Endothelial Function and Chronic Exposure to Air Pollution in Normal Male Subjects

Marie Briet, Cédric Collin, Stéphane Laurent, Alice Tan, Michel Azizi, Mohsen Agharazii, Xavier Jeunemaitre, François Alhenc-Gelas, Pierre Boutouyrie

Abstract—Exposure to urban air pollution, ultrafine particles or gases, is associated with acute cardiovascular mortality and morbidity. We investigated the effect of ambient air pollution on endothelial function in 40 healthy white male nonsmokers spontaneously breathing ambient air in Paris, France. Air pollutant levels (nitrogen, sulfur and carbon oxides, and particulate matter) were averaged during the 5 days preceding arterial measurements. Brachial artery endothelium-dependent flow-mediated dilatation and reactive hyperemia induced by hand ischemia and endothelium-independent glyceryl trinitrate dilatation were measured using a radiofrequency-based echo-tracking device at 2-week intervals. Flow-mediated dilatation was independently and negatively correlated with the average levels of sulfur dioxide (P<0.001) and nitrogen monoxide (P<0.01). Sulfur dioxide levels explained 19% of the variance of flow-mediated dilatation. An increase in gaseous pollutants, 2 weeks apart, was significantly associated with a decreased in flow-mediated dilatation. No association was found between air pollutants and glyceryl trinitrate–induced vasodilatation. Reactive hyperemia was significantly and positively correlated with particulate matter with aerodynamic diameters <10 μm and <2.5 μm (P<0.0001 and P<0.0001, respectively) and nitrogen dioxide (P<0.01). An increase in particulate matter, 2 weeks apart, was significantly correlated with an increase in reactive hyperemia. Endothelial function was impaired by ordinary levels of pollution in healthy young males, in an urban area, and may be reduced by 50% between the least and the most polluted day. Gaseous pollutants affect large artery endothelial function, whereas particulate matter exaggerates the dilatory response of small arteries to ischemia. (Hypertension. 2007;50:970-976.)

Key Words: brachial arteries ■ ultrasonography ■ pathology ■ mechanical stresses ■ air pollution ■ endothelium

Air pollution is a worldwide public health problem. Numerous short- and long-term epidemiological analyses in European and North American cities have clearly demonstrated an association between air pollution and cardiovascular morbidity and mortality. The American Heart Association recently pointed out the necessity to increase the research effort on the effect of air pollution on cardiovascular disease. Air pollution has been involved in arrhythmia, heart failure, acute myocardial infarction, cerebrovascular disease, and thrombocytic disease. Recently, particles levels have been correlated with an increase in cardiovascular events in healthy women. This study suggests that pollution toxicity interests not only patients with preexisting cardiovascular disease but also healthy subjects.

Most epidemiological studies focused on solid pollutants, ie, particulate matter ([PM] PM10 and PM2.5 with aerodynamic diameters <10 μm and <2.5 μm, respectively) but less attention was paid to gaseous pollutants, including carbon monoxide (CO), monoxide and dioxide of nitrogen (NO and NO2, respectively), and sulfur dioxide (SO2), despite the fact that gaseous pollutants are also involved in cardiovascular toxicity.

Endothelial dysfunction is an early feature of the atherogenic process and is a predictor of cardiovascular events and death in patients with hypertension, coronary heart disease, heart failure, and in a population-based cohort. The effect of air pollution on endothelial function is equivocal. Healthy subjects exposed to a high level of pollutants, either diluted diesel exhaust or concentrated ambient fine particles plus ozone, were accompanied by endothelial dysfunction or arterial vasoconstriction without endothelial dysfunction, respectively. In patients with diabetes, air pollutants at ordinary urban levels were correlated with an impairment of vascular reactivity and endothelial function.

We, thus, investigated the impact of various air pollutants at ordinary urban levels on endothelial function in healthy subjects, nonsmokers who were devoid of cardiovascular risk.
factors. The aim of the present study was to quantify the impact of gaseous and PM pollutants both on a large conducting artery, the brachial artery, through the investigation of flow-mediated dilation (FMD), and on small arteries through the investigation of reactive hyperemia in response to the release of hand ischemia.

Methods

Subjects
The present study is an ancillary investigation of a previously published study designed to evaluate the arterial effects of partial genetic deficiency in tissue kallikrein activity on endothelial function. In the main study, we screened 206 white male subjects aged 18 to 35 years for the kallikrein R53H genotype and the following inclusion criteria: strictly nonsmoker and not exposed to passive smoking, noncannabinol users (all of the subjects tested negative for urinary cotinine and cannabino levels), strictly normotensive, normal clinical examination, normal plasma creatinine and serum cholesterol concentrations (<5.2 mmol/L), and no proteinuria. Ten heterozygous subjects (R53H) and the first 30 consecutive homozygous subjects (R53R) were included. Subjects were studied twice at 2-week intervals, in a crossover design, after being randomly assigned to 1 of 2 experimental diets for 7 days: either a low-sodium and high-potassium diet or a high-sodium and low-potassium diet (Na+/K+ diet). All 40 of the subjects completed the ancillary study after giving written informed consent. The protocol to recruit study participants and all of the procedures were reviewed and approved by an institutional review committee (Paris-Cochin, France) and adhered to the principles of the Declaration of Helsinki.

Noninvasive Measurement of Flow-Mediated, Endothelium-Dependent Vasodilatation
Endothelium-dependent, flow-mediated dilatation of the brachial artery was studied in response to 5-minute hand ischemia and was compared with the endothelium-independent response to sublingual glyceryl trinitrate (GTN). The complete method has been described previously. Briefly, subjects were instructed to lie down in a temperature-controlled room (21°C to 23°C) with their right arm secured comfortably on a support. Measurements were performed between 9:00 and 11:00 AM. The diameter and wall thickness of the brachial artery and blood velocity profiles were continuously measured with a high-resolution radiofrequency-based echo-tracking system (Wall Track System, Esaote Pie-Medical) using a 7.5-MHz ultrasound probe. Diameter and blood velocity were measured at baseline (after 15 minutes of rest in supine position), during 5 minutes of hand ischemia, during 120 seconds of reactive hand hyperemia (produced by releasing a pneumatic wrist cuff inflated to 50 mm Hg above the systolic blood pressure for 5 minutes), and 3 minutes after administration of 150 μg of sublingual GTN (Natispray, 0.15 mg/dose. Procter&Gamble Pharmaceuticals, France). Postischemic flow-mediated, endothelium-dependent vasodilatation was determined as the maximal increase in brachial artery diameter during reactive hyperemia, calculated as the moving average of 3 consecutive diameter measurements. Endothelium-dependent vasodilatation was determined as the maximal increase in brachial artery diameter after GTN administration. We used hemiperc mean flow (maximum mean central velocity after ischemia release) as an index of reactive hyperemia, ie, the ability of peripheral small arteries to dilate after hand ischemia. The interobserver variations in the baseline diameter and percentage of postocclusion vasodilatation were 0.7% and 19.0%, respectively.

Air Pollution
Air pollution data were extracted from the AIRPARIF (http://www.airparif.asso.fr), a monitoring network of air pollution in the Paris conurbation. Measurements were made according to standard techniques and quality control.

We chose the measurement station closest to HEGP Hospital, ie, Auteuil station, which is 1000 m from HEGP Hospital. This automatic station gives hourly values of major air pollutants (NO, NO2, SO2, CO, PM10, and PM2.5). Preliminary analysis using the modelization facilities of AirParif (St v.4 Kisters France SAS) showed that HEGP Hospital was exposed to nearly identical levels of pollution compared with Auteuil station. We extracted the values of pollutants on the day of arterial examination (D0) and during the 5 days preceding it (5-D). We used the 24-hour average value of each pollutant, the morning average for D0, and the peak value of D0 in statistical analysis.

Statistical Analysis
Statistics were performed using NCSS 2004 software (Gerry Hintze). Data are expressed as mean ± SD. Relations between air pollutants and endothelial function were studied using multiple robust regression analysis, using each visit as an independent observation. We also built an air pollution score by adding the rank of each pollutant (SO2, NO, and CO) on a definite day (normalized between 0 and 100). Systematic adjustments were made on the R53R/R53H genotype, diet, subject factor, visit, and air temperature (24-hour average). We further studied the influence of changes in air pollutant concentration on changes in endothelial function between the 2 periods. Because of multiple testing, we only interpreted P < 0.01 as significant (Bonferroni correction).

Results

Subjects
Forty healthy men were studied. Arterial blood pressure and vascular characteristics are presented in Table 1.

Air Pollution
The observed air pollution during the study period was close to the average air pollution in Paris for the 2000–2006 period. Indeed, the mean values of 5-D air pollutants were at the 45th, 50th, or 55th percentiles of the 2000–2006 period. Changes in diameter after hand ischemia is negatively correlated with mean values of SO2 at D0 (P < 0.001; Table 2 and Figure 1) and NO (P < 0.01; Table 2). FMD was reduced by 50% between the least and the most polluted day, whereas endothelium-independent dilatation was not significantly modified (Figure 2).

Correlations Between Air Pollutants and Endothelial Function
After adjustment for Na+/K+ diet, R53R/R53H genotype, visit, and subject factor, independent negative relationships were observed between flow-mediated dilatation and 5-D mean values of SO2 (P < 0.001; Table 2 and Figure 1) and NO (P < 0.01; Table 2). FMD was reduced by 50% between the least and the most polluted day, whereas endothelium-independent dilatation was not significantly modified (Figure 2). Pollution score, taking into account levels of NO, CO, and SO2, was negatively correlated with flow-mediated dilatation (P < 0.001; Table 2). These correlations remained significant after adjustment for baseline diameter and average day air temperature. Flow-mediated dilatation was independently and negatively correlated with mean values of SO2 at D0 (P < 0.001). Correlations with D0 gaseous pollutants were in general accordance with 5-D correlations, but with lower significance, except for SO2, which explained 23% of the variance of flow-mediated dilatation (data not shown). No correlation was found between flow-mediated dilatation and NO2, PM10, and PM2.5 (Table 2). Changes in diameter after...
GTN were not correlated with air pollutants levels (data not shown).

**Changes in Air Pollutants and Changes in Endothelial Function**

Changes toward higher levels of pollution led to lower levels of endothelial function. In univariate analysis, changes in amplitude of flow-mediated dilatation were highly dependent on changes in SO2 ($r=0.43; P<0.01$), more weakly on NO ($r=0.39; P=0.015$) and CO ($r=0.39; P=0.015$), but not on changes in NO2, PM$_{2.5}$, or PM$_{10}$. Because changes in endothelial function between visits 1 and 2 were, by definition, strongly dependent on the initial value of endothelial function ($r^2=0.51; P<0.0001$), we further adjusted endothelial function changes to baseline values. In multivariate analysis, changes in SO2 and pollution score explained 10% and 13% of the variance of changes in the amplitude of flow-mediated dilatation, respectively (Table 2).

**Correlations Between Air Pollutants and Small Artery Reactive Hyperemia**

As described previously, the R53H genotype was significantly associated with higher blood velocity.$^{26}$ After adjustment for diet, R53R/R53H genotype, visit, air temperature,

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean ± SD</th>
<th>Minimum–Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>61±5</td>
<td>52–69</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>115±9</td>
<td>95–139</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>61±8</td>
<td>41–81</td>
</tr>
</tbody>
</table>

**Table 2. Independent Influence of Air Pollutants on Endothelial Function in Healthy Subjects**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>$R^2$ Increment</th>
<th>$\beta$-Coefficient</th>
<th>Lower CI</th>
<th>Upper CI</th>
<th>$P$</th>
<th>$R^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flow-mediated brachial artery dilatation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-D gaseous pollutants (% for 1 SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SO$_2$</td>
<td>19</td>
<td>-0.73</td>
<td>-1.08</td>
<td>-0.38</td>
<td>&lt;0.001</td>
<td>0.21</td>
</tr>
<tr>
<td>NO</td>
<td>10</td>
<td>-0.83</td>
<td>-1.42</td>
<td>-0.24</td>
<td>&lt;0.01</td>
<td>0.11</td>
</tr>
<tr>
<td>CO</td>
<td>8</td>
<td>-0.68</td>
<td>-1.22</td>
<td>-0.15</td>
<td>&lt;0.05</td>
<td>0.11</td>
</tr>
<tr>
<td>Pollution score</td>
<td>14</td>
<td>-2.28</td>
<td>-3.57</td>
<td>-0.99</td>
<td>&lt;0.001</td>
<td>0.16</td>
</tr>
<tr>
<td>NO$_2$</td>
<td>3</td>
<td>0.64</td>
<td>-0.26</td>
<td>1.55</td>
<td>NS</td>
<td>0.06</td>
</tr>
<tr>
<td>5-D PM (% for 1 SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{15}$</td>
<td>1</td>
<td>-0.32</td>
<td>-1.10</td>
<td>0.46</td>
<td>NS</td>
<td>0.04</td>
</tr>
<tr>
<td>PM$_{10}$</td>
<td>0</td>
<td>0.07</td>
<td>-0.62</td>
<td>0.76</td>
<td>NS</td>
<td>0.03</td>
</tr>
<tr>
<td>Changes in amplitude of flow-mediated dilatation between visits</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SO$_2$</td>
<td>10</td>
<td>-7.10$^{-2}$</td>
<td>-11.10$^{-2}$</td>
<td>-3.10$^{-2}$</td>
<td>0.002</td>
<td>0.69</td>
</tr>
<tr>
<td>Changes in pollution score</td>
<td>13</td>
<td>-3.10$^{-2}$</td>
<td>-4.10$^{-2}$</td>
<td>-2.10$^{-2}$</td>
<td>&lt;0.0001</td>
<td>0.74</td>
</tr>
</tbody>
</table>

All of the data were adjusted for diet, R53R/R53H genotype, subject factor, and visit. $R^2$ increment refers to the percentage of variance explained by the pollutant. NS indicates not significant.
and subject factor, the 5-D mean values of PM$_{2.5}$, PM$_{10}$, and NO$_2$ were significantly and positively correlated with small artery reactive hyperemia ($P<0.0001$, $P<0.001$, and $P<0.01$, respectively; Table 3 and Figure 3). Further adjustment on baseline diameter showed that larger diameter was associated with larger reactive hyperemia ($P<0.001$), but this adjustment did not affect the correlations with PM$_{2.5}$, PM$_{10}$, and NO$_2$. No correlation was found between mean value of SO$_2$, NO, and CO and small artery reactive hyperemia. Changes in the 5-D mean value of PM$_{2.5}$ between the 2 visits explained 13% of the variance of changes in small-artery reactive hyperemia after adjustment on baseline values. Similar results were observed when blood flow was used instead of blood velocity. No correlation was found between air pollutants and the hyperemic-ischemia mean flow ratio (data not shown).

Discussion

In the present study, we demonstrated that, in young healthy volunteers devoid of cardiovascular risk factors and strictly nonsmokers, exposition to ambient air pollution, notably gaseous pollutants (SO$_2$ and NO), led to a significant alteration in endothelial function. This important impairment was observed for relatively low levels of pollution. Indeed, Paris is exposed to dominant winds, has virtually no polluting industries, and charcoal or petrol heating is marginal. Thus, Paris is among the less polluted capitals in Europe. Nevertheless, FMD could be reduced by 50% between the least polluted and the most polluted day (Figure 2), a change which is comparable to the usual difference observed between diseased patients and healthy control subjects. These baseline correlations are reinforced, because changes in air pollution at 2-week intervals accounted for 19% of the variance of endothelial function. This result shows that the variability of measurement at repeated investigation is influenced by changes in air pollution. We did not find any correlation between air pollutants and endothelium-independent GTN-induced brachial artery dilatation (Figure 2). Thus, these results suggest a direct effect of air pollutants on endothelial function rather than an effect on smooth muscle relaxation.

Correlation between air pollutants and endothelial function is stronger with the 5-D mean value of air pollutant than with D0 value. This observation suggests a cumulative effect of air pollutant exposure on endothelial function.

An important result of the present study is that the negative correlation between air pollution and flow-mediated dilatation is the strongest for the SO$_2$ level. The principal source of SO$_2$ is the combustion of sulfur-containing fuels, diesel engines, and roasting of metal sulfide ores. Epidemiological studies are consistent with a toxic effect of SO$_2$ adversely acting on cardiac morbidity and mortality. SO$_2$ could induce pulmonary inflammation and general inflammation together with oxidative damage in the lung and heart. Experimental and epidemiological studies have demonstrated that acute systemic inflammation impairs endothelium-

**Figure 1.** Significant correlation ($P<0.001$ multivariate analysis after adjustment for diet, R53R/R53H genotype, subject factor, visit, and air temperature) between the mean levels of SO$_2$ during the 5 days preceding the examination and the change in brachial artery diameter during reactive hyperemia.

**Figure 2.** Box plot of flow-mediated dilatation and change in diameter after GTN as a function of 4 quartiles of SO$_2$ level. The box horizontal line represents the median, the box encloses the interquartile range (IQR; 50% of the distribution), and the whiskers represent adjacent values (25th percentile: $-1.5\times$IQR and 75th percentile: $+1.5\times$IQR).
dependent dilatation, and oxidative stress could lead to a reduction in NO bioavailability and subsequent endothelial dysfunction.

Among all of the pollutants studied, only gaseous pollutants were correlated with an alteration in large-artery FMD. No significant association was found with particulate matter. This result contrasts with epidemiological and experimental studies. PM, which is classified within defined size ranges, is very heterogeneous in its composition. We have no data about chemical composition of particles in our study, and the level of PM is not available in Paris. This variability in composition of PM may explain the disparity between the studies. Most experimental studies showed that both endothelium-dependent and -independent vasodilatation were altered after exposition to air pollutants in humans and animals. These studies used PM levels 5- to 10-fold higher than the one measured in Paris during the present study. At these high concentrations, particles may exert a toxic effect on vasomotor tone, beyond endothelial dysfunction. At the level of PM observed during the present study, we did not observe any change in GTN-induced vasodilatory response of the brachial artery but an exaggerated dilatory response of small arteries to hand ischemia. One particularity of our finding is that the absolute value of peripheral vasodilation, rather than the percentage of increase in flow, was correlated with PM levels. This unexpected effect may be related to a significant increase in inflammation after exposure to particles. Inflammatory states may have a dual effect on vascular function, both altering the endothelial response of large arteries and causing small-artery vasodilatation. We could not explore these mechanisms in the present study, and further experimental studies are necessary to understand the present findings.

### Methodologic Features and Limitations of the Study

The present study has several strengths. The subjects investigated in the present study constitute a homogeneous sample of young healthy males, with no previous exposure to tobacco and no cardiovascular risk factors. Thus, the confounding effects of age, gender, and cardiovascular risk factors can be ruled out. Second, measurement of endothelial function was performed with “gold-standard” techniques and repeated at 2-week intervals. Third, measurement of air pollution was performed by automatic devices and completely independent of vascular investigations.

Sunlight and humidity are known factors influencing the balance between air pollutants. Given the high variability of weather on a day-to-day basis, it was difficult to adjust beyond mean day temperature and building air pollution scores. Further adjustment on general weather could further reduce the variance of FMD.

One important limitation is that subjects were allowed to live outside the hospital during the study. Although all of the participants were living in the Paris area and had to come twice daily to the hospital for their meals, they could have been exposed to different levels of pollution during the study.

We chose to express FMD with reference to ischemia, not baseline. This is because of the fact that, in our setting, we observed that cuff inflation was accompanied by a sharp parallel decrease in blood flow and diameter (endothelium dependent), which represented one third of the global FMD.

### Table 3. Independent Influence of Air Pollutants on Small Artery Reactive Hyperemia in Healthy Subjects

<table>
<thead>
<tr>
<th>Parameters</th>
<th>R² Increment</th>
<th>β-Coefficient</th>
<th>Lower CI</th>
<th>Upper CI</th>
<th>P</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reactive hyperemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-D PM (% for 1 SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM₂.⁵</td>
<td>14</td>
<td>15.68</td>
<td>7.11</td>
<td>23.30</td>
<td>&lt;0.0001</td>
<td>0.24</td>
</tr>
<tr>
<td>PM₁₀</td>
<td>13</td>
<td>15.91</td>
<td>7.74</td>
<td>24.0</td>
<td>&lt;0.001</td>
<td>0.16</td>
</tr>
<tr>
<td>5-D gaseous pollutants (% for 1 SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SO₂</td>
<td>2</td>
<td>4.03</td>
<td>‐14.31</td>
<td>6.36</td>
<td>NS</td>
<td>0.17</td>
</tr>
<tr>
<td>NO</td>
<td>1.8</td>
<td>9.2</td>
<td>‐0.28</td>
<td>18.86</td>
<td>NS</td>
<td>0.1</td>
</tr>
<tr>
<td>CO</td>
<td>5</td>
<td>10.46</td>
<td>1.73</td>
<td>19.31</td>
<td>0.02</td>
<td>0.18</td>
</tr>
<tr>
<td>NO₂</td>
<td>8</td>
<td>13.8</td>
<td>3.6</td>
<td>24</td>
<td>&lt;0.01</td>
<td>0.18</td>
</tr>
<tr>
<td>Changes in endothelial function between visits (adjusted on baseline value)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Changes in PM₂.⁵</td>
<td>13</td>
<td>1.98</td>
<td>0.67</td>
<td>3.29</td>
<td>0.004</td>
<td>0.44</td>
</tr>
</tbody>
</table>

All of the data were adjusted for diet, R53R/R53H genotype, subject factor, visit, and air temperature. R² increment refers to the percentage of variance explained by the pollutant. NS indicates not significant.

**Figure 3.** Significant correlation (P<0.0001 multivariate analyses after adjustment for diet, R53R/R53H genotype, subject factor, visit, and air temperature) between the mean levels of PM₂.⁵ during the 5 days preceding the examination and the increase in blood flow velocity after the release of hand ischemia.
response. We verified that correlations were similar when FMD was expressed with reference to baseline, albeit with slightly lower levels of significance.

Although the dose of GTN used in the present study was lower than the one usually recommended, the vasodilatory response to GTN was large compared with FMD. This could limit the relevance of the absence of influence of air pollution on endothelium-independent vasodilation.

Conclusions and Perspectives
The present study demonstrates that 5-D average ambient air pollution is associated with altered endothelial function and that the changes in air pollution at 2-week intervals condition changes in endothelial function. In one of the least polluted capitals of Europe, endothelial function may decrease by 50% between the least polluted and the most polluted day, a change that is comparable to the usual difference observed between diseased patients and healthy control subjects. Because endothelial dysfunction is an early feature of vascular disease, the present study suggests that ambient air pollution should be taken into account when establishing the CV risk profile of a subject. Second, because gaseous air pollutants account for a significant part of the variability of endothelial function, it can be useful to monitor air pollution during clinical studies and adjust results on the level of gaseous air pollutants.

Source of Funding
This study was funded by the French Ministry of Health, Délégation à la Recherche Clinique, Assistance Publique-Hôpitaux de Paris, Programme Hospitalier de Recherche Clinique (PHRC AOR#01050).

Disclosures
None.

References
Endothelial Function and Chronic Exposure to Air Pollution in Normal Male Subjects
Marie Briet, Cédric Collin, Stéphane Laurent, Alice Tan, Michel Azizi, Mohsen Agharazii,
Xavier Jeunemaitre, François Alhenc-Gelas and Pierre Boutouyrie

_Hypertension_. 2007;50:970-976; originally published online September 17, 2007;
doi: 10.1161/HYPERTENSIONAHA.107.095844

_Hypertension_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2007 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://hyper.ahajournals.org/content/50/5/970

Data Supplement (unedited) at:
http://hyper.ahajournals.org/content/suppl/2007/10/18/HYPERTENSIONAHA.107.095844.DC1