MedicalXpress

Cutting the cord to determine babies' health risk from toxic exposure

December 3 2008

Despite the well-known dangers of first- and secondhand smoke, an estimated ten percent of pregnant women in the U.S. are smokers. Exposure of a developing baby to harmful cigarette byproducts from mothers who smoke affects an estimated 420,000 newborns each year and poses a significant health care burden.

Now, in the first study of its kind, a team of researchers has completed a global assessment of newborns' umbilical cord blood to better understand the fetal health risks from smoking mothers. The research was led by Johns Hopkins University and included Rolf Halden, a researcher from the Biodesign Institute at Arizona State University.

"Cigarette smoking is a massive onslaught on human physiology," said Halden, who works in the institute's Center for Environmental Biotechnology. Cigarette smoke is known to contain more than 4,000 chemicals, potentially affecting the health of a newborn baby on multiple levels, including low birth weight, premature delivery and small size for gestational age. The exact cause of these health effects continues to be the subject of investigation.

"Unfortunately, maternal cigarette smoking puts babies at risk of adverse birth outcomes and increases susceptibility to other diseases later in life," said Halden.

The research team's goal was to provide the first assessment of proteins detectable in infant blood and to identify possible molecular predictors,

or biomarkers, of fetal health risks.

The emergence of improved analytical tools allowed the researchers to address newborn health risks and explore the environmental effects of a well-known toxin in a level of detail not previously available. These tools include high-speed DNA sequencing, a powerful instrumental analysis called proteomic mass spectrometry to enhance the detection of proteins in complex samples, and bioinformatics, or the raw computing power to perform massive data crunching to tease out and identify biomarkers.

In doing so, the team described over 200 serum proteins contained in umbilical cord blood, the vital link between mother and developing baby that shares between the pair both essential nutrients as well as unwanted toxins absorbed by the mother.

"Modern tools in mass spectrometry and bioinformatics have enabled us to obtain a first view of proteins contained in fetal cord blood serum and to single out among these more than a dozen interesting ones whose concentrations change as a function of chemical exposure. These biomarkers of exposure and early effect are the gold of protein mining," said Halden, who is also an associate professor in the Ira A. Fulton School of Engineering.

Halden, who joined ASU's Biodesign Institute in 2008, initiated the study while at Hopkins along with lead author David R. Colquhoun, and colleagues Lynn R. Goldman, Frank R. Witter, Robert N. Cole, Marjan Gucek, Malini Mansharamani, and Benjamin J. Apelberg. The results were published in the early online edition of the journal *Environmental Health Perspectives* (www.ehponline.org).

To best obtain a snapshot of fetal proteins at birth, the study needed to obtain cord blood samples as soon as possible after newborn delivery. This required the coordinated efforts of multiple investigators and the

resources of the large teaching hospital at Hopkins to recruit study subjects. Among the participants were many doctors and nurses to help with deliveries and obtain cord blood samples along with graduate students who were on call and had to rush out in the middle of the night to collect samples, transfer and process them, and analyze the data from the study population.

The group started with a large pool of more than 300 cord blood samples, and after adjusting for parameters such as the age of the mothers, narrowed down their focus to a dozen babies, half from non-smoking mothers and the other half from pregnant smokers.

"The study was a little bit challenging in that we went out on a fishing expedition," said Halden. "We wanted to look at everything at the same time, and the ability to tease out from the soup of proteins only those of interest was the chief technical challenge of this project."

The team looked for new proteins or proteins levels that may have changed between the smoking and non-smoking groups. After analyzing more than 200 proteins through mass spectrometry in smoke-exposed and control groups, they found small changes in the levels of some proteins, which represented biomarkers of cigarette smoke exposure.

"Of 17 proteins that were significantly up- or down-regulated in the cord blood of babies born to smoking mothers, 14 have previously been described to be related to smoking in either adults or in the fetus," said Lyne Goldman, a professor in the Department of Environmental Health Sciences at Johns Hopkins' School of Public Health.

The protein biomarkers have been linked to key metabolic pathways involved in regulating nutrients, oxygen and inflammation processes.

After their analysis, the team also discovered some surprising results that

illustrate the subtlety of using biomarkers as an approach to peer into the molecular makeup of human health. "There was not a single protein unique to either the smoking or non-smoking group," said Halden. "The remarkable finding is that there were no unique biomarkers."

Halden explains that only through the combined use of the new technologies was the research team able to tease out the small differences in the proteins levels between the two study groups.

Asked about the reliability of the biomarkers that the research team identified? Halden said, "The truth is that we don't know yet. We only took a first snapshot of the protein profile in baby blood right after birth. But does it change over time and will the differences we detected persist? We don't know."

The group hopes to use the same techniques to examine a wide range of environmental exposures and their effect on human health. "These findings confirm and underscore the serious metabolic alterations that are occurring in utero to children of smoking mothers, alterations that may increase risk for chronic disease over a lifetime," said Hopkins colleague Frank Witter. "We hope that this method will be sensitive enough to detect proteomic changes associated with environmental exposures as well."

The ultimate hope is that through the use of biomarkers identified by the team, it may become possible to detect effects of toxic exposures early on, before the onset of disease. "This may open opportunities to improve health outcomes by reducing the occurrence and severity of disease from environmental exposures, said Halden."

Source: Arizona State University