Molecular analysis: a potential role in the management of periodontal disease?

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Traditionally, dental professionals have advised patients that if they maintain good oral hygiene and general health then they should avoid problems such as periodontal disease. However, we now know that it is not that straightforward. There are many risk factors that influence an individual’s susceptibility to periodontal disease. Some of these, such as smoking and oral hygiene, can be controlled. Clinicians often see patients who present with similar levels of oral hygiene and health but their periodontal disease progression can be wildly different: whilst one patient may present with minimal tissue changes, another may exhibit advanced disease. Brushing and interdental cleaning remain extremely important to maintain a healthy mouth, however recent research shows that genetic factors may have a major modifying influence. Examining such genetic factors could therefore be of assistance in patient management.

Patients are increasingly becoming aware that they have a responsibility to take control of their oral health and are achieving excellent oral hygiene, and yet experience shows that their periodontal disease continues to progress. Cutting edge molecular technology, which may determine a patient’s susceptibility to periodontitis and the presence of specific bacterial DNA, is now available.

Genetic assessment permits the determination of a patient’s genotype. Genetic testing for periodontal disease susceptibility works by measuring a gene which regulates the production of Interleukin 1A and 1B (IL-1B), inflammatory mediators which stimulate host cells and result in the destruction of bone and soft tissue around the tooth. The destruction of these structures happens as a result of the host inflammatory response to the presence of bacteria. The level of the response is determined by the patient’s specific genetic makeup, which influences the amount of IL-1B produced.

Testing is quick, easy and pain free simply requiring a buccal swab to be taken, air dried and placed in a test tube prior to being sent to the laboratory. Patients with a positive result (Fig.1) are found to have up to four times as much IL-1B in response to a bacterial challenge when compared to negative patients (Fig.2). Clinical studies also show positive patients to be 2.7 times more likely to lose their teeth during the maintenance phase of treatment. When heavy smoking is also a factor this figure rises to 7.7. On this basis, a patient with a positive result would require close monitoring and to be treated more aggressively if symptoms occur. If treated early then serious complications of periodontal disease, such as gingival recession and tooth loss, can be prevented. Early diagnosis and treatment are therefore crucial. Genetic testing provides a major advantage in diagnosing and treating those individuals most at risk and should be offered as the gold standard in the diagnosis of periodontitis.

Figure 1: Example of positive genetic test

Figure 2: Example of report of negative genetic test

Historically it has been thought that the impact of periodontal disease would be limited to the mouth and just result in tooth loss. However, in recent years it is becoming increasingly recognised that the effects of periodontal disease may compromise health at other body sites. Recent research reveals that periodontal disease is closely linked with systemic disease such as:

- Heart disease - In the presence of gingival inflammation, bacteria from the mouth enter the bloodstream (bacteraemia). These bacteria can attach themselves to platelets in the blood which in turn aggregate inside the blood vessel walls causing clots to form...
and narrowing of the arteries.

- **Stroke** - In a similar way, active periodontal inflammation may contribute to clotting due to recurrent bacteraemia thereby increasing the risk of a stroke or transient ischemic attack.
- **Diabetes** - The presence of gingival inflammation can make it more difficult for a diabetic patient to control their blood sugar levels. Elimination of such inflammation can directly improve diabetic control.
- **Lungs** - Certain types of bacteria that are found in periodontal disease have been implicated in predisposing to the onset of pneumonia and other respiratory disease. Maintaining low levels of bacteria in the mouth has been shown to reduce the risk of developing chronic lung problems.
- **Pre-term births** - It has been reported that women with periodontal disease are 7 to 8 times more likely to give birth prematurely to low birth weight babies. Researchers believe periodontal disease causes the body to release inflammatory mediators which produce pre-term birth. However, further scientific research is required to substantiate this association.
- **Other links** - Researchers are also presently researching similar links between periodontal disease and Alzheimer’s disease, rheumatoid arthritis and kidney disorders.

Periodontal disease is an inflammatory condition associated with the presence of bacteria within the tissues. In view of this it is important to know which bacterial species are present before treatment begins. The use of a bacterial DNA test enables clinicians to know the identity and level of bacteria present within the tissues. The test is a simple, safe and painless procedure. All supra gingival plaque should be removed from the site area with a sterile curette, then up to five small paper points placed in the deepest pockets for ten to fifteen seconds. If concentrations and type are required in specific sites these points are placed in individual tubes separately. If this is of no relevance then all points can be pooled together in one tube. These are then sent to a laboratory for analysis.

Knowledge of bacterial DNA prior to starting your treatment can determine the exact strain of bacteria present and then a treatment plan can be implemented. Some species of bacteria cannot be permanently eliminated by localised debridement alone and therefore the use of adjunctive, specific antibiotic therapy may be required.

The presence of “aggressive” bacterial species such as *Actinobacillus actinomycetemcomitans* (Aa), *Porphyromonas gingivalis* (Pg), *Tannerella forsythensis* (Tf), *Treponema denticola* (Td) and *Prevotella intermedia* (Pi) would indicate a need for appropriate antibiotics (Fig.3). It is then advisable to retake the test 4 – 6 months post treatment to ensure the “aggressive” bacteria have been eliminated.

Most patients find it reassuring to know whether or not they have aggressive strains of bacteria in their mouths (Fig.4). If the aggressive strains are not present, patients feel relieved, however it may be advisable to prescribe a course of Periostat: the doxycycline, an antibiotic with anti-enzymatic activity, reduces the likelihood of tissue destruction allowing the body to repair the damaged tissue. Patients who test positive for the aggressive strains of bacteria, on the other hand, gain a better understanding of why they have had such a difficult time controlling their periodontal problems in the past. It is often helpful to suggest to the patient that they contact their GMP to request some background tests. It would be important to measure blood glucose to exclude diabetes and undertake a full blood count to detect any immunosuppression.
Other uses of molecular based tests
In addition to the management of periodontal disease, the test described here could be useful in patients who are undergoing orthodontic treatment, where force will be placed on the bone and good oral hygiene will be more difficult to maintain.

If a link between periodontal disease and pre-term birth is substantiated in the future, a bacterial DNA test may be worth considering for patients that are thinking about becoming pregnant.

Patients about to undergo implant surgery should be recommended to take the test to ensure that any periodontal infection is under control to minimise the risk of peri-implantitis and implant loss.

While periodontal disease is serious, oral cancer can be life-threatening. In the UK there are over 7000 new cases of oral cancer per year, with the highest incidence, for both males and females, in Scotland. More recently there has been an interest in the presence of certain types of human papillomavirus (HPV) in the oral tissues and development of squamous cell carcinoma in the mouth. In the future there may be benefit from doing molecular tests for HPV in patients to determine if they are at a high risk of developing oral cancer.

Editor’s note: Throughout this paper the term Actinobacillus actinomycetemcomitans (Aa) is used. However the nomenclature for this bacteria has now changed to Aggregibacter actinomycetemcomitans (Aa).

About the author:
Gayle initially qualified with a BSc in Medical Biotechnology prior to becoming a qualified dental hygienist therapist. Having worked in both NHS and private settings she currently works in a cosmetic practice in Scotland, ‘Cherrybank Dental Spa’. In March 2012 Gayle lectured at the dentistry show in Birmingham on the role of hygienist therapist in practice, she has been shortlisted for young hygienist therapist of the year, written articles for dental newsletters and magazines and is looking forward to embarking upon the role as a lecturer for Ivoclar.

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www.perio.org
www.medicalnewstoday.com/articles/5982.php

http://www.haleperiodontal.co.uk/10/Bacteria-Testing.html


http://info.cancerresearchuk.org/cancerstats/types/oral/incidence/

http://clincancerres.aacrjournals.org/content/14/21/6723.full