

Chapter 3

Current Trends in Disease Recognition & Diagnosis - A Perspective From India

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Introduction

In an era of improved understanding of the pathogenesis of periodontal disease, the diagnostic process has never been more central to determining therapeutic methods (Offenbacher & Collins 1993, Armitage 1992). In this age of technological advance, there is no dearth of equipment to assist the periodontal clinician in this task. The multifaceted nature of periodontal disease has clearly laid itself out to be one that is constituted by selective phases of disease activity, a plethora of periodontopathic organisms and consequences that extend even beyond the oral cavity. And yet it is this aspect of periodontal disease that again makes it difficult to diagnose and therefore difficult to treat. In the light of our present understanding of periodontal disease dynamics, the lack of a static diagnostic point of reference therefore, is often one that is felt acutely, by the researcher and clinician alike.

Mounting evidence of the association between periodontal disease and systemic disease (Page 1998, Mealey 1999) has served to make periodontal diagnosis more important than it ever was before. Established findings have shown us the association between periodontal disease and cardiovascular disease (Beck *et al* 1996, Beck *et al* 1998), chronic obstructive pulmonary disease (Scannapieco *et*

al 1998, Travis *et al* 1994, Scannapieco & Mylotte 1996), cerebrovascular accidents (Grau *et al* 1995, Syrjanen *et al* 1988), diabetes mellitus (Loe 1993) and pre term low birth weight babies (Dasanayake 1998, Offenbacher *et al* 1996). Some preliminary evidence also exists for pathophysiological similarities between rheumatoid arthritis and periodontal disease as well.

Diagnosis is best understood in terms of the consequences of periodontal disease and the parameters affected by the process. It is the consequence of disease that we seek to measure, not only as our indicator of the presence and extent of disease but also as the therapeutic end point of success. In these terms, it becomes easier to classify diagnosis into clinical, radiological, microbiological and biochemical methods.

The value of a diagnostic test is largely defined by its ability to predict disease accurately. A test can give varied results that range from a true positive to a true negative or a false positive to a false negative. Depending on the co-relationships that a certain diagnostic test subscribes to, it is possible to determine the predictive value of a given test (Hill 1971, Sackett *et al* 1991). The ability of a diagnostic test to read as truly positive in the actual presence of disease is regarded as the sensitivity of a test. On the other hand, the

ability of a diagnostic test to read as a true negative in the actual absence of disease, is regarded as its Specificity (Hill 1971, Sackett *et al* 1991). These parameters can be evaluated by an objective estimation of the number of true/false positives or true/false negatives that result from the use of a particular diagnostic method. As an extension of these parameters, it is then possible to calculate the relative or absolute risk of a certain factor and obtain odds ratios that are a more objective representation of diagnostic evaluation. Diagnostic tests need to be understood in these terms and it is the onus of research to address these issues before expecting clinical application.

Clinical methods

Clinical methods of periodontal diagnosis have routinely relied on the periodontal probe as being an indicator of the primary consequence of periodontal disease i.e., the loss of periodontal attachment. Periodontal probing suffers from inherent limitations nevertheless and issues concerning probing like probing force, probing angle, the resistance of an inflamed periodontium to probing technique and the reproducibility of repetitive assessment (Badersten *et al* 1984), remain. These problems have been addressed to some limited extent by the use of constant force electronic (Clark *et al* 1992) or computer controlled probes like the Florida probe. But these probes offer considerable difficulty in terms of practicality of use and economic affordability.

The idea of having fiber optic devices at the end of investigative instruments is not new to medicine. Medical specialties have made extensive use of such instruments to reach inaccessible anatomic locations in the body and indeed have gone further by using such devices for non-invasive surgery as well. Undoubtedly some of the limitations of periodontal therapy such as visual and physical access to the

disease-involved site may be addressed by the incorporation of such technologies into investigative devices that are small enough to enter the periodontal structures. The Perioscope is one such device that uses fiber optic technology to illuminate the periodontal pocket, offering a magnified and clear view of the root surface and inaccessible areas such as trifurcations and bifurcations.

This technology can be used to detect subgingival calculus remnants, ulcerated sulcular epithelium, cemental perforations and the like. SEM studies (Armitage & Christie 1973) of teeth involved in more aggressive forms of periodontitis have provided key information about cemental abnormalities, particularly at the cementodentinal junction (Tamamoto 1999) and also extensive resorption lacunae that characterize the entire length of the root surface. It is possible that some of these findings, have implications for the refractory nature of periodontitis in some individuals and the clinical diagnosis of such abnormalities may be made more possible by devices like the Perioscope.

Clinical diagnosis also needs to keep in mind the implications that arise from the multifactorial nature of periodontal disease. While there is much attention paid to the relationship between periodontal and endodontic disease, the implications of restorative dentistry are less understood by the periodontist and the restorative dentist alike. The explosion of restorative materials, calls for greater attention to the interaction with the periodontium like never before. And while periodontal investigation of biocompatibility is not discounted, iatrogenic periodontal abuse from restorative abnormalities has nevertheless to be contended with.

The sacrosanct area of the biologic width (Vacek 1994) and its relevance to periodontal integrity and restorative longevity is probably most neglected. While fixed prosthodontics has

evolved to accommodate this key periodontal concept, routine interproximal dentistry continues to violate biologic principles (Yuodelis *et al* 1973) many times. Accommodating the periodontium to receive a restoration and the involvement of the periodontist in restorative dentistry are concepts that must become clinical reality. Equally, orthodontic movement is focused so much on the root surface, that the associated changes in soft tissue are often overlooked. The periodontium must not be loaded beyond the call of routine orthodontic principles.

Localised periodontal conditions associated with developmental abnormalities are not commonplace but are however a pertinent diagnostic implication the practitioner should be aware of. The prevalence of defects such as *dens in dente* (Roland 1979, Ruprecht *et al* 1987), enamel hypoplasia, the palatogingival groove etc. may also vary between different ethnic populations and data is limited in this regard. The ability of some of these defects to harbor local etiologic factors and provide a nidus for accumulation of bacteria is what makes them relevant. Early recognition of these factors by thorough clinical examination can serve to prevent such situations in some cases.

Radiological Methods

The advancements in radiography and imaging probably represent one of the most fascinating aspects of diagnostic technology. Routine roentgenograms have expanded to include larger areas of the facial structure and the use of orthopantomograms, coaxial images and computerized navigation of tomograms have become common. These techniques undoubtedly offer a larger picture of the effect of periodontal disease on osseous structures and have contributed tremendously to radiographic diagnosis. The use of computer algorithms to generate spiral computerized

tomographic images of osseous structures in 3-D is however new, at least in terms of its application for the diagnosis of periodontal disease. A simulated anatomic dissection offers a perspective that is unprecedented in the form of these imaging techniques. Bone can be viewed three dimensionally and the bidimensional limitations of the routine radiograph are easily a thing of the past.

Older radiographic techniques such as subtraction radiography (Grondahl & Grondahl 1983) and CADIA (Bragger *et al* 1988) were not accessible to the general dental practitioner for several reasons. Today direct digital radiography, either through the use of CMOS sensors or phosphor plates, offers a better opportunity to understand the consequence of periodontal disease on osseous density. Colorization of the 256 gray scales that constitute the spectrum of a black and white image has also made the interpretation of such images more contemporary. The elimination of radiographic magnification error in these techniques by calibration, has also served to make objective measurement possible. Computerized 3D reconstructions of these images also yield valuable, if only somewhat limited information. The benefits of decreased radiation with these techniques have also made their routine use in examination more realistic. It is now possible to show a patient 3D reconstructions of the alveolar structure and there is no doubt that these technologies go a long way in educating the patient and enabling him to accept periodontal treatment. Their use in maintenance and longitudinal assessment is also naturally obvious.

Microbiological Methods

Microbiological methods of periodontal diagnosis do not easily lend themselves to routine use in the hands of the general dental practitioner. The nature of investigation rarely

helps chair side use and this has contributed to their limited application. But periodontal disease is nevertheless bacteriologically mediated and therefore microbiologic diagnosis must form a mainstay of diagnostic investigation.

Microscopy of any nature is rarely definitive in its identification of periodontopathic organisms. The availability of specific immunologic staining reagents in some cases however makes such techniques continually viable. Such reagents do exist for a variety of periodontopathic organisms such as *P. gingivalis*, *P. intermedia*, *T. denticola*, and *A. actinomycetemcomitans*.

Culture methods (Slots 1986) continue to have some limited application as well. The use of selective and non-selective media can serve to isolate certain periodontopathic organisms and the relevance of such methods to testing antibiotic sensitivity in refractive forms of periodontitis continues. Quantification of microorganisms with some of these techniques is also possible in less equipped laboratories by the use of colony counting devices that are computerized and fairly efficient.

DNA probes (Grench *et al* 1986) based on a genomic understanding of bacterial microstructure are a more predictable, but expensive, method. DNA probes are available for *A. actinomycetemcomitans*, *P. intermedia* and *P. gingivalis* and these are well identified in genomic libraries that are commercially available. The degree of accuracy in organism identification is what makes the use of these techniques potent. The use of extended methodologies such as PCR (Griffen *et al* 1992) will also come into use in the future.

Enzymes, derived from either the host or the microbes, can also form useful markers for diagnosis. A trypsin-like enzyme (Loesche 1986) present in *T. denticola* and *P. gingivalis* is absent from at least 60 other subgingival plaque organisms. This enzyme can be detected by the hydrolysis of the trypsin

substrate benzoyl-DL-arginine naphthylamide (BANA) (Loesche 1985) with almost 88% accuracy. This forms the basis for a chromogenic chairside test that is user friendly and potentially useful in the hands of even a general dental practitioner.

Biochemical methods

Biochemical diagnosis revolves primarily around the estimation of one or more of four key products that are released as part of the pathogenic process of periodontal disease. These are usually either host derived enzymes (Loesche 1986), bacteriological products, inflammatory mediators or tissue breakdown products. Many of the studies that have identified techniques for objective estimation of these products revolve around the collection of gingival crevicular fluid. Techniques for collection (Brill 1969) of this fluid and its limited availability in quantity have however served to limit such applications to research. The translation to clinical use continues to be defiant and this is perhaps one reason why biochemical diagnosis does not find routine clinical application.

Salivary biochemistry on the other hand lends itself to far more clinical relevance and recent studies estimating CD14 levels and the like, serve to reinforce its potential. Biochemical assays exist for a variety of enzymes like aspartate aminotransferase (Chambers *et al* 1991), β -glucuronidase, alkaline phosphatase (Chapple *et al* 1994), dipeptidyl peptidase, elastase and cathepsins (Cox & Eley 2003). Inflammatory mediators like Prostaglandin E₂ (Offenbacher *et al* 1986) and cytokines of various types (Masada *et al* 1990) can also be estimated in saliva, gingival crevicular fluid or tissue samples. None of these techniques have however become commercially available as yet. Other salivary assays for the salivary peroxidase system and

salivary antioxidants (Moore *et al* 1994) hold promise too.

Biochemical assays for other markers in serum, like C reactive protein, also seem to offer potential for use.

Genetic tests for polymorphisms (Greenstein & Hart 2002, Kinane & Hart 2003, Greenstein & Hart 2002) in the IL-1 gene cluster are a new direction and economic limitations continue to be a stumbling block here as well. Variability between ethnic subpopulations also implies the need for more data, before the objective transition to a diagnostic assay of risk predictability can be made.

Conclusion

It seems that clinical diagnosis will continue to be the cornerstone of periodontal disease recognition even with its inherent limitations. A recent position paper of the American Academy of Periodontology substantiates this (AAP Position Paper on Diagnosis of Periodontal Disease). To quote from the paper: "Despite our increased understanding of the etiology and pathogenesis of periodontal infections, the diagnosis and classification of these diseases is still based almost entirely on traditional clinical assessments". To arrive at a periodontal diagnosis the dentist must rely upon such factors as: 1) presence or absence of clinical signs of inflammation 2) probing depths 3) extent and pattern of loss of clinical attachment and bone 4) patient's medical and dental histories; and 5) presence or absence of miscellaneous signs and symptoms, including pain, ulceration and amount of observable plaque and calculus.

There is no doubt that disease recognition has important implications for interventional therapy. The nature of periodontal disease itself is a hurdle but not a limiting factor to much needed research in this area.

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