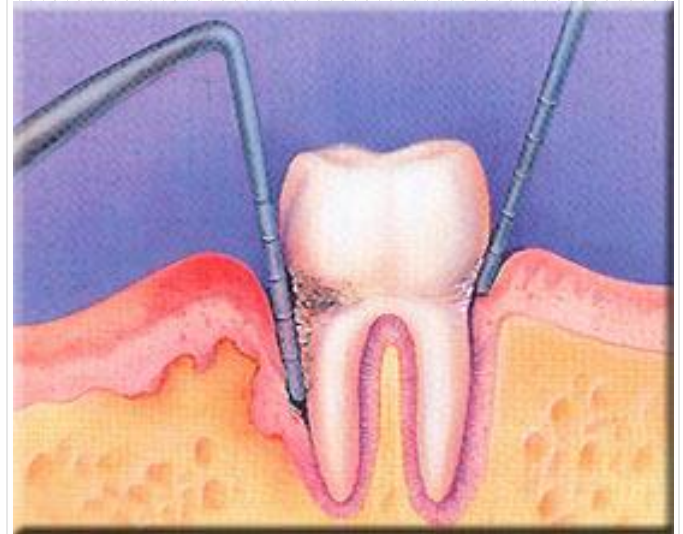


periodontal pathogens How to reach the Brain

Rasha Mohammed



Possible Link Between Chronic Periodontal Disease and Central Nervous System

- Infection and inflammation within the central nervous system (CNS) occur as consequence of systemic diseases. The only exception where a CNS infection is not acquired systemically is when bacteria are introduced to the brain by direct inoculation by neurosurgical intervention or penetrating traumas.

- Among the infections that precede CNS pathologies are: peripheral sepsis, pneumonias, urinary tract infections, sinusitis, otitis, and oral infections.
- Bacterial and viral pathogens gain access to the brain from sites of local infection by the bloodstream and lymphatics, and cause disruption of neurological homeostasis by compromising the integrity of the blood brain barrier (BBB) and bloodcerebrospinal fluid barrier

Brain abscess and periodontal pathogens

- Brain abscesses are most frequently caused by bacterial dissemination from a primary lesion at a distant site. One important site of primary infection can be the oral cavity

Four possible routes of odontogenic spread:

1. hematogenous systemic bacteria
2. direct venous drainage
3. introduction by foreign objects
4. lymphatic drainage.

- Consequently, it has been assumed that the patients with periodontal disease may have a much higher risk of developing bacteremia from daily oral activities and, hence, systemic diseases of oral origin.
- Bacteremia of periodontal origin may be associated with many systemic diseases such as endocarditis, meningitis, atherosclerotic vascular disease, and brain abscess.

SYSTEMIC INFECTION: FROM ORAL CAVITY TO BLOODSTREAM

- Most of the external organisms find oral cavity as a primary channel entering the human body. Periodontal pathogens possess several virulence factors such as lipopolysaccharide (LPS). These factors are capable of inducing pro-inflammatory cytokines (IL-1, IL-6, and TNF- α).

- The gingival epithelium provides physical, chemical, and immunological barriers that prevent the entry of microorganisms into the circulation. If this natural barrier, which is approximately ten-cell layer thick, is breached by periodontitis, bacteremia proliferates.
- As periodontal vasculature permeability increases, ulcerations in the pocket lining are generated due to buildup of sub- and supragingival plaque. Thereafter, periodontal bacteria propagate to distal organs, via the bloodstream or the lymphatic system, and result in inflammation of distant sites.

MECHANISMS INVOLVED IN SPREAD OF INFLAMMATION TO BRAIN

The two mechanisms involved in the brain which cause an increase in proinflammatory molecules, that is, via systemic circulation and/or neural pathways.

In the systemic circulation, proinflammatory molecules enter brain through areas which lack blood brain barrier (BBB). Alternatively these inflammatory molecules can also enter areas in brain with blood brain barrier through:

- (a) Fenestrated capillaries of the BBB**
- (b) Using cytokine specific transporters**
- (c) Increasing the permeability of BBB, or**
- (d) Endothelial cells of the brain are activated to produce cytokine inducing signaling molecules such as nitric oxide.**

Possible ways for microorganisms to reach the brain

- **Blood circulation**

In case of oral and periodontal diseases, the microbial-induced infection presents a infectious problem to the entire body. Further, specific microorganisms associated with the disease process release toxins that invoke an inflammatory response.

- Bacteria, bacterial toxins, localized tissue response cytokines, and other inflammatory mediators enter the vascular circulation and can activate a systemic response. This entry into vascular channels happens through the gingival sulcus area, which harbors a high microbial load in periodontal diseases.

- Various dental treatments such as brushing, chewing, flossing, and use of tooth picks can also cause bacteraemia (a condition when there is bacteria in the blood) in a patient with periodontitis. This condition can occur several times in a day and is estimated to last approximately 3 hours for oral bacteria.

- Bacteraemia can be controlled by the immune system of the body; however, in subjects with a reduced immunity (the elderly patients), patients suffering from diabetes, rheumatoid arthritis, or malignancies, bacteria distribute into the vascular channels.
- Within one minute after distribution into vascular channels, bacteria may reach distant organs such as the heart, brain, lung, and peripheral blood capillaries.

- **The blood–brain barrier**

All the blood capillaries in the body are lined with endothelial cells, which act as an interface between the blood and the wall of the blood capillaries. All the blood capillaries of the body and brain have endothelial cells; however, these vascular endothelial cells of the brain differ from rest of the body vessels due to the presence of tight junctions between them. This nearly creates an impermeable boundary between the brain and the bloodstream and is termed as “the blood–brain barrier” (BBB).

- The BBB helps in the blockage of the passage for certain harmful substances such as toxins and various bacteria.
- The BBB can prevent the microorganisms in the blood from accessing the brain.
- However, the aging process may favor the growth of oral microorganisms, mainly the anaerobic bacteria and facultative yeasts established in the early life, and may trigger proinflammatory responses that may weaken the BBB.

- MRI confirmed that there is loss in the integrity of BBB in a mouse with candidiasis. This loss in integrity can allow the microorganisms to spread through the blood stream to the brain and thus may lead to neurodegeneration.

THANK YOU