

How can saliva help us diagnose and care for newborn babies?

Caring for newborn babies, particularly those born prematurely, can be a tricky business. They are unable to tell caregivers how they are feeling or if something is wrong, and it can be hard to monitor their physical progress and needs using typical medical assessments. **Dr Jill Maron** from the **Women & Infants Hospital of Rhode Island**, USA, conducts research to develop diagnostic tests that use saliva to help clinicians learn more about the health of newborn infants so that they can monitor progress, diagnose problems and provide appropriate treatment when needed.



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Research project

Using saliva to diagnose and care for newborn and premature babies

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If you've ever been around a newborn baby, you'll know how much joy they can bring into the world. However, you'll also be aware of how difficult they can be to care for. Fear, worry and frustration are emotions that will be all too familiar to anyone who has looked after a baby that, for some unknown reason, won't stop crying.

Newborn infants are completely dependent on others to meet their needs, and the situation is

 Talk like a ...

neonatal paediatrician

Diagnostics — the process of determining the causes of a patient's symptoms

Enzyme — a protein that speeds up chemical reactions in the body. For example, digestive enzymes in saliva help to break down food

Neonatal — newborn, covering the first four weeks of life

Opioid — a highly addictive drug derived from the opium poppy that is often used in pain-relief medication

Paediatrics — the branch of medicine focusing on children

Premature — babies born more than three weeks before their due date

even more delicate with premature babies, who may weigh less than 500 grams, or the weight of a typical bag of pasta. "Premature infants are considered the most vulnerable patient population in all of medicine," says Dr Jill Maron of the Women & Infants Hospital of Rhode Island. "They are often very fragile to touch, and every organ system from their lungs and their heart to their brain and kidneys are underdeveloped and at risk of damage." Newborn infants are also unable to express how they are feeling or tell someone if they feel unwell. "Doctors who take care of

this population are often compared to veterinarians because they also care for patients who cannot easily communicate," continues Jill.

A key diagnostic used in medicine is the simple blood test. Unfortunately, repeated blood testing of premature infants not only inflicts harm to these infants but may also result in the need for blood transfusions due to their limited blood supply. Fortunately, Jill has discovered that another bodily fluid, which holds much of the same information as blood, can be used instead: saliva.



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What are the advantages and challenges of using saliva in neonatal diagnostics?

“Saliva is a window into our entire body and its function,” explains Jill. “It can be collected non-invasively and repeatedly, without inflicting any harm to the infant.” Although saliva is over 99% water, it contains nearly all the components found in blood, including proteins, genes, electrolytes and drugs.

However, using saliva to diagnose newborn infants comes with other challenges. For example, babies are unable to spit into a tube as other patients would. “Instead, we collect saliva samples using suction machines (like you might find at the dentist) or through absorbent sponges,” says Jill. “Still, newborn babies can only provide a small amount of saliva, which can be difficult to analyse if it’s not processed properly.”

Once the saliva sample has been taken, the next challenge is preserving it. “The mouth is filled with degradative enzymes that can destroy many of the proteins and genes that we are interested in analysing,” explains Jill. “The mouth is also filled with bacteria that can quickly replicate and ruin a sample.” New samples are immediately placed in a stabilising solution, protecting them from degradation and bacterial overgrowth.

What can saliva tell us about the oral feeding habits of premature newborns?

“Oral feeding maturity is one of the key factors that determines how long a premature baby will need to stay in hospital, as a baby cannot go home if he

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or she is unable to feed,” says Jill. “For over a decade, I analysed neonatal saliva to better understand developmental differences between those infants who could successfully orally feed and those who could not.” Previously, it was believed that an infant’s ability to suck, swallow and breathe without the risk of choking was the most important factor influencing their ability to feed. “While this developmental reflex is essential, salivary analyses taught me that this was not the whole story,” continues Jill. “To feed successfully, a baby must have mature and integrated sensory systems including taste, vision and smell, and a maturing memory system that allows them to remember how and when to eat.”

Being able to diagnose the specific problem preventing an infant from feeding means that Jill can personalise care to each infant, something that was previously very difficult. “By analysing an infant’s saliva, we have the potential to understand what therapy an individual baby may need to improve

feeding outcomes,” says Jill. “For example, if an infant is having difficulty with sensory integration, we can encourage the mother to hold the baby more often, which can potentially impact how quickly the infant can sense touch, smell, sound and taste.”

What can saliva tell us about the feeding behaviours of opioid-exposed newborns?

Neonatal Abstinence Syndrome (NAS) occurs when a baby is born dependent on drugs that the mother used during pregnancy, and it can cause specific problems with feeding. “Some infants struggle to feed and cannot seem to coordinate the suck, swallow, breathe reflex,” explains Jill. “On the other hand, some babies suffering from NAS eat excessively, consuming a greater number of calories than babies not exposed to opioids during pregnancy.”

Jill has linked this overeating to the process of drug withdrawal. “Our brains regulate our addictive behaviours by modulating reward signalling,” she explains. “When something feels good, our brains tell us to do it again – this can lead to addiction, whether it is to drugs, gambling, food or even shopping.” One of Jill’s mentees, Dr Elizabeth Yen, used neonatal saliva to show that excessive food intake in infants with NAS is likely a dysregulation of the reward signalling pathways, whereby infants use food to mimic the positive feedback they used to feel from opioids. “It’s as if they have traded one addiction for another,” says Jill. “And all of this was discovered through neonatal saliva.”

About *neonatal paediatrics*

Multidisciplinary work is important in the field of neonatal paediatrics. "From the start of my career, I have been dependent on colleagues from different scientific disciplines to move my work forward," says Jill. "Over the years, I have partnered with dentists, neuroscientists, chemists and speech pathologists to advance my research. Without their guidance, partnership and insight, the field of neonatal salivary diagnostics would not be where it is today."

Jill values being able to split her time between direct work with patients as a physician, and research as a scientist. "My

clinical work informs my science," she says. "By caring for patients at the bedside, I can more easily recognise the areas of research that will be beneficial to improve outcomes. However, one of the challenges of becoming a physician-scientist is the need to balance both jobs. Extended training in both areas is required."

Jill believes that neonatal paediatrics is an exciting and meaningful field to work in. "Neonatology is considered one of the newest fields in all of medicine. It has only been a subspecialty for about 60 years," says Jill. "Over that time, we have seen many advancements in the clinical

care that we can provide to premature infants, with some babies born as early as 22 weeks surviving. The next generation of neonatologists will be able to not only improve survival for our youngest patients, but also improve their long-term outcomes."

"There are still so many advancements to come, so the field is wide open in terms of potential research," says Jill. "The use of artificial intelligence, new diagnostic tests and the creation of smaller clinical assessment tools will lead to more and more babies surviving and thriving."

Pathway from school to *neonatal paediatrics*

To pursue a career in neonatal paediatrics, you will need to study biology, chemistry, physics, mathematics and statistics, as these subjects are required for medical school.

In addition, subjects such as genetics and physiology will be useful. Jill says, "Neonatologists are truly at the front line of genetics, as we are often the first to diagnose an infant with a genetic syndrome. Newborn babies are also wonderful teachers of physiology, as unlike adults, they don't have longstanding issues such as type 2 diabetes or coronary artery disease. Thus, you can learn and appreciate true pathology that is not complicated by other issues."

Look for internships or summer programmes to gain knowledge and experience in neonatal paediatrics or other areas of medicine. For example, Brown University, where Jill works, offers pre-college programmes covering a range of subjects in medicine, including topics such as genetics, addiction and laboratory work. Look at the course catalogue and apply here: precollege.brown.edu/apply

Explore careers in *neonatal paediatrics*

"Getting exposed to the field early is the best advice I can offer," says Jill. "Reach out to neonatologists or other advanced neonatal care providers and inquire about opportunities to shadow them. These experiences will give you the most realistic insight into the profession. If shadowing is not an option, ask to interview them about their job."

The American Academy of Pediatrics website has a career resources section with advice on options, financial support, job hunting and career progression: www.aap.org/en

In the UK, Great Ormond Street Hospital for Children runs the Young Visitors programme, providing short work placements for 16- to 19-year-olds who are interested in working in medicine: www.gosh.nhs.uk/learning/gosh-learning-academy/outreach-and-work-experience/gosh-young-visitors-programme

Jill recommends the books *Baby ER* by Edward Humes and *Almost Home* by Dr Christine Gleason.



Meet *Jill*

I have always loved science. Reading about biology and chemistry excited me as a student. I also loved interacting with people and helping them. These traits made medicine an ideal choice for me.

It is a true gift to be able to care for families in the neonatal intensive care unit (NICU). Admission to the NICU is always scary and unexpected. Taking this journey with the families reminds me of what really matters in life. The babies have also taught me so much about resilience. My profession has given me a unique perspective on how to prioritise my personal life and goals.

Being validated as a successful physician-scientist through grant awards and high-impact publications, along with my clinical leadership positions, has been my greatest accomplishment. I feel so fortunate to have been able to have an opportunity to improve the care and outcomes for newborn babies, both at the bedside and in the laboratory.

Being able to listen, adapt, multitask and think outside the box has helped me lead a successful career. Being brave enough to not fear failure is also important.

My long-term mentor, Dr Diana Bianchi, inspired me to become a physician-scientist. Watching her provide compassionate care and conduct research with the highest scientific rigour was the inspiration for my own career.

Medicine is a lifelong career. There were times in my journey when I was focused mainly on my clinical training, and other times when I focused more on my research. Later in my career, I took on leadership and administrative roles. However, I didn't do everything all at once. Pace yourself; it's a marathon not a sprint. You can do it all over the span of your career, but don't try to do it all at the same time.

In my spare time, I love to read, exercise, play piano and travel. I also love to be with my family and play with my two golden retrievers, Oliver and George.

Jill's top tips

1. Choose your career based on your passion. Medicine is a long journey that is both rewarding and exhausting. However, any job you love is not a job at all. It's a career that will give you great fulfilment.
2. Funding opportunities for research can change. Keep an open mind about where your next project or partnership may lead you.
3. Enjoy the journey and give yourself the freedom to change your mind. You never know where you will end up, and that's the fun of it!