HUDSON
INSTITUTE OF MEDICAL RESEARCH

SUMMER 2021

HUDSON **NEWS**

Hudson Institute of
Medical Research
27–31 Wright Street
Clayton VIC 3168
Australia

t: + 61 3 8572 2700
e: info@hudson.org.au
w: hudson.org.au

Please support our Infant and Children's Health Appeal

Director's message

Professor Elizabeth Hartland

Welcome to *Hudson News* Summer 2021

As we move into the festive season, I am deeply conscious that this can be a sad and difficult time for many people, following a year of continued unpredictability and challenge. From all of us at the Institute, we hope you continue to take care of yourselves and your loved ones and find time to enjoy the upcoming holidays.

In this festive issue of *Hudson News* we officially launch our **Infant and Children's Health Appeal** and share our groundbreaking research into inflammation that can occur in the early days and years of a child's life. Professor Marcel Nold and Associate Professor Claudia Nold are solving the biggest inflammatory challenges facing pre-term babies like baby Jack (opposite and page 4), while Professor Suzanne Miller (page 8) has identified a new anti-inflammatory treatment to give babies starved of oxygen at birth a better chance at life. While in our Cancer theme, Hudson Institute researchers have identified promising new therapeutic targets, providing new hope to the families of children with cancer, like Lachy (pages 6 and 7).

Inflammation contributes to more than half of all deaths worldwide, as well as widespread illness and disability. As the world's biggest killer, inflammation underpins hundreds of health issues across the human lifespan including cancer, pneumonia, endometriosis and infertility, infectious diseases, COVID-19, and numerous conditions facing newborn babies and infants.

The potential of medical innovation targeting the body's inflammation response is immense. Controlling the 'inflammation cascade' – a chain reaction that leads to severe, chronic inflammation – could help us tackle half of all human illness and disease.

Hudson Institute is home to Australia's largest group of inflammation scientists. Their focus is to find treatments that can be translated into best practice healthcare.

Cover - Isabelle and Lachy, story pages 6 and 7

Since the pandemic began, Hudson Institute has been part of the global fight against severe COVID-19 inflammation. Our scientists advise on how the immune system drives life-threatening inflammation during COVID-19 and provide clarity around which treatments are likely to work. Hudson Institute's COVID-19 global impact continues with our industry partner, Noxopharm, to test the properties of its approved cancer drug, Veyonda, which is now moving from safety trials into larger random controlled clinical trials to determine whether it could potentially halt the fatal inflammation caused by COVID-19.

The pandemic has highlighted a lack of critical infrastructure, including high-containment facilities, to fight infectious disease outbreaks. So, we are pursuing plans to establish a **National Centre for Inflammation Research (NCIR)** – a world-class hub focusing on acute inflammation (such as COVID-19 acute respiratory distress) as well as many other chronic inflammatory conditions.

For the people who depend on our research, like Carly and Ryan and Dani and Darren who you'll meet in the pages that follow, our science brings hope for new treatments and a better future.

However, it is only with your support that our scientists can solve the biggest health challenges facing our smallest and youngest patients. We hope you are inspired to give generously to our Infant and Children's Health Appeal, so together we can bring smiles to the faces of families who need it most.

We remain as grateful as ever for the unwavering support of our community, especially in the difficult environment in which we all find ourselves.

With gratitude

Professor Elizabeth Hartland
Director and CEO

In this issue

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Clayton VIC 3168

Tackling inflammation to save our tiniest patients

For premature babies, surviving birth is often the first of many challenges. Researchers are targeting inflammation, which underpins some of the most devastating illnesses affecting premature newborns.

Born too soon, these babies face a massive battle for survival outside the protection of their mothers' bodies. Without the vital time needed to develop, their tiny organs must cope with the demands of life outside the womb before they are ready, making them susceptible to fatal diseases. Those who survive often face a lifetime of health challenges.

Hudson Institute scientists are shedding light on how life-threatening inflammatory conditions develop in premature babies and, using their new knowledge, working on promising new anti-inflammatory approaches to improve the function and health of the lung, brain, immune and coagulation systems.

Groundbreaking research by Associate Professor Claudia Nold (Hudson Institute) and Professor Marcel Nold (Professor of Paediatric Immunology, Monash University's Department of Paediatrics; Hudson Institute; and Neonatologist at Monash Newborn, Monash Children's Hospital) is targeting two of the biggest inflammatory challenges facing preterm babies – BPD and NEC.

Continued pages 4 and 5

Preterm facts

- **One in 10** Australian babies is born premature.
- Globally, around **15 million** babies are born preterm each year and one million die as a result of preterm birth complications.

Dani and Darren holding baby Jack

PRETERM BIRTH

Baby Jack's story

The decision to start a family was an easy one for Darren and Dani. After six great years together, they knew they were ready for parenthood.

"It was the best news when Dani fell pregnant," says Darren, "Everything was going really well, we were blissfully looking forward to a November birth but that all changed in July."

"It was Saturday evening, I was watching TV and Dani came in around 11 pm and said she was bleeding," Darren recalls.

"We called the midwife and went to Wonthaggi Hospital and discovered that Dani was three centimetres dilated. It's fair to say, we were in a bit of shock."

Bubs is coming

Dani was rushed by ambulance to Monash Health in Melbourne, almost two hours away, at one o'clock on Sunday morning.

Baby Jack was born at just 24 weeks and weighing only 777 grams. Thankfully, it looked promising with Jack arriving above the expected weight for that age and breathing on his own.

One step forward

During his first two months, little Jack endured several setbacks, including having to be put on a ventilator when seizures prevented his breathing.

"He started to get better with the support of the team looking after him at Monash Health Newborn, but then he had a second seizure. We still aren't sure what is causing the seizures to happen," says Dani.

Continued page 4

Continued...

"It really turned our whole world upside down," says Dani. "There are good days, but it is often one step forward and two steps back. We know the potential risk of BPD and cerebral palsy. It's an emotional rollercoaster.

"We had some beautiful cuddles last week, but Jack is still on the ventilator. There is still a long way to go – we wait, and we hope. Today, we are just happy that Jack is breathing.

"There are lot of unknowns with premature babies. You keep wondering what else scientists can find out to help other parents. Great research will reduce the stress that parents have to go through.

> "We are obviously in the right place and miracles can happen. We are staying positive. Hopefully Jack will be OK and we can take him home."

Professor Marcel Nold is one of the neonatologists looking after Jack. The aim of research conducted by the team he leads with A/Prof Claudia Nold is to find new treatments that will give babies like Jack a better start to life.

On the wards, we experience the immense burden premature birth and its consequences place on the babies and their families every day," he says.

"Our tiny patients often need our care for several months, and a baby like Jack finally going home is for us and the family one of the brightest and most hopeful moments we all work towards. However, that joy is not rarely tempered when we look back at the family's long and hard journey, and also a time when we look forward, because we know things will not be a breeze from here either.

> "My team and I want to make a real difference to the lives of families such as Jack, Dani and Darren, by developing new treatments for severe early life disease and making sure these treatments become available to the young patients."

NEC – a deadly gut disease

Necrotising enterocolitis (NEC) is a disease of the premature gut and the most common cause of death due to gastrointestinal health issues in infants.

NEC triggers massive inflammation, causing parts of the small and/or large intestines to die. Widespread infection and multi-organ failure often ensue. It is a looming spectre that strikes unpredictably in preterm babies.

Diagnosis is difficult and there is no drug available to prevent or treat NEC. Around a third of babies with NEC require intestinal surgery, and up to two thirds of these don't survive. For babies who make it, NEC can also have long-term impacts on development, including on the gut and the brain.

Discovery hope

NEC research led by the Nolds offers fresh hope. Their discoveries have shed new light on how NEC develops and, as a result, identified new and existing drugs to treat the condition.

"Despite decades of research, NEC remains a major challenge in the neonatal intensive care unit because of its insidious onset, rapid progression, and the absence of an effective therapy," Prof Nold says.

"By the time we know a baby has NEC, the infant is often already in a critical condition with sepsis (widespread bacterial infection) and sometimes life-threatening multi-organ failure. This renders neonatologists powerless to treat or prevent what still is for many babies a deadly disease, and for survivors a severely disabling condition," he says.

Shielding therapy

The Nolds have discovered that an anti-inflammatory protein, IL-37, is lower in babies with NEC and when IL-37 is given as a supplement in preclinical models, it protects against NEC.

"Our data suggests that supplementing babies who have, or are at risk of developing NEC, with an IL-37 therapeutic or another drug that acts in a similar way, may prevent or treat the condition," Prof Nold says.

"Absolutely, IL-37 could provide our tiniest patients with a much-needed therapy to shield them from NEC."

Next steps

The Nolds are collaborating with academic and industry partners to solve the complex challenges a new drug faces on its path to becoming available to patients.

NEC facts

- NEC affects between one and three in **1000** live births.
- Up to **a third** of babies with NEC die – a number that has changed little over the past 50 years.
- NEC is one of the most common causes of death in premature babies between days **15 and 60** of life.
- Of NEC-afflicted infants, **15–30 per cent** need surgery – and up to two thirds of these babies don't survive.

L–R: Prof Marcel Nold and A/Prof Claudia Nold

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BPD – a devastating lung disease

The most common chronic illness in premature babies, affecting almost one in three, is the chronic inflammatory lung condition, bronchopulmonary dysplasia (BPD). Of all the conditions they could face, this is the one that's most likely to cause long-term health problems including respiratory issues, learning difficulties, impaired brain development and cerebral palsy.

BPD has no cure, and it causes considerable suffering for premature infants and their families.

"If we can lessen the burden of this significant complication, everyone stands to gain from it," says A/Prof Nold.

"As a mum myself, nothing in science would give me greater pleasure than to help other families by easing or even eliminating the burden of chronic diseases such as BPD."

What causes BPD?

Babies who are born preterm are often placed on essential and life-saving respiratory support to get crucial oxygen to the heart and all other organs. Sadly, because of this life-saving care, up to 60 per cent of the babies develop BPD soon after birth. BPD is caused by severe injury to the lung tissue and prevents normal lung growth.

"BPD is a devastating disease, and these babies often suffer lifelong conditions. When we tackle lung disease, the risk of developing many other problems is also reduced," says A/Prof Nold.

Combination therapy

Knowing that inflammation is a key driver of BPD, the team has discovered a safe and effective anti-inflammatory treatment that could save preterm babies.

Their discovery has shown that the natural protein IL-1Ra, which the body uses to curb excessive inflammation, is effective in preventing BPD.

"In preclinical timing and dosing studies, we determined that IL-1Ra works best to prevent the development of BPD when it was given immediately after birth, before chronic inflammation can establish itself, and at a lower, rather than higher dosage," A/Prof Nold says.

"We are hopeful that IL-1Ra could be a safe prevention strategy for at-risk premature infants. This is the first step towards a therapy for chronic lung disease in very vulnerable premature infants."

With no safe or effective treatment for these babies, this work provides families with new hope and a healthier lifelong outlook.

BPD facts

- Up to **60 per cent** of preterm babies will develop BPD.
- The anti-inflammatory drug IL-1Ra has been used safely by around **200,000** patients since its introduction in the early 2000s. complications.

Next step

Recruitment for a first trial of IL-1Ra in premature infants is planned for early 2022.

Have you considered what your legacy could achieve with a gift in your Will?

Leaving a gift in your Will to Hudson Institute will allow us to power new and innovative treatments and cures for this and future generations.

Our team is here to help with any queries. Please contact Connie Honaker at

t: + 61 450 524 565 | **e:** connie.honaker@hudson.org.au

Children like Lachy are benefiting from our coordinated research and clinical care programs.

Banking on better treatments for childhood cancer

Every year about 1000 young Australians are diagnosed with cancer and 5600 are undergoing treatment. Any cancer diagnosis is heart-wrenching, but for children it seems profoundly unfair.

By better understanding genetic variability in paediatric cancer patients, researchers can improve treatments, survival rates and quality of life for children with cancer.

Led by Hudson Institute of Medical Research and funded by the Children's Cancer Foundation, the Hudson-Monash Paediatric Precision Medicine Program (HMPPMP) brings together Victoria's leading childhood cancer researchers and clinicians to improve patient outcomes and train the next generation of paediatric cancer scientists and clinicians.

The program has developed a world-leading biobank – a collection of tissue samples – which allows researchers to work with real-life cancer cells. Now, using state-of-the-art functional genomic and multi-dimensional profiling technologies, the biobank is being used to develop the next generation of precision oncology treatments for paediatric cancer patients.

HMPPMP's Head of Research, Associate Professor Ron Firestein, says every child's tumour is genetically unique and responds to cancer treatment in a different way.

"This forward-thinking program has enabled scientists and clinicians to collaborate and build critical information into childhood cancer treatment pipelines," he says.

"This year, the team has identified a number of promising therapeutic targets for paediatric brain cancers and sarcomas using sophisticated genetic and drug screens."

Carly and Ryan with their children, Isabelle and Lachy

CHILDREN'S CANCER

Lachy's story

Daycare sniffles

Lachlan was a happy baby with beautiful blond wavy hair. He slept and fed well. The perfect baby.

At 18 months, Lachy developed fevers, vomiting and general tiredness. Doctors thought it was a daycare virus and he would get over it.

But when he didn't, his parents, Carly and Ryan, took him to the emergency department and he didn't leave hospital for a month.

Lachy had an 11 cm tumour in his abdomen. Within days he was diagnosed with Stage IV neuroblastoma, which had spread to his bone marrow.

Adjustment

"Diagnosis hit us like a ton of bricks. Neuroblastoma can be fatal and has a history of coming back. Cancer is bad enough, but when you hear it's a nasty one you think the worst – that you are going to lose your child," explains Ryan.

By the end of that week, Lachy had started chemo.

"It was a huge adjustment. But you've got to keep your kid happy, and you must move forward. You start the process."

Daunting treatment

Lachy's treatment plan kicked off with five rounds of chemotherapy over five months. Sadly, he lost his beautiful wavy blond hair. Then it was time for surgery to remove the tumour.

"The operation was a long 11 hours. They initially thought Lachy's kidney could be saved, but they had to take it out. That's rough," Carly says.

Next came a stem cell transplant using Lachy's cleaned cells to grow bone marrow.

"We knew this was the scary treatment, when things could go bad, because it wiped Lachy's immune system. He was in hospital isolation for his month-long recovery. We were his only two visitors.

"We got Lachy home just in time for Christmas; the best gift ever," says Carly.

In the New Year, Lachy went into two weeks of daily radiation therapy, which included having daily general anesthetics.

"That knocked him around. He would wake up and throw up. It was a dark time – you do your best not to think about it," says Ryan.

The final treatment was five rounds of immunotherapy. While it was less invasive, Lachlan's tiny body had to endure serious analgesics including morphine to control the pain.

Fourteen months after diagnosis, Lachy had ticked every box on his treatment plan.

"A lot of families don't get through that, so we knew that we were lucky," says Ryan.

One day at a time

Now, Lachy is one-year cancer free – and, amazingly, has grown back a full head of curly blond hair – a daily reminder of what he's lost and gained.

"Another four years and he can be officially cancer free. It's still a while to go, but we are thankful that things are going great and we're on the path to a cure. One day at a time," says Ryan.

"While Lachy is a happy healthy kid, we get incredibly nervous when it comes to our review dates. If bad news is going to come, that's the time." says Carly.

Ray of sunshine

It has been an ordeal for the whole family, including Lachy's seven-year-old sister Isabelle. "She saw things that she shouldn't, but she's an amazing young girl. It was tough on her, but she knew Lachy was sick and our focus was on him," says Ryan.

"Lachy was amazing. He would smile and get on with it. He is just such a trooper.

"All these kids with cancer, they have moments when they are really sick, but they are still kids. They have bright moments of happiness and that really makes you happy, it has a snowball effect.

"Lachy still faces challenges, some hearing loss, the loss of a kidney and some long-term stuff associated with radiation and treatment, but he's here with us, he's happy and we're on the path to being cured."

Medical research matters

Carly and Ryan are full of praise for the research that went into Lachy's treatment.

"It gives you hope, not just for your own child, but for others. It also shows in the results – when we were diagnosed it was 50/50 – we knew medical research could make that better," Ryan says.

Together we can invest in high-quality medical research that really matters for kids like Lachy.

Help us support research for safer and more effective treatments for childhood cancer, so children can be with their families.

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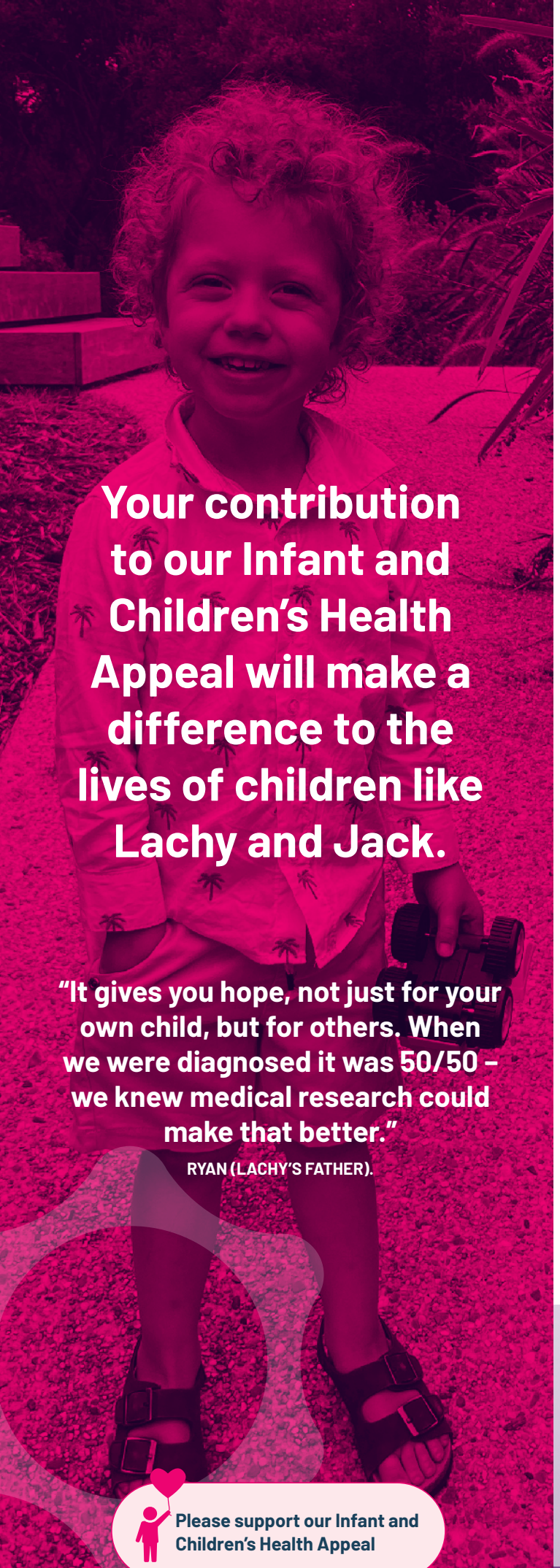

Transforming the lives of at-risk newborns

L–R: Prof Suzanne Miller and A/Prof Atul Malhotra

A naturally occurring sleep hormone could be a game-changer for protecting newborn babies from brain damage caused by oxygen deprivation at birth.

Hudson Institute is paving the way for a new treatment that could transform the way babies starved of oxygen at birth are treated worldwide.

Oxygen deprivation at childbirth, or birth asphyxia, kills one million babies globally each year. This severe lack of oxygen may go on to cause a condition known as neonatal encephalopathy (NE), causing conditions including cerebral palsy and intellectual disability.

In Australia, the current treatment for NE is therapeutic hypothermia or whole-body cooling, which slows the body down to allow it time to heal. Sadly, a quarter of these babies will die despite cooling, and another quarter will survive – but go on to live with life-long disability.

Professor Suzanne Miller and her team have spent the past decade working to understand the brain injury that occurs following birth asphyxia. Now, their work is paving the way for treatments that will transform the way babies starved of oxygen are treated at birth.

In a new pre-clinical study published in the *Journal of Pineal Research*, the team have discovered that combining hypothermia with the antioxidant melatonin provided significantly greater recovery from NE.

Prof Miller explains, "Often, we will never know the cause of the lack of oxygen to a baby, so finding an effective treatment after birth is crucial for providing babies and families with a better chance of life or life without disability."

Homing in on free radicals

Hypothermia as a treatment for NE reduces the risk of death or disability by around 30 per cent, but hypothermia alone is not sufficient. Scientists know that asphyxia at birth causes an influx of oxygen-damaging free radicals. Hudson Institute scientists are targeting those free radicals with the powerful antioxidant, melatonin.

"Melatonin has potent antioxidant and anti-inflammatory properties to fight against damaging free radicals, and here we showed that it significantly enhances brain protection of therapeutic hypothermia," Prof Miller said.

Associate Professor Atul Malhotra, study co-author and neonatologist at Monash Children's Hospital, says the results lay the foundation for a combined treatment, which has strong implications for reducing neonatal death and disability.

A/Prof Malhotra, who collaborates with colleagues in low- and middle-income countries including rural India, hopes melatonin therapy alone may be beneficial in settings where cooling is not available.

International clinical trial

With such positive pre-clinical results, Prof Miller's team is seeking funding to begin an international clinical trial, collaborating with teams in the UK and New Zealand.

What is the role of melatonin?

Asphyxia at birth causes a large influx of oxygen-damaging free radicals and inflammatory cells that wreak havoc on the brain.

While melatonin is best known for its role in driving the body's sleep and wake cycle, it is also a powerful antioxidant and anti-inflammatory and a proven safe and feasible treatment.

Melatonin helps to 're-balance' the scales and provides the body with the ability to fight against these damaging products.

Collaborators

Monash University, Monash Children's Hospital, Murdoch Children's Research Institute, University of Auckland.

Funders

NHMRC, Bill and Melinda Gates Foundation.

"Your gift today can help improve the lives of children like Lachy and Jack."

Professor Elizabeth Hartland
Director and CEO

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