Ilsa Buchholz doesn’t remember much about all the tests and procedures she underwent during her last visit to the clinic at the Children’s Hospital Research Institute of Manitoba.

After all, the nine-year-old was only five at the time, so her memory is a little hazy.

Nonetheless, she does have a pretty good idea of what to expect during her visit to the clinic today - her fifth visit to the health centre since she was born.

For example, she knows that she and her mom will have to fill out a lot of paperwork to answer various lifestyle questions, including how much time she spends in congested environments like traffic jams. And she also knows the clinic team will want to check her body fat by using a caliper to measure skin folds on her arms and back.

Less familiar are the myriad other tests she will undergo today. Among other things, the clinic team will measure her height and weight, and check the circumference of her waist. They will also take a blood sample, check her blood pressure, and give her a DXA scan to determine the density of her bones.

Then there’s the skin test, which involves gently pricking her arm to determine sensitivities to eggs, nuts and other common allergens. Eventually, her nasal passages will be swabbed and the secretions collected will be placed in a vial.

She will even undergo a breathing test - called “spirometry” - that measures lung function by testing how fast and how much air can be blown out of the lungs.

That’s a lot of testing for a little kid, but Ilsa doesn’t mind.

That’s because she knows the work being done here today is part of a very special initiative known as Canadian Healthy Infant Longitudinal Development (CHILD) Cohort Study. And she also knows the knowledge gained through this project is helping to improve the health of children just like her right across the country, and even around the world.
"I think that is very cool," says Ilsa.

Launched in 2008, the CHILD cohort study was designed to enable many different scientific investigations to be carried out over time as part of one major initiative.

The project involves collecting data on the health of 3,500 kids, as well as their moms and dads, from across the country for the first eight years of their lives. Scientists then tap into the data to gain new insights into a variety of health issues, including asthma, allergies and other diseases that emerge in early childhood.

The initiative - the largest undertaking of its kind in Canada, and one of the largest in the world - involves scientists in Toronto, Hamilton, Edmonton and Vancouver. Manitoba is playing a major role in the project. About 1,000 kids from this province are enrolled in the study, and local researchers are leading several branches of investigation.

Among them is Meghan Azad, a biochemist, epidemiologist and Canada Research Chair in Developmental Origins of Disease at the University of Manitoba. She co-leads the Manitoba site with Dr. Allan Becker, a pediatric allergist and professor in the Department of Pediatrics and Child Health in the Rady Faculty of Health Sciences at the University of Manitoba.

Azad's research focuses on how environmental exposures in early childhood - in addition to genetics - may lead to the development of asthma, allergies and even obesity.

For her and the many other scientists and medical doctors involved in the research, CHILD represents an unprecedented wellspring of data about children's health, starting in the womb and continuing through the early years of life.

As Azad explains, scientists the world over have recently become very interested in something called the "exposome," a term used to describe all the environmental exposures a person may experience in a lifetime and how they may impact a person's health.

Even before birth, children are exposed to many aspects of the world around them, and once born, they are quickly immersed in a soup of bacteria, chemicals and pollutants, says Azad, who is also an assistant professor in the Departments of Pediatrics & Child Health and Community Health Sciences in the Rady Faculty of Health Sciences at the University of Manitoba.

At its heart, CHILD is an investigation into the interplay between environment and genetics in the development of good health or allergies, asthma and other diseases that may emerge early, possibly even in utero, and lead to lifelong health consequences.

"Chronic diseases like asthma, diabetes and heart disease have a huge burden on society and human health, and we're learning more and more that they may have their origins very early in life, perhaps even before birth," Azad says. "So the hope is that by starting during pregnancy and following children as they grow, we can capture the necessary information to learn about those early origins of health," she says.

Becker concurs. As he explains, CHILD resulted from the recognition that asthma has reached epidemic proportion over the last few decades, especially in high-income countries.

"It was generally agreed that asthma is a gene-associated, environment driven chronic disease, and genes simply don't change that quickly," says Becker. "Therefore, the rise of asthma has to relate to environmental changes that must have begun in the last quarter of the 20th century."

In order to examine those changes, scientists needed a large birth cohort.

"The key in developing such a cohort was to ensure that all the relevant expertise was 'on board,' and our initial cadre of 40 clinicians and researchers provided the impetus for development of the cohort," says Becker.
Over the years, the health data collected through CHILD has yielded a number of important discoveries that have challenged long-held beliefs and changed the way doctors approach certain health-care issues.

Azad and her colleagues, for example, have produced important studies on breastfeeding and the microbiome, which is a term used to describe the bacteria living in our gut.

In fact, a study produced by Azad and her colleagues on gut microbiota (bacteria living in the intestinal tract) and its relationship with mode of delivery (vaginal versus C-section) and infant diet became one of the most widely read papers in the Canadian Medical Association Journal when it was published more than five years ago.

Through their work, the CHILD research team found that the microbiome of babies born by C-section was not as diverse as those of babies born vaginally.

"As babies slip through the vaginal canal, which is full of normal, healthy bacteria, they receive their first dose of microbes, which is missed with a C-section," Azad explains.

This is important because gut microbes help train the immune system. As a result, C-section babies who are lacking a "normal" microbiome may develop a faulty immune system, leading to asthma and/or allergies. In both cases, these conditions arise when the immune system overreacts when exposed to things like pollen or peanuts, misidentifying them as health threats that need to be eradicated.

But the team's work didn't end there. They also looked at how infants were breastfed and for how long.

After examining the feces in dirty diapers, among other tests, they discovered that children who were born by C-section and breastfed experienced a quicker "recovery" of their gut microbiomes. Azad thinks this is because breast milk provides a source of beneficial bacteria along with other compounds that support a healthy microbiome.

"Initially, when we published that paper, we could see that the babies' microbiomes were different, and then the bigger question becomes, 'Does that matter in terms of getting allergies and asthma later?" she says. "Now that they're turning eight years old, we can actually see who gets asthma, for example, and who does not."

The discoveries to date are already providing hearty food for thought for expectant and new moms as well as health-care providers. For example, parents and doctors are now thinking more carefully about opting for C-section as an elective procedure. Additionally, new moms now have more information about the importance of breastfeeding, especially if they did give birth by C-section, Azad says.

Like all good research, one finding leads to more questions, so Azad's work soon led to further research into the chemistry of breast milk.

"The more I learn about breast milk, the more amazing I think it is."

Her team has zeroed in on compounds called human milk oligosaccharides (HMOs).

"These are complex sugar molecules that don't get digested by the baby."

Many researchers were uninterested in these compounds because they served no nutritional purpose for babies. But Azad finds them fascinating because, while babies do not directly benefit from HMOs, their gut bacteria - critical to healthy immunity and digestion - do. Simply put, HMOs are dinner for the microbiome.

"We think those [HMOs] are probably important for helping develop the baby's gut microbiome, so we have linked up with Dr. Lars Bode, a world expert in HMOs, to measure them in the CHILD cohort," she says. "We're also..."
measuring other components in breast milk - including hormones like insulin, and fatty acids."

Azad and her team of doctoral, graduate, post-doctoral and undergraduate researchers are not alone in carrying out important work. Other CHILD research teams have also made important discoveries.

For example, a team led by Dr. Stuart Turvey and Dr. Brett Finlay at the University of British Columbia looked into the impact of antibacterial agents like antibiotics on childhood development and the potential for increased incidence of asthma and allergies.

Author of the bestselling book Let Them Eat Dirt: Saving Our Children from an Oversanitized World, Finlay hypothesized that exposure to these agents could be a key factor in the rise of allergy rates during the last few decades. (According to the United States-based Centers for Disease Control and Prevention, the prevalence of childhood food allergies has increased by 50 per cent between 1997 and 2011. CDC statistics also show that the number of people with asthma increased by 28 per cent between 2001 and 2011.)

To that end, research from the CHILD Cohort Study identified four gut bacteria critical in decreasing asthma risk in children. CHILD findings also suggest that the growing use of antibacterial agents - cleaning products included - may be killing off the good germs along with the bad.

“We still recognize that genetics are important, because allergies and asthma do tend to run in families,” says Azad. Indeed, children are more likely to develop these afflictions if their parents have them. "But there are lots of kids showing up with allergies who have no genetic history of the condition.”

Genetics haven't changed, she explains. "What has changed is our environment. We are using sanitizers everywhere, and more antibiotics. Allergies and asthma have become an epidemic that we're trying to figure out."

Closer to home, a Manitoba research team led by Kent HayGlass, Canada Research Chair in Immune Regulation, has made important discoveries regarding the immunity of healthy pregnant women.

“A lot is known about diseases of pregnancy - pre-eclampsia and gestational diabetes, for example,” says HayGlass, who is also a professor in the Department of Immunology at the University of Manitoba’s Rady Faculty of Health Sciences.

Much less research has focused on healthy moms having healthy babies - the usual outcome of pregnancy. Studies looking at the immune system in uncomplicated pregnancies are even more uncommon. So his team's work involved following 250 mothers from CHILD during pregnancy and for three years after giving birth.

Among the questions they sought to answer was whether a mother's immune system changed during a typical healthy pregnancy. For some time, researchers were at odds over whether a mother’s immune system was weakened during pregnancy to avoid rejecting the baby (but leaving the mother more vulnerable to infection), or whether it ramped up its protection of mother and baby, and increased the risk of the immune system attacking the genetically different fetus.

The research team found that a pregnant woman's immune system became more tolerant during day-to-day gestation, making more anti-inflammatory, and fewer pro-inflammatory, molecules. However, when they studied the response of immune cells that were stimulated with different bacteria and viruses, pregnant women were much more aggressive in combating infection. Thus, these women were more tolerant while healthy, but when exposed to infection they reacted more aggressively than when they were not pregnant. Thus, healthy pregnancy is a state of "higher innate immune attentiveness."

In other words, during pregnancy the immune system is both accepting of the fetus and more aggressive in guarding against various types of infection - a development that protects both mother and child against potential illness.
Research also revealed that these changes in a pregnant woman's immune system are temporary, returning to normal about one year after birth.

So far, the CHILD initiative has yielded more than a dozen key discoveries that are shedding new light on early childhood health issues. Here is a partial list of findings based on summaries from the CHILD website at www.childstudy.ca:

- Researchers at the University of Alberta found that children of women who consumed more fresh fruit during pregnancy enjoyed better outcomes for cognitive mental development early in life.

- A joint study between the University of Alberta and the University of Manitoba, involving Azad, found that infants with fewer gut bacteria at three months of age had an increased risk of sensitivity to milk, eggs and peanuts at age one, which is considered a risk factor for allergies later in life.

- A research team led by Azad discovered that children of women who consumed artificial sweeteners during pregnancy had a higher risk for early childhood obesity.

- Researchers at McMaster University in Hamilton found that infants who experienced a delay in the introduction of certain allergenic foods such as peanuts, eggs and milk had a higher risk of sensitivity to those foods at 12 months of age. That study supported the findings of a study done in the United Kingdom that suggested children introduced to peanuts earlier in life had much less risk of developing a peanut allergy. It's also worth noting that the CHILD research did not just apply to those with a genetic risk for peanut allergies, which was the focus of the study that came out of England, but to all young children.

- Azad's research team at the University of Manitoba found that babies who are breastfed longer have a lower risk for asthma later in life. The protective effect is even more pronounced for children of women who have asthma.

- Researchers at the University of Alberta found that children living in a home with a cat or dog have less risk of childhood allergies and obesity. They found that babies exposed to furry pets also had certain bacteria that may protect them against obesity and allergies.

[A summary of all CHILD cohort study research discoveries can be found here.]

The heart of CHILD is the study participants. Without their commitment to the study, this research simply would not be possible. Participants like Ilsa, and their families, are the reason the study continues to be successful.

While the list of discoveries is already extensive, there's more to come as researchers gather information and conduct experiments from the latest round of medical examinations, and make that data available to researchers around the world.

For example, researchers are hopeful they will find answers to long-standing questions like: Why do some children outgrow their allergies while others have them for life? They are also looking for links between early exposures and health problems that may occur later in development.

But exploring these connections is also dependent on financial support. CHILD has been funded for the last 10 years by the Canadian Institutes of Health Research and the Allergy, Genes, and Environment (AllerGen) network. Now, it needs additional support to keep the research going.

Currently, CHILD only has funding for the latest round of medical exams for participants at eight years of age. Like the other CHILD scientists, Azad would like to see ongoing financial support. "My hope is to get funding so we can continue following these kids well into their adult years," Azad says.

Certainly, the discoveries made so far bolster the argument for continuing this highly influential study. The findings have provided expecting parents with the information they need to make more informed decisions during pregnancy and the early years of a child's life. And they also show that investments in research can give health-care providers the information they need to help prevent various diseases and conditions.

"There is a lot of focus in medicine on the development of new treatments and cures, which is important, but ideally, we'd rather prevent diseases in the first place," says Azad. "To do that, we need to know how they get started, and that's what CHILD is allowing us to do."

Joel Schlesinger is a Winnipeg writer.