

Findings may offer new clues to development of heart disease

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Robyn McGregor with daughters Janet Love and Cathy McGregor (left to right).

Credit: University of Auckland

Aucklander Cathy McGregor grew up knowing she was "some kind of a miracle baby". When her mother, Robyn, was pregnant with her, her specialist had told her not to expect a live baby. Robyn had been diagnosed with rhesus disease, in which antibodies in the mother's blood attack her baby's red blood cells, causing potentially fatal fetal anaemia. Robyn had the highest recorded level of antibodies at that time, in 1977.

Her specialist was pioneering New Zealand doctor, Sir William Liley, of National Women's Hospital in Auckland. Fourteen years earlier, working with the Liggins Institute's namesake, Sir Graham (Mont) Liggins, Liley had developed a procedure to transfuse healthy [red blood cells](#) into anaemic babies through the mother's abdominal wall. He performed the first ever successful human blood transfusion before birth in the world. Within a few years, the technique – radical for its time – halved the number of stillbirths due to fetal anaemia.

So it was that Cathy McGregor received four blood transfusions while in her mother's womb, five more when she was a newborn and another two in her first year of life, surviving her eight-weeks-premature birth to become a healthy child and adult. Now 39, she's a fit, energetic mother-of-two involved in three family businesses.

Today, results from a study she participated in could offer fresh clues to how certain experiences before or just after birth, such as anaemia, might influence a person's risk of developing [heart disease](#) later in life.

The study, which involved almost 100 New Zealanders like Cathy who had life-saving blood transfusions for anaemia before birth, has found differences in their adult hearts and blood vessels.

Researchers at the Liggins Institute, based at the University of Auckland, were intrigued by animal evidence that fetal anaemia and transfusions led to changes in heart structure in adulthood. Wanting to find out if the same was true in humans, they combed medical records of births from 1963-1992, and set about tracking down the first people in the world who'd received transfusions in utero for this condition – sometimes with only the mother's name and child's date of birth to go on.

"The mothers were crucial to making this study work", says researcher Dr Alexandra Wallace, a research fellow at the Liggins Institute and paediatrician at Waikato Hospital. "Some had had a number of babies who died and then they had a baby who received a transfusion and survived. They were so immensely grateful to Liley."

Of the 228 adult survivors the researchers identified, 95 were able to participate, and had a brother or sister unaffected by fetal anaemia who could take part with them. All study participants underwent heart-related blood tests, and an MRI scan to determine the size and shape of the heart, and the function of important blood vessels. The sibling comparison minimised the impact of genetic and lifestyle factors known to influence [heart disease risk](#).

Overall, there was no difference in the incidence of heart disease between affected and unaffected siblings, which didn't surprise the researchers - the affected adults were aged between 18 and 47 years at the time of the study, younger than the age at which heart disease usually appears.

But they did find differences in heart structure. Survivors of fetal anaemia had smaller hearts and thicker-walled main heart chambers. They also had lower levels of HDL cholesterol – the "good" cholesterol which helps protect from heart disease. Also, there were signs the inner lining of their [blood vessels](#) was working differently.

"We can't say whether the changes we saw will result in increased rates of heart disease when these people get older," says Dr Wallace.

"They might have more heart disease as a group, or earlier onset of heart disease, or there may be no difference – their bodies might have managed to cope with and adapt to these differences."

Researchers plan a follow-up study on the same participants when they're older.

No differences were detected in other heart disease risk factors including body size, blood pressure, glucose tolerance, smoking, alcohol use, and exercise participation.

Based on these findings, people who had fetal anaemia and blood transfusions shouldn't panic, Dr Wallace says. "The best thing to do is to maintain a healthy lifestyle and have routine monitoring of your heart health through your family doctor."

Because the affected adults all had both fetal anaemia and transfusions, it's impossible to say from this study which one led to changes to their hearts. "But anaemia is the likely culprit because of the stress this places on the developing heart," says Dr Wallace.

Cathy McGregor says she was excited about participating in the study – "I was actually thinking of it as a free 'warrant of fitness' for myself!" Her big sister, Janet Love, joined as her sibling comparison – "Janet was a really good sport," McGregor adds.

About one in seven couples possess the genetic make-up to have a child with rhesus disease. Because the mother's antibodies deplete the baby's oxygen-carrying red blood cells, the baby's heart must work much harder to pump oxygen around the body. Without treatment, the heart may fail

before the baby is born.

Often the firstborn isn't affected, but the disease becomes increasingly severe with every baby after. (Robyn McGregor had previously given birth to three children, but her fourth pregnancy ended in miscarriage; Cathy was the result of her fifth pregnancy.)

Dr Wallace: "It's remarkable that Liley had the courage to do what he did. It's made such a huge difference to so many babies and families around the world."

Today, it's possible to prevent rhesus disease in most cases by giving at-risk mothers antibody injections during pregnancy. But a small number still receive blood transfusions before birth for fetal anaemia in New Zealand.

And the study findings may also be relevant for preterm babies, as most develop anaemia in the first few weeks after birth, and some are treated with blood transfusions. It's known that babies who are born small, either because they are born preterm or had poor fetal growth, have an increased risk of coronary heart disease and other chronic diseases in adulthood.

"If people who had fetal anaemia have differences in their hearts, it's quite possible that those born preterm who experienced anaemia have similar differences," says Distinguished Professor Jane Harding from the Liggins Institute, a preeminent New Zealand paediatrician who led the research team.

"Currently, there is no single, agreed degree of severity of anaemia at which doctors treat preterm babies with transfusions. Our findings suggest that this might be important not only in the short term, but to optimise their heart development for life."

More information: Alexandra H Wallace et al. Long-term cardiovascular outcome following fetal anaemia and intrauterine transfusion: a cohort study, *Archives of Disease in Childhood* (2016). DOI: [10.1136/archdischild-2016-310984](https://doi.org/10.1136/archdischild-2016-310984)

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