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All in Good Time

Amid ever-changing advice about when to introduce allergenic foods to babies, CHILD Study research sends a clear signal

Wait a year before introducing peanuts to your allergy-prone baby. Better yet, wait three years. Avoid eating eggs while you're breastfeeding. No, eggs are fine. But definitely keep your baby away from dairy. Introduce some foods early yet breastfeed exclusively for six months. Confused yet? Imagine the turmoil for new parents trying to protect their babies from developing food allergies.

Dr. Malcolm Sears, Professor
McMaster University

Until recently, parents were instructed to hold off on feeding certain foods to babies at risk of food allergies: peanuts, tree nuts, milk, eggs and soy were all on the list of foods to avoid until well after baby's first birthday. Today, parents are told the opposite: get babies eating these foods ASAP. What happened? Why such a dramatic shift in thinking?

In a nutshell: better research. After years of study, scientists now have a clearer understanding about the best time to introduce potentially allergenic foods to infants—and waiting is not the answer.

A 2017 study led by Dr. Malcolm Sears, a respirologist and professor of medicine at McMaster University in Hamilton, Ontario, is one of several large studies to reach this conclusion. The research involved a national team of investigators participating in AllerGen's CHILD Study—a major Canadian research effort involving nearly 3,500 Canadian children and their families across four provinces. Concerned about the rise in allergies to peanuts and other common foods, Dr. Sears and his team set out to gain insight into "which pattern of food exposure in early childhood was the least likely to lead to allergy."

Using data from more than 2,100 CHILD Study infants and their parents, the team analyzed information about the babies' diets at three, six, 12, 18 and 24 months of age. They paid particular attention to the age at which parents introduced peanut, egg white, and cow's milk products such as yogurt, cheese and ice cream.

The researchers then grouped the children into three categories based on the baby's age of first exposure to these test foods: early (before six months of age), usual (between seven and 12 months of age), and delayed (after 12 months of age).

When the babies were seen at age one year, they were tested for sensitization to cow's milk, egg white, and peanut. "Sensitization means you react to a skin allergy test, which isn't the same as having symptoms of allergy," notes Dr. Sears. "However, sensitization can be an early sign of a future problem and a substantial number of sensitized children do go on to develop an allergic disorder."

The researchers looked for connections between the timing of the exposure to these foods and the babies' skin test results. The analyses left little doubt: delaying the introduction of any one of these foods beyond the first year of life significantly raised the odds of sensitization to that food. How significantly? "Infants who avoided cow's milk products in the first year of life were nearly *four times* as likely to be sensitized to cow's milk at age one," says Dr. Sears. "That's huge!" Delaying the introduction of eggs and peanuts until after the baby's first year *nearly doubled* the risk of sensitization to those foods at age one.

After controlling for other factors that could also affect allergy risk, such as ethnicity, breastfeeding status or whether a mother had allergies herself, the findings remained conclusive. "We were pleased that the results were so clear—it wasn't just a case of maybe, possibly, or could be," says Dr. Sears, though he is quick to add: "However, this was an observational study, not a clinical trial, so we cannot claim 'cause and effect.' Nonetheless, we believe our results strongly indicate that when

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In the CHILD Study, 76% of parents introduced egg to their infants at seven to 12 months of age, while only 3% did so before six months. With peanut, only 1% of parents ventured an exposure before six months and 63% avoided feeding peanut entirely during their babies' first year.

it comes to timing the introduction of these foods, earlier is better."

The early introduction of eggs—before one year—seemed to be especially beneficial: exposure to eggs significantly reduced the odds of developing sensitization to any of the three foods tested, according to Dr. Sears.

Dr. Sears notes that the majority of food allergies are related to the immune protein immunoglobulin E (IgE). When a food allergy occurs, the body's immune system triggers cells to release IgE to neutralize the food allergen, resulting in allergic symptoms. "We think that early exposure to allergenic foods may help babies become tolerant to these foods, so that they do not produce excess IgE, which in turn reduces sensitization," he says.

Taking a LEAP forward

The CHILD Study's results bolster the growing body of research that has reached similar conclusions. In 2015, the United Kingdom's landmark LEAP (Learning Early About Peanut Allergy) study found that introducing peanuts early in life to allergy-prone infants decreased their likelihood of having a peanut allergy at age five by more than 80%.

Studies of farm animals and dust mites have further challenged the misperception that exposing young children to allergens promotes allergic reactions. If anything, "these studies showed that introducing children early to these allergens protects them, rather than increasing their risk," says Dr. Sears.

Such discoveries have led researchers to speculate that peanut avoidance is actually fuelling the spike in peanut

allergy. "It's possible that the more we avoid it, the worse the epidemic," says Dr. Sears. "Introducing peanuts earlier could give us a chance of turning things around. In Israel, babies start eating peanut-containing foods very early, and peanut allergy is virtually unknown there."

Which raises the question: why did it take so long to discover the advantage of early exposure? As Dr. Sears sees it, the avoidance strategy made intuitive sense to both doctors and parents. "Previously, it was thought that waiting to introduce peanut allowed the gut and immune systems to mature and would help prevent allergies, so it's understandable that parents might be anxious about introducing foods to an infant when there's a risk that the child might be allergic."

Previous recommendations calling for delayed food introduction rested on limited evidence and targeted at-risk infants only. Nonetheless, the practice of avoidance took hold in the general population over time. In the CHILD Study, 76% of parents introduced egg to their infants at seven to 12 months of age, while only 3% did so before six months. With peanut, only 1% of parents ventured an exposure before six months and 63% avoided feeding peanut entirely during their babies' first year.

This is why Dr. Sears views the scientific method as paramount. "You challenge ideas and accepted practice by rigorously studying them until you can either confirm or refute them," he says. "Our results and other recent studies have demonstrated, with little remaining doubt, that introducing potentially allergenic foods early is the way to go."

The bigger picture

The study's findings were published in *Pediatric Allergy and Immunology (PAI)* in 2017, though Dr. Sears began thinking about this line of investigation as early as 2002. Then in 2008, AllerGen and the Canadian Institutes for Health Research (CIHR) awarded a $12 million grant to launch the CHILD Study, with Dr. Sears as its Founding Director.

"CHILD is a longitudinal study, meaning health data are gathered regularly on the same infants as they grow and develop over many years," he explains. "This means we can examine a wide range of health problems, see what factors are associated with them, and better understand how these problems develop over time. We already knew that food allergy was a driver of asthma, so it made sense to use CHILD data to look at factors that could affect the risk of food allergy, such as the timing of first exposure."

In step with the collaborative mindset championed by AllerGen, the *PAI* article lists 11 researchers as co-authors, including the CHILD Study's current Director and co-Director, Dr. Padmaja Subbarao (The Hospital for Sick Children) and Dr. Stuart Turvey (The University of British Columbia), respectively.

The paper's lead author, Maxwell Tran, is an AllerGen trainee and medical student who worked in Dr. Sears' lab while still an undergraduate student in McMaster University's Bachelor of Health Sciences program. Tran spotted Dr. Sears' study in a research directory. "I reached out to his lab, one thing led to another, and before long I was his summer student," an opportunity made possible by AllerGen's *Undergraduate Summer Studentship* program.

Tran also had a very personal interest in Dr. Sears' work. "Growing up, I had pretty severe asthma and food allergies," he says. As background work for the research leading to the *PAI* findings, Tran did a thorough review of the existing research literature, where he found "a lot of controversy about when to introduce potentially allergenic foods to children. This confirmed that there was a clear need for studies like this one."

More work to be done

As often happens with research discoveries, these CHILD findings have raised many new questions related to the optimal timing of first exposure: Is five months of age better than six months to introduce allergenic foods? Is four months even better? How does early introduction fit with recommendations to breastfeed exclusively for six months? Is early introduction recommended for children who have a parent or sibling with a food allergy? Dr. Sears and the CHILD researchers intend to explore such questions in new analyses using an even larger subset of the CHILD Study participants.

There's also work to do on the public education front. To this end, Dr. Sears, Maxwell Tran, and their team are working to get the word out to the wider clinical community—and to parents directly. In 2017, Tran wrote a short AllerGen Research*SKETCH* lay summary to make the team's findings accessible to a broad Canadian audience.

In line with the evidence supporting early introduction of foods, newer feeding guidelines recommend "breastfeeding exclusively for four months, then continuing to breastfeed while starting to introduce allergenic substances at four to five months," says Dr. Sears. But while the message is clear—early is better—Dr. Sears understands that parents and caregivers may take time to adopt the new guidelines. "That's why it will be important for family doctors, pediatricians and allergists to speak in a unified and reassuring voice. We hope our study will help them do that."