

Risk of disease partially set in womb, scientists say

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Pregnant women sacrifice many of life's simple pleasures - caffeine, sushi, a glass of wine - in the hope that their baby will be born healthy. But according to a provocative new field of research, what happens during pregnancy can have lasting consequences that emerge decades after the child leaves the hospital. Studies are finding that adult illnesses like heart disease, stroke, cancer and diabetes can have roots in the mysterious months we spend in the womb.

Although genetics and [lifestyle choices](#) certainly influence an adult's risk of getting a disease, researchers now believe that the food a pregnant woman eats, her weight and fitness, her [stress level](#), and the drugs, pollutants and infections she is exposed to can trigger changes that also make her baby vulnerable to disease after birth.

For example, scientists have found that a diet containing excessive protein can suppress [fetal growth](#) and lead to adult-onset hypertension. Expectant mothers who starved during their final trimester as a result of the Dutch famine of 1944-45 were more likely to have babies who later developed [Type 2 diabetes](#). And the children of [obese mothers](#) also are at high risk of Type 2 diabetes and [metabolic syndrome](#).

"Human beings break down the same reason cars break down; they're either driven on bad roads or made badly in the first place," said David Barker, a professor of [clinical epidemiology](#) at England's University of Southampton, who in 1989 initially advanced the idea that [coronary heart disease](#) might originate in fetal life. "Some people are just strong

and some are not. Being made bad means, biologically, that you have fewer functioning units."

Experts stress that this field of study is relatively new and that the physical mechanisms that might explain the correlations between [stressors](#) in the womb and mechanical problems down the road are unclear.

It is also not lost on researchers that some pregnant women already are wracked with guilt over forgetting their prenatal vitamins or eating hot dogs instead of broccoli.

"I feel like a walking bomb," said Chicago's Amy Elstein, 28, who is five months pregnant and fears that her stress levels are affecting her baby. "It's like my body is not my own. Everything I put into it - what I eat, what I breathe - I worry that will have an effect on my child."

"Pregnancy feels like a period in your life when you want very badly to do the right thing, but you don't have control of what's going to happen, so women look for areas they can control," said Dr. Ann Borders, an assistant professor of obstetrics and gynecology at Northwestern University. "We're trying to help women be aware of unhealthy stresses but not freak out that they're hurting baby for long term."

The current advice for pregnant women still stands: Eat nutritious foods, exercise, reduce stress and avoid smoking and drinking.

But Barker and other scientists in the field want to step up prenatal care radically because they believe the diets of girls and young women are determining the health of the next generation.

Eventually, this area of research "will make a huge impact on not just what we tell women during pregnancy, but what our children's health will

be," said Alan Guttmacher, director of the National Institute of Child Health and Human Development.

It was once widely assumed that, aside from cigarette smoke, drugs and excessive alcohol, the uterus, or womb, sheltered the fetus from environmental influences. Scientists also thought that the growing fetus could siphon off necessary nutrients from a mother like a parasite to ensure its survival.

Two decades of research into the fetal origins of disease, however, have challenged both assumptions and led to a revolutionary shift into the thinking about health and development.

According to Barker's widely accepted fetal origins theory, also referred to as the developmental origins of health and disease, stressors in the womb can permanently change a fetus's body structure, physiology and metabolism. Those changes then can lead to a higher risk of illness in the future.

Though some research looks at the effects of environmental exposures and psychological stress, much attention centers on nutrient deprivation, which occurs when the mother isn't getting amino acids, glucose and lipids to the developing baby quickly enough to meet its growing needs.

For example, most pancreatic beta cells - they produce the insulin that regulates blood sugar - are produced during fetal life, said Dr. Susan Ozanne, a British Heart Foundation senior fellow at the University of Cambridge. If the environment in the womb is suboptimal, as when a mother isn't getting enough protein to the fetus, the baby can wind up with fewer beta cells.

"This causes us problems later on, particularly if we place high demands on our body to produce insulin by becoming obese or eating high-sugar

diets. Then we don't have enough beta cells to produce the amount of insulin we need," Ozanne said.

Nourishing a fetus, however, involves more than just eating the right foods. A woman's body composition also can affect how well her placenta transfers nutrients to the fetus.

"Different types of women provide different levels of access to her nutrients," said Kent Thornburg, director of the Heart Research Center at Oregon Health and Science University. "Thin mothers with low amounts of muscle are less able to handle protein than more muscular women, for example. Women who carry large amounts of fat are in a constant state of mild inflammation, which affects the formation and function of the placenta."

Fetal programming may work in at least two ways. One is that nutrient deprivation may simply stunt the growth of organs or tissue.

If a fetus can't get enough nutrients, scientists believe, it adapts by diverting sustenance to organs crucial for survival, such as the brain and heart. That can compromise other organs, such as the kidneys, lungs and pancreas, leaving the developing baby more vulnerable to illness down the road.

"The idea of the human baby as an efficient extraction of nutrients from mother is completely wrong," said Barker, also a professor of medicine at Oregon Health and Science University. Muscle growth also can be sacrificed, as an undernourished fetus will try to maintain levels of blood glucose by making its muscles resistant to the effects of insulin. This thrifty handling of sugar turns into a liability after birth, when sugar from freely available food floods the blood and obesity can make the body even more resistant to insulin, which leads to diabetes.

The other proposed mechanism is epigenetics, a process by which stressors modify the body's DNA in ways that affect the functioning of key genes.

Ozanne and her colleagues at Cambridge found that rat pups whose mothers ate a low-protein diet during pregnancy had low levels of activity of a gene called HNF4. That "leads to a reduction in the number of pancreatic beta cells that develop in the fetus, making them less able to produce sufficient levels of insulin in adulthood," Ozanne said.

Fetal exposure to the stress hormone cortisol appears to trigger both processes.

The placenta normally shields a fetus from exposure to cortisol, but if a mother is chronically stressed - constantly in fight-or-flight mode - it can't produce enough enzymes to do the job. If the fetus is exposed, Thornburg said, cortisol not only slows growth in most organs, "it also modifies genes through epigenetic mechanisms to make them lose their protective functions."

Chicago's Sara Strother, 30, who is due in December, said she keeps her stress levels down with yoga and avoids pesticides, plastic containers, cigarette smoke, alcohol, chemicals found in commercial cleaning products, airplanes (because of radiation exposure), even people with negative attitudes.

"You name it, I am paranoid," Strother said during a recent Mother Me childbirth education class at Sweet Pea's Studio in Chicago.

Early in Strother's pregnancy, she bought a juicer and binged on carrot juice. She then panicked after reading that high doses of vitamin A could be harmful. Her midwife eased her concerns: Carrots are OK. High doses of vitamin A supplements may not be.

Elstein, a recruiter, said she also tries to be careful about what she eats, drinks and inhales. She holds her breath around buses and moved out of the house for two days when a room was painted. "I'm so scared something will go wrong and I will blame myself, so I cope by trying to control what I can to ease my concerns."

Eventually, she talked to a therapist who reminded her that many people have babies in less than ideal circumstances and things work out.

"That's what I try to remind myself when I get nervous or scared," she said. "The cells are dividing and there's nothing I can do to stop this train from leaving the station."

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