

# **Diagnosis of Active Chronic Periodontitis – Is There a Better Way?**

Ali Khadivi, Hon. B.MSc., Ronit Weizblit, Hon. B.Sc., Sara Rahman, Hon. B.Sc.,  
Dave Ho, B.Sc., Aleem Kherani Hon. B.Sc.

## TABLE OF CONTENTS:

	Page Number
Abstract.....	1
Introduction.....	1
Methods.....	3
Definition of Terms.....	3
Search Strategy .....	3
Determination of Relevance .....	5
Results.....	7
Discussion .....	9
Conclusion.....	12
Appendix 1 - Checklist.....	13
Appendix 2 – Evidence tables.....	14
Acknowledgements .....	19
Literature Cited .....	20

## **ABSTRACT**

Techniques for periodontal disease diagnosis are evolving. As microflora in the affected periodontal pocket are becoming better understood, the aim to improve accuracy of prognosis and treatment remains. One of the main disadvantages of traditional periodontitis diagnostic tests is their inability to predict current disease activity (Eley & Cox, 1998). As a result, clinicians are unable to easily differentiate cases requiring aggressive treatment in active periodontitis versus from inactive cases. The need for accurate diagnostic tests to predict active periodontal disease remains a focus in periodontal research.

An evidence-based review was conducted to determine if there exists a test to diagnose active chronic periodontal disease. Key words used include: active, ongoing, current, chronic periodontitis, progressive periodontitis, diagnostic test, predictor, prediction, indicator, indication, and marker. A total of 207 articles were identified, and based on elimination due to relevance and quality; 29 studies were considered appropriate for review. Using a recommended quality and validity checklist, 5 articles met final evidence criteria.

Results show fair evidence that Gingival Crevicular Fluid (GCF) components can be useful for improving the diagnosis of active chronic periodontitis. However, due to the lack of specificity, cost-effectiveness, or clinical ease, none of the tests are superior to the current diagnostic procedures employed (measurements of attachment loss, probing depth, bleeding on probing, and radiographic analysis). The need for more specific and sensitive tests still stands.

## **INTRODUCTION**

Chronic periodontitis is the loss of periodontal ligament and bone support. Upon initiation, the disease will progress in bursts of activity of unknown duration if untreated, and can exist in active (recurrent) and inactive (refractory) states (Persson, et.al., 1989). Chronic

periodontal disease is a prevalent condition, occurring mostly in adults (R. Turnbull, personal communication, December 5, 2006). Chronic periodontitis is a disease of multifactorial etiology; influenced by oral hygiene, smoking, education and socio-economic status (SES), age, pregnancy, genetics, and systemic diseases (Pihlstrom, 2001). These risk factors may influence age of onset, duration and severity of the disease, but their role in determining whether disease is active or inactive is unknown. Ultimately, periodontal diseases can negatively impact an individual's quality of life, as it affects social interaction, aesthetics, function, and the costs of dental treatment. In order to control the progress of chronic periodontitis, early diagnosis of active disease is crucial.

Accurate diagnosis is imperative as it can determine the impact of disease and future treatment decisions. Several diagnostic tests aim at distinguishing indicators for healthy sites and periodontal disease sites. This is a complex matter as the periodontal pocket contains hundreds of species of bacteria, among the numerous environmental constituents of this microenvironment (e.g. toxins, host-immune products, etc.) A select few components of this biomass are responsible for inducing the initiation and progression of chronic periodontal disease (Tenenbaum, et.al., 2005). The healthy periodontal pocket primarily consists of gram-positive facultative anaerobes, non-motile cocci and bacilli, and few spirochetes and motile organisms. Contrastingly, a chronic periodontitis pocket contains an increased mass of bacteria with predominantly spirochetes, motile rods, and gram-negative anaerobes (R. Ellen, personal communication, February 6, 2007). Although no one organism is responsible for causing chronic periodontitis, certain bacteria are present in higher numbers during diseased states (Eley & Cox, 1998). Diagnostic difficulty arises because some of these species are present in a healthy oral flora, and composition of the flora in healthy or inactive sites can vary between patients (Eley & Cox, 1998). Current tests aim to detect pathogen levels, their toxic by-products, and/or the immune system response to these

pathogens in Gingival Crevicular Fluid (GCF) of active and inactive diseased sites as a means of diagnosis (Fine et.al.1986). This paper is a systematic review of the literature to determine if there exists a test to diagnose active chronic periodontal disease.

## METHODS

A systematic review of the literature was conducted to identify, select and critically appraise relevant articles.

### Terms Defined

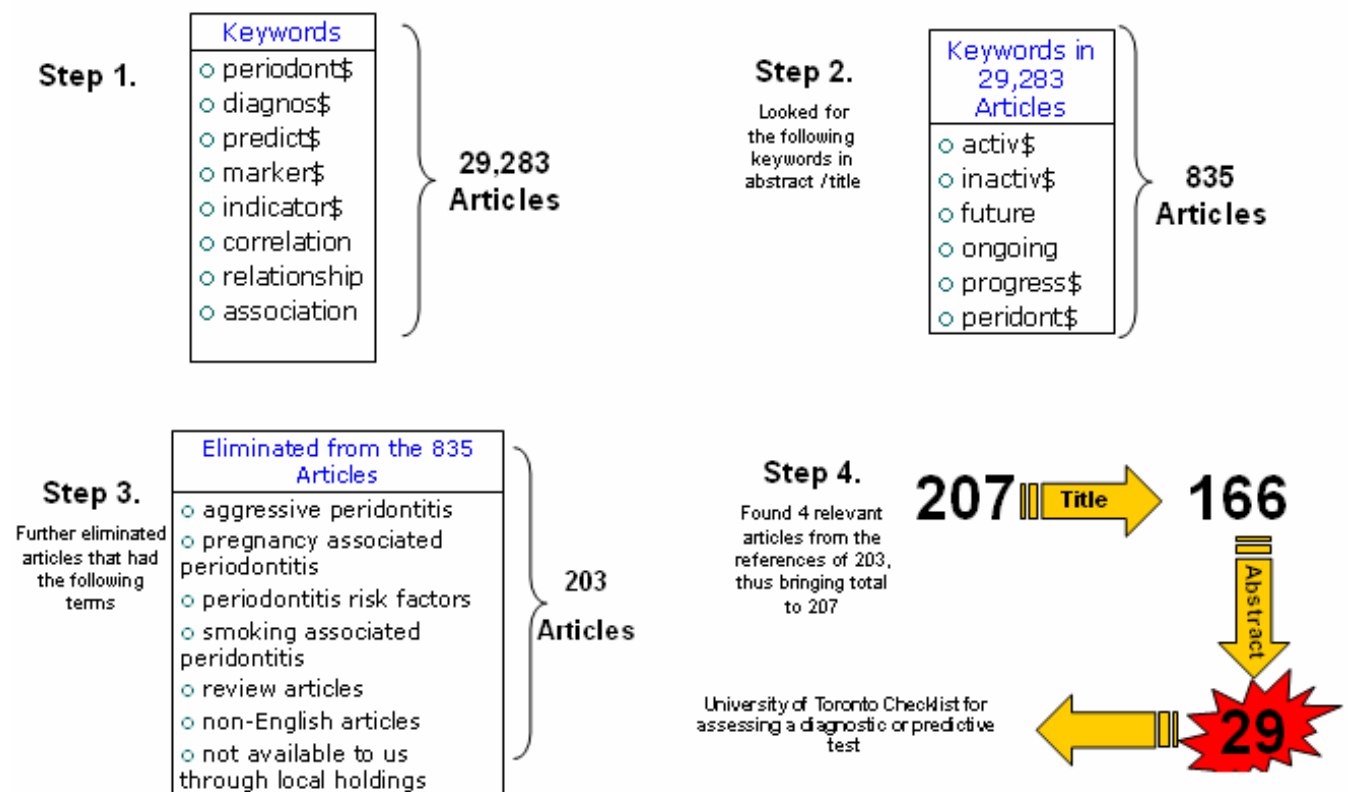
<b>Definitions:</b>
<u>Disease Activity:</u> Destruction of periodontal tissues is currently taking place. The progression of periodontal disease as measured by a change in probing attachment level or alveolar bone support determined radiographically (Lamster, et.al., 1993).
<u>Chronic periodontitis:</u> Inflammation of the gingiva, resulting in loss of clinical attachment due to periodontal ligament destruction and loss of the adjacent supporting bone (“Parameter on Chronic Periodontitis With Slight to Moderate Loss of Periodontal Support”, 2000).
<u>Diagnostic test:</u> A technique to increase the probability of correctly determining the cause of a patient’s signs and symptoms (Needleman & Moles, 2000).
<b>Key Words:</b> Active, Chronic, Periodontal Disease, Diagnostic Test
<b>Gold Standard:</b> Histology

### Search Strategy

A literature review was conducted online using the multifile database Ovid Medline (1966-present), which includes the following databases: ACP Journal Club (ACP), Cochrane

Central Register of Controlled Trials (Central), Cochrane Database of Systematic Reviews (CDSR), and the Database of Abstracts of Reviews of Effects (DARE), and PubMed Journals@Ovid Full Text and Ovid Healthstar. MeSH (Medical Subject Headings) were used to expand on the vocabulary so as to conduct a more extensive search. The following keywords were used in the search: periodont\$, diagnos\$, predict\$, marker\$, indicator\$, correlation, relationship or association (the "\$" is a truncation technique that retrieves unlimited suffix variation). A combination of these search terms resulted in a total of 29283 search results. To narrow the search further to include studies dealing specifically with *active* periodontitis, specific key words indicating disease activity were identified in the abstract and/or the title (activ\$ or inactiv\$ or future or ongoing or progress\$, periodont\$). This narrowed the search down to 835 search results. Next, studies related to aggressive periodontitis, pregnancy associated periodontitis, periodontitis risk factors, and smoking-associated periodontitis were eliminated from the search. Similarly, review articles, non-human and non-English articles, and articles not available in local holdings at the University of Toronto were also eliminated. This produced a final count of 203 articles from the online databases.

Of the 203 articles from the online databases, a search of the references within these articles was conducted. A total of 4 articles were obtained in this manner (Figure 1).



**Figure 1.** Step by Step Search Technique.

### Determination of Relevance

Of the total 207 articles, 41 were eliminated at the title stage, and 137 were eliminated at the abstract stage. Articles were considered irrelevant if they dealt with specific target populations (i.e. elderly patients, HIV patients), or the treatment of periodontitis as opposed to its diagnosis. The remaining 29 that were not eliminated were selected for reading. Of these, articles were considered relevant based on the following criteria:

- 1) The study must be a primary study
- 2) The study must report test performance using sensitivity/specificity, likelihood ratios, or ROC curves

3) The study must be of good design, specifically cohort or case-control studies.

Each study was graded relative to CFTPHE and a recommended quality and validity checklist (See Appendix 1). We gave one point to studies that:

1. **Were ethical.** Such studies did not pose any physical or psychological harm to subjects.
2. **Clearly defined the test's cut-off values.** Such studies specified exact values for a positive or negative reading for chronic and active periodontitis as indicated.
3. **Evaluated the test against a valid gold standard.** All studies were allotted a score of zero due to an ideal gold standard of histological section.
4. **Determined the test results and disease status independently.** Such studies were specified as double-blind studies.
5. **Evaluated the test using patients with a range of severity of disease.** These studies used patients with variation in attachment loss and bone loss.
6. **Evaluated the test among patients with diseases that might be confused with, or closely related to active chronic periodontitis.** These studies also used the test in patients with gingivitis, aggressive periodontitis, or stable chronic periodontitis (as opposed to active chronic periodontitis).
7. **Reported test performance using sensitivity/specificity, likelihood ratios or ROC curves.** Standard and comparable measures.
8. **Reported the effect of moving the cut-off point.** Studies that describe the effect of moving the cut-off point on sensitivity and specificity.
9. **Had tests which gave better results than the current or standard test.** Since all studies had used current or standard tests (probing depths and/or radiographic bone

loss) in place of a gold standard to compare their diagnostic tests to, diagnostic tests could not have given better results than the gold standard. We were therefore unable to give one point to any of the studies in this instance.

10. **Tests that were likely acceptable to patients**, in terms of time, cost, efficiency, and comfort.

It is important to recognize that since numbers 3 and 9 outlined in the checklist above could never score points, the checklist was actually being scored out of 8 instead of 10, and the cut-off would therefore be 5 out 8. A total of five articles were considered relevant according to the above criteria. All of these articles evaluated the diagnostic efficacy of GCF components from subjects with chronic active periodontitis.

## **RESULTS**

All studies were cohort or case-control studies. No randomized trials were available in the literature. All studies looked at GCF and the biological markers contained within to determine the activity level of periodontal disease.

Eley & Cox (1996) compared the GCF contents of cathepsin B to probing depths to determine the success of cathepsin B as a marker for active disease. Seventy-five patients with moderate chronic periodontitis were tested; with a high degree of specificity and sensitivity (99.8% and 100%, respectively), it was found that cathepsin B was able to better identify active pocket destruction than other markers in GCF. The authors did not themselves test other markers and used values obtained elsewhere.

Persson et al. (1992) compared periodontal probing values with aspartate aminotransferase (AST) levels found within GCF. Twenty-five patients with moderate to

advanced periodontal disease were tested. The study found statistically significant differences in AST values with patients at various levels of disease. With a high degree of sensitivity (93%), the study found that 800  $\mu$ IU was the best cut-off to determine active disease. It was determined that AST levels are a reasonable indicator of active disease when used in conjunction with clinical judgment. This study had a small population, and there was no indication of the cost of this type of diagnostic test.

Palcanis et al. (1992) compared GCF elastase levels against various other measures of disease activity including CAL, probing depth, bleeding on probing (BOP), gingival inflammation score, plaque index, and subtractive radiography. Thirty patients were examined over a 6-month period; the study demonstrates that GCF elastase levels are significantly higher in sites with active chronic periodontitis in comparison to inactive sites. When the standard test used to detect disease consisted of a combination of radiographic bone loss and loss of attachment levels, the elastase test showed sensitivity and specificity values of 82% and 66%, respectively.

Hemmings et al.(1997) tested the Periocheck and Perioscan methods of diagnosing periodontal disease activity. Nineteen patients were tested in this study that revealed that the Periocheck and Perioscan were able to detect activity with a high sensitivity (88% and 99% respectively) and low specificity (61% and 55% respectively). This study used a small population size, was not able to make statistically valid conclusions, and had a potentially high occurrence of false positives.

Nakashima et.al.(1996) measured the following biological measures: functional elastase (FEL), antigenic elastase (AEL), alpha-2 macroglobulin (a2M), alpha-1 antitrypsin (a1AT), prostaglandin E2 (PGE2), alkaline phosphatase (ALP), osteocalcin (OC), beta-glucuronidase (BG), AST, and collagenase(COL)) in GCF in an attempt to identify periodontal disease activity . Using 8 subjects, investigators found no difference between active versus inactive sites in all

biological markers except PGE2 expressed as a ratio to neutrophil (PMN) count, ALP, BG, and COL. Via linear discriminant analysis, it was determined that total amounts of PGE2, COL, ALP, a2M, OC, and AEL yielded a higher predictive value (with sensitivity of 80% and specificity of 91%) for active disease than any single measure, thus suggesting that a combination of biochemical assays is needed to detect active chronic periodontal disease.

## **DISCUSSION**

Upon reviewing the available literature, several approaches to the diagnosis of active chronic periodontitis have been assessed among various studies. GCF appears to be a rich source of biological markers of disease ranging from host and bacterial enzymes to immune response elements. As a result, much research has focused on examining how the amounts of different GCF elements vary with disease status.

Most of the studies showed fair evidence to support a link between active chronic periodontitis and specific GCF elements. However, the number of subjects in each study did not exceed 75. This relatively small sample size in each case negates the strength of the findings.

In addition to the small subject pools observed, no mention was made as to the geographic or socioeconomic representations of the patients participating in the study. While these patient factors could act as predictors of active disease, investigators have not specifically tested these groups. Reviewed studies have excluded subjects who were pregnant, or had a systemic condition that could affect periodontal health (i.e. medication or disease), but there was no apparent control for subjects based on environmental, or social factors. As such, the presence or absence of a specific factor in GCF could be due to another variable, previously unaccounted for.

The purpose of this literature review is to find a diagnostic test that can detect active periodontal disease in an otherwise healthy individual. In order to do so, factors influencing disease should first be assessed in the absence of any confounding variables. As such, searches were further refined by eliminating articles that pertained to disease modifiers, such as smoking status (Figure 1). Although eliminated, these ten studies are not without merit; some focused on establishing associations between smoking and periodontal disease, rather than on assessing the efficacy of smoking as a diagnostic tool (Gelskey, 1999). Several eliminated articles did look at smoking status in relation to changes in biomarkers, such as salivary IL-1 $\beta$ , albumin and AST (Nishada et al., 2006); and salivary proteolytic enzymes (Liede et al., 1999). However, these studies did not specifically pertain to active chronic periodontitis diagnosis.

A diagnostic test will be subject to much variation among practitioners, as has been demonstrated in the reviewed articles. Tasks as simple as sampling the patient's GCF can be consistent within one provider but can vary markedly compared to another. For example, GCF was sampled from each test site in most of the articles reviewed. When doing so, the chromatography paper used to collect the samples was inserted into the sulcus to depths ranging from just 1mm into the entrance of the pocket (Hemmings et al., 1997) to the full depth of the pocket (Nakashima et al., 1996). Due to this variability in sampling techniques, different biochemical markers could be attributed to active disease if the distribution of GCF elements changed with depth of the pocket.

The current method by which practitioners assess disease status involves a combination of clinical measures that can include CAL, BOP, probing depths, and radiography, all taken over a period of time. It was used as a basis for comparison against the proposed diagnostic tests. However, the different studies lacked uniformity in the combination of measures used. For example, despite its limited role in prompt therapeutic intervention, the use of radiography to

track bone loss over time is important because it offers a more definitive view of how alveolar bone changes during the course of active periodontitis. While some studies do employ radiographic evidence of bone loss, others rely solely on periodontal probing and CAL to define disease. Thus, this lack of consensus on an adequate current standard of testing could reflect over- or underestimated sensitivity and specificity values.

While many studies focus on the ability of a single factor to function as a measure of disease presence and activity, there appears to be a lack of agreement concerning what this marker is. For example, some investigators postulate that GCF cathepsin B levels may be a useful indicator of susceptibility to periodontal progression (Eley & Cox, 1996), while others have determined that GCF enzymes such as AST are only moderate indicators and are therefore only indicated for use as adjunctive methods of diagnosis (Persson et al., 1992). It has also been suggested that a combination of factors may lead to increased predictability over any single factor (Nakashima et al., 1996). If so, it would stand to reason that conducted biochemical tests should encompass a broader spectrum of characteristic factors in order to establish an accurate diagnosis.

Furthermore, with an increasing focus on the use of biochemical assays in the diagnosis of active chronic periodontitis, the issue of its practicality in a real clinical setting comes into question. The ability of any of these tests to be performed chairside is not entirely clear. While all tests reviewed posed a negligible amount of discomfort to the patient, potential costs – in terms of both chair-time and finances – were not stated in any of the articles. Given the specific assays that must be conducted, incurred costs could theoretically be high, which may be met with resistance from the patient or practitioner in electing this hypothetical method of diagnosis.

A search of the Cochrane Database of Systematic Reviews – which compiles worldwide reviews on the effects of healthcare interventions – returns no reviews pertaining to diagnostic tests for periodontal disease ([www.cochrane.org](http://www.cochrane.org)). Given the current lack of an efficient and fully

reliable diagnostic test in identifying disease status, the absence of a full-scale review of the literature further underscores the need for increased attention given to ascertaining an efficient and efficacious method of diagnosis. Doing so could lead to the further development of prompt and early treatment strategies for patients at risk.

## **CONCLUSION**

In conclusion, there is fair evidence suggesting that various GCF components have the potential to offer improvements over current diagnostic methods. However, the differing study designs, potential costs, and assays of different indicators do not offer a compelling argument in favour of one test over another, and consequently, no diagnostic test is superior to the methods currently being practiced. Further research must be undertaken in order to find an effective diagnostic test. For now, the profession will have to rely on the current method of CAL, BOP, probing depths, and radiography.

## APPENDIX 1

Table 1: Checklist for Assessing a Diagnostic or Predictive test

1. Was the study ethical? (1)
2. Is the test clearly described (including the cut-off values)? (1)
3. Was the test evaluated against a valid gold standard? (1)
4. Were the test results and disease status determined independently? (1)
5. Was the test evaluated using patients with a range of severity of disease? (1)
6. Was the test evaluated among patients with diseases that might be confused with, or are closely related to the disease of interest? (1)
7. Is the test performance reported using sensitivity/specificity, likelihood ratios or ROC curves? (Note: if predictive values, only, are reported, was the background prevalence of disease similar to that of your patients) (1)
8. Is the effect of moving the cut-off point reported? (1)
9. Does this test give better results than the current or standard test? (1)
10. Is the test likely to be acceptable to patients? (1)

Adapted from: Fletcher, Fletcher and Wagner. Clinical epidemiology – the essentials. 3<sup>rd</sup> ed.

1996, and Sackett et al. Evidence-based medicine: how to practice and teach EBM, 1997.

## APPENDIX 2

Evidence Table 1  
Eley, B.M., Cox, S.W. (1996)

Design & Population	Diagnostic Test & Control	Outcome	Critical Appraisal	Conclusion & CTF Rating
<p><b>Cohort</b></p> <ul style="list-style-type: none"> <li>patients with chronic periodontitis</li> <li>34 Males, 41 females</li> <li>Age 28-61</li> </ul> <p>(N = 75)</p>	<p><b>Diagnostic Test:</b> Test sites were the MB sites of the 1st &amp; 2nd molars and premolars</p> <p>GCF collected by use of chromatography paper 1mm subgingival for 30 sec and subjected to Florometric assay (enzyme assay)</p> <p><b>Control:</b> Determined retrospectively on the basis of close similarities between them and then attachment loss site</p>	<ul style="list-style-type: none"> <li>Rapid Attachment loss (RAL) were statistically significantly higher than those control sites for both total Cathepsin B activity and Cathepsin B concentration</li> <li>Diagnostic Test Based on GCF of 7.5 uU/30s: Sensitivity=100%, Specificity= 99.8%, PPV=86.53%, NPV=100%</li> </ul>	<p><b>Checklist Score:</b> 7/10 = 70%</p> <ul style="list-style-type: none"> <li>no mention of other possible markers in the study, by testing others this would have strengthened their finding</li> <li>overall a good study</li> </ul>	<p><b>Conclusion:</b></p> <p>Overall patient level comparisons showed that mean GCF cathepsin B levels were significantly higher in attachment loss patients than non-attachment loss patients and thus it might be possible to detect patients susceptible to periodontal progression using GCF cathepsin B levels</p> <p><b>CTF Rating:</b> Level II-2 B</p>

Evidence table 2  
Persson GR et al. (1992)

Design & Population	Diagnostic Test & Control	Outcome	Critical Appraisal	Conclusion & CTF Rating
<p><b>Cohort</b></p> <ul style="list-style-type: none"> <li>patients with moderate to advanced periodontitis</li> </ul> <p>(N = 25)</p>	<p><b>Diagnostic Test:</b></p> <ul style="list-style-type: none"> <li>All first molars and lateral incisors were tested with probing depth and Gingival crevicular fluid samples taken at 3 month intervals.</li> <li>Gingival crevicular fluid AST level(600,800, 1000,1200)<math>\mu</math>IU at confirmed diseased sites was compared to levels at non diseased sites</li> </ul> <p><b>Control:</b></p> <ul style="list-style-type: none"> <li>Sites with &lt;2mm attachment loss were considered healthy</li> </ul>	<ul style="list-style-type: none"> <li>Statistically significant differences in AST values were found for different disease categories</li> </ul> <p>AST 800 <math>\mu</math>IU Sensitivity = 93% Specificity = 68%</p>	<p><b>Checklist Score:</b> 7/10 = 70%</p> <ul style="list-style-type: none"> <li>Depending on the cut off chosen various levels of sensitivity and specificity can be obtained. Clinical judgment is thus required in addition to this test to be able to determine risk status and decided on an appropriate AST level cutoff. )</li> <li>Small population used. Cost of test was not indicated</li> </ul>	<p><b>Conclusion:</b></p> <ul style="list-style-type: none"> <li>This test when used in collaboration with clinical judgment presents an additional tool for the clinician</li> </ul> <p><b>CTF Rating:</b> Level II-2 B</p>

Evidence table 3  
Palcanis, KG, et al. (1992)

Design & Population	Diagnostic Test & Control	Outcome	Critical Appraisal	Conclusion & CTF Rating
<p><b>Cohort</b></p> <ul style="list-style-type: none"> <li>30 patients chosen on basis of progressive periodontal disease</li> <li>Age 21-73</li> <li>excluded subjects based on factors that could affect periodontal health (pregnancy, medication, etc)</li> </ul> <p>(N = 30)</p>	<p><b>Diagnostic Test:</b></p> <ul style="list-style-type: none"> <li>5 sites per patient</li> <li>GCF collected every 2 months for 6 months for detection of elastase</li> <li>Strip placed into sulcus for 15 sec and subjected to spectrofluorometric analysis of elastase</li> </ul> <p><b>Control:</b></p> <ul style="list-style-type: none"> <li>Inactive sites in the same patient</li> </ul>	<ul style="list-style-type: none"> <li>Statistically GCF elastase scored significantly. higher compared to normal at sites</li> <li>Periodontal attachment loss (2.81 +/- 0.29 vs. 2.03 +/- 0.07, P&lt;0.0005) and bone loss (2.32 +/- 0.17 vs. 2.01 +/- 0.08, P&lt;0.05)</li> <li>Sensitivity = 82%; Specificity = 66%</li> </ul>	<p><b>Checklist Score:</b> 6/10 = 60%</p> <ul style="list-style-type: none"> <li>range of severity tested, cut- offs defined and moved</li> <li>no controls included in the same study</li> </ul>	<p><b>Conclusion:</b></p> <ul style="list-style-type: none"> <li>elastase is significantly higher in sites w/ progressive periodontal attachment and bone loss</li> </ul> <p><b>CTF Rating:</b> Level II-2 B</p>

Evidence table 4  
Hemmings, K.W., Griffiths G. S., & Bulman J.S (1997)

Design & Population	Diagnostic Test & Control	Outcome	Critical Appraisal	Conclusion & CTF Rating
<p><b>Cohort</b></p> <ul style="list-style-type: none"> <li>10 females, 9 males</li> <li>Median age=36.6</li> <li>Patients had moderately severe chronic periodontitis</li> </ul> <p>(N=19)</p>	<p><b>Diagnostic Test:</b></p> <ul style="list-style-type: none"> <li>5 diseased sites per patient</li> <li>Criteria for treatment was: a minimum pocket depth of 5mm, BOP 1+, and radiographic bone loss</li> <li>5 disease sites: Use of Perioscan to check plaque sample and use of Periocheck for crevicular fluid proteases</li> </ul> <p><b>Control:</b></p> <ul style="list-style-type: none"> <li>2 healthy sites per patient</li> <li>Criteria for being deemed as a control: pockets under 3mm, BOP 0, no radiographic bone loss</li> </ul>	<ul style="list-style-type: none"> <li>Inter and intra-examiner reproducibility had good agreement for both Perioscan and Periocheck (60 – 90%)</li> <li>Perioscan: Sensitivity = 99% Specificity = 55%</li> <li>Periocheck Sensitivity= 88% Specificity= 61%</li> </ul>	<p><b>Checklist Score:</b> 5/10 = 50%</p> <ul style="list-style-type: none"> <li>Small pop'n size (20pt's, 126 useable sites of data), problems with tests: insufficient number sites with deterioration to make statistically valid conclusions</li> <li>disease active = defined as &gt;2mm attachment loss, but this can be false +ve</li> <li>flaws in test design: gingival bleeding made reading some results impossible</li> </ul>	<p><b>Conclusion:</b></p> <ul style="list-style-type: none"> <li>It was time consuming to provide a full mouth evaluation with these tests for any patient</li> <li>In the future it may be necessary to use a combination of a highly sensitive test with a highly specific test to gain the best predictive value for clinical use</li> </ul> <p><b>CTF Rating:</b> Level II-2 B</p>

Evidence table 5  
Nakashima, K, et al. (1996)

Design & Population	Diagnostic Test & Control	Outcome	Critical Appraisal	Conclusion & CTF Rating
<p><b>Cohort</b></p> <ul style="list-style-type: none"> <li>• 5 females, 3 males</li> <li>• Mean age=43.1</li> </ul> <p>(N=8)</p>	<p><b>Diagnostic Test:</b></p> <ul style="list-style-type: none"> <li>• 10 active sites and 43 inactive sites out of 330 sites in 8 subjects were monitored</li> <li>• GCF collected at 0,3,6,9,12 mos for PMN counts and biochemical analysis (FEL, AEL, a2M, alAT, PGE2, ALP, OC, BG, AST, COL)</li> </ul> <p><b>Control:</b></p> <ul style="list-style-type: none"> <li>• inactive diseased sites of the same oral cavities compared to sites w/ active periodontal disease</li> </ul>	<ul style="list-style-type: none"> <li>• ALP, BG, COL were significantly higher in active versus inactive sites</li> <li>• PGE2 alone was not significantly different between active and inactive, but as a ratio of PMN count is significantly different</li> <li>• linear discriminant analysis determined that PGE2, COL, ALP, a2M, OC, and AEL were best combo for discrimination between active and inactive sites</li> </ul> <p>Sensitivity = 80%; Specificity = 91%</p>	<p><b>Checklist Score:</b> 5/10 = 50%</p> <ul style="list-style-type: none"> <li>• only 8 subjects</li> <li>• moving threshold values higher increased false negative rate; decreasing threshold decreases false positive rate</li> </ul>	<p><b>Conclusion:</b></p> <ul style="list-style-type: none"> <li>• Combination of several GCF biochemical parameters gives a more reliable prediction of periodontal disease status compared to a single marker.</li> </ul> <p><b>CTF Rating:</b> Level II-2 C</p>

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