# Fetal alcohol syndrome heart defects may be caused by altered function, not structure

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Recent data shows that more than 500,000 women in the U.S. report drinking during pregnancy, with about 20 percent of this population admitting to binge drinking. Even one episode of heavy drinking can lead to the collection of birth defects known as fetal alcohol syndrome (FAS). Along with growth retardation, head and face abnormalities, and neurological problems, FAS also causes heart problems in just over half of those with this condition. Though much research has focused on looking for the cause of these alcohol-induced heart defects, they remain largely a mystery.

To investigate this question, Ganga Karunamuni of Case Western University and her colleagues studied heart formation in quail embryos, whose heart development is very similar to that of humans. The researchers used an innovative imaging technique, optical coherence tomography, to compare embryos exposed to a single, large dose of alcohol to those who hadn't received alcohol. They looked both at how alcohol changed the function of the developing hearts as well as their structure. They found that significant changes in heart function appeared to come well before changes in structure that are hallmarks of the well-known FAS heart anomalies. These changes in function, the study authors suggest, might be the cause of the structural problems that arise later by exerting forces on the heart that change its development.

The article is entitled "Ethanol Exposure Alters Early Cardiac Function in the Looping Heart: A Mechanism for Congenital Heart Defects?" It appears in the Articles in Press section of the *American Journal of*

*Physiology – Heart and Circulatory Physiology*, published by the American Physiological Society.

## Methodology

The researchers studied three sets of quail embryos. In one set of these embryos, the researchers injected a quantity of alcohol into their shells proportional to the amount that would be considered a single episode of binge drinking in a pregnant woman. They purposely chose a time during early development in which embryos are especially vulnerable to the effects of alcohol. In another set of embryos, the researchers injected their shells with saline, a placebo not known to have any harmful effects. The researchers left a third set of embryos to develop without any interventions.

Using an imaging modality called optical coherence tomography, which gives the ability to peer through layers of tissue, the researchers kept an eye on the developing hearts at a particular stage when the primitive heart switches from a tube shape to a loop-shaped circuit. The researchers compared both heart blood flow and anatomy at this stage between the three different sets of embryos. They also compared heart anatomy between the different sets both at this looping stage and at a stage closer to hatching.

## Results

As expected, the researchers found that the hearts of embryos exposed to alcohol had dramatic defects close to hatching, including thinner walls separating the heart's four chambers and damaged valves. Long before these defects formed, the researchers saw significant differences in heart blood flow between embryos that weren't exposed to alcohol and those that were. In those whose shells weren't injected with alcohol, a small

portion of the blood flowed backward through the heart circuit after each beat. In those exposed to alcohol, a much larger portion of blood flowed backward in the circuit. These malfunctioning hearts had smaller "cardiac cushions"—collections of cells that later become chamber walls and valves—compared to unexposed hearts.

## Importance of the Findings

The authors suggest that this improper function may itself steer developing hearts in the wrong direction during development, setting the stage for larger defects to arise. Previous studies have shown that because cells in the heart and elsewhere are responsive to mechanical forces, those forces exerted by blood flow can affect heart formation. By learning more about these functional changes in the early heart, the researchers suggest that it may eventually be possible to redirect blood flow to a more healthful pattern, thereby rescuing FAS hearts before they form defects.

"With an average of 4 million U.S. pregnancies per year, there will be approximately 10,000 cases of alcohol-induced congenital heart defects ," the study authors write. "Continued study of the mechanisms involved in the development of alcohol-induced cardiac birth defects is warranted in order to implement effective treatments and/or prevention strategies."

**More information:** ajpheart.physiology.org/conten … /ajpheart.00600.2013

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