Good Morning

I am here today to discuss with you the results of a recent research study investigating potential mechanisms for the health impacts of diesel exhaust particles (DEP) and by association to particulate matter in general.
We have all heard about the harmful effects of DEP in Board meetings over the past several years. Many regulatory actions have been taken to reduce emissions of DEP to minimize these effects. Additional regulations will be considered at today’s Board meeting.

In 1998, the Air Resources Board identified diesel exhaust particles as a Toxic Air Contaminant. It poses a serious potential to cause cancer in people exposed to levels commonly found in California.

DEP often contributes a considerable portion of PM2.5 mass in urban areas and may cause some of the various health impacts associated with PM exposure. PM effects of concern include increased mortality and morbidity observations from heart and lung related causes. However, finding mechanistic explanations for these effects has remained elusive.

DEP have recently been found to play a role in causing or worsening existing allergies and asthma, especially when other allergens are present. The pollutant can reduce visibility and may play a role in global climate change.
This study I'll be discussing was performed by Dr. Nemmar from a research group in Belgium.

READ TITLE

The objective of this study was to investigate possible mechanisms to explain observations of cardiovascular morbidity and mortality found in epidemiological studies. DEP was employed as a surrogate PM.
Experimental Approach

- Fluid suspensions of DEP placed into hamsters trachea
- Blood coagulation and markers of lung inflammation measured shortly after exposure

Protocols Developed from Prior Studies
- Investigators found ultrafine PM administered into airways quickly entered circulating blood

In this study, hamsters were employed as experimental test animals. They were surgically prepared to accept a liquid suspensions of DEP into the trachea (throat). The particles were from a reference material that is available for research on effects, chemistry and the physical properties of DEP. The particles were placed in solution and treated to encourage individual particles to be separated from the bulk material. Several concentrations of DEP containing fluids were instilled in to groups of animals to allow an evaluation of the role of dose in producing effects.

Following treatment with DEP the animals were allowed to develop measurable responses.

1. Thrombosis (coagulation/clotting)--was assessed by measuring the intensity of light passed through an experimentally damaged vein or artery. Less light passed when coagulation processes occurred.

2. Lavage fluid assays--fluid was retrieved from lungs. The cellular content of this fluid was separated and evaluated. The remaining non-cellular fluid was also assayed. Cells and chemicals of interest relate to irritation/injury responses.

3. Platelet function (related to clotting) in collected blood was assessed.

The protocols are an extension of previous work by the authors where ultrafine particles were administered to the airways of hamsters as a liquid suspension. These particles appeared in circulating blood soon after the exposure. This suggests that inhaled PM might also do so and could explain how PM could impact cardiovascular function.
The investigators report that for each of the effects they measured that effects increased as the administered dose increased.

The following findings were reported--

There was 2 to 7 times more blood coagulation in treated animals than controls as dose went from low to high (over a concentration range of 100 fold). The graph shows this clearly. The effect happens quickly, in less than an hour.

There was an increase in macrophage and neutrophil cells retrieved in lung lavage. The neutrophils are markers of airway damage and inflammation. This effect also happens very quickly, in one hour.

Proteins retrieved from lung fluids increased as the dose increased. The proteins indicate airway damage and leakiness technically referred to as “epithelial permeability”

Histamines in retrieved lung fluid increased dramatically---2-10x above control animals. This indicates a marked allergy/asthma health impact potential as well as the initiation of complex physiological processes and it was detected after one hour following exposure.
There are limitations imposed by the protocols.

The DEP exposure was performed by liquid administration into the throat. The liquid was fairly concentrated, when compared to an inhaled DEP from the atmosphere.

The DEP differs from what is found in the atmosphere. Exhaust particles in the atmosphere start as finely structured chains of smaller DEP. The sonication of reference material disrupts this structure and may impact the chemistry as well.

In the pictures we can see the structure and nature of ambient DEP on the left and particles employed in this study on the right.

DEP was employed in this study to represent atmospheric PM. It is possible that it may have unique toxic properties.
What are the implications of this study?

Probably the most important implication is that this study identifies a new reason for us to be concerned about the health impacts of DEP--cardiovascular response and lung injury--beyond its potential to cause cancer after many years exposure. Here we have seen clear responses after only an hour.

The study reinforces this concern by providing plausible biological mechanisms to explain how these effects cardiovascular effects might occur.

The findings also provide strong evidence that could explain the observations of epidemiological studies that consistently find increases in deaths and hospitalizations of people when PM levels increase in ambient air. Until recently, there has been very little mechanistic explanations for these findings.

Lastly, the findings of this study suggest the need to conduct relevant experimental studies to confirm whether these effects occur in people exposed to PM or DEP.