reflect a greater awareness of the "benefits" of aspirin among older physicians, a higher incidence of aches and pains and coronary risk factors with advancing age or the urge to prevent "impending" ischemic cardiac event!

This survey was conducted before publication of the Physicians Health Study in the United States or the British Male Physicians trial in the United Kingdom. Thus, our results probably were not influenced by publication of these reports and subsequent media coverage of the "benefits" of aspirin. A major limitation of this survey, however, is relatively small number of participants. Another limitation of this survey is that most respondents were from the Northeast United States and, therefore, whether these data represent attitudes of most US physicians cannot be ascertained. However, the striking increase in aspirin intake with increase in age provides a basis to conduct larger surveys to assess physicians' attitudes toward novel therapy.

Lastly, intake of a relatively small dose of aspirin suggests awareness among physicians that 325 mg may be adequate to prevent coronary events, possibly by differentially inhibiting platelet function.

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**Pulmonary Extraction of Immunoreactive Atrial Natriuretic Factor in Dogs**

Eric R. Bates, MD, Mark J. McGillem, BS, G. B. John Mancini, MD, and Roger J. Grekin, MD

Atrial natriuretic factor (ANF) is a hormone predominantly secreted by the cardiac atria. It stimulates the kidney to produce natriuresis and diuresis, and vasodilates vascular smooth muscle. The half-life of the hormone is a few minutes, suggesting that breakdown occurs in many tissues. Significant extraction of ANF has been demonstrated across the capillary beds of liver, kidney and limb. Pulmonary extraction of the hormone has not been shown in dogs or man, however, even though rat lung homogenates destroy ANF and isolated rabbit lungs remove ANF, perhaps because blood samples in the in vivo studies were obtained from systemic arteries instead of pulmonary veins. If ANF is released into the left atrial cavity through the thebesian veins, systemic arterial sampling could underestimate pulmonary extraction of ANF. The purpose of this study was to determine whether ANF is extracted across the canine pulmonary perfusion bed.

Surgical exposure of the heart and femoral vessels was accomplished in 15 mongrel dogs. Blood samples were withdrawn from catheters in the femoral vein, pulmonary artery, pulmonary artery wedge, pulmonary vein, left atrium, aorta and coronary sinus. Levels of immunoreactive ANF (IR-ANF) were measured by radioimmunoassay after extraction with Sep-Pak cartridges. Antibody was obtained from Peninsula Laboratories, Inc.

Results are listed in Table I. IR-ANF levels significantly increased from the femoral vein to the pulmonary artery. Levels were significantly decreased in the pulmonary artery wedge position and the pulmonary vein, compared with the pulmonary artery. There was a significant step up in the left atrium, compared with the pulmonary vein and the pulmonary artery wedge. Left atrial and aortic levels were not statistically different. Coronary sinus levels were 3 times higher than systemic levels.

Although 2 human studies reported equivalent ANF levels in pulmonary arteries and systemic arteries, pulmonary wedge or pulmonary venous sampling was not performed and it was concluded that ANF was probably not extracted in the lung. Also, Wesselsouch et al found no extraction between right ventricular and left ventricular sampling sites in the dog. Rodeheffer et al reported a decrease in ANF levels in the capillary wedge position, compared with equivalent levels in the pulmonary artery and aorta. They suggested that the hormone was extracted by the lung and secreted from the left atrial endocardium, rather than attenuated by the sampling technique, because high ANF concentrations were found in left atrial tissue from a patient undergoing cardiac transplantation.

This study, using pulmonary venous sampling in the dog, demonstrates that ANF is partially extracted during pulmonary transit. The results confirm that samples obtained from the pulmonary wedge position accurately reflect pulmonary venous levels of IR-ANF. For unclear reasons, an amount of ANF approximately equivalent to

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that extracted in the lung is released into the left atrial cavity, presumably through the thebesian veins in the left atrial endocardium, and restores systemic arterial levels to those found in the pulmonary artery.

These data suggest that the lung is an important site for ANF extraction. The decrease in plasma ANF across the lung (pulmonary artery to pulmonary vein) was 17.7 ± 4.1 pmol/liter as compared with 17.3 ± 4.9 pmol/liter across the lower extremities (aorta to femoral vein). Because pulmonary blood flow is equal to systemic blood flow, these results suggest that a large proportion of ANF extraction occurs in the lung. It is possible that patients with pulmonary dysfunction have impairment of this extraction resulting in decreased clearance of the peptide. Such a mechanism could contribute importantly to the elevated ANF levels present in patients with congestive heart failure and pulmonary hypertension. Careful clearance studies will be required to ascertain the relative roles of increased secretion and decreased clearance of the peptide in these patients.

The lung may also be an important target organ for ANF. Large numbers of ANF receptors in the lung have been demonstrated using autoradiography. No evidence has been presented to date, however, as to whether these are clearance receptors (c receptors) or biologically active receptors (b receptors). Based on the high degree of clearance of ANF by the lung, it is likely that large numbers of the c receptors are present. Some evidence has been presented to suggest that ANF has biologic effects on lung tissue. Large doses of the peptide have been reported to protect against chemical-induced pulmonary edema. ANF also dilates pulmonary arteries and has been shown to have bronchodilator properties.

### Table 1: Immunoreactive Atrial Natriuretic Factor Levels in 15 Mongrel Dogs

<table>
<thead>
<tr>
<th></th>
<th>FV</th>
<th>PA</th>
<th>PAW</th>
<th>PV</th>
<th>LA</th>
<th>AO</th>
<th>CS</th>
</tr>
</thead>
<tbody>
<tr>
<td>pmol/liter ± SE</td>
<td>30 ± 8</td>
<td>60 ± 14</td>
<td>45 ± 11</td>
<td>41 ± 11</td>
<td>51 ± 13</td>
<td>48 ± 12</td>
<td>145 ± 34</td>
</tr>
<tr>
<td>p Value</td>
<td>0.0002</td>
<td>0.02</td>
<td>NS</td>
<td>0.03</td>
<td>NS</td>
<td>0.003</td>
<td></td>
</tr>
</tbody>
</table>

AO = aorta; CS = coronary sinus; PV = femoral vein; LA = left atrium; NS = not significant; PA = pulmonary artery; PAW = pulmonary artery wedge; PV = pulmonary vein; SE = standard error.