

# Comment on: Cani et al. (2007) Metabolic Endotoxemia Initiates Obesity and Insulin Resistance: *Diabetes* 56:1761–1772

Toshiyuki Saito, Hideaki Hayashida, and Reiko Furugen

The recent article by Cani et al. (1) interests us very much. We have reported that obesity and periodontitis were associated for the first time in 1998 (2). Further study revealed that hepatic impairment was more strongly associated with periodontitis than obesity indexes (3). Our results showed that periodontitis increased with elevated serum levels of aspartate aminotransferase, alanine aminotransferase, and cholinesterase and an aspartate aminotransferase-to-alanine aminotransferase ratio of less than one, suggesting that hepatic steatosis is associated with periodontitis. Adjustment for neither BMI nor body fat attenuated these relationships. Tomofuji et al. (4) reported that chronic administration of lipopolysaccharide (LPS) to the periodontal pockets in a rat model of periodontitis increased serum LPS, fatty liver lesion, tumor necrosis factor- $\alpha$ , and 8-hydroxydeoxyguanosine in the liver. We reported that past development of glucose intolerance was significantly associated with deeper periodontal pockets, suggesting that a periodontal gram-negative pathogen, such as *Porphyromonas gingivalis* and *Actinobacillus actinomycescomitans*, is one cause of glucose intolerance (5). Periodontal treatment to remove these bacteria appears to reduce circulating tumor necrosis factor- $\alpha$  levels (6). Many studies have clarified that these bacterial infections are

associated with arteriosclerosis, cardiovascular disease, and stroke.

Although 10–20% of the population has moderate-to-severe periodontitis, 21–80% of adults have some form of periodontal disease. The ulcerated area inside periodontal pockets with these subgingival bacteria is estimated to be as much as 72 cm<sup>2</sup> in patients with severe periodontitis (7). Periodontal gram-negative pathogens could be another source of LPS in addition to intestinal bacteria, at least in the case of severe periodontitis. Periodontitis might lead these people to obesity/diabetes.

## REFERENCES

1. Cani PD, Amar J, Iglesias MA, Poggi M, Knauf C, Bastelica D, Neyrinck AM, Fava F, Tuohy KM, Chabo C, Waget A, Delmée E, Cousin B, Sulpice T, Chamontin B, Ferrières J, Tanti JF, Gibson GR, Casteilla L, Delzenne NM, Alessi MC, Burcelin R: Metabolic endotoxemia initiates obesity and insulin resistance. *Diabetes* 56:1761–1772, 2007
2. Saito T, Shimazaki Y, Sakamoto M: Obesity and periodontitis. *N Engl J Med* 339:482–483, 1998
3. Saito T, Shimazaki Y, Koga T, Tsuzuki M, Ohshima A: Relationship between periodontitis and hepatic condition in Japanese women. *J Int Acad Periodontol* 8:89–95, 2006
4. Tomofuji T, Ekuni D, Yamanaka R, Kusano H, Azuma T, Sanbe T, Tamaki N, Yamamoto T, Watanabe T, Miyauchi M, Takata T: Chronic administration of lipopolysaccharide and proteases induces periodontal inflammation and hepatic steatosis in rats. *J Periodontology* 78:1999–2006, 2007
5. Saito T, Shimazaki Y, Kiyohara Y, Kato I, Kubo M, Iida M, Koga T: The severity of periodontal disease is associated with the development of glucose intolerance in non-diabetics: the Hisayama study. *J Dent Res* 83:485–490, 2004
6. Iwamoto Y, Nishimura F, Nakagawa M, Sugimoto H, Shikata K, Makino H, Fukuda T, Tsuji T, Iwamoto M, Murayama Y: The effect of antimicrobial periodontal treatment on circulating tumor necrosis factor-alpha and glycated hemoglobin level in patients with type 2 diabetes. *J Periodontol* 72:774–778, 2001
7. Page RC, Offenbacher S, Schroeder HE, Seymour GJ, Kornman KS: Advances in the pathogenesis of periodontitis: summary of developments, clinical implications and future directions. *Periodontol* 2000 14:216–248, 1997

From the Department of Oral Health, Unit of Social Medicine, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan.

Address correspondence and reprint requests to Toshiyuki Saito, Nagasaki University, Oral Health, Unit of Social Medicine, 1-7-1 Sakamoto, Nagasaki 852-8588, Japan. E-mail: syto@nagasaki-u.ac.jp.

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