Gingival crevice fluid – an introduction

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Studies on gingival crevice fluid (GCF) extend over a period of about 50 years. The pioneer research of Waerhaug in the early 1950s was focused on the anatomy of the sulcus and its transformation into a gingival pocket during the course of periodontitis (24). In the late 1950s and early 1960s a series of groundbreaking studies by Brill et al. laid the foundation for understanding the physiology of GCF formation and its composition (4). The studies of Löe et al. contributed to this understanding and started to explore the use of GCF as an indicator of periodontal diseases (17). Egelberg continued to analyze GCF and focused his studies on the dentogingival blood vessels and their permeability as they relate to GCF flow (6). The GCF studies boomed in the 1970s. The rationale for understanding dentogingival structure and physiology was created by the outstanding electron microscopic studies of Schroeder (20) and Listgarten (16). Presence and functions of proteins, especially enzymes in GCF were first explored by Sueda, Bang and Cimasoni (3, 6). It was soon understood that enzymes released from damaged periodontal tissue possessed an enormous potential for periodontal diagnosis. Ohlsson, Golub and Uitto discovered that collagenase and elastase in GCF are derived primarily from human cells, most notably neutrophils, and that their activity is correlated with gingival inflammation and gingival pocket depth (12, 18, 22). Migration of neutrophils and their function in gingival tissue and GCF were clarified by the excellent investigations of Attström et al. (2). In 1974 the first edition of the monograph *The Crevicular Fluid* by Cimasoni was published (6). This comprehensive review gave a big boost to GCF studies and towards the end of the first millenium the research on GCF increased dramatically. Today the PubMed computer search of the National Library of Medicine (USA) revealed 1656 studies on different aspects of GCF. This volume of *Periodontology 2000* reviews some of these studies.

The review by Griffiths examines the hypothesis of Alfano (1) which states that in health GCF represents the transudate of gingival tissue interstitial fluid but in the course of gingivitis and periodontitis GCF is transformed into true inflammatory exudate. In his review the author discusses the GCF composition and evaluates different methods for GCF sample collection, their advantages and pitfalls (14). The flow rate of GCF may increase about 30-fold in periodontitis compared to the healthy sulcus. However, its resting volume also increases at the same time with the formation of gingival pockets. Therefore, even though the GCF flow rate when accurately measured with an electronic device clearly reflects the periodontal disease process, the method of fluid collection has to be selected to provide a clear distinction between the resting volume and the flow rate of GCF. These issues are thoroughly examined in the review by Goodson (13).

Junctional epithelium is a unique tissue. Nowhere else in the body does nonkeratinizing epithelium face an inert hard tissue. This situation poses an exceptional challenge to the junctional epithelium in the dentogingival area to protect the periodontium, and consequently the whole body, against the several hundred bacterial species that are present in the oral cavity. The structure and metabolism of junctional epithelium are discussed in the review by Pöllänen et al (19). The different strategies used by junctional epithelium to overcome the microbial challenge and reasons for the failure of the defence systems are also described. GCF plays a special part in maintaining the structure of junctional epithelium and in the antimicrobial defence of periodontium. Leukocytes, especially neutrophils, are key players in the battle against bacteria in the sulcular region. The article by Delima and Van Dyke deals with cells of the GCF and the fine balance between the protective and destructive roles of neutrophil-mediated host defense (7). Either defective or excessive neutrophil
Gingival crevice fluid (GCF) is a complex mixture of substances derived from serum, leukocytes, structural cells of the periodontium and oral bacteria (Fig. 1). These substances possess a great potential for serving as indicators of periodontal disease and healing after therapy. Some of the suspected periodontopathogens, such as *Porphyromonas gingivalis* and *Treponema denticola* produce broad-spectrum neutral proteinases as part of their virulence arsenal. These proteinases may be detected in plaque and GCF samples of periodontitis patients. The properties of the oral bacterial enzymes and their value in evaluating periodontal status are discussed in the review by Eley and Cox (10).

The host-derived substances in GCF include antibodies, cytokines, enzymes and tissue degradation products. The antibodies in gingival crevicular fluid are comprised of both locally and systemically synthesized molecules and they reflect periodontal colonization by particular microbial species. Antibodies are key players in the protection of the body against pathogenic bacteria. However, they may also be crucial in eliciting destructive inflammatory reactions in the periodontium. Antibodies in GCF and strategies for using them to maintain local and systemic homeostasis are discussed in the issue by Ebersole (8).

Bone-specific markers such as the collagen telopeptide fragments and osteocalcin in GCF may reflect periodontal bone resorption. Giannobile et al. review these factors in this volume (11). The article by Champagne et al. explores the inflammatory mediator levels in subjects with periodontal diseases. Their results suggest that some inflammatory mediator levels increase with time in periodontitis patients both in active and stable periodontal sites and that the risk for periodontitis is related to the overall systemic inflammatory response of an individual (5).

Proteolytic enzymes are released in periodontal tissues during inflammation from leukocytes, activated structural cells of epithelium and connective tissue. Of these enzymes, matrix metalloproteinases (MMPs) have the main responsibility for degradation of periodontal tissues. Recent studies have shown, however, that MMPs also have specific functions in controlling tissue defense reactions and repair. In an attempt to find a specific MMP indicator for periodontal diseases focus should be directed to proteinases that are released during the active tissue destruction episodes of the diseases, rather than those released from neutrophils throughout the inflammatory process. Also active rather than total (latent plus active) enzyme activities should be measured. Different techniques to measure host cell proteases and interpretation of the results are discussed in the article by Uitto et al. (23).

It is obvious that GCF provides a unique window for analysis of periodontal condition. Collection of GCF is a noninvasive and relatively simple procedure. The potential of GCF in early detection of periodontitis and healing of periodontal tissues following therapy was already understood in the 1950s. However, in the third year of the second millennium we still do not have a practical and accurate periodontal indicator based on GCF. What are the barriers to their development? Periodontal diseases, their microbial causes, cell regulation and tissue reactions during inflammation and healing have proved to be extremely complex issues. We still do not have a clear picture of the pathophysiological events leading to tissue destruction connected to periodontitis. We do not know the actual roles of different GCF enzymes in inflammation and tissue repair. We have only just started to understand the role...
of different pathogenic bacteria in the periodontitis process. Several tests have been developed that are aimed at specifically and sensitively revealing the metabolic status of periodontal tissues. Some of them have shown good specificity and sensitivity values as well as potential for predicting disease progression. Unfortunately only a handful of GCF tests have made their way into clinical practice. Clinicians are still missing a practical test based on enzymes, tissue degradation products or cytokines that accurately indicates an initial periodontitis process, active disease periods or effective healing. It is the hope of this editor that the reviews in this volume of *Periodontology 2000* will serve as a stimulus for studies resulting in further understanding of periodontal tissue physiology. This will eventually pave the way for the development of practical GCF indicators that will aid in the accurate diagnosis and appropriate treatment of periodontal diseases.

**References**

8. Ebersole J. Humoral Immune Responses in Gingival Cre-