

Alcohol may amplify chronic rejection in lung transplants

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A recent study using an animal model of lung transplants shows that chronic alcohol consumption by the donor promotes scarring and airway injury after transplantation.

The results raise questions about human lung donors with a history of alcohol abuse, say authors Patrick Mitchell, PhD, a postdoctoral researcher, and David Guidot, MD, professor of medicine at Emory University School of Medicine and director of the Emory Alcohol and Lung Biology Center.

The study will be published in the Dec. 1 issue of the *American Journal of Respiratory and Critical Care Medicine*. Its findings have prompted doctors at Emory to begin a clinical study of the post-transplant effects of alcohol use among lung donors.

"There are reasons to be concerned that chronic alcohol abuse by donors could increase the risk of complications in the transplanted lung," Dr. Guidot says. "Our goal is not to exclude donors, which would be the worst case scenario. Rather, it is to understand the biology, so that we can know how to intervene and make outcomes better."

Dr. Mitchell, who designed the animal experiments, says that the team's long-term goals are to develop biological tests to measure the effects of alcohol on the lung and ways to compensate for those effects.

About a sixth of deceased organ donors have a history of heavy alcohol consumption, defined as two or more drinks per day, according to the United Network for Organ Sharing (UNOS) database. That's more than triple the rate in the general population.

Previous studies have shown that donor alcohol abuse increases the risk of heart failure after heart transplantation. But so far, clinical data describing the effect of alcohol abuse on lung transplants has

been scarce.

"There is considerable evidence that alcohol abuse increases the risk for lung disease and lung injury," Dr. Guidot says. "So it is a natural progression to look at lung transplants."

In lung transplantation, chronic rejection comes in the form of obliterative bronchiolitis, a slow destruction of the lung followed by remodeling of the lung into scar tissue and irreversible airflow limitation.

"Chronic rejection remains the major barrier to successful lung transplantation and unfortunately, suppressing the immune system doesn't change the outcome," he says.

Lung transplantation treats the end stage of several diseases, including emphysema and cystic fibrosis. About 1,000 patients receive lung transplants annually in the United States and are chosen from a waiting list of around 4,000. Because of the lack of suitable donors, hundreds of people die annually waiting for a transplant.

Although almost three-quarters of lung transplant recipients survive the first year after surgery, obliterative bronchiolitis affects the majority after five years, Dr. Guidot says.

To examine the effects of alcohol on lung transplantation, the researchers used a model in which they transplanted a trachea from one strain of rat to another.

Feeding alcohol for eight weeks to rats that became tracheal donors increased the degree to which scar tissue overran the transplants, the study shows. The "alcoholic" rats consumed 36 percent of their calories in alcohol.

Donor alcohol consumption did not worsen chronic rejection in transplants within an inbred rat strain,

but it did add to the incompatibility between the immune systems of rats from an "outbred" strain of rat that is less uniform genetically.

Alcohol appeared to depress the number of white blood cells in the donor trachea pre-transplant but increased the production of growth factors that promote the expansion of scar tissue.

Monitoring alcohol's effects of acute and chronic graft rejection after lung transplantation in humans is the next logical step, the Emory doctors say.

Andres Pelaez, MD, a pulmonary medicine specialist at Emory's McKelvey Lung Transplant Center, will study lung transplant patients for a minimum of two years' observation. In parallel, his team will examine the prevalence of alcohol abuse in the potential donor pool, he says.

"This study is uniquely poised to gather new information important for lung transplantation," Dr. Pelaez says.

Source: Emory University

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