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The Expanding Scope of Periodontics – A Review Article

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ABSTRACT

Periodontology is widely recognized as the dental speciality pertaining to the ailments of the tissues surrounding and supporting the tooth. In the past decade a significant amount of research in periodontology was directed towards applications of advanced fields of studies like genomics, proteomics, nano-technology, bio-photonics, etc. The aim of the present review article is to outline the scope of periodontology, by briefing current practices and emphasizing the more recent and advanced developments.

Key Words: Advances in Periodontology, Biophotonics, Genomics, Nanotechnology, Periodontal Vaccine, Probiotics, Proteomics, Tissue-engineering

INTRODUCTION

Periodontics as a speciality is considered to have begun during the mid-nineteenth century when John W. Riggs (1811-1885), now popular for defining the term "Riggs disease", started confining his practice to treating diseases of the periodontium[(1)]. Over the centuries, periodontics has come to include under its umbrella, an enormity of scientific disciplines.

DISCUSSION

In the present article, periodontology is briefed in terms of its conventional diagnostic aids and therapies, and the more recent and advanced developments are then discussed.

Diagnostic Aids

Periodontics encompasses a plethora of conventional and advanced diagnostic tools including probes, radiographic techniques and microbial analyses.

Probes: These are physical devices used to measure the distance from the bottom of the pocket to a reference line (usually the cemento-enamel junction)[(2)]. An overview of all the periodontal probes developed is shown in Table 1.

Radiographic diagnostic aids include

1. Digital Subtraction Radiography (DSR):This has been used in the post treatment assessment in regenerative procedures[(3)]. It is a great tool in conducing longitudinal assessments.
2. Computer-assisted densitometric image analysis system (CADIA): or advanced than DSR, CADIA has been shown to detect the changes in the density of the crestal even bone before the crestal height reduces[(4)]. CADIA can also be employed to evaluate the results of regenerative procedures.
3. Tuned aperture computed tomography (TACT): It has been shown to be more accurate for quantifying osseous changes in healing bone defects and has proposed as an alternative for pre-surgical implant planning[(5)].
4. Cone-beam computed tomography (CBCT): Studies have been done validating the usefulness and accuracy of CBCT in visualizing periodontal structures and in regenerative procedures[(6)].
5. Micro CT: In a study by Park[(7)] et. al., it was demonstrated that Micro CT is reliable approach for quanti-

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tative assessment of the alveolar bone.

6. Optical coherence tomography (OCT): OCT renders early detection of subgingival calculus possible as dental calculus has been found to have strong scattering properties and can be differentiated from Enamel[8].
7. Magnetic resonance imaging (MRI): In a study, including 25 patients with dental implants, by Gunzinger[9] et. al., it was discussed that MAVRIC (multi-acquisition variable-resonance image combination) reduced the artifacts from dental implants (which is one of the major issues for the use of MRI in oral cavity).

Other imaging techniques

1. Ultrasound Imaging: It has been shown that this imaging modality is highly accurate and repeatable for periodontal evaluation[10]. Various systems employing ultrasound have been developed for the detection of subgingival calculus, i.e., Detectar®, Keylaser II®, and Dental Endoscope.
2. Photoacoustic Imaging technique: This imaging technique integrates visible and near infrared excitation with acoustic detection and its application has been demonstrated in measuring periodontal pocket depths[11].

Diagnosis through Microbial Analysis: It has been observed that microbial analysis of the significant organisms in periodontal diseases helped in the clinical decision making process for the adjunctive use of systemic antibiotics[12].

Some of the methods of microbial analysis include:

1. Microscopic assays
2. Culture assays
3. Immunologic assays
   - direct immunofluorescence
   - direct immunofluorescence
4. DNA probe assays
5. Enzyme-based assays

Periodontal Therapy

The core of periodontal therapy includes various non-surgical and surgical modalities. Non-surgical therapy is mainly focused at eliminating plaque and plaque retentive features (calculus, overhanging restoration margins etc) through scaling, root planning and is always combined with oral hygiene instructions.

Surgical therapy is indicated when there are deep obstinate periodontal pockets despite good plaque control. Other surgical procedures include those that correct a variety of natural and pathological aberrations in the periodontium (curettage, gingivoplasty, gingivectomy, muco-gingival surgeries, crown lengthening surgery, root resection procedures and periodontal reconstructive procedures). Different approaches in surgical periodontology (conventional scalpel and laser surgeries, cryosurgery, electro cauterization, piezosurgeries) provide a diverse treatment options for diverse conditions. These therapies constitute the core of periodontics (Table 2).

Scope of Periodontics

The scope of periodontics extends substantially into the other specialities of dentistry.

Periodontics-Orthodontics

The significance of the implications of orthodontic therapy in periodontics can not be over-stated as the medium for orthodontic tooth movement is the periodontal ligament, a central component of the periodontium. In a patient with compromised periodontal health, meticulous care must be provided to ensure the orthodontic therapy is carried out in inflammation-free periodontal tissues. Another interesting overlap between the principles of these two specialities is the 'Periodontally Accelerated Osteogenic Orthodontics' where orthodontic tooth movement is accelerated by way of integrating selective alveolar corticotomy and particulate bone-grafting with orthodontic-therapy[13]. Temporary anchorage devices or mini-implants are often used for orthodontic anchorage.

Periodontics-Prosthodontics

The success of the outcome of any prosthodontic treatment is based on the solid foundation of the periodontium and on restoration designs that are conducive to periodontal health.

Periodontics-Oral Surgery

Many a surgical procedures constitute this interdisciplinary interface such as frenectomy, frenotomy, ridge augmentation procedures, etc. During orthognathic surgeries, there is convincing evidence that suggests, there is significant incidence of periodontal injury in the region of segmental osteotomy[14]. It has been reported that orthognathic surgeries have a marked effect in the development of gingival recessions[15].

Periodontics-Restorative Dentistry

When planning a restoration, consideration must be given to the margin placement, restoration contours and contacts, embrasure shape, and polish of the restoration, so that it is conducive to periodontal health.

Periodontics-Endodontics

There is an intimate relationship between the periodontium and the endodontium through the apical foramen, lateral canals, accessory canals and dentinal tubules. Such a natural continuum in the anatomy predisposes to a pathological continuum as well.

Periodontics-Forensics

The interplay in these departments is appreciated during age estimation using tooth cementum annulations (TCAs) and amino acid racemization (sample taken from gingiva, as it is the most accessible), Gingival epithelium assessment, and using implants (that endure the thermal insults due to the high melting point of titanium) and implant recognition software for identification[16].

Periodontology and Geriatrics

Age-related changes are seen in every tissue of the periodontium in the elderly (thinning of the epithelium, reduced keratinization, flattening of rete pegs in gingiva; increase in the fibrous component in the connective tissue; increase in the width of cementum; resorption of bone). In this group of patients the treatment protocol must reflect the consideration of any other systemic and psychological diseases, resistance and regenerative potential, state of host immune response. In an article by Ira B. Lamster[17] it is discussed that there is a present-day demographic shift where the count of older adults (>65 years) surpasses the count of young individuals (<5 years) and that by 2050 the number of people of age 65 and older will reach 1.5 billion, hence, dental professionals must boost their knowledge necessary to care for older population as this will turn out to be an appreciable part of the future of dental profession.

Periodontal Medicine

Periodontics has ramifications in a multitude of systemic conditions. Periodontal disease has been inflicted as having reverberations in cardiology (Porphyromonas *gingivitis* secretes an enzyme gingipain[18] that is associated with activation of the thrombin receptor on the platelet leading to platelet aggregation), pulmonology (respiratory pathogens may attach to the excessive plaque in patients with periodontitis and act as a source of infection to distal portions of respiratory tracts[19]; dental plaque has been suggested as a critical reservoir for harboring the micro-organisms responsible for hospital acquired pneumonia in institutionalized elderly[20]), pregnancy (Periodontitis is notably associated with preeclampsia and is considered a risk factor[21]), stroke, osteoporosis. Periopathogens also possess the reputation of being capable of causing bacteremia and subsequently focal infections[19]. Hence, periodontology should be reflected as an essential part of preventive medicine.

Tissue Engineering

Tissue engineering has gained favor in periodontics due to its potential in periodontal tissue regeneration and is based on three approaches: (i)Protein (proteins affecting the growth, differentiation and maturation are used) (ii) Cell (Mesenchymal stem cells are used) and (iii) Gene therapy based methods[22]. Gene therapy is an encouraging therapeutic modality in periodontics. Depending on the method of introduction of the gene vector, it can be either in vivo (where they are delivered directly at the target site) or ex vivo (where the target cells are extracted, processed with gene vectors and implanted at the target site).

Host Modulation

Host modulation is gaining importance as a periodontal therapy. Here various therapeutic agents (Table 3) are used to down-regulate the biologic function of pro-inflammatory mediators in the host.

Biophotonics

A popular stream for current researchers in periodontology is 'Biophotonics'. It deals with the area overlapped between photonics and biomedical sciences. Various periodontal applications of biophotonics have been listed in table 4.

Photodynamic therapy (PDT) is one such application where when used an as adjunct to SRP has shown improved results. The three elements of photodynamic therapy are oxygen, photosensitizer and light. The triplet state photosensitizer, that forms after excitation of photosensitizer with light can react with biomolecules in two ways: Type I and Type II[25].

Type I: Direct electron/hydrogen transfer

Type II: formation of singlet oxygen

Photodynamic anti-microbial chemotherapy (PACT) had been observed to show efficacy against bacteria (including drug-resistant strains), yeasts, and parasites[26].

Micro-dentistry

Concepts of micro-dentistry, in the context of periodontology engendered a periodontal endoscope (The Perio-Scope) that harbors fibre-optic technology for illumination, magnification and video-recording for visualizing sub-gingival tissues[27]. This allows instrumentation in the most efficient way possible ensuring a thorough debridement. Using the similar technology, endoscopic capillaroscopy systems have been developed for the imaging of periodontal-pocket and gingival crevice micro-vasculature[28]. This currently aids in understanding the pathological process but in future may prove to be an effective diagnostic aid.

Genomics, Proteomics and Nanotechnology

Future of periodontics powered by genomics, proteomics and nanotechnology seems immensely promising. Nutrigenomics is a newly unravelling scientific sphere that is believed to have implications in the development of periodontal diseases. Epigenetic variations (like DNA methylation, histone modifications, chromatin remodelling) in genes regulating nutrients can increase the probability of micronutrient diseases like obesity and type 2 Diabetes Mellitus that have propensity for periodontal manifestations[29].

Introduced by Kellam and Weiss, Infectogenomics deals with the influence of host genetic variability on microbial colonization and governs the outcome of infection by various pathogens[30]. A variety of genetic factors have been recognized to impact periodontal pathogen invasion. Mutations in the genes expressing a few pattern recognition receptors (TLRs and NLRs) evoke an altered host response to microbial invasion[31]. Polymorphisms in the IL-1 gene have been extensively implicated in the pathogenesis of chronic periodontitis[32,33]. Other gene polymorphisms (in genes expressing cytokines) associated with periodontitis are of tumour necrosis factor-α (TNF-α), MMP8, nuclear factor kappa β (NF-κβ), Vitamin D receptor etc[31].

Genome-Wide Association Studies: These have broadened the current knowledge of the genetic implications of Chronic Periodontitis. In a study by Rhodin[34] et. al., *NIN* and *ABHD12B*(severe CP), *KCNK1*(red complex), and *DAB2IP*(*Pg*) were identified in loci that have been previously suggested as associated with chronic periodontitis and two novel associations were detected, i.e., *WHAMM* and *AP3B2*.

Proteomics, currently a propitious research frontier in periodontics, is the study of proteomes and their functions. Haigh BJ et. al. in a study applying quantitative proteomic analysis on saliva from subjects with severe periodontitis reveled altered abundance in 15 proteins and of those S 100 proteins showed the most prominent change[35]. Parotid secretory protein and haptoglobin have the potential to act as biomarkers for detecting and monitoring periodontitis.

Biomarkers for periodontal disease can be classified into (i) Proteomic (ii)Genetic (iii)Microbial (iv)Other[36](Table 5). Proteomics and Genomics, along with salivary diagnostics, when applied to periodontology are vastly promising as they may reveal such biomarkers for diagnosis and targets for disease intervention.

Recent developments in the micro-fabrication technology and MEMS helped develop 'lab-on-chip' (LOC) systems which are used as point-of-care (POC) testing devices for periodontal diagnosis. This LOC system executes complex assays within a short period of time and with small samples[37]. Some of the commercially available POC systems for use on saliva include: Oral fluid nanosensor test (OFNASET, University of California, Los Angeles [UCLA] Collaborative Oral Fluid Diagnostic Research Laboratory, led by Dr. David Wong[38]), Electronic taste chips (Rice University in Houston, Texas), OraQuick, Integrated microfluidic platform for oral diagnostics. Gingival Crevicular Fluid and Plaque have also been as oral diagnostic substrates for POC tests like Periogard and Perioscan (BANA) respectively[39].

Dentistry is entering the era of 'Personalized-medicine' and it is more applicable in periodontology than in any other aspect of dentistry. Personalized medicine disposes the concept of 'one-size-fits-all' and precisely tailors a health care regimen for the individual based on the genomic-proteomic profile of the patient and risk factors associated. Personalized-medicine is progressively becoming more practically relevant with the advent of sophisticated diagnostic advances, salivary diagnostics. In a study by W.V. Giannobile at. al.[40], association of tooth loss with 1 *vs.*2 annual preventive visits was tested among high-risk patients (≥1 of the risk factors: smoking, diabetes or interleukin-1 genotype) and low-risk patients (no risk factors). It was found that in the low-risk group the second annual preventive visit did not have significant effect on tooth loss outcome whereas in the high-risk group, the subgroup with 2 annual preventive visits showed lower event (tooth loss) rates than the subgroup with 1 annual preventive visit. Hence, it was concluded that stratification of patients based on associated risk factors and gene biomarkers could be beneficial in resource allocation for preventive medicine.

With the advent of nanotechnology new domains opened up for research in periodontology. Nano-materials in the form of nanotubes, hollow spheres, core shell structures are gaining importance in the context of controlled drug release. Triclosan loaded nanoparticles have been tested through emulsification-diffusion process[41] and gained positive response. Scaffold systems have also been constructed at a nanoscale for periodontal tissue regenerations procedures. Applications of nanotechnology in periodontology have been listed in table 6.

Dermatoglyphics in Periodontics: It has been shown by Vaidya[47] et. al. that more whorls and less arches in both right and left hands, in the fingerprints, were seen in patients with chronic periodontitis. Dermatoglyphics could potential act as a useful tool for the prompt diagnosis and prevention of those oral diseases that are directly or indirectly influenced genetically.

Probiotics

Applications of probiotics (e.g., lactobacillus acidophilus) are encouraging (Table 7) as they have proven to reduce the pHof the oral cavity and posses an antioxidant property that reduce the formation of plaque and calculus. Dendritic cells up-regulate the expression of Th1 (T-helper cell 1: for intracellular pathogens) and Th2 (T-helper cell 2: for extracellular pathogens) after being stimulated by Probiotics. Probiotics enhance immunity through "toll like receptors"[48].

Periodontal Vaccine

A promising avenue for research has opened up after realization of the prospective applications of periodontal vaccine. Why is the drive for periodontal vaccine compelling? Apart from being the most culpable disease for tooth loss world wide, periodontitis is implicated for having systemic sequelae like atherosclerosis, diabetes mellitus, respiratory infec-

tions, pre-term low-weight birth, rheumatoid arthritis, etc. Hence, inventing new prevention methods is compelling. Periodontal vaccination can be active, passive or genetic[56] (Table 8).

Stem Cell Therapy

Periodontal ligament stem cells (PDLSCs) are present in the peri-vascular space of the periodontal ligament and are considered to be a sub-population of the Mesenchymal stem cells having resemblance to pericytes[57]. In an experimental study by Kengo Iwasaki et. al[58], periodontal ligament stem cells were transplanted into surgically created periodontal defects in rats and it the results revealed periodontal regeneration is induced by transplanting PDLSCs. Although there currently are gaps in making periodontal-regeneration using stem cells practical, the presence of gripping evidence for the potential of its applications is driving a large chunk of research in this avenue to make this a clinical reality.

Extracorporeal Shock Wave Therapy

Exploration for newer and better treatment modalities resulted in the introduction of Extracorporeal Shock Wave Therapy (ESWT) into dentistry. ESWT uses shock waves of a certain energy to cause a sudden and transient pressure disturbance in the targeted tissue that triggers a response. In a review by Munivenkatappa Lakshmaiah Venkatesh Prabhuji[59] et. al., it is discussed that ESWT has a potential for bone regeneration, rapid periodontal healing, anti-inflammatory properties, etc., and that ESWT can be implemented in periodontal therapy following appropriate modifications.

Artificial Intelligence

Although it is still at a very initial state, a lot of researched is being directed at incorporating Artificial Intelligence (AI) into dentistry. Softwares are being developed that combine more precise CBCT scans with machine learning to detect even the slightest anomalies based on a number of previous scans and provide an appropriate treatment plan. Such a software can be helpful in that the patient is aware of the nature of their problem just a few minutes after the scan and has in mind a probable treatment plan that makes the work of the dentist more convenient. Artificial intelligence could be applied in the context of implantology for automatic selection of optimal implant sites and angulations for a given patient.

Advancements in the teaching of Periodontics: Virtual Reality and Haptics: Two visuo-haptic systems named Periosim and periodontal simulator (University of Illinois at Chicago, USA) simulate three dental instruments, i.e., a periodontal probe, an explorer and a scaler. This is used to train students in different aspects of periodontololgy[60].

CONCLUSION

The scope of periodontology in the past decade has expanded rapidly into various scientific fields of study and the future trends will embrace concepts like:

- biophotonics
- stem cell biology
- periodontal vaccines
- nanotechnology (powered by genomics and proteomics)

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Conflict of Interest

The authors declare no conflict of interest.

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Table 1: Periodontal Probes Overview

Periodontal Probes	1st Generation • Conventional instruments • No probing-pressure control	• William's Probe
		• CPITN Probe
		• UMich O Probe
		• UNC-15 Probe
		• Naber's Probe
	2nd Generation • Pressure sensitive (Not exceeding 0.2N/mm²)	• True pressure Sensitive (TPS) Probe
		• Electronic pressure sensitive probe
		• Yeaple (Jojen Technologies LLC,15 Coach Side Lane Pittsford, NY 14534 USA)
	3rd Generation • Automated	• InterProbe (The Dental Probe, Inc., Glen Allen, VA 23058)
		• Foster-Miller (Alabama) Probe
		• Florida Probe System (Florida Probe Corporation 3700 NW 91st Street, C-100 Gainesville, FL 32606 USA)
		• Florida Probe with PASHA* probe
		• Toronto Automated Probe
		• Accutek Probe
	4th Generation • 3-D probes	
	5th Generation • 3-D Probes • Non-Invasive	Ultrasonographic Probe (US) Probe
	Most Recent Advancement	Non-Invasive periodontal Probing through Fourier-Domain Optical Coherence Tomography
Non-Periodontal Probes	Calculus Detection	Detec-Tar (Dentsply Professional, York, PA, USA)
	Gingival Temperature	Periotemp Probe (Abiodent Inc, Danvers, MA)
	Periodontal Disease Evaluation System	Diamond Probe/Perio 2000 System (Diamond General Development Corp., 333 Parkland Plaza, Ann Arbor, MI 48103-6202)
	Tooth Mobility	Periotest (Siemens AG, Bensheim, Germany)
*Pressure-controlled, Automated, Standardized Hand-Piece		

Table 2: Core of Periodontal Therapy

Non-Surgical	Delivering Oral Hygiene Instructions	
	Supra-gingival and Sub-gingival Scaling	
	Elimination of other plaque retentive features	
	Management of risk factors like Smoking	
	Anti-microbial/Anti-plaque agents/Systemic antibiotics	
Surgical	Soft Tissue	Gingivectomy
		Gingivoplasty
		Curettage
		Mucogingival Surgeries
		Pocket reduction and elimination procedures
		Lip-repositioning
		Vestibuloplasty
		Frenotomy
		Frenectomy
	Hard Tissue	Resective Osseous Surgeries
		Regenerative Osseous Surgeries

Table 3: Host-Modulation Drugs

Category	Class	Example	Mechanism of Action	Ref.
Antiproteinases	Tetracyclines	Subantimicrobial-dose doxycline	Inhibits collagenase activity	(23) (24)
		Chemically modified tetracyclines (CMT-1,2,3,4,5,6,7,8)	Inhibition of MMPs, pro-inflammatory cytokines, inducible nitric oxide synthase (iNOS)	
Anti-inflammatory drugs	Salicylates	Asprin	Down-regulation of prostaglandins (among which PGE2 is reported to be increased in periodontitis)	(23)
	Indomethacin			
	Propionic acid derivatives	ibuprofen, flurbiprofen, naproxen		

Table 4: Biomedical Sciences + Photonics = Biophotonics

Clinical Applications	Diagnosis	In vitro imaging and spectroscopy (for optical diagnosis)
	Treatment	Thermal Interaction
		Laser Tissue Welding
		Photodynamic Therapy
		Bioimaging
Research Applications	Photomechanics	
	Spectroscopy	Absorption, Fluorescence
		Infrared (IR)
		Mass Spectroscopy
		Nuclear Magnetic Resonance Spectroscopy
		Nuclear Quadrupole Resonance Spectroscopy
		Ultraviolet–visible spectroscopy or ultraviolet – visible spectrophotometry (UV/VIS)
		Raman Spectroscopy
	Fibre Optic Sensors (Biosensors)	

Table 5: Biomarkers in Periodontal Disease (36)

Proteomic	alkaline phosphatase
	Aminopeptidase
	Translactoferin
	IgM
	MMP-9
	MMP-13
	Lactoferrin
Genetic	IL-1 polymorphisms
	IL-10 polymorphisms
	Tumor necrosis factor Polymorphisms
Microbial	Aggregatibacter actinomycetemcomitans
	Porphyromonas gingivalis
	Prevotella intermedia
	Peptostreptococcus
	Campylobacter rectus
	Mycoplasmas
Other	Calcium
	Cortisol
	Hydrogen sulfide
	Methyl mercaptan
	Pyridine

Table 6: Nanotechnology In Periodontology

			Ref.
Diagnosis	lab-on-a-chip (LOC) assay system	Valuable in detection of diagnostic periodontal biomarkers and in assessment of disease severity	(37)
Bone Grafting	Nanocrystalline Bone grafts in Bone Regeneration	Nanosized particle bone grafts have improved osteoconductive properties than traditional Hydroxyapetite.	(42)
Implants	Nanostructured Diamond	ultrahigh rigidity	
	Nanostructured Hydroxyapatite Coatings	Enhance osteoblastic activity	(43)
	Nanostructured Metallo-Ceramic Coatings		
Drug Delivery	Nanoparticles	triclosan-loaded nanoparticles have been tested for the treatment of periodontal disease	(41)
Periodontal Tissue Engineering	Nanofibers	Nanofiber materials have been reported to have been fabricated for three-dimensional cell culture and tissue engineering	(44)
Local Anesthesia	Nanotechnology based anesthetic suspensions	Numerous micron size active analgesic moving dental robots suspended in a colloidal suspension	(45)
Dentifrobots	In the form of tooth pastes and mouthwashes	Perform continuous calculus debridement	(46)

Table 7: Probiotics in Periodontal Therapy

		Ref.
Lactobacillus reuteri	Use of *L. reuteri* lozenges has shown to improve clinical effectiveness in moderate and deep pockets	(49)
Lactobacillus helveticus	Has been reported to up-regulate the expression of β-defensins in oral cavity, decreasing the no. of P. gingivlalis	(50)
Lactobacillus salivaris	Has been observed to decrease the amount of periodontopathic bacteria	(51)
Lactobacillus brevis	Down-regulates the inflammatory cascade	(52)
Lactobacillus gasseri	Has been shown to reduce alveolar bone loss and disorganization of periodontal ligament	(53)
Weissella cibaria	Inhibits volatile sulphur compounds (VSCs)Production	(54)
	Inhibits biofilm formation	(55)

Table 8: Periodontal Vaccines

Active Immunization	Whole cells
	Sub-unit vaccines
	Synthetic peptides as antigens
Passive Immunization	Monoclonal antibody
	Plantibodies
Genetic Immunization	Plasmid vaccines
	Live, viral vector vaccines