Oxidative stress has been associated with immune dysfunction and implicated as a risk factor for periodontitis and atherosclerosis. Diminished systemic antibody neutralization of periodontal pathogens might increase the impact of those pathogens upon systemic acute phase responses. Objective: Determine whether oxidative stress modifies the association between pocket depth (PD) and plaque (Pl) with serum neutralizing IgG antibody levels to oral pathogens (Ab's), and thereby enables a stronger relationship between PD (and selected Ab's) with serum C Reactive Protein (CRP). Methods: Dental exams of subjects (n=6605) in the Atherosclerosis Risk in Communities Study determined full mouth PD and Pl. Serum samples were assayed for CRP with a high sensitivity assay, for serum 8-iso-PGF2a (measure of oxidative stress independent here of smoking) by ELISA, and for Ab's to 17 oral bacteria by 17 different ELISA's. Subjects within highest quartiles of extent PD 5+mm, CRP, or Pl scores ≥ 1 were considered high. The top quartile of 8-iso-PGF2a subjects were designated oxidatively stressed (Ox-S) and remaining subjects Non-Ox-S. Multivariate logistic models employed nesting of variables to determine significant (p<0.05) associations between variables. Results: All significant relationships between Pl or PD with 17 Ab's were direct amongst Non-Ox-S subjects (OR's: 1.2-1.6 and 1.2-2.7, respectively) but were inverse for Ox-S subjects (OR's: 0.48-0.65 and 0.38-0.66, respectively). Suggesting altered Ab responses to oral bacteria in Ox-S subjects. In Non-Ox-S-subjects CRP was not related to PD but inversely related (OR's: 0.59-0.80) to Ab's, while in Ox-S-subjects CRP was directly related to PD (OR: 1.6) and selected Ab's (OR's: 1.3-1.6). Conclusion: Systemic oxidative stress is linked with altered associations between plaque and PD and serum antibodies to oral bacteria and accompanied by a stronger association between extent PD and serum CRP. Grant support: NIDCR R01-DE11551, GCRC RR-00046, and T-32 (DE-007310) and multi-center contracts from Heart Lung and Blood Institute.