



## The intriguing commonality of NETosis between COVID-19 & Periodontal disease



### ABSTRACT

NETosis, being an alternative form of cell death is the creation of web-like chromatin decondensates by suitably primed neutrophils as a response to stimulus aimed at containing and eliminating the same. In certain situations, it causes more harm than benefit in the form of bystander damage directly or via activation of autoimmune mechanisms. Such pathophysiology finds evidence in both Periodontal disease and COVID-19. Coupled with impaired removal, NETs have been implicated in both these disease forms to promote a state of inflammation and be a source of constant harm to the tissues involved. This potentially forms groundwork to implicate Periodontal disease as predisposing towards adverse COVID-19 related outcomes.

First reported by Brinkman in 2004, Neutrophil Extracellular Trap (NET) production is an alternative form of cell death, differing from the likes of necrosis and apoptosis. It is essentially the creation of extracellular neutrophil traps to contain and eliminate insult. NETs are nuclear chromatin in decondensed form in a web-like configuration [1]. These are associated with a number of antimicrobial factors such as peptides and histones. NETosis, or the process of NET production is accomplished by suitably primed neutrophils and their composition varies according to the insult incurred. NETosis is a catastrophe at the cellular level in that it results in cell death and often causes bystander damage either directly or through autoimmune mechanisms [1].

NETosis has found a plausible role to play in the pathophysiology of periodontal disease with mediators such as interferon alpha which are implicated in the stimulation of NET release being reported at higher levels in Periodontitis patients. Another issue apart from the obvious bystander damage caused by NET formation is their impaired removal as is observed in Periodontal disease [1].

Viral evasion of host defense is well documented, with recent findings also pointing towards this as a stimulus for NETosis. Viral stimulated NETs have been reported to undergo unregulated systemic circulation which elicits the expression of chemokines, immune complexes and cytokines which culminates in inflammation [2].

Studies conducted on bronchoalveolar lavage fluid from patients afflicted with Acute Respiratory Distress Syndrome (ARDS) and those with acute exacerbation of Chronic Obstructive Pulmonary Disease have reported increased NETs [2]. Advanced stages of COVID-19 have exhibited a hyper-inflammatory state or a proverbial 'cytokine storm' along with an ARDS-like condition [2].

This knowledge, with its translational implications would point to the possibility of an increased level of NETs in patients of both COVID-19 and Periodontal disease. This introduces the possibility of patients suffering from Periodontitis at an increased risk of COVID-19 related adverse outcomes, possibly adding, after due clinical validation, to the existing list of conditions predisposing to developing severe forms of the disease.

### Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### References

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