Please note: Dr. RuDusky has reported that he has no relationships relevant to the contents of this paper to disclose.

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REPLY: Bad Air Revisited

We thank Dr. RuDusky for taking an interest in our work. Our study was intended to address the role of a respiratory filter intervention during controlled pollution exposure in patients with heart failure (HF). In 2007, HF was associated with 39.4% of all hospitalizations due to cardiovascular diseases in Brazil, and it may be responsible for 6.3% of all causes of deaths in South America (1). Regarding hypertension, it is a leading risk factor for cardiovascular disease and a significant cause of morbidity and mortality as long as it remains uncontrolled (2). A large body of evidence indicates that patients with hypertension are characterized by endothelial dysfunction (3). We excluded volunteers with uncontrolled hypertension because it could play an important role as a confounder and selection bias, especially in a small sample of patients with HF. Blood pressure (BP) was recorded during the initial pre-study evaluation and history and also at the beginning of each session. Uncontrolled hypertension was defined as an average systolic BP ≥140 mm Hg or an average diastolic BP ≥90 mm Hg, among those with diagnosed hypertension and who are currently using BP-lowering medication. As outlined in the article, patients with HF were receiving optimal medical therapy, and 2 volunteers from the control group were receiving beta-blocker therapy.

Although our neutral findings of heart rate variability (HRV) could be explained by the optimal beta-blocker therapy in the HF group, it is noteworthy that diesel exhaust exposure (DE) also did not affect HRV in the control group. This suggests that the use of cardiovascular therapies might not be the primary explanation for the absence of an effect of air pollution on autonomic function. There are several methodological differences between the recent study by Lee et al. (4) and ours that can explain these contradictory findings. Lee et al. (4) assessed lagged nocturnal effects of fine particulate matter (PM2.5), whereas we conducted an experimental short-term study with controlled DE exposure that provided a precisely defined PM2.5 concentration in a regulated environment. We cannot state whether longer-term air pollution exposure could affect the HRV in optimally treated HF patients.

The epidemiologic association between air pollution exposure and exacerbation of cardiovascular disease is well established, yet the mechanisms underlying the increased risk of cardiovascular events are incompletely understood. Increasing concern relating to the health effects of air pollution has led many individuals to use facemasks to reduce personal exposure (5). There is, therefore, a need to consider approaches that can reduce effects of ambient air pollution exposure on both a societal and a personal level. Reduction of traffic emissions involves economic and political difficulties. The pioneering demonstration that a simple filter intervention can reduce the adverse effects of pollution in patients with HF could provide an inexpensive strategy for preventing HF decompensation. Given the worldwide prevalence of exposure to traffic-related air pollution, we speculate that patients with uncontrolled hypertension may benefit from the filter intervention as well.

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Antibody-Based Protection of von Willebrand Factor Degradation

Recently, Bartoli et al. (1) reported on the use of doxycycline to reduce ADAMTS-13-mediated von Willebrand factor degradation during supraphysiological shear stress. We have read their article with interest, noticing reference in their discussion to one of our recent publications that appeared in *Thrombosis and Haemostasis* (2). However, we would like to correct some significant misinterpretations of our data as cited by the investigators. Indeed, our antibody is referred to as a monoclonal antihuman ADAMTS-13 antibody. This is incorrect. In fact, we have reported on the discovery and characterization of a monoclonal antihuman von Willebrand factor antibody, designated Mab508. This is not only clearly written in the abstract, but our article also describes in detail the epitope within von Willebrand factor that is recognized by this antibody. Describing our antibody as being antihuman ADAMTS-13 is therefore an important oversight.

Second, the investigators suggest that our antibody blocks ADAMTS-13 activity by 83% and that such widespread inhibition may inadvertently provoke a hypercoagulable, thrombotic thrombocytopenic purpura-like state and thrombosis. The investigators seem to confuse 2 types of experiments reported in our article. First, we clearly show that the anti-von Willebrand factor antibody blocks binding and degradation of von Willebrand factor by ADAMTS-13 by a maximum of 50%. The figure 83% actually refers to the inhibition of the high-molecular weight multimers, not of von Willebrand factor as a whole. This is an essential difference, as it actually prevents (rather than induces) Mab508 from provoking the occurrence of ultralarge von Willebrand factor multimers that could potentially induce thrombotic thrombocytopenic purpura-like symptoms. This specificity is an important strength of our antibody, particularly when compared with the nonspecific inhibition of ADAMTS-13 and other proteases that is achieved when using doxycycline.

We hope that this letter clarifies the scope of our article (identification of an anti-Von Willebrand factor antibody that partially interferes with ADAMTS-13-mediated degradation).

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Please note: Drs. Lenting, Denis, and Susen are inventors on a patent related to Mab508 that is owned by Inserm-Transfert SA. Dr. van Belle has reported that he has no relationships relevant to the contents of this paper to disclose.

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REPLY: Antibody-Based Protection of von Willebrand Factor Degradation

Thank you for the opportunity to respond to Dr. Lenting and colleagues. In our paper that examined doxycycline to reduce ADAMTS-13-mediated von Willebrand factor (vWF) degradation during left ventricular assist device (LVAD)-like shear stress (1), we referenced a recent paper by Rauch et al. (2).

In their study, Rauch et al. (2) used a monoclonal antibody (mAb508) to block ADAMTS-13/vWF interactions in order to preserve high-molecular-weight vWF multimers. We acknowledge that “anti-ADAMTS-13” antibody was incorrect terminology and that their antibody is in fact an anti-vWF antibody that blocks the ADAMTS-13/vWF interaction. We congratulate Dr. Lenting and colleagues for this important mechanistic work with potential therapeutic implications. However, we disagree with statements made in their recent Letter to the Editor. Other than correcting the terminology, our concern that mAb508 therapy may lead to hypercoagulability and thrombosis remains unchanged.