





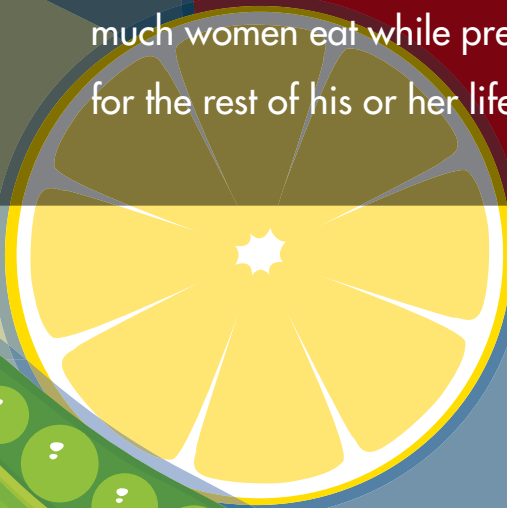
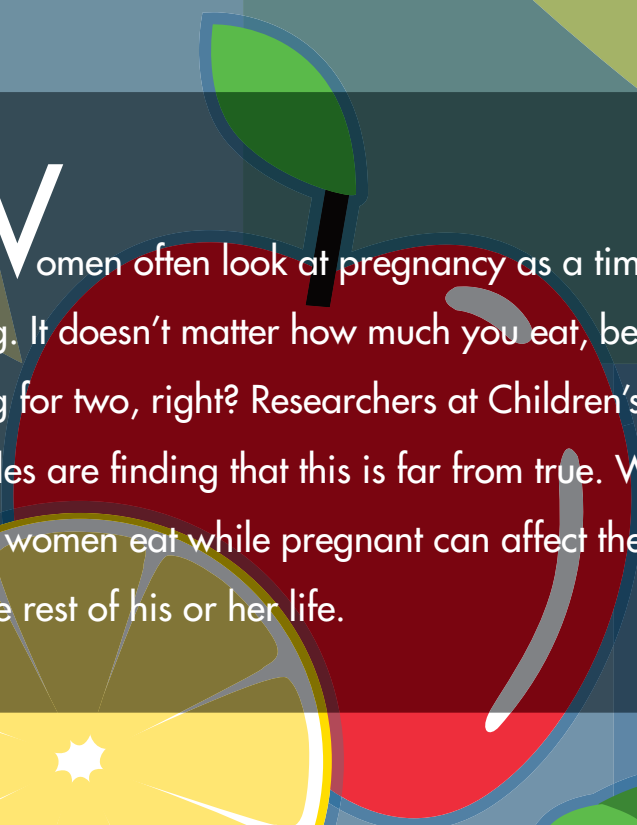




BORN TO BE OBESE

How perinatal nutrition can lead to lifelong risk of obesity and diabetes



Women often look at pregnancy as a time for guilt-free eating. It doesn't matter how much you eat, because you're eating for two, right? Researchers at Children's Hospital Los Angeles are finding that this is far from true. What and how much women eat while pregnant can affect their child's health for the rest of his or her life.

Childhood obesity is an alarming trend. Recent statistics estimate that 22 million children under the age of 5 are overweight worldwide. And epidemiological evidence confirms that obesity and other diseases can have their underpinnings in a mother's diet during pregnancy.

Data go all the way back to a famine in the Netherlands during World War II—studies have shown that children born during the famine had higher rates of obesity, diabetes and other health problems. Researchers at The Saban Research Institute of Children's Hospital Los Angeles are exploring the reasons for this connection.

"We've known for decades that the brain is very important to regulating appetite," says Sebastien G. Bouret, PhD, who is studying the role of perinatal hormones and nutrition in lifelong appetite regulation. "In addition, the human body evolved to promote weight gain to protect us from environmental challenges like famine.

"We have found that obesity risk is greatly influenced by two factors: the nutritional and hormonal conditions of the mother during pregnancy, and the nutritional and hormonal conditions of the infant—with both malnutrition and over-nutrition increasing a child's risk."

The hormone leptin, derived from fat cells, is key to this process. Findings from Bouret's lab indicate that the majority of neurons in the hypothalamus, a part of the brain that plays a role in eating and body weight regulation, develop during mid-gestation under the influence of leptin. Alterations in the intrauterine environment like maternal obesity may have long-term and potentially irreversible consequences on the number of cells comprising the hypothalamus during a period in development when this part of the brain is especially vulnerable.

Bouret, an assistant professor of Pediatrics at the Keck School of Medicine of the University of Southern California, was awarded a four-year, \$1.68 million grant from the National Institutes of Health and the National Institute of Diabetes and Digestive and Kidney Diseases to support his lab's research. His most recent discovery indicates that ghrelin, a hormone produced by the stomach, also plays a major role in brain growth.

"Timing is everything," Bouret says. "Ghrelin initiates hunger, and leptin controls satiation. We've discovered that ghrelin, like leptin, also acts very early in life to affect other processes, such as brain development. While leptin promotes growth of the hypothalamus, ghrelin seems to tell it when to stop."

His research may provide new insight into how prenatal nutrition leads to obesity and diabetes in children, as well as point to new treatments for these disorders. Bouret stresses that based on these discoveries, early intervention is the key. "Many key physiological processes, including appetite regulation, are established during the perinatal period—that time just prior to and soon after birth—affecting a child's entire life. By managing an optimal metabolic environment in pregnant mothers and children, we may promote a lifetime of metabolic health."

"These studies are providing new ways for us to impact the obesity epidemic," says Richard B. Simerly, PhD, deputy director of The Saban Research Institute and director of the Institute's Neuroscience Program. "By understanding the effects of too little or too much nutrition during pregnancy and early infancy, we have an opportunity to intercede and prevent a lifetime of serious health problems resulting from childhood obesity."



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