

US EPA ARCHIVE DOCUMENT



Effects of Diesel Exhaust in a Rat Model of Sleep Apnea

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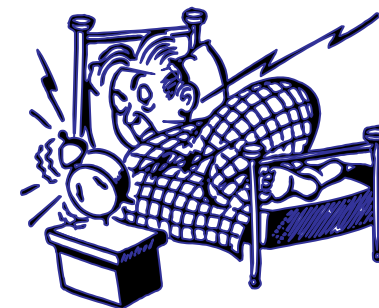
Benjimen R. Walker, Ph.D., UNM HSC

Pre-existing Cardiovascular Disease and Air Pollution

- *Air pollution increases cardiovascular mortality*
 - *Meuse Valley in Belgium*
 - *Donora, Pennsylvania*
 - *The “London Fog” incident of 1952*
- *Allowable levels of pollution also linked to cardiovascular disease*
 - *Hospital admissions for heart failure and myocardial infarction strongly correlate with daily PM levels*
 - *Pre-existing cardiovascular disease increases risk for pollution-induced cardiovascular events.*

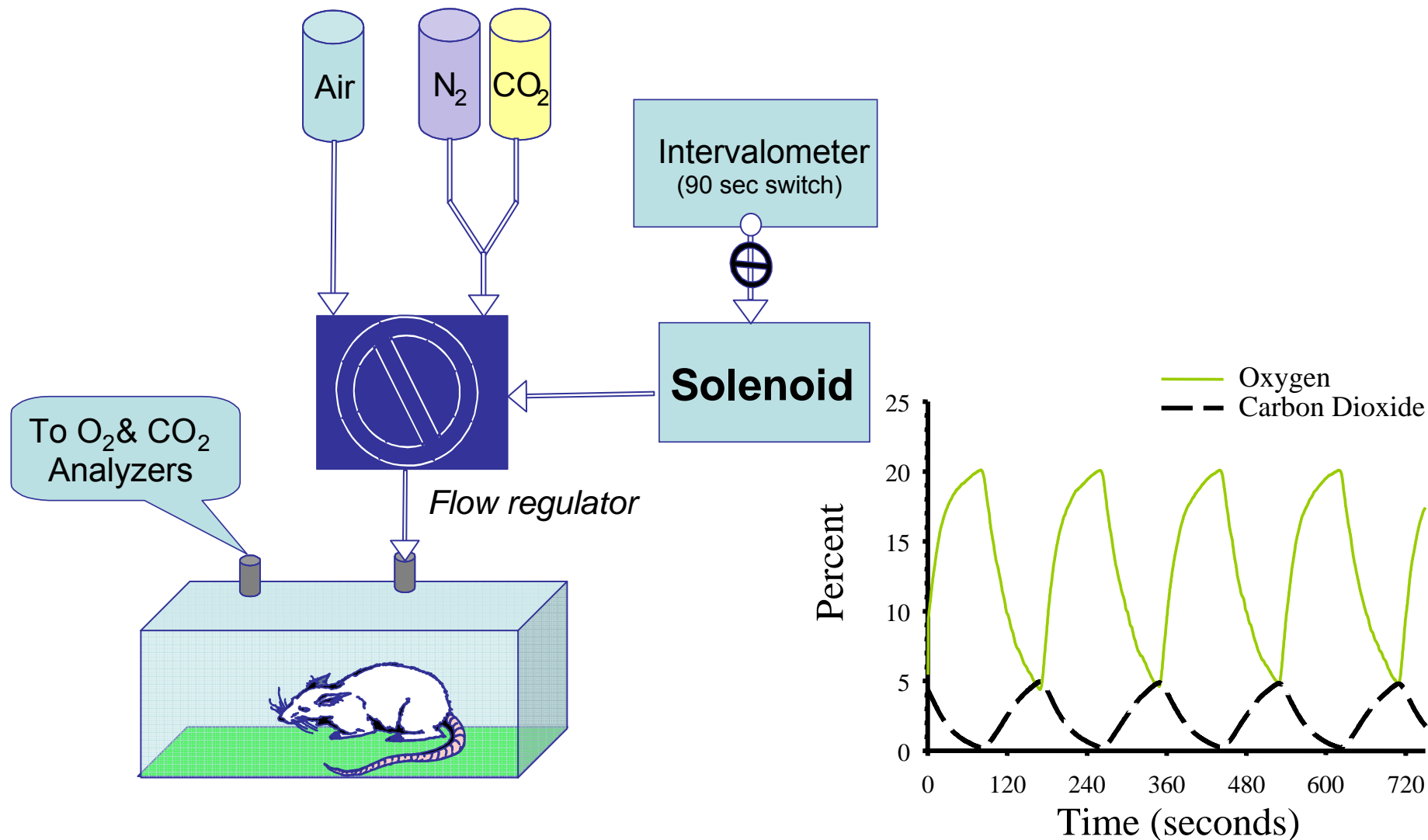
Impact of Sleep Apnea

- Sleep apnea affects approximately 20% of American adults.
- Sleep apnea appears to cause or exacerbate systemic hypertension.
- Sleep apnea is associated with ischemic heart disease, heart failure, stroke, cardiac arrhythmias, and pulmonary hypertension.

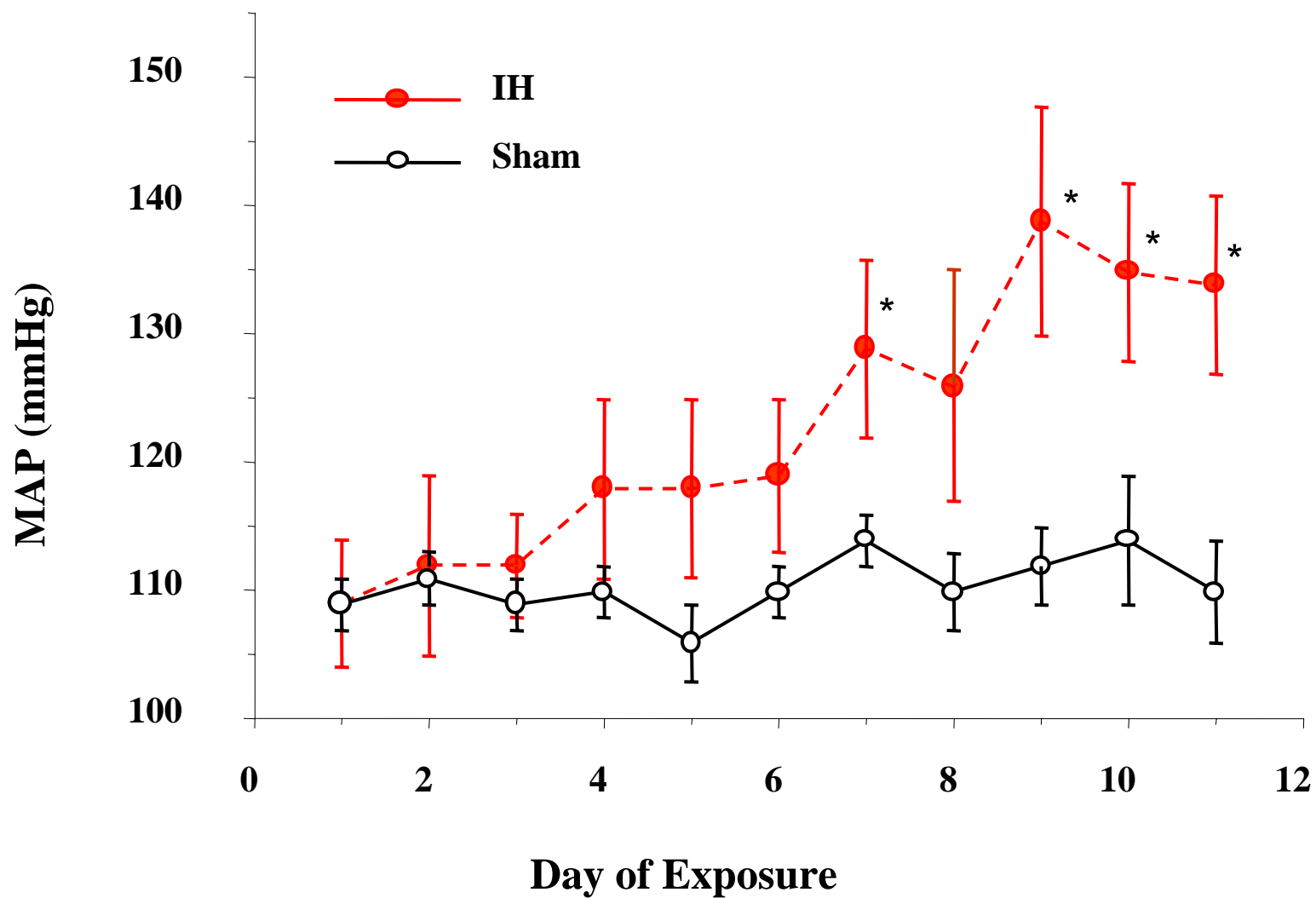


Sleep apnea might therefore injure blood vessels to make them more susceptible to air pollution-induced damage.

Rat Model of Sleep Apnea (intermittent hypoxia exposure)

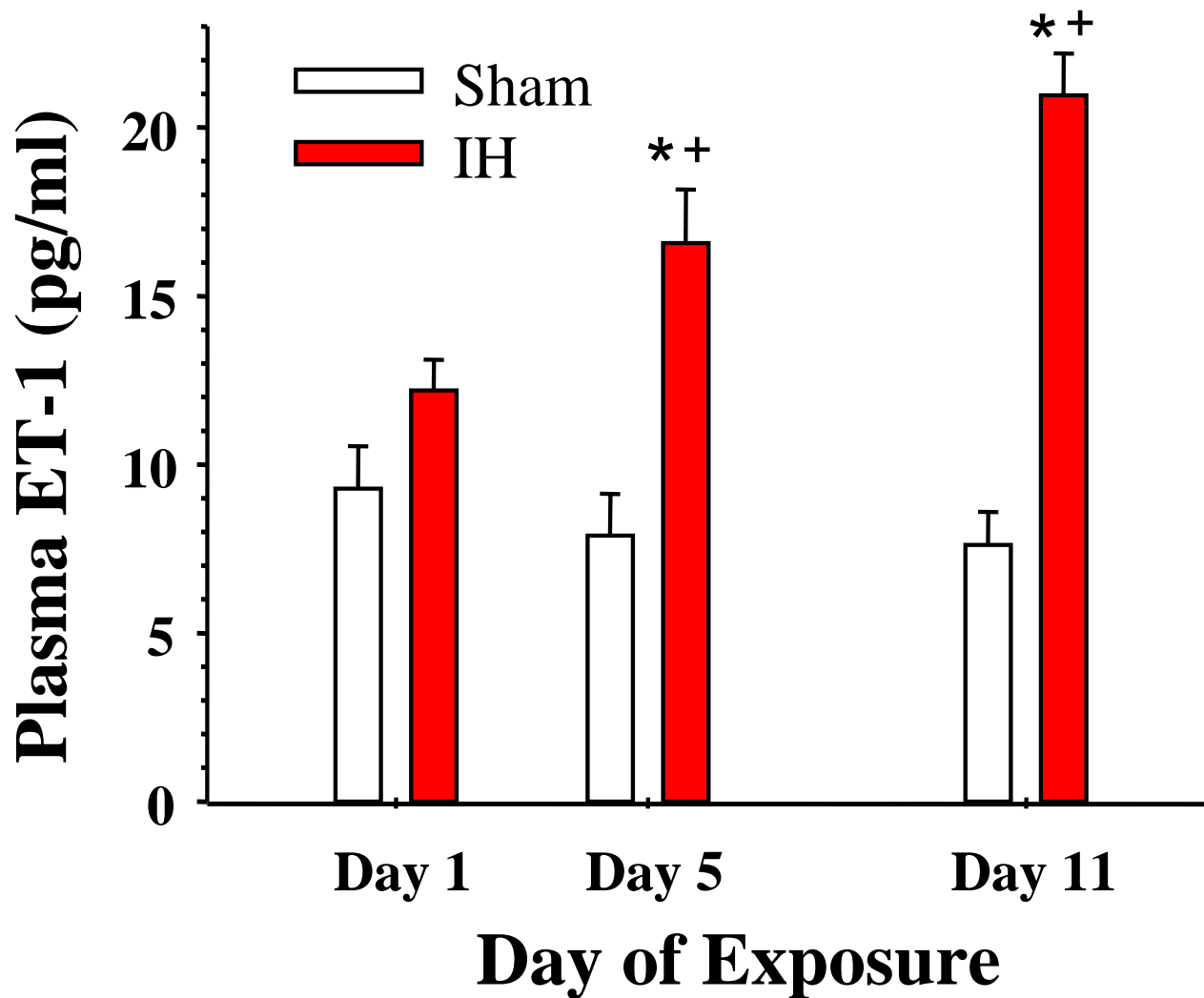


IH Elicits Hypertension in Rats

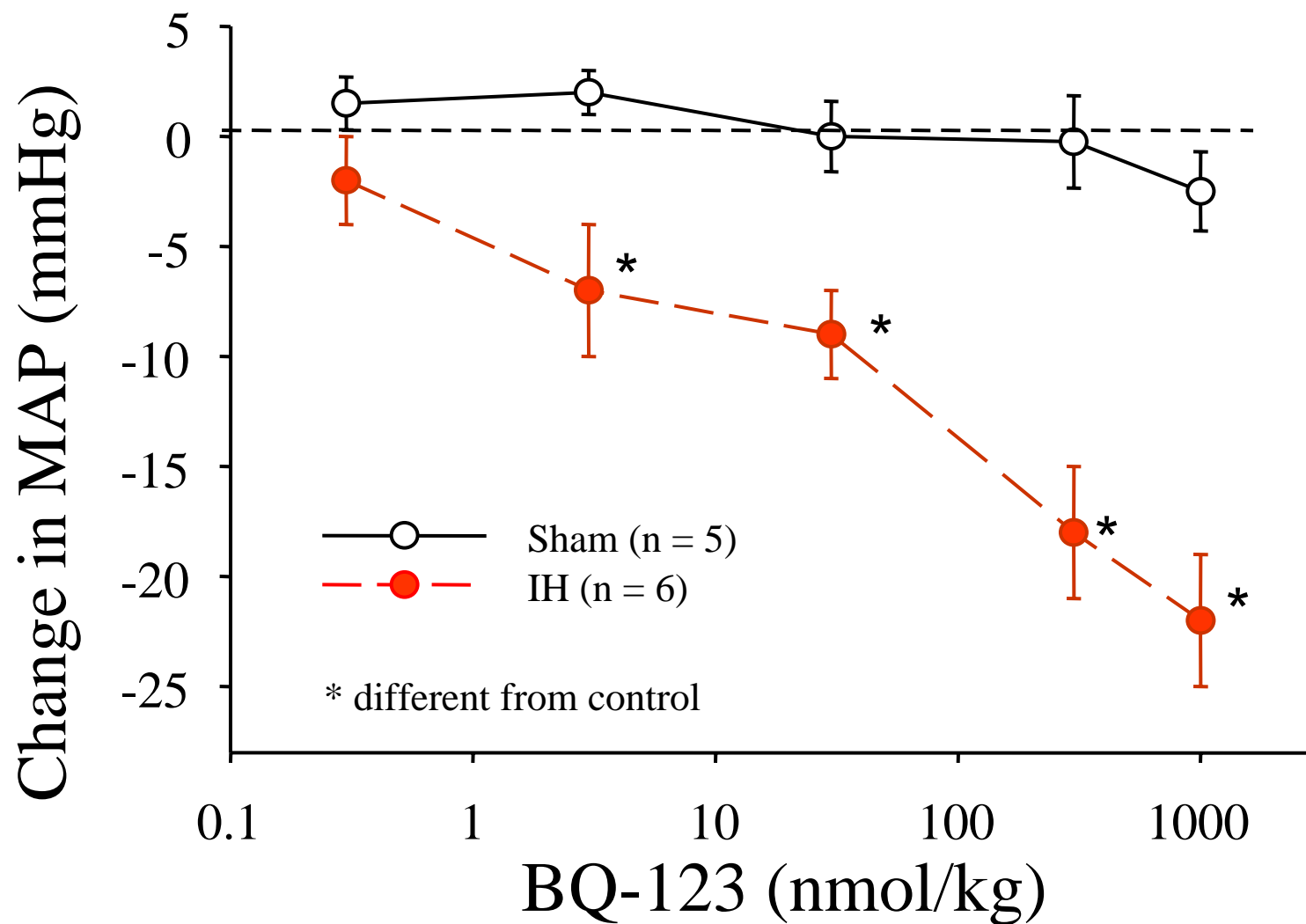


Kanagy et al Hypertension 2001

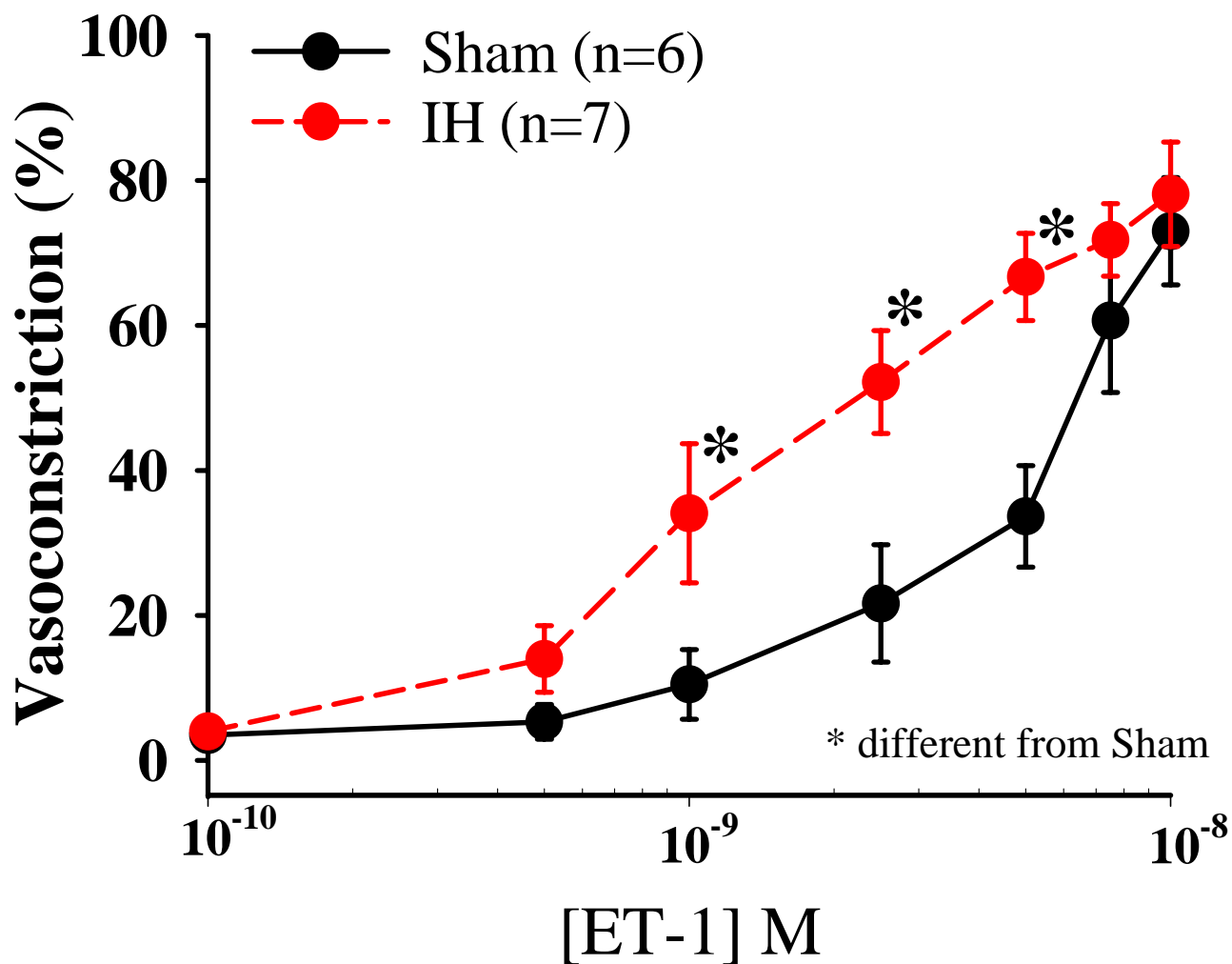
IH Exposure Increases Plasma ET-1



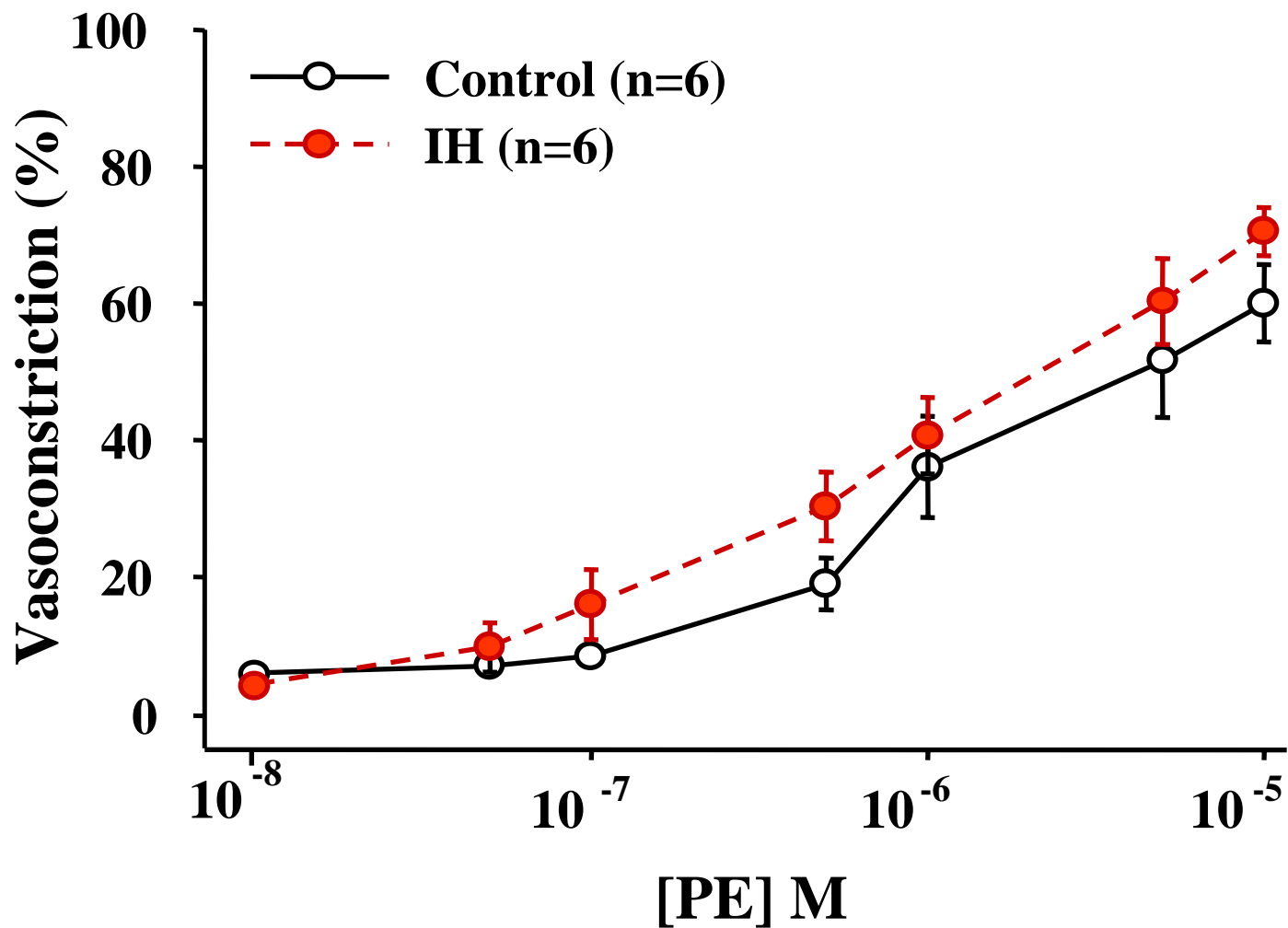
ET_A-Receptor Blockade Decreases Blood Pressure in IH Rats



IH Mesenteric Arteries Are More Responsive to Endothelin than Sham Arteries

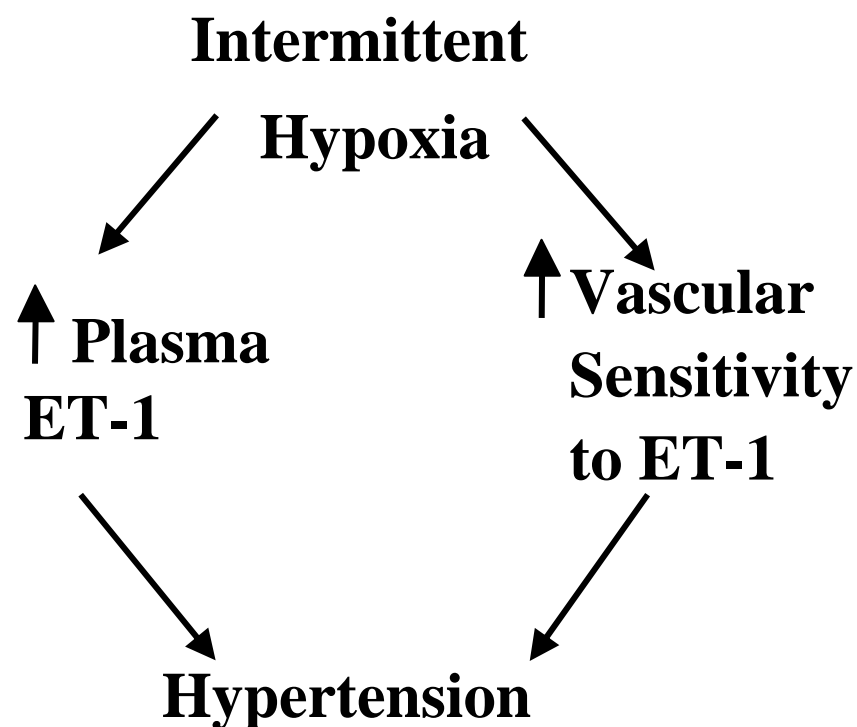


Sensitivity to PE is not Altered in IH Arteries

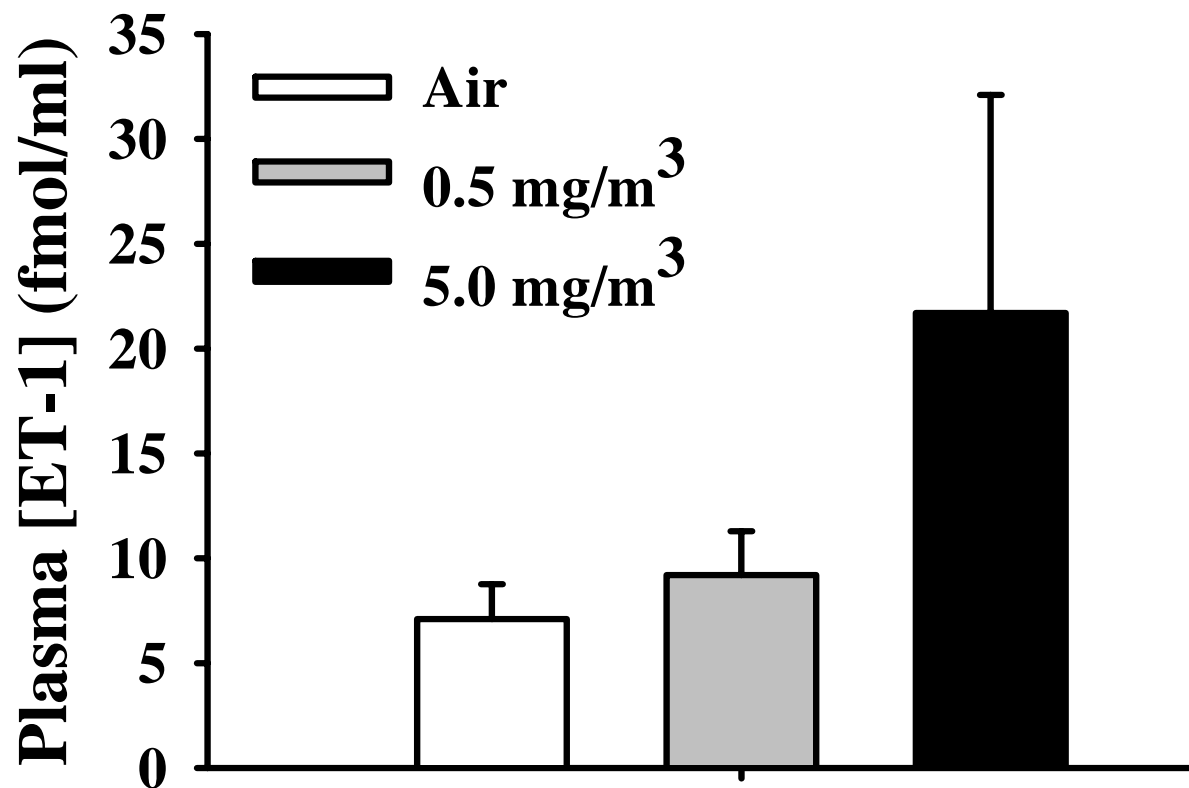


Endothelin-Dependent Hypertension IH in Rats

- IH exposure causes endothelin-dependent hypertension in rats.
- IH elevates circulating levels of endothelin.
- IH increases vascular sensitivity to endothelin.



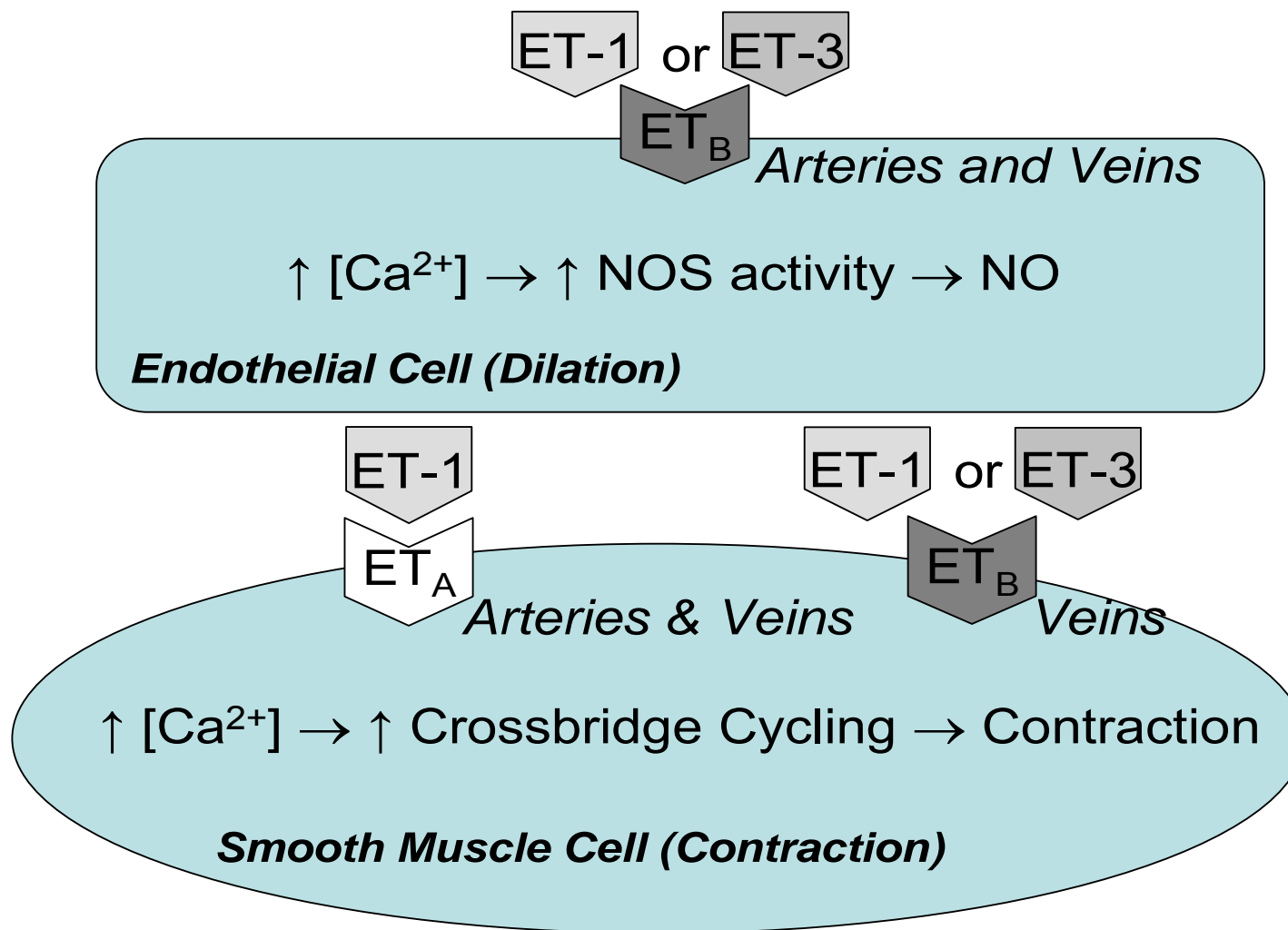
Exposure to Diesel Exhaust Increases Plasma ET-1



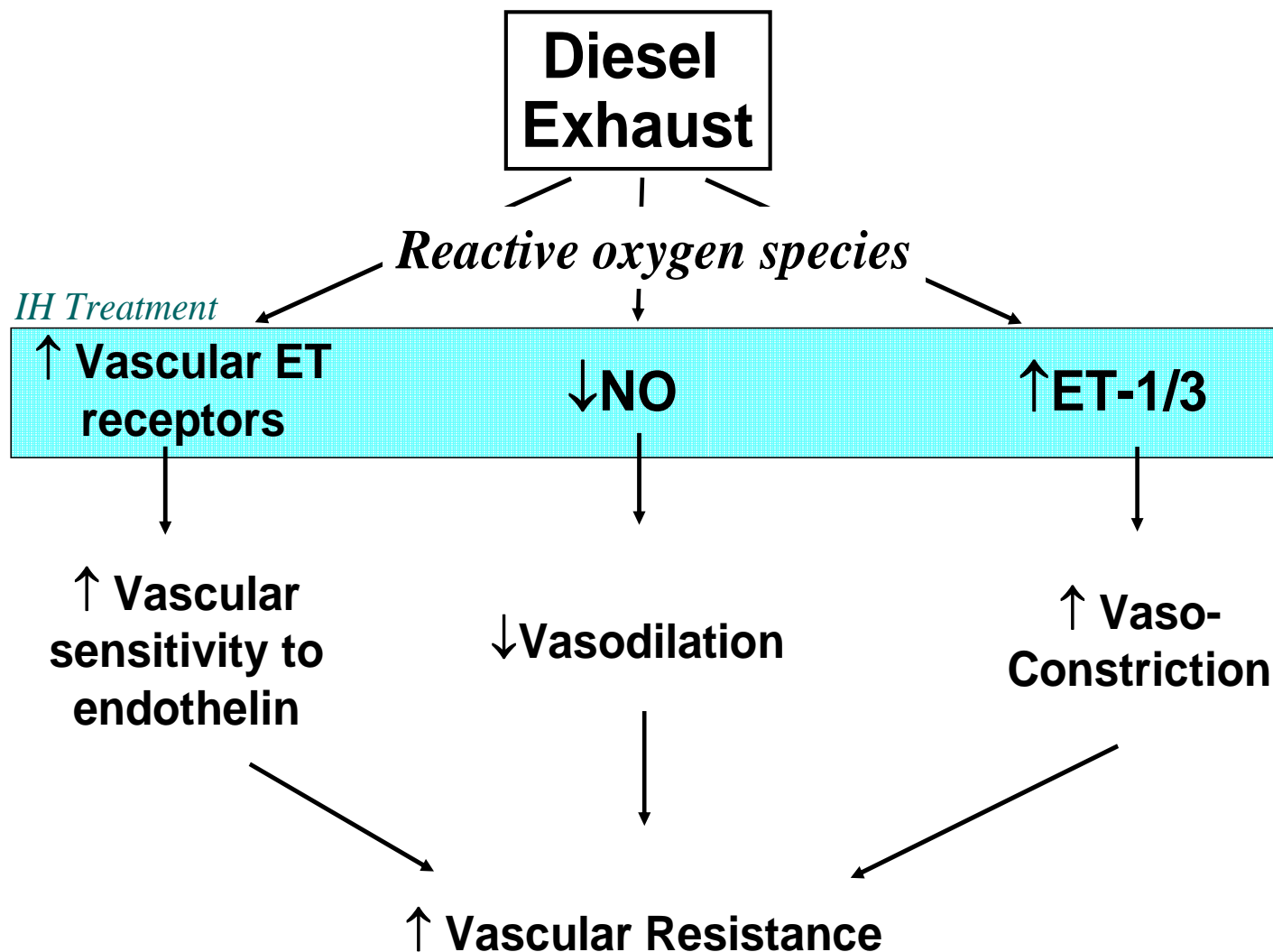
Hypothesis

Inhalation of whole DE augments ET-vasoconstriction in ET-sensitized rats.

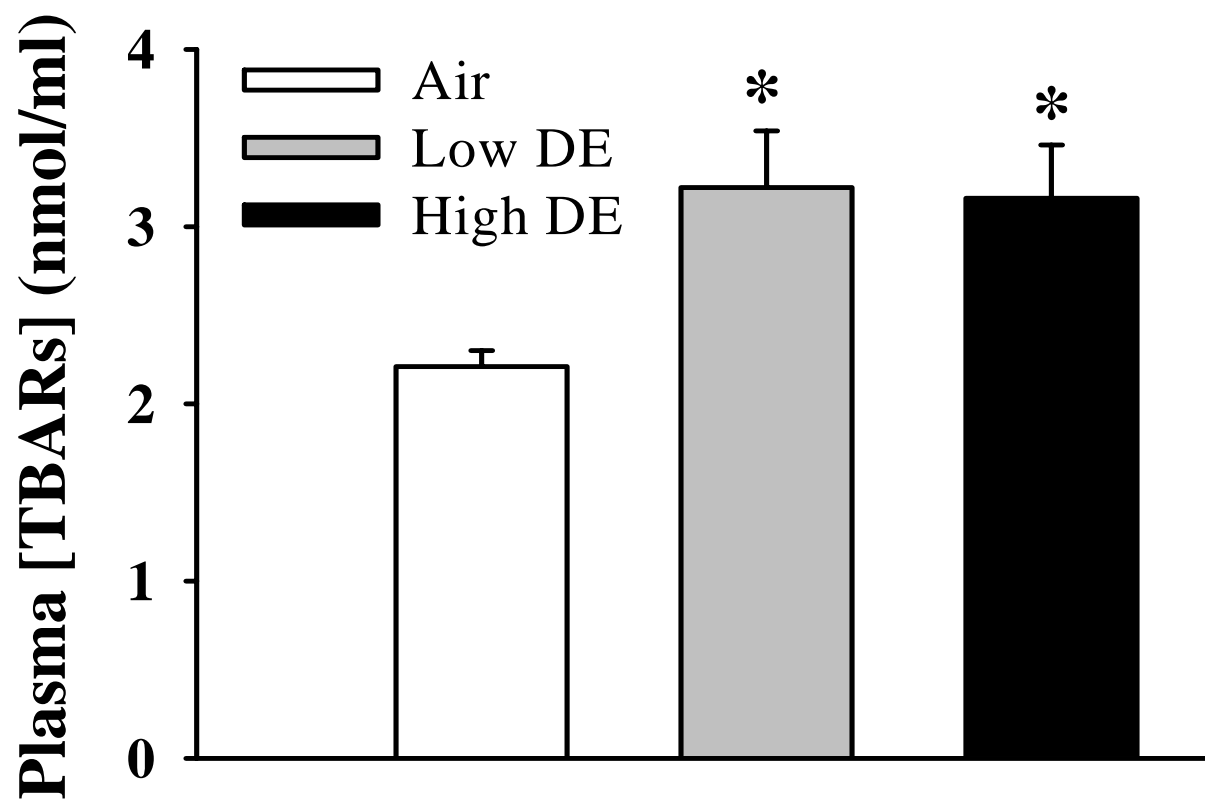
Mechanism of Endothelin Vasoconstriction



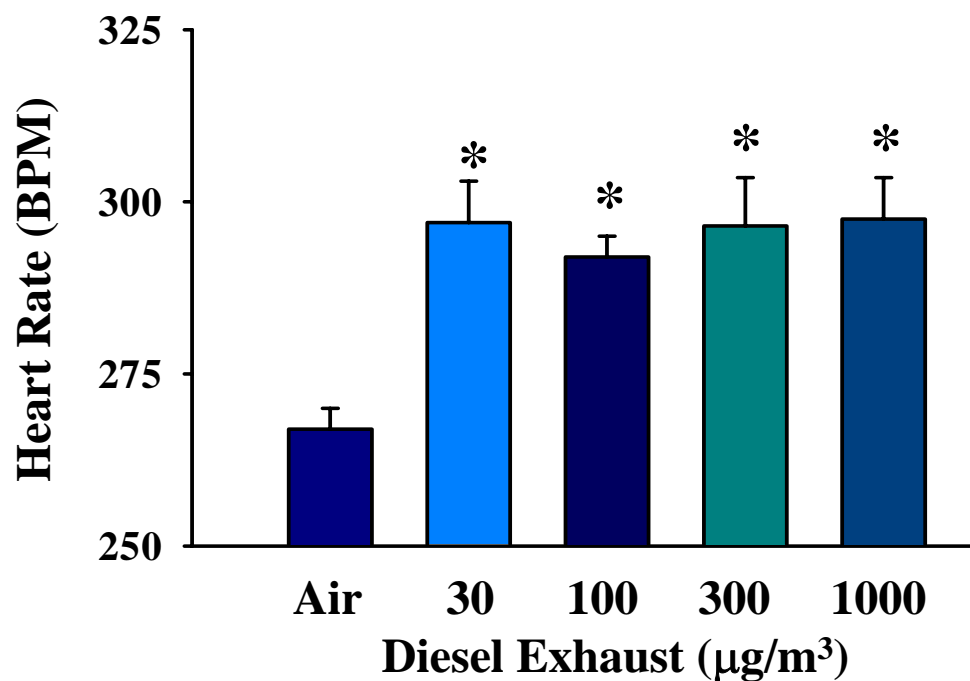
Proposed Actions of DE in IH-Exposed Rats



Diesel Exhaust Increases Oxidative Stress

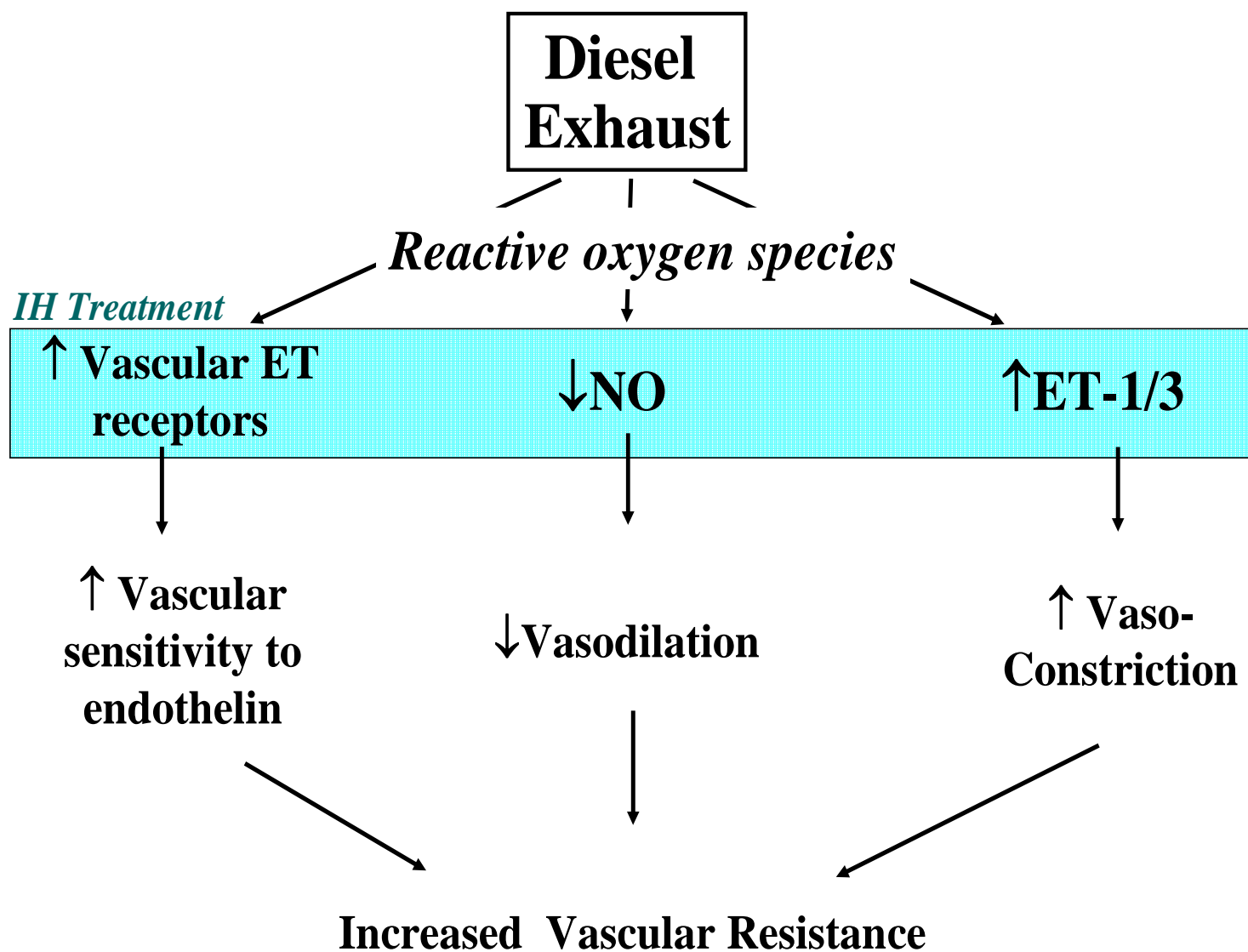


Diesel Exhaust Affects Heart Function



Campen et al., Cardiovasc. Tox., 2003

Proposed Mechanism



Contributors

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NIH
AHA
EPA
NIEHS (core facilities and
equipment)

