



## NUTRITION & YOUR CHILD

### MATERNAL NUTRITION BEFORE PREGNANCY LEAVES PERMANENT MARKS ON CHILD'S GENOME

Over 10 years ago a landmark mouse study showed that a mother's diet before and during pregnancy can change her offspring's coat color by affecting the establishment of epigenetic marks on the genome. It has remained unknown, however, whether such effects also occur in humans. Now, by studying naturally-occurring seasonal differences in the diet and nutritional status of women in rural Gambia, a team of researchers at the USDA/ARS Children's Nutrition Research Center at Baylor College of Medicine and at the London School of Hygiene & Tropical Medicine and Medical Research Council Unit in The Gambia, found that mothers' nutrition around the time of conception causes epigenetic changes in their offspring that result in permanent systemic effects. A report on their research appears in the journal *Nature Communications*.

Previous research has shown that seasonal changes, during the rainy and dry seasons in rural Gambia, affect maternal nutritional status, causing infants born during the food-scarce rainy season to weigh less than those born during the dry season. In the current breakthrough, researchers showed that these seasonal variations also cause permanent changes to the child's epigenome, which regulates how a person's genes function.

The research focuses on special regions of the human genome called metastable epialleles. At these regions, DNA methylation (an epigenetic mark that controls gene expression) is established in the early embryo and then maintained in various tissues during fetal development and for the rest of life. Researchers previously found in rural Africans that the season in which conception occurs is associated with DNA methylation at metastable epialleles, but it was unclear exactly how this happened.

To further investigate, a team led by Dr. Branwen Hennig at the London School of Hygiene & Tropical Medicine and Dr. Robert Waterland at Baylor conducted this prospective study to determine specifically whether maternal nutrition around the time of conception affects establishment of DNA methylation at these genomic regions in offspring, and whether these effects indeed occur systemically.

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### REVISIONS TO DIETARY REFERENCE FOR CALORIC INTAKE IN PRESCHOOLERS

Dietary reference intakes are recommendations for nutrient intakes that include energy, protein, carbohydrate, and fat as well as vitamins and minerals. In the case of energy (i.e., calories), the recommendations aim to balance energy expenditure at a level of physical activity consistent with health and to support adequate growth in children. Based on new data in children between 3 and 5 years of age, researchers at the USDA/ARS Children's Nutrition Research Center at Baylor College of Medicine suggest lower dietary reference intakes for energy in preschool aged children. The report appeared recently in *The American Journal of Clinical Nutrition*.

Dr. Nancy Butte, professor of pediatrics at Baylor and first author of the paper, and colleagues published new data from 97 healthy, normal weight preschool aged children who completed a protocol that entailed the doubly labeled water method, wearing accelerometers, which measure physical activity, and heart-rate monitoring devices. The doubly labeled water method uses a stable isotope that tracks the end products of metabolism—carbon dioxide and water. Study participants drink a special type of water which is enriched with two isotopes, and participants go about their normal routine for 10 to 14 days and collect their urine samples once a day. The urine is analyzed for the two isotopes. By calculating carbon dioxide production, researchers are able to estimate total energy expenditure over a two-week period. Based on this information researchers can determine how many calories the individual needs to eat. Consequently, the doubly labeled water method has been used to develop dietary reference intakes for energy.

The dietary reference intake equation for energy uses gender, height and weight and requires input of the study participants' activity level— sedentary, low active, active or very active. The use of activity monitors, step counters or heart rate monitors may assist in the assignment of physical activity levels.

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# EXPERTS PROVIDE INPUT ON EFFECTIVENESS OF EXERGAMES



Exergames, or fitness video games, are becoming increasingly popular among children and adults, but how much they contribute to increasing physical activity is still uncertain. Dr. Tom Baranowski, professor of pediatrics at the USDA/ARS Children's Nutrition Research Center at Baylor College of Medicine and editor-in-chief of *Games for Health Journal*, recently published three articles in the journal identifying key components that need to be explored to make these video games more effective in increasing physical activity in children.

These articles highlight several important ideas. First, Baranowski and colleagues identified what developers of exergames could do to enhance their ability to increase physical activity. They identified several key components:

- **Sensors** – Monitor physical activity during game via sensors placed on the child during play to be sure children are being active while playing the games
- **Fun** – Identify what makes an activity fun and explore how this could be used to enhance physical activity in games
- **Values** – Because people tend to engage in behaviors that are congruent with their values, research needs to be done on what children value and how exergames could be positioned to increase those values
- **Persuasive messaging** – Providing tailored, individualized messages within the games that restate the values that are provided by the player
- **Story** – Use a story to explain how characters overcome barriers to being physically active and thus teach children to overcome their own barriers to being physically active
- **Goal setting** – Provide opportunities to set and achieve goals
- **Feedback mechanisms** – How to provide feedback in exergames is not well known and more research needs to be done in this area

In a round table discussion, Baranowski and colleagues next discussed the benefits of games having different levels of play that often get progressively more difficult. Baranowski notes that the idea behind levels in a game is a concept of flow—what keeps people involved in a game is that they want to face a challenge that they are competent to face. If the game is too easy, players are bored and if it's too hard, players are frustrated. People need an activity that presents them with a challenge at their level of competence, said Baranowski. However, in some cases, levels are critical, but there are times when they are not. It depends on what you are trying to achieve. Baranowski concludes that "levels are just one tool in the game developers' toolbox and should be used when levels of increasing difficulty make sense from an educational or behavior change perspective."

Lastly, Baranowski highlights the difficulty in comparing new video games presented in journal articles, "Some authors present certain aspects of games and others present other aspects," he said. "It makes it impossible to do comparisons of games."

As a result, he identifies several key game components and aspects of video game that should be reported in an article about every new game so that future research will have the data needed to compare videogames across various areas of study.

With these three papers, Baranowski identifies several areas that can help further development and evaluation of games for health.

"We're very early in the use of video games for promoting health behaviors. Lots of interesting things have been done, but not all studies show a benefit. We need to explore how we can enhance these games," said Baranowski.

Support this research came from the USDA/Agricultural Research Service (cooperative agreement 58-6250-0-008).

Houston-area residents are invited to participate in the following nutrition research projects designed to help CNRC scientists learn more about the nutritional needs of children. Free parking is provided. For most studies, financial compensation is provided and transportation may be available.

## FOR MORE INFORMATION, CONTACT

Marilyn Navarrete at 713.798.7002 or rilynn@bcm.edu.

## VOLUNTEERS

### Seeds

Help researchers learn about children's eating experiences by participating in healthy eating classes and eating activities with other families. All moms will be compensated for their time each testing day. The classes will be held in the following zip codes: 77004 and 77039. Please call Sandra Lopez at 713-798-6779 or Andrea Jaramillo at 713-798-6747 for more information.

### Type 1 Diabetes Study

Adults ages 18 to 50 who have been diagnosed with type 1 diabetes for more than a year are needed for a study that will evaluate the usefulness of a mini-glucagon dose for treatment of low blood sugar. To qualify, your diabetes must be well controlled and you must be on an insulin infusion pump. Study involves blood tests. For more information call 713-798-7003 or 713-798-7002.

### Games for Health **NEW!**

Children 10 to 12 years old are needed for a six-month study to understand how to help them eat healthier and be more physically active. Must play two "Games for Health" video games and provide three blood samples. Sign up at [www.g4hstudy.org/s3/Eligibility](http://www.g4hstudy.org/s3/Eligibility). Watch game trailers at <https://www.youtube.com/watch?v=K89f7lqFJ-w> and [https://www.youtube.com/watch?v=3e2z0L\\_bpZM](https://www.youtube.com/watch?v=3e2z0L_bpZM).

### Cardiovascular Study

13- to 18-year-old adolescents and young adults (normal weight and overweight) with and without type 2 diabetes are needed for a research study investigating risk for heart disease in youth. Study involves body composition, heart scan and blood tests.

### Fatty Liver

11- to 21-year-old overweight adolescents and young adults with and without liver disease are needed for a research study investigating risk for early heart disease in youth. Study involves body composition, liver scan and blood tests.

### Pregnancy & Child Health

Did you have a pregnancy complicated by preeclampsia or a baby with low birth weight? Can a complicated pregnancy in mom put the child at risk for future health problems? To answer this question, we are conducting a research study that looks at pregnancy history and its effect on the child's health. 8- to 11-year-old children of both eclamptic and non-preeclamptic pregnancies are needed as well as 8 to 17 year olds of pregnancies with high blood pressure. Study involves body composition and blood tests.

# LESSONS LEARNED AT CNRC HAVE GLOBAL IMPACT

A healthcare professional in Thailand who has been a leader in promoting breast feeding and other nutrition initiatives says she gained valuable knowledge from the USDA/ARS Children's Nutrition Research Center at Baylor College of Medicine.

Now the director of the Queen Sirikit National Institute of Child Health in Bangkok, Thailand, Dr. Siraporn Sawasdivorn, visited the CNRC about two decades ago as part of Emory University's Hubert H. Humphrey Fellowship.

"Participation in the Humphrey Fellowship significantly strengthened my professional skills and my health management practices," she said. "Additional growth as a health practitioner and planner was made possible by professional visits to the National Institutes of Health and the CNRC, where breastfeeding and child nutrition were among the topics shared."

The fellowship, including her three-month long visit to the CNRC, served to broaden her view of community nutrition and helped her gain insight on how to move health issues to policy and the importance of health social marketing.

Since completing the fellowship, she has made significant strides in promoting the health benefits of breastfeeding in Thailand. She was named the first general secretary of the Breastfeeding Center in Thailand in 2002, and has served in her current role since 2007. She launched a collaboration with the royal family to promote breastfeeding, working closely with the Crown Prince's wife to support these efforts.

She has promoted breastfeeding-friendly hospitals, adding a program to promote breastfeeding among the staff of the National Institute of Child Health so that they can set the example for others, and has developed marketing and educational materials, including a textbook on the practical management of breastfeeding.

She also has focused efforts on the importance of breastfeeding for sick babies, organizing a three-day conference that included seminars on breastfeeding promotion, how human milk helps sick babies, maximizing milk supply for mothers of sick infants, breastfeeding support for moms of hospitalized babies and optimizing breastfeeding for late preterm babies.

Researchers and leaders at the CNRC are committed to promoting children's nutrition not just at home but internationally.

"In the 35 year history of the CNRC, our faculty have worked on research and policy activities internationally in dozens of countries, and we will continue to share our research expertise worldwide," said Dr. Dennis Bier, director of the CNRC.

The study required measuring maternal nutritional status very early in pregnancy—potentially before the women even knew they were pregnant. To do so, more than 2,000 women of childbearing age were enrolled from 34 villages in rural West Africa. They were visited monthly for one year and asked to indicate when they had their last menstrual cycle. At the first indication of a missed cycle, a blood sample was taken to confirm pregnancy and to measure 13 blood biomarkers of maternal nutritional status.

At the same time, 30 women of childbearing age across three of the same villages were visited monthly and had their food intake measured and provided blood samples for biomarker assessment. Seasonal patterns of nutritional status in this 'indicator group' were used to extrapolate the values for the main group back to the actual time of conception.

Researchers followed the main group of women after childbirth and took blood samples along with hair follicle DNA samples from the infants at around 6 months of age. They found that babies who were conceived in the rainy season had higher DNA methylation at six metastable epialleles. Remarkably, a nearly identical effect was found in both peripheral blood and hair follicle DNA.

"This suggests all the cells in these kids' bodies have the same markers associated with their season of conception," said Waterland.

Of all of the biomarkers they measured, researchers found that maternal homocysteine and cysteine concentrations in their blood around the time of conception were the strongest predictors of their infants' DNA methylation at these metastable epialleles.

"These were found to be the best biomarkers for predicting the nutritional influence on the baby's methylation. In both cases, the effect was negative. Higher homocysteine and cysteine predicted lower methylation in the kids," said Waterland. "So this very clearly answers the question, was it nutrition? Yes, maternal nutrition at the time of conception absolutely is affecting DNA methylation at these metastable epialleles in the children and that's apparently affecting all the cells in their body. These early nutritional effects on the human epigenome are almost certainly happening all over the world."

"Our ongoing research is yielding strong indications that the methylation process can be disrupted by nutrient deficiencies and that this can lead to disease. Our ultimate goal is to define an optimal diet for mothers-to-be that would prevent defects in the methylation process. Preconceptional folic acid is already used to prevent defects in embryos. Now our research is pointing toward the need for a 'cocktail' of nutrients, which could come from the diet or from supplements if necessary," said Andrew Prentice, professor of international nutrition at the London School of Hygiene & Tropical Medicine and head of the MRC International Nutrition Group.

Others who took part in the study include Paula Dominguez-Salas, Sophie E. Moore, Sharon E. Cox, Anthony J. Fulford, and Matt Silver of the London School of Hygiene & Tropical Medicine; Eleonora Laritsky, Maria S. Baker, and Yongtao Guan of Baylor and the CNRC; Andrew W. Bergen and Gary E. Swan of SRI International; Roger A. Dyer and Sheila M. Innis of the University of British Columbia; and Steven H. Zeisel of the University of North Carolina at Chapel Hill.

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## DIETARY REFERENCE CONTINUED FROM PAGE 1

"The two basic determinants of your energy requirements are your body size and level of physical activity," said Butte.

When researchers measured total energy expenditure in preschoolers and compared them to the equations in the current recommendations, they saw that the current recommendations overestimate energy expenditure of preschoolers.

Based on these data, they generated four new equations for the four activity levels that are more appropriate for preschoolers.

Butte notes that the existing equations can overestimate the energy needs of preschool children by as much as 50 percent, which could lead to overconsumption of calories and the development of obesity.

"We're hopeful that people who are working with preschool aged children will use these new equations," said Butte. The dietary reference intakes are used for feeding children in institutional settings such as hospitals or early childcare centers.

Others who took part in the study include William W. Wong, Theresa A. Wilson, Anne L. Adolph, Maurice R. Puyau of Baylor and the CNRC and Issa F. Zakeri of Drexel University.

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