Noninherited Risk Factors and Congenital Cardiovascular Defects: Current Knowledge


EXECUTIVE SUMMARY

Over the past decade, there have been major breakthroughs in understanding inherited causes of congenital cardiovascular defects (CCVD), including the identification of specific genetic abnormalities for some types of malformations. Relatively less information has been available on noninherited modifiable factors that may have an adverse effect on fetal heart development. However, a growing body of epidemiologic literature on this topic highlights the need for a review of the current state of knowledge on modifiable risk factors for abnormalities in cardiac development.

The Congenital Cardiac Disease subcommittee of the American Heart Association Council on Cardiovascular Disease in the Young convened a writing group to review and summarize the current state of knowledge regarding noninherited risk factors for structural cardiac anomalies. An explicit goal was to provide guidance to potential parents that could reduce the likelihood that their child would have a major cardiovascular malformation. The group focused on factors that influence cardiac development during weeks 2 through 7 of gestation and was limited to parental exposures during the first trimester of pregnancy and the 3 months before pregnancy that could result in structural abnormalities. Exposures that may cause other types of cardiac injury were not considered.

Much of the data came from well-designed case-control studies, with few prospective sources of information. However, results of the comprehensive literature review confirmed the increasing amount of information available about nongenetic influences on major cardiac anomalies. The major findings included:

1. Periconceptional intake of multivitamin supplements that contain folic acid may reduce the risk of CCVD in offspring, similar to the known risk reduction for neural tube defects that is seen with folic acid intake.
2. Some maternal illnesses, including phenylketonuria (PKU), diabetes, rubella, and other febrile illnesses, are associated with increased risk for CCVD. Risk from PKU and diabetes may be attenuated by treatment. The increasing prevalence of type 2 diabetes among women of childbearing age in recent decades makes the identification and implementation of effective prevention strategies a high priority.
3. Certain maternal therapeutic drug exposures, such as thalidomide and isotretinoin, are associated with an increased risk for CCVD. Numerous other drugs have been studied with inconclusive results.

4. Data regarding risk from maternal nontherapeutic drug exposures are inconclusive.

5. Maternal environmental exposure to organic solvents may be associated with increased risk for CCVD; data for other environmental exposures are inconclusive.

6. Data about paternal exposures are limited and inconclusive.

Caveats regarding interpretation of possible exposure-outcome relationships from case-control studies were highlighted by the authors, with an emphasis on the need for additional study. In particular, future information from the National Children’s Study may help clarify potential policy recommendations. However, recommendations to prospective parents were made and are summarized. These recommendations were based on either clear evidence or the precautionary principle that suggests reasonable prudent behavior based on the current state of knowledge. It is important to note that these recommendations were aimed at minimizing potential prenatal exposure to risk factors for congenital heart defects only and not other adverse health outcomes. Prospective parents should discuss important health behaviors that may affect a pregnancy, such as nutrition, physical activity, lifestyle, use of medications, and occupational and nonoccupational exposures, with their primary care provider or obstetrician.

**RECOMMENDATIONS TO PROSPECTIVE PARENTS BASED ON EVIDENCE AND THE PRECAUTIONARY PRINCIPLE**

Women who wish to become pregnant should:

1. take a multivitamin with folic acid daily;
2. obtain preconception and prenatal care with specific attention to detection and effective management of PKU and diabetes and vaccination for rubella;
3. discuss any medicine use with their doctor, even over-the-counter medications;
4. avoid contact with people with influenza or other febrile illnesses; and
5. avoid exposures to organic solvents.

*These are recommendations based on evidence available in the medical literature to reduce risk of offspring with a congenital heart defect only. Prospective parents should discuss other important health behaviors with their health care provider and/or obstetrician.
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