View Abstract

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	ABSTRACT BODY: **Objectives:** Unlike chronic periodontitis (CP), refractory periodontitis (RP) is characterized by progressive loss of clinical attachment despite ongoing periodontal therapy and low levels of microbial biofilm. Neutrophils are first responders during acute infection, but also play a monitoring role at the oral mucosa and are the primary leukocyte subtype in the mouth. The purpose of this study was to assess and differentiate the unique properties of neutrophils in the two patient populations. **Methods:** Patients entering the Centre for Advanced Dental Research and Care (CADRC) were divided into chronic periodontitis or refractory periodontitis groups based on previously established criteria. Non-periodontitis healthy controls were also assessed. A clinical exam along with blood and saliva samples were collected. We developed a multi-colour flow cytometry panel to assess surface cluster of differentiation (CD) markers of oral neutrophils. Surface expression of these markers acts as a surrogate of the neutrophil activation state. **Results:** We found that, despite progressive pocket depths and loss of attachments, patients with RP resembled healthy controls with respect to oral neutrophil load (*p*-value = 0.158) and surface expression of oral neutrophil activation markers (CD66a, *p*-value = 0.302; CD63, *p*-value = 0.926; CD11b, *p*-value = 0.158). In contrast, increased oral inflammation based on oral neutrophil counts (*p*-value < 0.0001) and activation markers (CD66a, *p*-value = 0.029; CD63, *p*-value = 0.001; CD11b, *p*-value < 0.0001) was found in patients with CP, compared to healthy controls. The percentage of sites that exhibited bleeding on probing (BOP) was 8.6 ± 3, 32.1 ± 3.6 and 62 ± 2.0 for health, RP and CP, respectively. **Conclusions:** Radiographic and clinical measures (probing depths, bone loss) shown in patients with RP mimic similar measures derived from patients with severe CP (apart from the severity and rapidity of bone loss in

	the former). However, our findings suggest that the two conditions could be manifested, at least from the point of view of innate immunity, by wholly different pathophysiological mechanisms. At the least, these findings also support the notion that RP and CP should be classified as separate entities, as has been alluded to by the new American Academy of Periodontology (AAP) classification system.
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