

Each year, more than 150,000 infants in America are born with serious birth defects.

But, a remarkable vitamin — consumed in daily doses equivalent to the size of George Washington's pupil on the \$1 bill — is helping reduce the three most common congenital defects: neural tube, craniofacial and heart defects.

Researchers and health-care professionals know that women of reproductive age who consume folic acid reduce the risk of giving birth to children with neural tube defects, but they don't know why.

In studies around the world, the use of folic acid by women in the earliest stages of pregnancy has been shown to reduce the occurrence of these defects by as much as 70 percent. Now, scientists are focusing on how folic acid gives this protection.

"Folic acid is a great public health victory because it's cheap, safe and effective," said Richard Finnell, Ph.D., professor and director of UNMC's Center for Human Molecular Genetics.

"But, finding the cause of these birth defects has eluded the best labs and the best minds."

Dr. Finnell's hypothesis

# THE miracle OF FOLIC ACID RESEARCH

by Karen Burbach

explores the role of folic acid in DNA synthesis. Rapidly developing cells have a high demand for folic acid because it is needed for

DNA synthesis. As a result, problems arise for the embryo when there are insufficient amounts of folic acid available. Dr. Finnell theorizes that a lack of folic acid causes some important genes not to operate optimally.

Dr. Finnell is testing his hypothesis with genetically altered mice, the first in the world developed specifically to help explain how folic acid protects against common human birth defects.

The mouse model allows researchers to explore how the movement of folic acid within cells provides protection against cleft lip and palate and against neural tube defects, which involve the brain and spinal cord.

Another UNMC investigator, using a completely different approach, has arrived at a different hypothesis about folic acid and congenital defects.

Thomas Rosenquist, Ph.D., professor and chairman of cell biology and anatomy, and director of research development, is using thousands of chicken embryos to test how such birth defects may be linked to elevated levels of homocysteine, an amino acid associated with heart disease and stroke. Research has shown that when folic acid decreases, homocysteine levels always increase.

Neural tube and related defects occur in humans when mothers have elevated levels of homocysteine,



JoAnn Frederick

and the same is true when chicken embryos are exposed to elevated levels of homocysteine, Dr. Rosenquist said. He believes that elevated homocysteine keeps the embryos from having access to an essential substance that promotes normal development.

Whether the embryo is most effected by a lack of DNA or a damaged effect of homocysteine, neural tube defects occur early — within the first six weeks of human development. "By the time a woman realizes she's pregnant it's often too late," he said.

The recommended daily allowance for folic acid for most adults is 400 micrograms. But, for women contemplating pregnancy, or for those who have had a pregnancy that resulted in a birth defect, it is better to take 4 milligrams, or 4,000 micrograms.

Folic acid is found in green leafy vegetables, orange juice, beans and breakfast cereals, as well as in all multi-vitamins. Because it is water soluble, folic acid cannot be stored in the body, so it must be taken every day.

Overall, the United States spends about \$8 billion a year on the 18 most common birth defects. Of those, neural tube, craniofacial and heart defects rank at the top. Such defects include spina bifida, cleft palate and cleft lip, and septal defects in the heart.

"If we prevent 50 to 75 percent of these we can save billions in pure medical costs, let alone family suffering," Dr. Finnell said.

Although best known for its prevention of birth defects, folic acid also plays a positive role for other conditions. It is essential for the production of red blood cells and tissue cells, normal growth, maintenance of a healthy intestinal tract, and prenatal nourishment. Since it reduces the body's levels of homocysteine, folic acid has a positive effect on cardiovascular disease and colon cancer.

"The long-term goal for my lab, as well as Dr. Finnell's and other research groups, is to see a reduction of defects in babies," Dr. Rosenquist said. "That's our motivating factor." d