

SMOKELESS TOBACCO AND PERIODONTAL DISEASE

To the Editor:

Fisher *et al.* (2005) claim to have published the first report of an association between smokeless tobacco (SLT) use and periodontal disease, based on odds ratios of about 2 that are only marginally statistically significant. However, their analysis is deficient. They did not control the reported association for education and socio-economic status (SES), two of the strongest correlates of periodontal disease that are also strongly and inversely correlated with SLT use. It is a certainty that control for education and SES will reduce the odds ratios and render them non-significant.

For over two decades, it has been standard practice to control for education and SES in studies of periodontal disease (Ismail *et al.*, 1983). In fact, Fisher *et al.* included at least seven references that address this matter, the most relevant of which was derived from the same dataset that they used (Tomar and Asma, 2000).

Fisher *et al.* did not entirely ignore education. They reported that study subjects lacking a high school education were about three to four times more likely to have periodontal disease than were graduates, making education the third most important (after age and diabetes) correlate of periodontal disease in their own study. Thus, it is surprising that education was omitted from the multiple logistic regression analysis that they performed.

The Fisher *et al.* paper appeared as a Rapid Communication, a category the *Journal* designates for "definitive reports of findings of unusual significance" (*Journal of Dental Research* Instructions to Authors). Until the deficiencies in their analysis are corrected, their report is not definitive or significant.

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- Journal of Dental Research Instructions to Authors, available at <http://jdr.iadrjournals.org/misc/ifora.pdf>
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The authors reply:

We appreciate Rodu and Cole's interest in our study and would like to address their concerns. Socio-economic status (SES) is a complex construct involving education, income, wealth, occupation, and a variety of other cultural factors. While variables for education and income are included in the NHANES III dataset, many of the other elements comprising SES are not available. We did not include the specific variables for education and income in our multivariable models, because of our concern for data sparseness in expanding the number of variables beyond those we presented in our paper. The problem we worked to avoid was the introduction of bias in our estimates of the association between smokeless tobacco use and severe active periodontal disease, while adequately controlling for confounding in our models to the degree that the data would allow. Unlike the Tomar and Asma report (2000) to which Rodu and Cole refer in their letter, our inclusion of smokeless tobacco use, analysis of interproximal periodontitis, and inclusion of analyses restricted to 'never-smokers' added extra limitations in sample size that Tomar and Asma did not experience.

However, we did not completely omit capturing important dimensions of SES in our multivariable models. Our considerations for selection of variables to control for in testing the association between smokeless tobacco use and severe active periodontal disease led us to include the variable 'having a dental visit in the past year', which is directly related to socio-economic status and closely associated with educational levels (Burt and Eklund, 2005), captures access to dental treatment, and influences periodontal status—established demographic factors that are also closely related to SES and periodontal status in the US (age, gender, and minority status), as well as established biologic risk factors for periodontal disease (cigarette smoking and diabetes).

Rodu and Cole mention that "it has been standard practice to control for education and SES in studies of periodontal disease". While we agree that it is important to adjust for SES in multivariable analyses where the data are available and sufficient to allow for appropriate adjustment, we believe that it may be debatable that it has been "standard practice to control for education and SES". A recent and very relevant critical review of the analytical epidemiology of periodontitis for the period 1994-2004 (Borrell and Papanau, 2005) includes a useful summary (although not intended to be exhaustive) of reports of risk factors associated with the onset and progression of periodontitis. Education or income was not reported as being considered in 29 of the 40 studies of associations with periodontal disease presented in the two tables in that paper. Of the remaining 11 studies, 6 studies considered education and income, 2 studies considered education only, and 3 studies considered income only.

We would also like to clarify the statement by Rodu and

Cole that we "claim to have published the first report of an association between smokeless tobacco use and periodontal disease". We actually reported:

"To our knowledge, this is the first report of the association between smokeless tobacco use and *severe active* [emphasis added] periodontal disease. Similar results were found for the association between smokeless tobacco use and interproximal severe active periodontal disease. When we removed the effect of smoking by restricting the analysis to never-smokers, the strength of the association between current smokeless tobacco use and both severe active periodontal disease and interproximal severe active periodontal disease was similar to that found for all adults, after smoking was taken into account in the multivariable analyses."

We believe that our study design and analytical approach are substantially supported by the current knowledge base and scientific evidence.

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DIFFUSION COEFFICIENT OF FLUORIDE IN DENTAL PLAQUE

To the Editor:

A recent paper by Watson *et al.* (*J Dent Res* 84:451-455, 2005) reported *ex vivo* measurements of fluoride ion penetration into dental plaque formed on removable implants worn by human volunteers. These data showed that brief exposures—30 sec to 2 min—of plaque biofilms to 1000 ppm fluoride were insufficient to deliver the full concentration of fluoride throughout the depth of the biofilm. Here, I report the extraction of a numerical estimate of the effective diffusivity of fluoride in dental plaque from these valuable data. The reason to bother determining the diffusion coefficient is that this is an intrinsic parameter that can be compared between studies and can form the basis of predictive calculations.

Application of the diffusion equation to the data of Watson *et al.* yields a value of the effective diffusivity of fluoride ion in plaque of $5.5 \times 10^{-6} \text{ cm}^2 \text{ s}^{-1}$. This value is 43% of the diffusion coefficient of the ion in pure water at the measurement temperature of 20°C. This value of the fluoride diffusion coefficient in dental plaque is in reasonable agreement with the value reported by McNee *et al.* (*Arch Oral Biol* 25:819-823, 1980), which was 23% of the value of the fluoride ion diffusion coefficient in water.

Together, these studies suggest that the effective diffusion coefficient of fluoride in dental plaque is approximately one-third its value in water.

With this result, the transient penetration of fluoride to the tooth surface beneath biofilms of various thicknesses was solved, illustrating the highly non-linear nature of this transport process. In a 100-micron-thick plaque, a 20-second exposure will deliver 91% of the applied fluoride concentration to the tooth surface. In a 500-micron-thick plaque, the same application of 20 sec achieves only 0.14% of the applied fluoride concentration at the base of the biofilm. What these calculations illustrate is that the extent of fluoride penetration depends strongly on the thickness of the plaque. With a five-fold difference in the plaque thickness, fluoride penetration goes from being essentially complete to being insignificant.

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The authors reply:

We thank Dr. Stewart for taking the time and trouble to calculate diffusivity data from the information in our recent paper.

Similar calculations were performed and are published in Dr. Watson's PhD Thesis (University of Leeds, UK, January, 2005). Results were similar at $1.5 \times 10^{-6} \text{ cm}^2 \text{ s}^{-1}$; differences may be due to the use of a slightly different diffusion constant for fluoride (Chu *et al.*, 1989).

We were cautious in exploring diffusivity in this way for the reasons below, but perhaps we have been a little too strict and denied ourselves some element of prediction, which Dr. Stewart points out.

The predictions fit quite well for short exposure periods, but there is a large discrepancy between predicted and measured values in biofilms exposed to 1000 ppm fluoride ion for 30 min.

The non-linear nature of the transport process is due, we surmise, to interaction with the biomass. Such interaction will depend upon the nature of the diffusing species and the nature of the biomass itself. Both the nature of the biomass and its architecture may be related to the time period over which the biofilms form, as well as to biofilm thickness. We have not yet carried out detailed studies on the chemical nature of the biomass, and how this relates to architecture, thickness, and the period of plaque development. We avoid the use of the term "biofilm age", since this is a natural biofilm formed *in vivo*, and we would require data concerning turnover rate.

In this respect, the precise location of penetrating species with regard to biomass is important. With this in mind, we refer you to our recent publication in the *Biofilm Club Proceedings* for this year (Robinson and Watson, 2005). This indicates that some species may penetrate the biomass quite well, while others, more polar in nature, seem mainly to attach to the biomass surfaces which line relatively open channels.

With regard to biofilm thickness, Dr. Stewart's point is well made, that plaque thickness is an extremely important determinant of fluoride penetration. However, while fluoride may penetrate thin biofilms more effectively, one of the aims behind the study was to simulate plaque biofilms at caries-prone sites, *i.e.*, between the teeth and in molar fissures. Because they are difficult to remove, plaque biofilms at these sites tend to be relatively thick.

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