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1. Full Title: The role of diet in periodontal disease and host inflammatory response
   Abbreviated Title (length 26): Diet & periodontal disease

2. Writing Group (list individual with lead responsibility first):
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3. Timeline:
   Begin preliminary analyses in September 1998. Begin final analyses after conclusion of

4. Rationale:
   Of all dietary fatty acids, polyunsaturated fatty acids (PUFAs) of the n-3 series, primarily
   eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), have been most
   extensively investigated because of their presumed anti-inflammatory properties. EPA
   and DHA, which are abundant in fish, have been found to suppress the production of
   arachidonic-acid derived eicosanoids which modulate the production of pro-inflammatory
   cytokines (Blok et al., 1997). However, few studies have evaluated the possible effects of
   dietary n-3 PUFAs on periodontal conditions. Campan et al. (1997) recently published
   findings from a small pilot study suggesting that fish oil supplements may reduce
   gingival inflammation, but a larger study is needed to establish efficacy. Most
   anti-inflammatory effects of n-3 PUFAs have been found using dietary supplements of
   fish oil that provide much higher doses of these fatty acids than normally consumed in
   the diet, but infrequent fish consumption may also provide benefit. For example, in ARIC
   the prevalence of chronic bronchitis, emphysema, and spirometrically-detected chronic
   obstructive pulmonary disease was inversely associated with dietary intake of fish and n3
fatty acids in a dose-dependent manner among smokers, even though the median fish consumption was only 1.4 servings per week (Shahar et al., 1994).

In addition to effects of n-3 fatty acids, total dietary fat intake and intake of antioxidants may also modify the host periodontal response. Mouse models of infection suggest that the PGE$_2$ response to periodontal pathogens is modified by total dietary fat levels (Gibbs et al., 1998). There is a clearly defined role for free radicals or reactive oxygen species in periodontitis, but little research has been performed in this area. Essential nutrients such as vitamins C and E may protect against oxidant-mediated inflammation and tissue damage by virtue of their ability to scavenge free radicals. Previous research suggests some role for vitamin E supplementation in the maintenance of periodontal health; ascorbic acid may influence early stages of gingivitis, particularly crevicular bleeding.

5. Main Hypothesis:
Greater habitual dietary intake of fish or n-3 fatty acids of marine origin, as determined by a food frequency questionnaire, is associated with decreased prevalence, extent, and severity of periodontal conditions, reduced levels of prostaglandin E2 and thromboxane B2 measured locally in samples of gingival crevicular fluid, and reduced levels of C-reactive protein measured in serum.

Greater habitual dietary intake of fat as a percent of calories is associated with increased levels of prostaglandin E2 in gingival crevicular fluid.

Greater intake of antioxidants (e.g. vitamin E, vitamin C) is associated with decreased prevalence, extent, and severity of periodontal conditions.

6. Data (variables, time window, source, inclusions/exclusions):
Data will include food frequency data collected at visit 1 (all participants), visit 2 (subset of participants), and visit 3 (all participants), fish oil supplementation measured at visit 3, dietary supplement data, periodontal conditions, inflammatory mediators in gingival crevicular fluid, and serum C-reactive protein measured on dental examinees at visit 4. We will evaluate the following as possible confounders: current smoking status and cumulative smoking exposure (cigarette years), diabetes, alcohol consumption, oral hygiene behavior, use of steroids, use of aspirin and non-steroidal anti-inflammatory drugs, hormone replacement therapy, and sociodemographic characteristics (gender, age, ethnicity, education), other nutrients (e.g. calcium).

Nutrient intakes will be adjusted for total energy intake in some analyses to minimize the extraneous variation in nutrient intake and to reduce confounding, if present, by body size, physical activity, and metabolic efficiency. Population-based surveys indicate that dentate individuals with fewer teeth consume more calories, fewer vegetables, less fiber, and more cholesterol and saturated fat compared to individuals with most of their natural teeth (Joshipura et al., 1996). Because tooth loss due to periodontitis may lead to changes in dietary patterns, we will stratify our analysis on number of teeth to evaluate the potential confounding effects on the association between diet and periodontal disease or...
markers of inflammation.

REFERENCES:
5) Shahar E, Folsom AR, Melnick SL, Tockman MS, Comstock GW, Gennaro V, Higgins MW, Sorlie PD, Ko W-J, Szklo M. Dietary n-3 polyunsaturated fatty acids and smoking-related chronic obstructive pulmonary disease.