Chapter 1. Introduction

Periodontal Disease and Periodontitis

Periodontal diseases are bacterial infections that occur at or below the gum line; they include both gingivitis and periodontitis. The former affects only the gingival tissue, while the latter not only affects the gingivae but also the bone supporting the teeth. This systematic review concerns chronic periodontitis, which itself is typically described as mild, moderate, or advanced on the basis of gingival inflammation, pocket formation, loss of gingival attachment, bone resorption, and number of teeth involved.[1,2] According to the Surgeon General's report on oral health, most adults are affected by these infections; a decade ago, nearly 36 million persons ages 35 through 79 had some form of periodontitis.[1,3] Of persons ages 45 to 54 (one of the two most affected age groups), 14 percent have severe periodontitis.[1,4] Prevalence rates and severity of periodontitis are higher among males than females and among blacks and Mexican Americans than whites.[1]

Expenditures on dental services were estimated in 1998 to be almost $54 billion; they were expected to exceed $60 billion in 2000.[4] Of this dental bill, perhaps nearly $5 billion is now spent on periodontal services (in 1999, an estimated $4.4 billion was spent on periodontal procedures alone).[1] As documented in the Surgeon General's report, periodontal diseases can be associated with a variety of other serious health conditions (e.g., diabetes, cardiovascular disease, stroke); the diseases themselves and the need to seek dental or periodontal care can have impacts on numerous quality-of-life indicators (e.g., social interaction, limitations in usual daily activities, psychological status and sleep, and diet and nutrition) that reflect patient-oriented concerns.

For the past 100 years, many investigations have attempted to define the etiologic agents of these diseases.[5] The microbiology of periodontal infections is quite complicated, and numerous bacterial agents have been implicated in their etiology. Perhaps as much as 50 percent of the subgingival flora of chronic periodontitis has not yet been characterized (Gary Armitage, DDS, Personal Communication, May 7, 2003). Nonetheless, small groups of specific bacterial species are now considered to be important in the initiation or progression (or both) of periodontitis;[6] often mentioned are *Bacteroides forsythus, Porphyromonas gingivalis, Treponema denticola,* and *Actinobacillus actinomycetemcomitans*.[7-9]

Scaling and root planning (SRP) is generally the first treatment employed for periodontitis. It is considered a nonsurgical procedure for which local anesthesia is often given to numb the infected gingiva (gums) around the teeth to be subgingivally scaled and planed. Scaling may be performed with hand instruments alone or with the aid of an ultrasonic scaler. It is done to clean teeth thoroughly below the gum line, removing bacterial plaque, calculus (tartar), debris, necrotic tissue, and pus from pockets that form around infected teeth. Root planing involves cleaning and smoothing the root surface of an infected tooth after scaling so that the gingival tissue can heal close to the root, shrinking the tissue and reducing the depth of the pocket that had formed. SRP is intended to reduce the bacterial load, shrink swollen and inflamed gingiva, and recondition the subgingival ecology, making it biologically compatible with optimal healing and reattachment of epithelium to the root surface.

Two commonly used clinical measures of periodontal disease progression and restoration of oral health are probing depth (PD, sometimes referred to as probing pocket depth) and clinical

attachment level (CAL). These measures are made with specially marked periodontal probes held parallel to the tooth and inserted under the free gingival margin and gently "walked" to the base of the sulcus (i.e., pocket). The probes are typically marked with rings or bands that measure distance in millimeters. The PD is generally measured as the distance from the base of the sulcus to the top of the free gingival margin. The CAL is often measured as the difference between the PD and the distance from the free gingival margin and a natural fixed anatomical marker on the tooth called the cemento-enamel junction (CEJ). As the name implies, the CEJ is where the cementum and enamel on the tooth are joined. Specially fabricated stents are also used as an alternative to a fixed anatomical landmark to measure changes in CAL.

Concerted clinical effort at SRP is aimed at reducing the bacterial load and thus reduce the subsequent risk of periodontitis (Figure 1, Line segment A-B). The recognition that specific bacteria rather than nonspecific "plaque" are the etiologic vector for periodontitis has led to the development of antimicrobial treatment approaches for reducing or eliminating these bacteria and the infections (Figure 1, Line segment A-C). Antimicrobial agents could both reduce the bacterial load and shift the bacterial ecology from "disease promoting" to "health promoting." If mechanical therapy and antimicrobial therapy are both effective, then the combination of the two could potentially be even more effective (Figure 1, Line segment B-D), lowering both the risk of further disease and reducing the bacterial load to further promote periodontal health. This systematic review examines the evidence for this combined approach to therapy for periodontitis.

Specifically, we examine the evidence, for adults with chronic periodontitis, as to whether SRP accompanied by an adjunctive antimicrobial agent, compared to SRP alone, improves outcomes that persist over time. The primary outcomes of interest in this report are PD reductions, CAL gains, and secondarily, reductions in selected pathogens. The clinical rationale for this question relates to developments in controlling periodontal infections.

Controlling Periodontal Infections

The juxtaposition of three developments makes concerted efforts to control periodontal infections more realistic today than in the past. The first major advance was the development of molecular diagnostic tools that can rapidly and inexpensively examine large numbers of plaque samples and identify specific microbial species. A second advance was the recognition that specific microbial complexes occur together in plaque. The third was the development of new tools to reduce the supra- and subgingival bacteria, such as chlorhexidine mouthwash, triclosan dentifrice, electronic toothbrushes, and systemic and local drug delivery systems. From data derived from these three scientific avenues, three strategies have been proposed for reducing the risk of periodontal diseases. Each attempts to intercept the disease process at critical points in its development.

1. Reduce supragingival plaque. Supragingival plaque reduction by home care and professional cleaning is the most universally practiced periodontal treatment available; it is considered essential in the treatment of periodontal diseases.

2. Control pathogen transmission. Introduction of an antibacterial mouthwash and toothpaste may insulate sites from infected pathogen reservoirs elsewhere in the mouth. Hujoel et al. tested rinsing once per week and observed a 45 percent reduction in tooth loss after 1 year.[10] Quirynen et al.[11] and De Soete et al.,[12] examining one-stage, full-mouth disinfection,

observed a parallel significant reduction in periodontal pathogens and improvement in clinical health following chlorhexidine rinses.

3. Disinfect pathogen reservoirs. Many investigators have recognized disease reservoirs as seeding sources for intraoral spread of disease and as an important consideration in determining therapeutic outcome.[13] Of the infection sources in the oral cavity, untreated sites elsewhere in the mouth represent the most obvious potential source of re-infection. At least three mechanisms are used to address this threat: SRP; local drug delivery; and systemic antibiotics.

SRP. SRP has been used effectively in periodontal therapy for more than 1,000 years.[14,15] The concept that eliminating periodontal pockets that support pathogen growth decreases the risk of periodontal disease is generally accepted. Some clinical studies indicate that most patients with periodontal disease can be maintained by regular SRP alone.[16-19] By itself, SRP produces a very modest transient reduction in bacteria; they can return to pretreatment levels within 2 weeks.[20,21] When total bacterial load changes, a subset of bacteria associated with periodontitis is also depressed, including *P. gingivalis*, *B. forsythus*, and *T. denticola*.[22] The microbial impact, however, appears to be short lived with sites re-infecting after 3 months. This suggests that a more effective initial therapy might reduce the labor of continued maintenance and also further reduce the disease risk.

Local drug delivery. Several local antibacterial agents have been tested for intra-pocket delivery. These include doxycycline gel, metronidazole gel, chlorhexidine chips, minocycline microspheres, and tetracycline fibers. All these agents, either alone or in combination with SRP, appear to reduce pocket depth[23] and may also alter oral bacteria.

Systemic antibiotics. A host of systemic antibacterial agents has been tested: amoxicillin, metronidazole, metronidazole plus amoxicillin, azithromycin, clindamycin, and ciprofloxacin. The studies, some considered in recent systematic reviews examining these antibacterial agents, either alone or in conjunction with mechanical therapy, suggest that antibacterial therapy alone may, in some cases, be as effective as SRP therapy.[15,24]

Origins of this Evidence Report

This is the fourth in a series of systematic reviews of dental topics prepared for the Agency on Healthcare Research and Quality (AHRQ) with the support and collaboration of the National Institute of Dental and Craniofacial Research (NIDCR) (for Acknowledgments, see Appendix A). The first was a review of dental caries diagnosis and management that cut across the entire population and stages of life.[25] The second report, rather than focusing on a specific dental disease condition or a particular treatment approach for the general population, dealt with several aspects of the treatment of a special population subgroup – persons infected with human immunodeficiency virus (HIV) and those living with acquired immune deficiency syndrome (AIDS).[26] The third report reviewed the cardiovascular effects of the use of epinephrine – an ingredient of dental anesthesia and retraction cord inserted around teeth to reduce bleeding – in hypertensive dental patients.[27]

The specific clinical question to be addressed in this evidence report emerged from a working group meeting that NIDCR convened on the National Institutes of Health campus on April 2, 2001. This invited group of eight experts from the field of periodontics represented the range of experience, activity, and perspective within the discipline, including academia, public

health, clinical practice, and research. In selecting the area of periodontal disease, NIDCR sought to include in its array of evidence reports the next largest domain of the profession's clinical activities after dental caries, for which we had already prepared a report. In bringing together the working group, NIDCR was opening the topic selection process to the needs and sensitivities of the field.

A set of six questions emerged from the working group meeting. Two involved diagnostic issues; one related to distinguishing aggressive from chronic periodontitis, and the other to assessing the validity of methods to predict periodontal destruction. Four questions addressed disease management or treatment issues. These included assessments of the effectiveness of SRP compared to other treatments, the nature of professional maintenance needed after periodontal therapy, how risk factors modify the outcomes of periodontal therapy, and whether predictable therapies exist for regenerating supporting tissue lost to periodontal disease. For a variety of reasons, the group rated the question of the effectiveness of SRP therapy for chronic periodontitis as the top issue for the NIDCR to consider in the evidence report.

The project team subsequently refined and clarified the question through discussions with the NIDCR staff and later through communication with the Technical Expert Advisory Group (TEAG) assembled for this particular topic area. The original question on effectiveness of SRP was too broad to be covered in a single evidence report, as it would have involved too much literature and required more time and resources than were available. The consensus decision, therefore, was to focus on the primary comparison of interest: In adults with chronic periodontitis, does SRP therapy in conjunction with the use of chemical antimicrobial agents, when compared to SRP alone, improve clinical outcomes that persist over time?

Among many possible indicators of improved clinical outcomes, we chose to use reported measures of PD reduction, gain in CAL, and pathogen reduction, with no accompanying increase in adverse events. To answer the key question, the project team systematically identified, critically appraised, and synthesized the evidence emanating from published primary human clinical trials research that produced data to allow examination of this question.

The question reflects two fairly common concerns in dentistry. First, practicing dentists may not be aware of the available research with respect to the effectiveness over time of therapies adjunctive to SRP for persons with chronic periodontitis. Second, the research may not be as comprehensive or definitive as it should be. Thus, all judged this particular focus to be of clinical, research, and practical significance.

Technical Expert Advisory Group

AHRQ guidelines require identification of a technical expert advisory group (TEAG) for evidence reports, in this case in the specialized area of managing periodontal diseases. Our TEAGs advance AHRQ's broader goals of (a) creating and maintaining science partnerships and public-private partnerships and (b) meeting the needs of an array of potential consumers and users of its products. Thus, a TEAG is both an additional resource and a sounding board throughout the project.

The TEAG for this systematic review comprised six individuals who are acknowledged technical or clinical experts in this area (Table 1). One member specifically represented the

American Academy of Periodontology (AAP) and another the American Dental Association (ADA), both potential user groups.

To ensure scientifically robust work, we asked the TEAG to provide reactions to work in progress and to advise on substantive issues or possibly overlooked areas of research. TEAG members participated in e-mail communications

- to discuss the key clinical questions, initial drafts of causal pathways, and proposed inclusion and exclusion criteria for research articles;
- to provide comments concerning the article abstraction forms, the content proposed for inclusion in the evidence tables, and the final versions of the key clinical question; and
- to discuss the proposed content of the evidence tables and the completeness of the search.

Because of their extensive knowledge of the literature and ongoing research in this specialized area of dentistry dealing with treatment of chronic periodontitis, as well as their active involvement in the associated professional societies, we also asked TEAG members to participate in the peer review process by commenting on the draft evidence report, and four did so.

Organization of this Report

The remainder of this evidence report is organized in the following manner. Chapter 2 provides details about our literature search and review methodology. Specifically included are the analytical framework for our key clinical question and our approach to conducting the systematic review, applying the inclusion/exclusion criteria, abstracting data from articles, maintaining quality control, and similar details. Chapter 3 presents the results of our analyses. Chapter 4 gives our concluding discussion, and Chapter 5 notes weaknesses and gaps we found in the research and offers recommendations for a research agenda related to the question addressed on the added effectiveness of therapies adjunctive to SRP in treating chronic periodontitis. Chapter 6 provides the references cited in the body of the evidence report.

Chapter 7 contains the evidence tables and supporting information. Finally, the complete bibliography of literature considered and used in developing the evidence report (including all articles reviewed in the literature search and all references cited in Chapters 1 to 5) appears in Chapter 8. The three appendices provide acknowledgments (Appendix A), our data abstraction form (Appendix B), and the quality review checklist (Appendix C).