



Landmark Studies in Periodontology

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Abstract

Gingivitis is defined as inflammation of the gingiva without attachment loss while Periodontitis, a chronic multifactorial inflammatory disease associated with a dysbiotic plaque biofilm and characterized by progressive destruction of the tooth supporting apparatus. Since 18th century, several concepts and hypothesis were trying desperately to define these two terminologies and to find the exact pathogenesis and progression of these diseases. There are several paradigm changes that tried to describe the initiation, progression and pathogenesis of these two diseases- 1870-1920- based on the clinical features of the disease, 1920-1970- based on the pathology of periodontal diseases while from 1970- present- based on infection and host response paradigm. There are several landmark publications which influenced us to think differently, radically, challenged our existing system, enriched our knowledge, influenced our thinking and changed the entire clinical concept of Periodontology. The aim of this review is to enlist all the landmark papers and their assumptions and ideas that contribute to our worldwide or create the framework from which you operate every day.

Keywords: Gingivitis, Periodontitis, Paradigm, Landmark, Pathogenesis

INTRODUCTION

In cricket, we always remember the names of Kapil Dev, Sourav Ganguly, Mahendra Singh Dhoni, but why? Because they have created certain exceptional and noteworthy and their contribution is considered to be landmark in the history of Indian cricket. So what is a landmark study and how to establish it? Is it based on number of citations the article has received? Well, that's one way to classify something as a landmark study as an objective parameter. Moreover, to be eligible to be called a landmark study, the publication should have- 1. Challenge Existing Paradigms (change from degenerative disease to inflammatory periodontal disease), 2. Advance our knowledge (In 1965, dental plaque-initiated Gingivitis, and removal of plaque reversed this inflammation), 3. Influenced our thinking (Guided Tissue Regeneration –

Predictable Regeneration), 4. Changed the entire clinical practice of Periodontology (Implants in edentulous areas) i.e. a paradigm shift. Now what is a paradigm shift? It is a collection of beliefs and concepts held by a group of people, a set of theories, assumptions and ideas that contribute to your worldwide or create the framework from which you operate every day.

Paradigm shifting studies in Periodontology can be seen under- 1. Etiology of Periodontitis, 2. Pathogenesis of Periodontitis, 3. Management of Periodontitis.

Landmark studies on Etiology of Periodontitis

The most often-cited papers in Periodontology are those by Harold Loe and John Silness in which they

described the criteria for the Gingival Index (GI) and Plaque Index (PI)- cited : 4,161 & 4,368 times. These indices continue to be used because they are somewhat reproducible, easy to record, and emphasize that an early stage of periodontal disease (i.e., Gingivitis) is strongly associated with the presence and amount of dental plaque adjacent to the gingival margin. The GI and PI clinical assessments were subsequently used by Loe and his colleagues in a classic series of studies on experimental Gingivitis in which the etiological link between dental plaque and Gingivitis was firmly established.¹ Periodontal disease became established as an infectious disease and in turn affected most aspects of clinical Periodontology. That idea that Periodontitis was an infectious disease caused by bacteria in dental plaque and removing plaque could halt the disease was a game changer for Periodontology as it led to non-surgical and surgical plaque removal therapy- and hence definitely a landmark study.

Indices form an integral part to define and establish a disease. Quigley and Hein's plaque index (1962) followed by Turesky's modification in 1970 paved the way to establish strongly the etiological link between plaque and Gingivitis. Other indices which strongly can be stated as a landmark are of Russell's Periodontal Index, 1956, CPITN index, 1982, Sulcus bleeding index of Muhlemann and Son 1971, Modified sulcus bleeding index by Mombelli 1987, Mobility index by Miller (1950s), Glickman and Carranza 1972, Lindhe 1997 helped us to detect and diagnose the progression and severity of the disease.

Dental plaque is defined clinically as a structured, resilient, yellow-grayish substance that adheres tenaciously to the intraoral hard surfaces, including removable and fixed restorations.² Several hypotheses came into existence to establish the link of plaque with periodontal diseases- 1. Non-specific plaque hypothesis (Loesche W. J, 1976), 2. Specific plaque hypothesis (Loesche W. J, 1976), 3. Updated plaque hypothesis- Unified theory (Theilade, 1986) 4. Ecological plaque hypothesis (Marsh P.D, 1994), 5. Keystone Pathogen Hypothesis (Hejishengalis G, 2012), 6. The polymicrobial synergy and dysbiosis model of periodontal disease etiology (Hejishengalis G and Lamont R. J. 2012). On the structure and formation of dental plaque, extensive studies was done by Philip. D. Marsh and some of his classical papers are- 1. Dental plaque as a biofilm and a microbial

community – implications for health and disease³, 2. Dental Plaque as a Microbial Biofilm⁴, 3. How is the development of dental biofilms influenced by the host?⁵.

The re-establishment and maintenance of periodontal health are the main objectives of periodontal treatment and periodontal instruments have been designed specifically to achieve this goal. An influential paper was Sigurd Ramfjord's description of how to use a calibrated periodontal probe to conduct a periodontal examination with respect to cemento-enamel junction (CEJ) in which a site-specific probing depth and clinical attachment loss could be measured. He advocated that a periodontal examination should measure the amount of clinical damage (i.e., clinical attachment loss, CAL) by using a periodontal probe- an idea that has stood the test of time – CAL measurement/ Probing Pocket Depth determination with the help of a probe served as a surrogate for Periodontal Disease determination and hence definitely a landmark paper.⁶ Ramfjord and his colleagues also reported that probing depths were important because deep periodontal pockets form in many cases of Periodontitis and the deeper they are, harder they are to clean. This led to an important question- "How deep is this deep? Is it too deep to treat surgically or non-surgically? What is that factor to determine whether we should proceed with scaling and root planing or whether we should perform Open flap debridement?" Jan Lindhe (1982) in a classical paper "Critical Probing Depth"⁷ answered to this question. According to him the critical probing depth for nonsurgical therapy (scaling and root planing) is 2.9 mm while for surgical therapy it is 4.2mm- a study way ahead of his time and hence the moniker- a landmark study.⁷

Talking about pocket depths, let's next see a study on the development of pockets and its progression from shallow to deep. The development and progression of Periodontitis was brought into limelight by the results of a highly cited landmark publication in 1986 in the natural history of periodontal disease in humans- The Sri Lankan Tea Plantation Workers Study.⁸ (Citation number- 595) This longitudinal epidemiological study confirmed.

1. Gingivitis does not always progress to Periodontitis;
2. Some cases of Periodontitis progress slowly,

3. And in other situations, loss of attachment may occur in rapid episodic bursts.

These observations led to the conclusion that, based on rates of progression, there are multiple forms of Periodontitis.⁸

Landmark Studies on Pathogenesis

Gingivitis is defined as inflammation of the gingiva without attachment loss. The first histological classification of Gingivitis was given by R. C Page & H E Schroeder into- 1. Initial 2. Early 3. Established and 4. Advanced lesion⁹ while a classification based on clinical features was given by Angelo Mariotti in 1999¹⁰ and if this Gingivitis is left untreated it will progress into Periodontitis. In this journey from Gingivitis to Periodontitis several changes are seen and classical papers by several authors explain these phenomenon- 1. Change in bacterial composition (Lindhe J, 1980)¹¹, 2. Change in cellular composition (Seymour. G. J, 1979)¹², 3. Periodontal disease: pathogenesis (Offenbacher S, 1996, cited by- 788)¹³, 4. Role of inflammatory mediators (Page R. C, 1991, cited by- 649)¹⁴ etc. Alteration of the alveolar bone is an important feature of Periodontitis and several landmark classifications have been given by various authors that paved way for future treatment plan- 1. Goldman and Cohen, 1958, 2. Prichard 1965, 3. Karn K. W. 1983, 4. Grant. D. A, 1988, 5. Papapanou N.P & Tonetti M. S. 2000.

Bacteria within the plaque can exert its pathological effect when it comes within the 'Radius of action'. Though this concept was introduced by Waerhaug in 1952, but it was Garant & Cho, who gave this term in 1979 and suggested that locally produced bone resorption factors may need to be present in the proximity of bone surface to exert their action and Page & Schroeder, 1981 postulated a range of effectiveness of about 1.5 to 2.5mm within which bacterial plaque can induce loss of bone.¹⁵

Whether trauma from occlusion (TFO) has a direct correlation with the pathogenesis of Periodontitis is still a debatable topic. Extensive work and several classical papers starting from Karolyi's hypothesis (1901), Stillman (1917, 1925), Orban & Weinman (1933), Box (1935), Stones (1938) all did not meet to a conclusion whether TFO has a role in pathogenesis of Periodontitis or not. Glickman (1955-1971) performed studies in animal models and human autopsies to find

the exact co-relation between them and in 1967 gave the altered path of destruction and mentioned that "trauma from occlusion is an etiologic factor of importance in situations where angular bony defects combined with infra-bony pockets are found at one or several teeth".¹⁶ Waerhaug was against "altered pathway of destruction" and concluded that occlusal trauma played no part in periodontal destruction and the angular defects and infrabony pockets are the result of inflammation induced by subgingival plaque.¹⁷

Sigmund Socransky opposed Koch's postulate and his paper on "Criteria for the infectious agents in dental caries and periodontal disease"¹⁸ had been quoted, according to Google Scholar, just 94 times but had nevertheless an immense impact on pivotal clinical studies designed to "prove" that certain species or groups of species were involved in the etiology of Periodontitis- a definite landmark paper. Again, Haffajee AD, Socransky SS in 1994¹⁹ in one of the landmark papers mentioned- Bacteria play a critical role in the pathogenesis of Periodontitis. (Citation number- 1171) The discovery that bacteria of the oral cavity, which play a critical role in periodontal disease pathogenesis, organize themselves in a biofilm; and that the pathogenesis of Periodontitis is same as that of any chronic disease- complex and multifactorial. In 1998, they again published another landmark paper with a citation number of 1819 where they mentioned about different complexes of bacteria.²⁰ Also in 2002, another classical paper by them where they mentioned in details about the pathogens of refractory Periodontitis which is still a debatable topic.²¹

Another author, Jørgen Slots, a Danish-born periodontist has immense impact in the field of Periodontology. Several of his papers are highly cited landmark papers and he worked extensively on bacteria and viruses and their role in the pathogenesis of Periodontitis- 1. Subgingival microflora and periodontal disease (cited by- 718), 2. Selective medium for isolation of *Actinobacillus actinomycetemcomitans* (cited by- 680), 3. Black pigmented *Bacteroides* species, *Capnocytophaga* species and *Actinobacillus actinomycetemcomitans* in human periodontal disease (Cited by- 888), 4. Human virus in Periodontitis (Cited by- 153).

Landmark Studies in periodontal pathological conditions

1. Recession i.e. apical shifting of the marginal gingiva exposing the root of the teeth. The first classification of recession was given by Sullivan & Atkins in 1968, but the landmark classification was given by P. D. Miller in 1985.²² Though it has certain drawbacks, but because of its simplicity and ease to remember, have to be called as a landmark paper. However, in the new 2017 classification system²³ it was replaced with Cairo's classification of recession.²⁴

2. Furcation defect is bone loss, usually a result of periodontal disease, affecting the base of the root trunk of a tooth where two or more roots meet (bifurcation or trifurcation). Several classifications are there, but the landmark classification was given by Irvin Glickman 1953²⁵ which still has an impact in the dental world. On the basis of vertical component of furcation involvement, a landmark classification was given by Turnow and Fletcher in 1983²⁶ which also has a great impact to determine the prognosis of furcation involved tooth.

As Periodontitis is called a Multi-factorial Disease what about the other Etiologic Factors? Pathogenesis of Periodontitis is modulated by various factors, including local, host, and environmental factors. Extensive work was done by Genco and Grossi on these risk factors and some of their landmark studies with high citation numbers- a) Current views of risk factors for periodontal disease, Genco RJ, 1996 (Cited by-620)²⁷, b) Assessment of risk for periodontal disease I, Grossi SG, 1994 (Cited by- 912)²⁸, c) Assessment of risk for periodontal disease II, Grossi SG & Genco RJ, 1995 (Cited by- 611)²⁹. Now different risk factors with their landmark studies are discussed below-

1. Smoking- Through various landmark studies like- a) Evidence for cigarette smoking as a major risk factor for Periodontitis, Haber J, 1993 (Cited by- 503)³⁰, b) The effect of smoking on mechanical and antimicrobial therapy, Kinane DF, 1997,³¹ c) Smoking- attributable Periodontitis in United States, Tomar SL, 2000 (Cited by- 548).³² Though smoking can be regarded as a major causal contributing factor for the development of Periodontitis has been suggested but intervention studies on the effects of smoking cessation on periodontal health are not still paradigm - shifting.

2. Stress- Belting and Gupta (1961)³³ using the Russell Periodontal Index, found that periodontal disease was

more severe in the psychiatric patients as compared to controls when oral hygiene frequency, level of calculus, age, bruxism and clenching were held constant. Though there are certain landmark papers by Linden GJ (1996)³⁴, Genco RJ (1999)³⁵ but still no conclusive studies with paradigm shifting effect on stress mitigation having an effect on Periodontitis.

3. Genetics- Despite interesting findings from the Michalowicz Twin Studies³⁶ and interleukin-1 polymorphism studies by Kornman³⁷, the genetic susceptibility of Periodontitis is still not at a paradigm shifting stage – yet.

Landmark Studies in Perio-Medicine

1. Cardiovascular disease- Probably the most often quoted early paper is by Mattila et al.,³⁸ who found that the association between poor dental health and coronary heart disease. Frank DeStefano,³⁹ later described periodontal disease as an independent risk factor in the US population, thus supporting the findings of Mattila in Europe. He described a two-component mechanistic working model that linked periodontal disease to cardiovascular disease via systemic bacterial dissemination interacting with the vasculature and activation of some reactive proteins which acts as a triggering factor for cardiovascular disease.

2. Diabetes and Periodontitis- Herald Loe in a classical paper mentioned Periodontitis as the 6th complication of Diabetes,⁴⁰ and a bi-directional relationship was established between them by Preshaw P.M in 2011.⁴¹ Lim et al, 2006 did a study in Periodontitis patients & reported that the severe Periodontitis patients were associated with poor glycemic control.⁴²

3. Pregnancy- Steven Offenbacher explored the ability of infections with oral organisms to induce obstetric complications in pregnancy and in a landmark paper (Cited by- 1115) mentioned that Oral organisms like *Porphyromonas gingivalis* and *Campylobacter Rectus* were capable of eliciting a wide range of obstetric complications including fetal growth restriction, placental damage and early parturition. Hence oral infection in humans could lead to increased risk for preterm/low birth weight deliveries.⁴³

Thus the Perio-Systemic link is a game changer as it has the potential to alter the clinical practice of periodontics profoundly.

Landmark studies in the management of Periodontitis

Historically treatment for Periodontitis included a range of therapies including dietary changes, gingival massage, local application of chemicals, removal of local irritants and surgical resection of affected tissues etc. In 1869, Riggs JW first publicly described a new treatment for the cure of inflammation of the gum- A thorough curetting of the gums to remove local irritation along with dental calculus- 1st known instance of the nonsurgical removal of acquired deposits. Zinner in 1955⁴⁴ showed that ultrasound could be used to remove deposits from the teeth- stated that the instruments were acceptable alternatives to

hand scalers as he were found to be as effective in the removal of calculus. In 1983, Echeverria B and Caffesse RG⁴⁵, challenged the value of gingival curettage and concluded that gingival curettage did not improve the condition of the periodontal tissues more significantly than scaling and root planing (SRP) and in 2015, SRP was mentioned as the Gold Standard treatment regimen for Periodontitis.⁴⁶

Periodontal Flap- From 1918⁴⁷ onwards, several designs and techniques have been introduced in Periodontics (Fig 1) but the landmark technique was given by Ramfjord and Nissle, 1974⁴⁸ which is still used in 21st century.

Research workers	Technique proposed
Leonard Widman (1918)	Original Widman flap
Neumann(1920)	Introduced mucoperiosteal- Neumann flap
Kirkland (1931)	Modified flap operation
Nabers (1954)	Repositioning of the attached gingiva
Ariáudo & Tyrell (1957)	Modified Nabers procedure
Friedman(1962)	Apically repositioned flap
Morris(1965)	Unrepositioned mucoperiosteal flap
Ramfjord & Nissle (1974)	Modified Widman Flap

Fig 1- Different flap techniques

When talking about osseous resective surgery, it was Rudolf Kronfeld in 1935 who mentioned that bone was not infected or necrotic and therefore do not need to be removed.⁴⁹ He outlined the principles of osseous surgery for the purpose of re-contouring the bone so that the elimination of the periodontal pocket was predictable and less likely to return over time. In another landmark paper Nathan Friedman mentioned in details about osteoplasty and ostectomy in 1955.⁵⁰ It was Clifford Ochsenbein, who in 1958 described in details about the instruments required to perform osseous resective surgery.⁵¹

The concept of “Muco-gingival surgery” was first introduced by Nathan Friedman, 1964⁵² but the term was changed to “Perio-plastic surgery” by P. D. Miller in 1993⁵³ which was accepted in the Proceedings of the 1996 World Workshop in Periodontics.⁵⁴

The concept of Host Modulation was introduced by Golub⁵⁵ in a landmark paper (Cited by- 517) for local delivery to the periodontal pocket as a sub-antimicrobial dose of tetracycline & doxycycline to suppress collagenase activity in the periodontal pocket and to prevent tissue breakdown. In another classical paper Radvar M⁵⁶ mentioned that tetracycline results were superior especially in sites with suppuration. Thus host modulation can add an incremental advance in the success of periodontal therapy.

Currently, in this modern world patients today not only value their teeth but also express desire to save natural dentition in favour of extraction whenever possible. Regeneration of the lost tooth structure is the treatment of the hour to preserve the natural dentition and to prevent numerous undesirable sequel after extraction. Melcher did extensive studies on regeneration and his

concept of compartmentalization paved way for success in regenerative therapy. Some of his landmark papers, which stood ahead of time are- 1. On the Repair Potential of Periodontal Tissues, 1976⁵⁷, 2. Cells of periodontium: their role in the healing of wounds, 1985⁵⁸. Guided Tissue Regeneration is also an aspect which help to regenerate lost periodontal structures. The technique using barriers was introduced by Nyman et al. in 1982. The term GTR was coined by Gottlow et al. in 1986. This method of enhancing periodontal regeneration was also referred to as “Controlled Tissue Regeneration” by Gottlow I, Nyman S, Karring T, Lindhe I. (1984). Some of the landmark papers on GTR with high citation numbers which changed and challenged the existing paradigm are by the work of- 1. Gottlow J, 1986⁵⁹ (Cited by-747), 2. Dahlin C, 1988⁶⁰ (Cited by-666) 3. Gottlow J and Nyman S, 1984⁶¹ (Cited by-635).

To regenerate lost periodontal structures, bone grafts form an important part. Extensive work in this field was done by Hyatt and Butler (1957)⁶², several landmark papers by Ellegaard B & Karring T (1973)⁶³, Mellonig J. T. (1993).⁶⁴ Thus it has to be stated that regeneration of Periodontium on Root Surfaces previously denuded by Periodontitis – definitely paradigm shifting study.

After hard tissue grafts, next comes the soft tissue grafts. Langer and Langer’s study in 1985 (Cited by-621) on Connective Tissue Grafts shattered a long-held principle that denuded root surfaces could not be covered predictably with soft tissue grafts.⁶⁵ Although several variations have developed revolving this landmark paper, but still today connective tissue graft still remains the gold standard for root coverage procedures.

The introduction of dental implants as part of Periodontics shifted the end points of treatment for Periodontitis almost instantaneously with Branemark’s studies in the mid-1980’s and Periodontics was changed forever. Indeed, this shift was so dramatic that some feel it has threatened the profession, with many clinicians practicing more like Implantologists than “TRUE” Periodontists. The most notable and landmark work was done by Per-Ingvar Brånemark (May 3, 1929 – December 20, 2014)- “Father of modern Dental Implantology”. Other classic landmark studies were conducted by- 1. Albrektsson T et al, 1986 (Cited by- 2140)⁶⁶, 2. Adell

R et al. 1989 (Cited by- 1531)⁶⁷, 3. Extensive work on peri-implant soft tissue by M. A. Listgarten, 1991⁶⁸. Implant will be incomplete without mentioning the extensive work of Carl. E. Misch, his book and work totally changed and challenged existing thoughts, beliefs and concepts about implant dentistry.

Conclusion

The continued growth of our profession depends on our ability to recognize these “game changers” and use them to our patient’s advantage and finally we should remember the enormous contributions of them all, who shaped our profession. We stand on their shoulders, but we also have a responsibility to honor their memories by assuring that we know the history of Periodontology PROPERLY.

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