# The effects of diesel exhaust inhalation on cardiovascular function_dataset

## Introduction:

Air pollution serves as a major risk factor for the development of asthma, respiratory disease and heart disease. Diesel particulate and fumes are a major contributor to air pollution. Workers in a number of different occupations, including mining, oil and gas exploration and refining, and drivers of heavy equipment who are regularly exposed to diesel exhaust while on the job, and persons living in areas with high levels of air pollution, are at an increased risk for developing asthma, cardiovascular disease and certain cancers.

Understanding the physiological and cellular effects of diesel exhaust inhalation on Various organs in the body is critical for identifying exposure-induced biological and physiological markers of disease or dysfunction. The experiments in this manuscript, focus on the effects of diesel exhaust (DE) inhalation on peripheral and cardiovascular function. In the current studies, we hypothesized that the development of cardiovascular disease in workers regularly exposed to DE is the result of the inhalation of volatile gases and particulate within the vapor that affect the cardiovascular system by altering physiological and cellular processes that affect peripheral vascular responsiveness to agents that cause blood vessels to constrict and vessels that cause blood vessels to dilate, blood pressure, cardiac output and kidney function (kidney function as it may contribute to changes in blood pressure). We also predicted that these changes in physiology would be associated with changes in the expression of proteins and the production of genes that play a role in regulating oxidative stress, responses to decreases in oxygen, and markers of kidney function that are associated with blood pressure.

## Methods

*Animals:*

- Male Sprague-Dawley rats were obtained from Hilltop Lab Animals, Inc. (Scottdale, PA)
- Animals were housed in cages ventilated with HEPA (high efficiency particulate air)-filters under climate-controlled conditions and a 12-h light/12-h dark cycle (lights on 0600 h).
- All procedures were approved by the NIOSH Animal Care and Use Committee and were in compliance with the Public Health Service Policy on Humane Care and Use of Laboratory Animals and the NIH Guide for the Care and Use of Laboratory Animals.

*Exposures:*

- Rats in whole body chambers were exposed to a target concentration of 0.2 $mg/m^3$ or 1 $mg/m^3$ DE or purified air for 6 h/d, 4 d/week.
- Animals were euthanized (i.p. injection of pentobarbital, 100 mg/kg b.w.) 1, 7 or 27 d following the exposure.

*Microvessel:*

- Ventral tail arteries from the C18-20 region of the tail were dissected, mounted on glass pipettes in a microvessel chamber (Living System; Burlington, VT), and perfused with bi-carbonated HEPES bufferwarmed to 37°C.
- After an hour acclimation period, the chamber buffer was replaced with fresh HEPES buffer and responsiveness of the arteries to phenylephrine (PE)-induced vasoconstriction and acetylcholine (ACh)-induced re-dilation was measured.

*Procedures for* in vivo *hemodynamic measurements*

- A Mikro-Tip® ultra-miniature PV loop catheters (SPR-901; Millar, Inc., Houston, TX) was inserted into the left ventricle through the carotid artery.
- Systolic (SBP), diastolic (DBP), mean arterial blood pressure (MAP) and left ventricular function were measured.
- Parallel conductance volume was calculated by the software and used for the correction of the cardiac mass volume, and each rat was euthanized by exsanguination under deep anesthesia at the conclusion of the experiment.

*Measuring oxidative stress:*

- Heart and kidney tissues were homogenized and total ROS were measured using 2′7′-dichlorofluorescien diacetate (DCFH-DA; Sigma-Aldrich, St. Louis, Mo).

*Quantitative reverse transcriptase polymerase chain reaction (qRT-PCR)*

- qRT-PCR was performed on heart and kidney tissues.
- Transcripts indicative of changes in inflammatory cytokines, apoptotic factors, and factors involved in vasomodulation, vascular remodeling and ionic status in the heart and kidney.

*Enzyme linked immunosorbent assays:*

- An ELISA to measure super-oxide dismutase-2 (SOD2; R&D Systems, Minneapolis, MN) in heart and kidney extracts.
- Data were reported as the concentration of SOD/total protein.

Reference:

Krajnak K, Kan H, Thompson JA, McKinney W, Waugh S, South S, Burns D, Lebouf R, Cumpston J, Boots T, Fedan JF. Biological effects of diesel exhaust inhalation. III cardiovascular function. Inhalation Toxicology, DOI: 10.1080/08958378.2024.2327364

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