

# Folic Acid Cut Congenital Heart Defects Risk

BY BRUCE JANCIN  
Denver Bureau

NEW ORLEANS — Periconceptual folic acid supplementation appears to reduce by close to 20% the overall risk of congenital heart defects, a case-control study conducted in the Netherlands has shown.

This finding has important public health implications in light of the enormous number of babies born with congenital heart defects each year worldwide, Dr. Ingrid van Beynum said at the annual scientific sessions of the American Heart Association.

Indeed, congenital heart defects are the most common form of all birth defects. In the United States alone, 40,000

**Mothers who took periconceptual folic acid supplements reduced the risk of congenital heart defects in their babies by a highly significant 18%.**

affected babies are born each year. Periconceptual folic acid supplementation at 400 mcg/day is already recommended for the prevention of neural tube defects, but surveys indicate many women do not follow this guidance. The added benefit of a reduced risk of congenital heart defects might be more persuasive, she said.

Consumption of folic acid-fortified foods typically gets a mother only one-

quarter of the way to the recommended periconceptual 400 mcg/day, noted Dr. van Beynum of Radboud University Nijmegen (the Netherlands) Medical Centre.

She presented an analysis of a decade's worth of data from EUROCAT (European Surveillance of Congenital Anomalies), a comprehensive birth defects registry covering three Northern Dutch provinces.

In 1995, the year before the study period began, the Dutch government launched a major media campaign encouraging women to take 400 mcg/day folic acid starting 4 weeks before conception and to continue the supplements until 8 weeks afterward.

The cases comprised 611 mothers who gave birth to babies with isolated or complex heart defects unrelated to either a genetic abnormality or a syndrome; 2,401 mothers who gave birth to infants with noncardiac congenital malformations and a known chromosomal defect served as controls.

Diabetic mothers, those who had used folate antagonists, and mothers of babies with neural tube defects, limb reduction, hypospadias, or oral cleft palate were excluded from both groups in the analysis.

Of the Dutch mothers included in the study, 62% were regular users of folic



**A ventricular septal defect is shown with myocardial motion imaging. Such defects were 31% less frequent in women who took periconceptual folic acid supplements.**

acid supplements periconceptually; 38% were not. The incidence of any congenital heart defect was 28.5% in nonusers compared with 23.2% in users, for a highly significant 18.5% relative risk reduction in the women who took folic acid supplements.

After investigators adjusted in a multivariate model for potential confounders including the baby's year of birth, maternal age, smoking and alcohol consumption during pregnancy, and maternal body mass index and education level, the estimated relative risk reduction associated with maternal periconceptual folic acid supplements remained at 18%, owing to the fact that

the prevalence of potential confounders in cases and controls was similar.

There was a particularly impressive 38% reduction in the adjusted risk of isolated septal heart defects in the folic acid group. Ventricular septal defects—the most common type of congenital heart defects—were reduced by 31%, while isolated atrial septal defects were decreased by 46%.

There were no significant differences between folic acid supplement users and nonusers in the incidence of right- or left-sided outflow obstruction or complex heart defects.

However, the 23% relative reduction in the risk of conotruncal heart defects

among folic acid users might well have achieved statistical significance with a larger patient sample size, according to Dr. van Beynum.

Although a randomized, placebo-controlled, clinical trial is acknowledged to be the highest form of scientific evidence, a definitive randomized trial of periconceptual folic acid supplementation for the prevention of congenital heart defects would be ethically impossible because of the treatment's established effectiveness in preventing neural tube defects.

Data from EUROCAT and other comprehensive registries will have to do, she noted. ■

## Sudden Death Risk in Congenital Heart Disease a Mystery

BY MITCHEL L. ZOLER  
Philadelphia Bureau

TORONTO — Experts are looking for the best way to assess the risk for sudden death in adults with congenital heart disease.

Adults with congenital heart disease face a threat from sudden cardiac death that is far higher than that of the general population, with a mortality risk of 0.9 events per 1,000 patients per year in patients who are younger than age 20 years. But as of now, there is no good way to distinguish patients with the highest risk from those congenital heart disease patients who have a substantially lower risk.

"No single hemodynamic or electrophysiologic risk factor appears to be sufficiently predictive," Dr. Louise Harris said at the 14th World Congress on Heart Disease. About a quarter of the deaths that occur in adults with congenital heart disease are sudden cardiac deaths.

Researchers may eventually develop a scoring system that takes into account several risk factors, she said. Recent findings have established that patients with

congenital heart disease may have abnormalities in several organ systems, and risk assessment needs to take all these variables into account. Renal function, for example, is impaired in a significant percentage of patients with congenital heart disease, and was linked with an increased risk for death (Circulation 2008;117:2320-8).

"Sudden cardiac death is not one physiologic entity, but a manifestation of a number of disorders," said Dr. Harris, a cardiologist in the congenital cardiac center for adults at Toronto General Hospital.

The risk for sudden cardiac death is highest in patients who survived any of four types of congenital heart diseases: tetralogy of Fallot, transposition of the great arteries, coarctation, and aortic stenosis. Of these, the most studied have been patients treated for tetralogy of Fallot.

**'No single hemodynamic or electrophysiologic risk factor appears to be sufficiently predictive' of sudden cardiac death in congenital heart disease patients.**

Most sudden cardiac deaths in congenital heart disease survivors involve an electrophysiologic disorder, such as an arrhythmia. These can be ventricular tachycardia, ventricular fibrillation, an atrial arrhythmia, or asystole. But sudden death can also occur secondary to a vascular catastrophe, including pulmonary embolism or an aneurysm rupture. He-

modynamic abnormalities causing both mechanical and structural issues, such as acute heart failure, also cause sudden death.

In patients who survived tetralogy of Fal-

lot, a QRS duration of more than 180 msec is a reliable predictor of ventricular tachycardia and sudden death. Patients with a QRS duration this long have had a greater-than-twofold increased risk of sudden death, compared with patients who had a shorter QRS interval, said Dr. Harris at the congress, which was sponsored by the Interna-

tional Academy of Cardiology. Indicators of hemodynamic abnormalities—such as increased right ventricular dimension, decreased right ventricular function, or a left ventricular ejection fraction of less than 40%—boost the risk for sudden death when they are coincident with prolonged QRS in patients who had tetralogy of Fallot.

In addition, inducible sustained monomorphic or polymorphic ventricular tachycardia during an electrophysiology study predicted sudden death with a sensitivity of 77% and specificity of 79%.

Other noninvasive electrophysiologic measures—such as a signal-average ECG, T-wave alternans, and ambulatory ECG monitoring—have been less reliable for predicting risk.

A significant limitation on risk stratification of congenital heart disease patients is that this strategy presumes that identifying a high-risk patient is to be followed by an intervention that improves the patient's outcome.

So far, there is insufficient evidence to prove that effective interventions are available to help these patients, Dr. Harris said. ■