Diesel Exhaust Is Linked To Cancer Development Via New Blood Vessel Growth

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(PhysOrg.com) -- Scientists here are the first to demonstrate that the link between diesel fume exposure and cancer lies in the ability of diesel exhaust to induce the growth of new blood vessels that serve as a food supply for solid tumors.

The researchers found that in both healthy and diseased animals, more new blood vessels sprouted in mice exposed to diesel exhaust than did in mice exposed to clean, filtered air. This suggests that previous illness isn't required to make humans susceptible to the damaging effects of the diesel exhaust.

The tiny size of inhaled diesel particles, most less than 0.1 microns in diameter, potentially enables them to penetrate the human circulatory system, organs and tissues, meaning they can do this damage just about anywhere in the body. A micron is one millionth of a meter.

Diesel exhaust exposure levels in the study were designed to mimic the exposure people might experience while living in urban areas and commuting in heavy traffic. The levels were lower than or similar to those typically experienced by workers who use diesel-powered equipment, who tend to work in mines, on bridges and tunnels, along railroads, at loading docks, on farms and in vehicle maintenance garages, according to the U.S. Department of Labor.

"The message from our study is that exposure to diesel exhaust for just a short time period of two months could give even normal tissue the

potential to develop a tumor," said Qinghua Sun, senior author of the study and an assistant professor of environmental health sciences at Ohio State University.

"We need to raise public awareness so people give more thought to how they drive and how they live so they can pursue ways to protect themselves and improve their health. And we still have a lot of work to do to improve diesel engines so they generate fewer particles and exhaust that can be released into the ambient air."

The research appears online and is scheduled for later print publication in the journal *Toxicology Letters*.

The researchers experimented with mice that resembled two conditions that could be present in a human body. In one, the scientists implanted a small platform seeded with normal endothelial cells, the cells that line blood vessels, under the skin of the mice. This was designed to mimic relatively normal conditions in human bodies for cell growth.

In the other, the researchers created an environment that would follow a significant loss of blood flow to a section of a vessel, called ischemia, in the hind limbs of the mice. This generated severe hypoxia, an area with low or no oxygen, a condition that is present in certain diseases.

Both types of mice were then exposed to either whole diesel exhaust containing particles at a concentration of about 1 milligram per cubic meter, or to filtered outdoor air, for six hours per day five days a week. The rest of the time they breathed filtered air in their cages. Effects of the exposure were measured after two weeks, five weeks and eight weeks of the exposures.

Though some blood vessel growth and chemical changes could be seen in the mice after two weeks of exposure, "generally, the longer the

exposure, the more effects we could see," said Sun, also an investigator in Ohio State's Davis Heart and Lung Research Institute. "It's difficult to translate outcomes from an animal study directly to the human experience, but the bottom line is, the shorter the exposure to diesel exhaust, the better."

The exposure to diesel exhaust caused a six-fold increase in new blood vessel formation in the ischemic hind limbs after eight weeks and a four-fold increase in vessel sprouting in the normal hind limbs of the mice in the same amount of time, compared to mice breathing filtered air.

The researchers also saw significantly more blood vessel growth in the implanted cells and in rings of tissue taken from the aortas of mice exposed to the exhaust compared to the control mice exposed to clean air. In fact, the researchers found that three types of blood vessel development occurred in these areas after exposure to the diesel exhaust: angiogenesis, the development of new capillaries; arteriogenesis, the maturation or re-started growth of existing vessels; and vasculogenesis, the formation of new blood vessels.

All of these processes are associated with tumor growth, but unprogrammed angiogenesis in particular can wreak havoc in the human body, Sun said.

"Whenever you talk about a solid tumor, angiogenesis is one of the fundamental mechanisms behind its development. Angiogenesis provides the means for tumor cells to grow because they have to have a blood supply. Without a blood supply, solid tumors will not grow," he said.

"We want our bodies to generate new blood vessels only when we need them. And then stop producing them when we need them to stop."

Though the researchers have not defined every mechanism behind these

processes, they sought to explain at least a few ways in which blood vessels are able to sprout or mature after exposure to diesel exhaust.

They observed that diesel exhaust exposure activated a chemical signal, vascular endothelial growth factor, which has long been associated with new blood vessel development. The exposure also increased levels of a protein, hypoxia-inducible factor 1, that is essential to blood vessel development when oxygen levels are low. At the same time, the presence of the exhaust lowered the activity of an enzyme that has a role in producing substances that can suppress tumor growth.

The scientists also tracked low-grade inflammation in tissues exposed to the exhaust, which is often associated with tumor development.

Though the tiny size of diesel exhaust particles may contribute to their ability to penetrate all areas of the body, Sun noted that their complex chemical composition, and the way in which those chemicals are released once particles enter the body, also influence how they react with human cells.

Gasoline exhaust particles are larger than diesel fume particles, but it's premature to suggest that they are any less dangerous to humans, Sun said.

"The bigger particles are known to be harmful primarily for upper respiratory tract illnesses. Larger particles also can't travel long distances - they tend to fall to the ground," he said. "Smaller particles hover in the air for a long time and can have long-term impact on humans when inhaled."

Sun and colleagues are now conducting a study testing whether the exhaust particles promote tumor development and metastasis.

More information: www.elsevier.com/wps/find/jour … cription#description

Source: The Ohio State University (news : web)