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Gingival Crevicular Fluid (GCF): A Diagnostic Tool for the Detection of Periodontal Health and Diseases: A Review

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Abstract: ***GCF (Gingival Crevicular Fluid) is the fluid found in gingival crevice and it mainly consists of substances derived from serum, leukocytes, bacteria, activated epithelial cells, connective tissue cells, and bone cells as these possess a great potential for serving as indicators of periodontal disease and healing after therapy. It plays a special part in maintaining the structure of junctional epithelium and the antimicrobial defense of periodontium. Some of the suspected periodontal pathogens such as*** **Porphyromonas gingivalis** ***and*** **Treponema denticola** ***produce broad-spectrum neutral proteinases as part of their virulence arsenal. Present review article gives a brief of every aspect about GCF.***

Keywords: Cells, Exudate, Fluid, Gingival crevicular fluid, Gingiva, Inflammation, Leukocytes, Periodontium

1.Introduction

Gingival crevicular fluid (GCF) is an inflammatory exudate derived from the periodontal tissues. [1] It mainly consists of substances derived from serum, leukocytes, bacteria, activated epithelial cells, connective tissue cells, and bone cells as these possess a great potential for serving as indicators of periodontal disease and healing after therapy. [2] **(Figure 1)**

GCF plays a special part in maintaining the structure of junctional epithelium and the antimicrobial defense of periodontium. Analysis of periodontal condition can be easily done by collection of GCF which is a non-invasive and relatively simple procedure. [3]

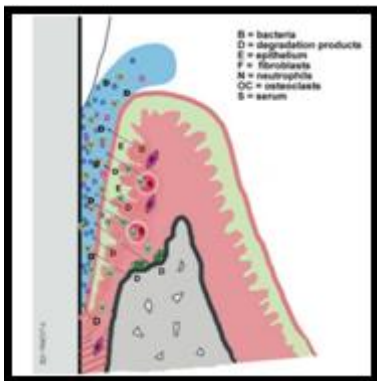

Figure 1: Gingival Crevicular Fluid

Junctional Epithelium the Antimicrobial Defense [4]

The junctional epithelium is firmly attached to the tooth and thus forms an epithelial barrier against the plaque bacteria and allows the access of GCF, inflammatory cells, and components of the immunological host defense to the gingival margin. It also exhibits rapid turnover, which contributes to the host-parasite equilibrium and rapid repair of damaged tissues.

GCF is an exudate of varying composition found in the sulcus/periodontal pocket between the tooth and marginal gingiva. It contains components of serum, inflammatory cells, connective tissue, epithelium, and microbial flora inhabiting the gingival margin or the sulcus/pocket. In the healthy sulcus, the amount of GCF is very less.

During inflammation, the GCF flow increases and its composition start to resemble that of an inflammatory exudate. The increased GCF flow contributes to host defense by flushing bacterial colonies and their metabolites away from the sulcus. The main route for GCF diffusion is through the basement membrane and then through the junctional epithelium into the sulcus.

Mechanism of Gingival Crevicular Fluid Production [5]

A. Molecular sieving:

Two events occurring in the inflammatory process are responsible for molecular sieving:

- A rise of hydrostatic pressure within the microcirculation.
- Unlocking of endothelial cell junctions. (**Figure 2)**

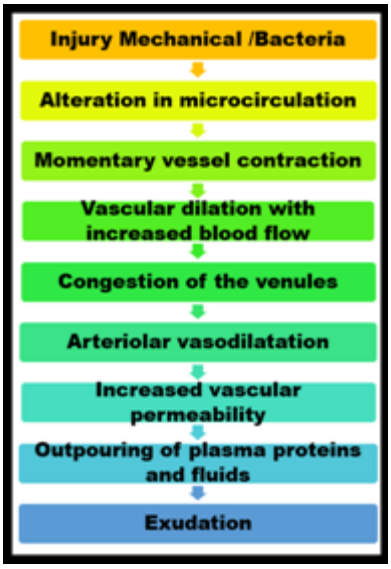

Figure 2: Mechanism of Gingival Crevicular Fluid

Permeability of Junctional and Oral Sulcular Epithelia

Albumin, Endotoxin, Thymidine, Histamine and Phenytoin are the substances that have been shown to penetrate the sulcular epithelium. The main pathway for the transport of substances across the junctional and sulcular epithelia seems to be the intercellular spaces which according to **Schroeder and Munzel Pedrazzoli** form 18% of the total volume of the junctional epithelium and 12% that of the oral sulcular epithelium. [6]

Three routes have been described: [7]

- Passage from CT into the Sulcus.
- Passage from the Sulcus into the CT.
- Passage of substances through Pathological or Experimentally modified Gingival Sulcus.

Gingival Crevicular Fluid [8]

GCF flow is the process of fluid moving into and out of the gingival crevice or pocket. It is a small stream, usually only a few microliters per hour. Fluid flow is a rate measure. It is the volume that crosses a defined boundary over a given time, mathematically symbolized as dV/dt, the first derivative of volume with respect to time.

GCF flow rates in health and disease. Shallow sulci in healthy subjects have GCF flow rates of 3-8 µl/h, Pockets with intermediate periodontal disease have GCF flow rates of approximately 20 µl/h. GCF flow at sites with advanced periodontal disease as high as 137 µl/h have been observed.

Factors Stimulating Gingival Crevicular Fluid Flow [9]

A. Gingival inflammation, mastication of coarse food, pocket depth, intracervical scraping, scaling, and histamine topical application.
B. Enzymes and sex hormones: Female sex hormones increase the gingival fluid flow because they enhance vascular permeability.
C. Circadian periodicity: There is gradual increase in gingival fluid amount from 6 AM to 10 PM and a decrease afterward.
D. Post-periodontal surgery, restorative procedure, strip placement, mobility, increased body temperature, and salivary contamination.
E. Ovulation, hormonal contraceptives, and smoking.
F. Systemic disease.

2.Methods of Collection of GCF

Intracrevicular washing (Gingival washing), Capillary tubing or Micropipette, Absorbing paper strips and Preweighed twisted threads.

1. Gingival washing methods [10]

In this technique the gingival crevice is perfused with an isotonic solution, such as Hanks' balanced salt solution, usually of fixed volume. The fluid collected then represents a dilution of crevicular fluid and contains both cells and soluble constituents such as plasma proteins.

2. Capillary tubing or micropipettes [11]

Capillary tubes of known internal diameter are inserted into the entrance of the gingival crevice following the isolation and drying of a site. GCF from the crevice migrates into the tube by capillary action and because the internal diameter is known the volume of fluid collected can be accurately determined by measuring the distance which the GCF has migrated. (**Figure 3)**

Figure 3: Clinical picture showing gingival crevicular fluid collecting using a Capillary tubing or micropipettes

3. Absorbent filter paper strips [12]

Considerable variations are there in the application of the filter paper strip method of collection. Positioning of paper strip (Extracrevicular method), Positioning of paper strip just at the entrance of the crevice (Intracrevicular method 'Superficial') and Positioning of paper strip at the base of the pocket (Intracrevicular method 'Deep'). (**Fig-4)**

Figure 4: Clinical picture showing gingival crevicular fluid collecting using an Absorbent filter paper strips

The fluid volume on the strips was quantified by a number of ways:

1. Originally, strips were stained with a protein disclosing dye such as ninhydrin at concentration varying between 0.2% and 2%. The stained area can be measured by using a magnifying device such as a graded microscope.
2. The strips were weighed before collection within a scaled microcentrifugation plastic tube and the weighing was repeated immediately after collection in the same microtubule.
3. An electronic method has been devised for measuring the fluid collected on a blotter (PerioPaper) using an electronic transducer (Periotron). **Figure 5**. This electronic device measures the changes in capacitance across the wetted strip. This change is converted into a digital readout that can be correlated to the volume of GCF.

Figure 5: PERIOTRON 8000

Preweighed twisted threads [13]

Weinstein et al inserted preweighed twisted threads into the gingival crevice around the tooth, and determined the amount of fluid collected by weighing the sample thread.

Problems with GCF Collection and Data Interpretation [14]

Contamination, Sampling Time, Volume determination, Recovery from strips and Data reporting.

Composition of GCF [15]

Gingival fluid is composed mainly of blood electrolytes and organic molecules, i.e. albumins, globulins, lipoproteins or fibrinogen and cellular components. In addition, the gingival fluid also contains of peptides, bacteria and enzymes. (Table 1) The presence of immune cells is associated with active transport, while the rest of components, depending on the size of molecule, show a passive filtration.

Table 1: Comparing the content of the individual cells of the immune system in gingival crevicular fluid and in peripheral blood

Cell type	GCF	Peripheral blood
Neutrophils	91-97%	60%
Monocytes / Macrophages	2-3%	5-10%
Lymphocytes	1-6%	20-30%
T lymphocytes	29%	50-75%
B lymphocytes	71%	15-30%

Over half a century ago **Sharry and Krasse** [16] proved that nearly 50% of cells collected from the gingival groove, even with clinically healthy surroundings, are leukocytes, while derived from other areas of the oral cavity - contained only 2% of leukocytes. Neutrophils (PMNs - polymorphonuclear leukocytes) constitute 91-97% of the immune system cells and quantitatively prevail among all leukocytes in gingival fluid. The remaining (2-3%) are monocytes/macrophages, T lymphocytes (29%), B lymphocytes (71%) (**Table 2).** The ratio of T cells to B is 1: 2, 7 which is different than in peripheral blood.

Table 2: Inflammatory mediators present in the gingival crevicular fluid

The mediators of the immune response	• Total and subgroups of immunoglobulin IgG • The mediators of the inflammatory response • Arachidonic acid derivatives such as PGE2 • Cytokines, such as IL-1, IL-2, IL-4, IL-6, TNFα	
Enzymes and enzyme inhibitors	**Proteolytic enzymes**	**Hydrolytic enzymes**
	Collagenase	Arylsulfatase
	Elastase	β-glucuronidase
	Cathepsin-B	Alkaline phosphatase
	Cathepsin-G	Acid phosphatase
	Cathepsin-D	Myeloperoxidase
	Tryptase	Lactoferrin

		Lysozyme
Bone-specific proteins	• Osteonectin • Phosphoprotein (N-propeptide) • Osteocalcin • Telopeptide of type I collagen • Tissue breakdown products	

3.Role of GCF as a Diagnostic Aid

Need for Diagnostic Tests for Periodontal Disease [17]

Disease activity may occur in episodes or bursts at a limited no. of sites during a defined interval, with the clinical duration of activity occurring in short periods from days to months. Evidence also indicates that at some sites, patients manifest periodontal breakdown that is slow but continuous in progression. There is need to distinguish between stable and progressive disease sites and to assess if these sites are adequately treated.

Requirements of a Diagnostic Test [15]

- Should be able to detect subclinical disease
- Information gained should be relevant to diagnosis, treatment or predictive tests
- Able to be accurately repeated in a number of different clinical situations and levels of disease severity
- To detect disease presence and evaluate severity
- To predict the subsequent clinical course and prognosis
- To estimate responsiveness to treatment before therapy
- To assess actual response to treatment after completion.

Drugs in the Sulcular Fluid [12]

Metronidazole and tetracycline can eliminate tissue bacteria, and in conjunction with scaling and root planning, they suppress actinomycetemcomitans levels. Tetracycline in low doses inhibits the activity of collagenase and other collagenolytic enzymes.

4.Conclusion

The studies of GCF chemistry have suggested the importance of an exuberant PMN response to subgingival plaque in the active phases of periodontal destructions. Furthermore, the accumulated data regarding the functional status of PMN at sites of infection and inflammation suggest that the tissue destruction associated with an influx of PMN is a result of PMN hyperactivity.

The search for markers of periodontal disease activity and progression has accelerated over the last decade and research is being aimed at establishing a more objective and quantitative methodology, capable of rapid diagnosis prior to the appearance of clinical signs of destructive disease. GCF has emerged in the last decade as a new domain for improved periodontal diagnosis and therapy.

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