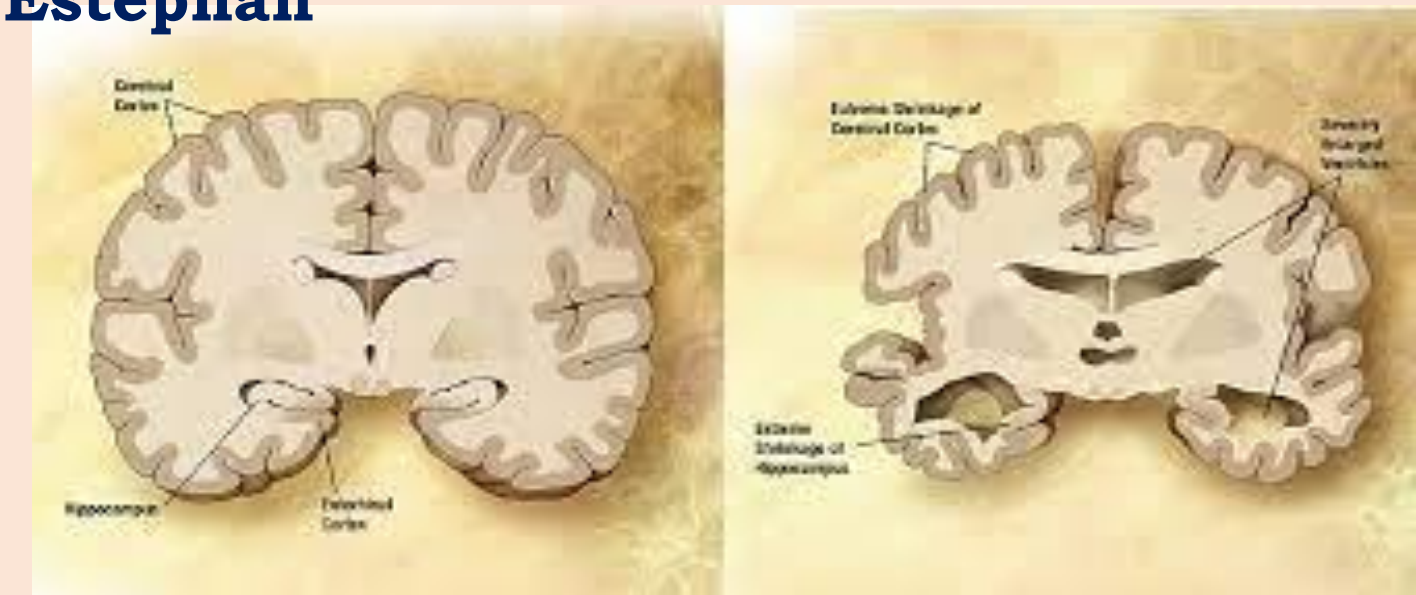
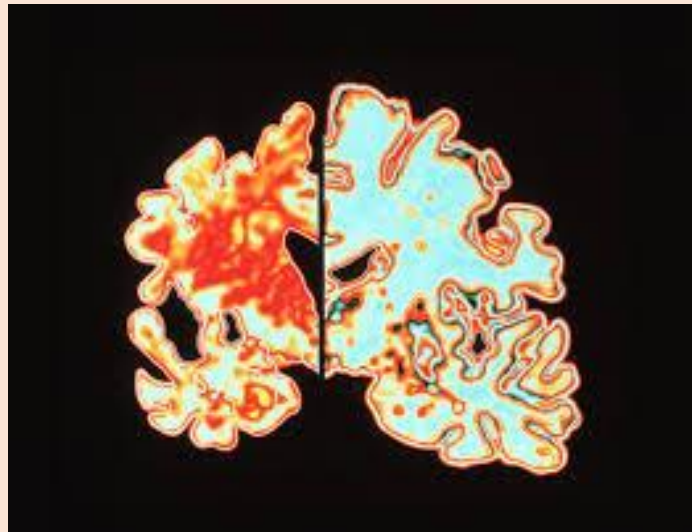
Can oral microbial infections be risk factor for neurodegenration?

By: Assist. Prof, Maha Fadheel Estephan



Various neurodegenerative diseases, e.g., Alzheimer's disease (AD), Parkinsonism etc., lead to loss of structure or function of the building units of the nervous system, i.e., neurons. Recent researches have described the role of systemic inflammation in the pathogenesis of various neurodegenerative disorders



Although chronic inflammation is not the causative agent of neurodegenerative disorders, it may modulate the neuropathology. In various prospective studies, it has been shown that an increase in the level of serum proinflammatory cytokines may precede neurodegenerative disorders.

oral cavity harbours more than 200 bacterial species and exhibits large variations at different oral sites. Various oral and periodontal diseases such as caries, chronic and aggressive periodontitis, mucositis, and gingivitis are associated with changes in the oral microflora and/or predominance of various anaerobic microorganisms.

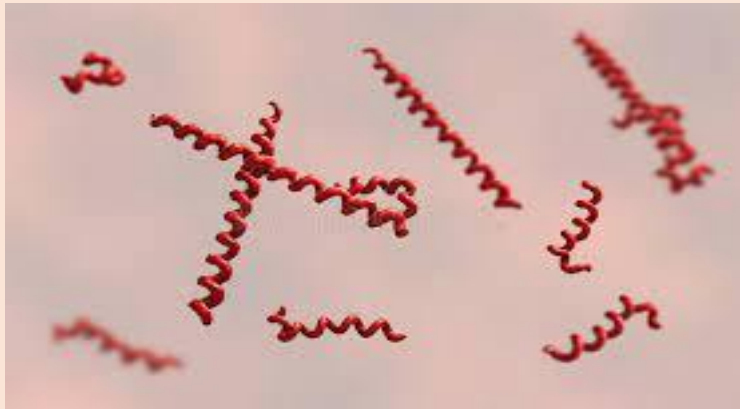
periodontal pathogenic bacteria and neurodegeneration

Many pathogens involved in chronic periodontitis are associated with the development of several inflammatory sites at distant organs. Some of the pathogens include *Treponema forsythia*, *T. denticola*, and *P. gingivalis*. *T. denticola*, a spirochete, was found in the brain of a patient with AD.

Spirochetes are strongly neurotropic in nature (i.e., they effect the neurons), and via the lymphatic system, they can spread along the nerve fibres.

They have been identified in the trigeminal nerve and ganglia.Spirochetes with their antigens and DNA have been identified to be associated with AD and are strongly considered to be the causative agents of dementia. In studies conducted at various laboratories, spirochetes have been found in association with AD.

The seven different oral Treponema species were found in 14 out of 16 AD brain samples. The viability of spirochetes in the brain was even checked by growing them from brains of several AD patients.It was found that there existed a co-infection in AD which included several other oral varieties of spirochetes (*T. socranskii*, *T. amylovorum*, *T. denticola*, *T. pectinovorum*, *T. medium*, and *T. maltophilum*). Spirochetes could reproduce biological and pathological hallmarks of AD when exposed to mammalian neuronal and glial cells in organotypic cultures.



Some of the other important periodontal pathogens related to AD are *Fusobacterium nucleatum* and *Prevotella intermedia*. The NHANES (National Health and Nutrition Examination Survey) study showed that the antibody levels of these organisms in serum were found to be considerably increased (α = 0.05) in AD patients in comparison to that in controls.

In periodontitis, bacteria along with some other molecules such as pathogen-associated molecular patterns (PAMPs) initiate the inflammatory response. PAMPs include LPS, peptidoglycan, capsular proteins (for virus), flagellin, fimbrillin, bacterial DNA, some proteases, and other modifying enzymes that stimulate the host immune response.

The PAMPs stimulate host's pattern recognition receptors (PRRs) to produce cytokines, which bring the appropriate immune cells to the infection sites.

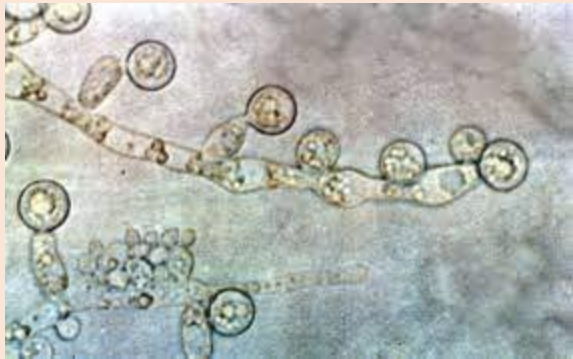
In addition, bacterial metabolic products result in the secretion of neuropeptides (calcitonin gene-related peptide, vasoactive intestinal polypeptide) by the periodontal pocket epithelium, which then promote the vasodilation of local blood vessels and permit an influx of neutrophils which come in response to the chemokines.The immune response that precedes the bacterial infection protects the periodontal pathogen by compromising the host's innate immunity in several ways.

The local inflammatory responses at the site of infection are often linked to CNS disorders such as AD and Parkinson's disease (PD). The role of the peripheral nervous system is still unclear. Recent studies have shown that the risk of developing AD significantly increases following the occurrence of a peripheral infection and that the systemic infection could lead to a faster cognitive decline.It was even reported that peripheral overexpression of IL-1β accelerated the disease process in an animal model of PD.These studies supported the observation that the overexpression of peripheral inflammatory products leads to more neurodegeneration

oral viruses, yeasts, and neurodegeneration

In various gingival and periodontal diseases, high counts of viruses, such as cytomegalovirus and Epstein Bar virus (EBV), have been reported along with the increase in the number of periodontopathogens.This increased count of the virus impairs the local host defence and synergistically aggravates the aggressiveness of pathogenic microflora.In various studies, viral-associated proteins in significantly increased proportions have been reported in amyloid containing plaques. This shows the role of viruses in the pathology of neurodegenerative diseases.

High counts of *Candida albicans* and *C. glabrata* have been reported in elderly patients. Increased numbers of oral yeast cells have been found in the periodontal pocket in the root canal, especially in patients suffering from denture stomatitis. Fungal proteins, polysaccharides, and DNA have been detected in the brain tissue of neurodegenerative diseases, suggesting the role of fungi in the etiopathology of neurodegenerative disorders.




Thank
you