Endothelial Function in Patients with HIV Infection

To the Editor—Although I agree with Solages et al. [1] that HIV-infected individuals have impaired endothelial function, our studies [2, 3] were not accurately described in their discussion. I disagree that their study “did not substantiate” [1, p. 1331] our observations. Their article actually confirmed our findings.

In contrast to Solages and colleagues’ attribution, we did not show that lipids or insulin resistance predicted brachial artery flow-mediated vasodilation (FMD) [2]. We showed that, among HIV-infected individuals, receipt of a protease inhibitor, blood pressure, heart rate, and brachial artery diameter predicted FMD ($R^2 = 67.1\%$). In a separate model restricted to subjects receiving protease inhibitors, we again found that artery diameter and blood pressure predicted FMD, but the best models also included lipoprotein parameters ($R^2 = 70.6\%$). We then showed that most (but not all) of the protease-inhibitor effect on FMD was related to high-density lipoprotein (HDL) cholesterol, triglyceride-rich lipoproteins, and glucose [2], which suggests some degree of mediation of the protease-inhibitor effect by lipoproteins and possibly by insulin resistance.

On the basis of our findings, impaired FMD would not be expected in a cohort with normal lipids and without lipodystrophy.

Subjects in our study who received protease inhibitors had a mean total cholesterol level of 219.8 mg/dl and a mean triglyceride level of 391.1 mg/dl [2]. Respectively, these values are $\sim 22\%$ and $\sim 147\%$ higher than those in the article by Solages et al. [1], in which essentially normal lipid values were reported and an unexpectedly low (6%) incidence of lipodystrophy was described. Without dyslipidemia or lipodystrophy, impaired FMD would not have been expected in patients in their study who received protease inhibitors, thereby confirming our findings. Indeed, Solages and colleagues’ finding that $\alpha$-HDL triglycerides predicted FMD seems to support a relationship between lipoproteins and endothelial function [2].

Referring to another article of ours [3], Solages et al. [1] stated that use of pravastatin “did not lead to a significant improvement in FMD” [1, p. 1331]. Although this is correct from a statistical standpoint (the $P$ value was .08), our finding of improved endothelial function recently was confirmed in a larger study in which pravastatin treatment led to a statistically significant increase in FMD ($P = .03$) [4]. Of note, changes in FMD in our study were predicted by lipoprotein and glucose levels [3].

Finally, I am concerned about the predictive model described on page 1328 of Solages et al. [1], which only accounts for 26% of the variability in FMD in patients with HIV infection. This is very low and suggests that unaccounted variables, such as blood pressure, heart rate, or brachial artery diameter (the denominator of the equation for calculating FMD), or measurement imprecision may be at play. The association with HIV load was of borderline statistical significance; however, linear associations with log parameters that have a finite lower bound (<50 copies/mL) are difficult to establish and interpret.

The perils of cross-study comparisons and the limitations of all cross-sectional studies, including ours, are well known. Prospective studies [5, 6] appear to suggest that viral control is an important short- and long-term determinant of endothelial function, whereas classical risk factors are more important long-term determinants of atherosclerotic burden.

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References

Seasonality of Respiratory Syncytial Virus Infection

To the Editor—Dr. Gavin Donaldson recently compared climate change and the pattern of epidemics of respiratory syncytial virus (RSV) infection in England and Wales for 1981–2004 [1]. His conclusion—that the warming of the temperature may be shortening the RSV infection season and, thus, decreasing the disease burden—is interesting, but it should be taken within the context of the global dynamics of RSV transmission. An equivalent analysis performed on the total annual number of hospitalizations for RSV infection, rather than on the timing of the end of the RSV infection season, would better test this hypothesis.

In contrast with Donaldson [1], we do not believe that within-school cross-infection has been ruled out. The combination of the short-lived immunity to RSV infection and the duration of the school year may explain the seasonal signal of RSV infection in many countries. Three studies provide evidence that younger children acquire infection from school-aged children within the household [2–4], indicating a significant contribution of within-school transmission to the overall transmission of RSV. A range of dynamic behaviors can result from the interplay between the time-scales of the acquisition and loss of immunity in a population and a seasonal signal for transmission [5, 6]. Therefore, temperature may be a part of but not the whole of the explanation for the seasonal dynamics in the United Kingdom, and it cannot be extended to a global explanation. In Finland, for example, RSV-related hospital admissions follow a 2-year cycle, beginning in the first winter, with a minor peak in the following spring (usually May) and a major peak in the second winter (usually December). The epidemiology of RSV infection in Finland has been described elsewhere [7] and has been described in comparison with that of England and Wales [6]. Similar cycling of early and late outbreaks has been observed elsewhere; recent data indicating similar outbreak patterns have been published from Germany, Switzerland, and Chile [8–10].

Because the number of diagnoses of RSV infection in the spring is increasing or decreasing in alternating years in several countries with different weather conditions, the end of the RSV infection season cannot be associated with the spring temperature. In addition, circulation of RSV is detected during most of the summers before major peaks but not after them. The decline of the infection rate after the minor peaks could be explained by several factors, including seasonal climate factors, such as higher temperature and more UV light. The most important factor is probably less indoor crowding of the transmitter population because of the summer vacation of school children and the reduced numbers of younger children in day care centers.

The vast majority of the children hospitalized with RSV infection are infants and toddlers, who catch their infections from older siblings or in day care centers. Assumming that the average virulence of the circulating virus strains remains the same, the size and density of the most susceptible child population are the main determinants of the RSV infection epidemic, or what we recognize as one. Regarding the length of the RSV infection season, nativity, urbanization, and travel are likely to be more important changes in the environment of the virus than the climate warming.

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References


