regulation of numerous key cell cycle regulators, which permit progression within the cell cycle from G1 to S phase, leading to an increased proliferation potential and survival rate. [23,24]

Stretching of gingival tissue speeds up the healing process by minimizing damage to bone and periodontium thus preserving the health of gingival tissue and bone cells. It allows good clot formation in which PdlSCs venture out in a highly inflamed infected environment. The firm attachment of the clot to bone serves as a scaffold for the stem cells to move along the root surface. [25]

Table 2: Comparison of healing after scaling, root planing and flap surgery with tip

	Healing After Scaling & Root Planing [26]	Healing After Flap Surgery [26]	Healing after Tri- immune- phasic periodontal therapy [17]
1 <sup>st</sup> day	<ul style="list-style-type: none"> <li>Blood clot fills the pocket which is totally or partially devoid of epithelial lining.</li> <li>Hemorrhage with dilated capillaries &amp; PMNs.</li> </ul>	<ul style="list-style-type: none"> <li>Connection between flap and tooth by blood clot</li> </ul>	<ul style="list-style-type: none"> <li>Blood clot fills in and is firmly attached to the clean bone serves as a scaffold.</li> </ul>
2-7 days	<ul style="list-style-type: none"> <li>There is rapid proliferation of granulation tissue with decrease in number of small blood vessels as the tissue matures.</li> </ul>	<ul style="list-style-type: none"> <li>Gap between Flap and tooth or bone .</li> <li>Epithelium migrates over border of flap.</li> <li>Minimal inflammatory response when flap is in close adaptation.</li> </ul>	<ul style="list-style-type: none"> <li>The stem cells move along it and up the root surfaces at the rate of 0.5mm per day for eight days and thicken the layer on the clot.</li> </ul>
After 1 week	<ul style="list-style-type: none"> <li>Restoration and epithelisation of gingival sulcus</li> </ul>	<ul style="list-style-type: none"> <li>Granulation tissue cover the dead bone</li> <li>Epithelium attachment to root surface by hemidesmosome</li> </ul>	<ul style="list-style-type: none"> <li>Periodontal pocket starts to fill in.</li> </ul>
After 2 weeks	<ul style="list-style-type: none"> <li>Immature collagen fibres appear.</li> <li>Normal colour, consistency, surface texture, and contour of the gingiva are attached.</li> <li>Gingival margin is well adapted to the tooth.</li> </ul>	<ul style="list-style-type: none"> <li>Collagen fibers begin to appear parallel to tooth surface</li> <li>Union of flap to the tooth is still weak because of presence of immature collagen fibers.</li> <li>A thin layer of epithelium and</li> </ul>	<ul style="list-style-type: none"> <li>Pockets have filled in.</li> <li>Esthetic restorations can start.</li> </ul>

		highly inflamed granulation tissue <ul style="list-style-type: none"> <li>• Sequestration and severe osteoclastic activity involving exposed bone surface was seen.</li> </ul>	
After 1 month:	<ul style="list-style-type: none"> <li>• Formation of long, thin junctional epithelium with no new connective tissue attachment.</li> </ul>	<ul style="list-style-type: none"> <li>• Fully epithelised gingival crevice with well defined epithelial attachment.</li> <li>• Beginning of functional arrangement of supracrestal fibers.</li> </ul>	<ul style="list-style-type: none"> <li>• Pockets fill in from the bottom with very dense, partially mineralized connective tissue [MAC] and finally will become acellular.</li> <li>• The final healed result with the bone crest cortical layer reformed and the disappearance takes about nine months.</li> </ul>

**Coronoplasty and splinting:** <sup>[16,17]</sup>

The primary objective of performing this procedure is to redistribute the forces on all the teeth by controlling the occlusal forces thereby preventing tooth mobility which would further prevent tissue damage.

**Oral hygiene reinforcement**

In addition to brushing and flossing, use of oral hygiene kit following bone one session treatment is recommended for maintenance oral hygiene subgingivally and thereby eliminating the pathogenic bacteria all the way down the attachment and into the root concavities where the brush and floss can't reach. Oral hygiene kit consists of Perio-Aid which consists of a handle and disposable hygienic points called aeros that fit into the end of the handle. This oral hygiene routine develops a new kind of attachment which is formed from the differentiated osteoblasts and keeps the tissue bit open and stops the epithelial attachment favoring the slower healing from bottom up which is similar to a membrane. A firm attachment with lack of bleeding or plaque on the tip gives the positive feedback which is evaluated with the squeaky clean sound against the tooth.

**Instructions:** It is to be used twice daily for 8 days and once daily for lifetime. <sup>[16]</sup>

**Life Style, Nutrition and Exercise:** <sup>[17]</sup>

- Eat balanced diet by consuming at regular intervals and by avoiding excessive sugar intake and frequency and by avoiding inbetween snacking.
- Increase intake of vitamins and minerals. Vitamin C and Zinc are most important.
- Avoid Smoking as it reduces circulation & depresses certain immune cells
- Regular exercise increases circulation to bring in building blocks and oxygen to the tissues as well as the vitamins and minerals that permit proper uptake.

**Conclusion**

Tri-immuno-phasic periodontal therapy has opened up new horizons in treatment of periodontal diseases by overcoming the limitations of traditional treatment modalities by fashioning a situation whereby the body can get out of its defensive phase and embrace the regeneration phase to heal back a new attachment. Early intervention and proper execution could save the patient being subjected to unnecessary invasive surgical procedures and thus improving the periodontal condition of the individual.

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