

## FAILURES ARE AS IMPORTANT TO KNOW AS SUCCESSSES

by Richard E. Tremblay, CEECD Director

**The title of this editorial comes from a letter written in 1847 by Charles Darwin, who probably made more observations and performed more experiments than any other scientist. However, that was not enough to satisfy a brain that craved "facts." Long before the age of Google and e-mail, he sent thousands of letters to other observers of "nature" around the globe, hoping to learn from their experiments. Knowing very well how easy it is to deceive yourself by putting too much credence in your pet ideas, he asked his correspondents to describe their failed attempts at proving their hypothesis as carefully as their successful ones.**

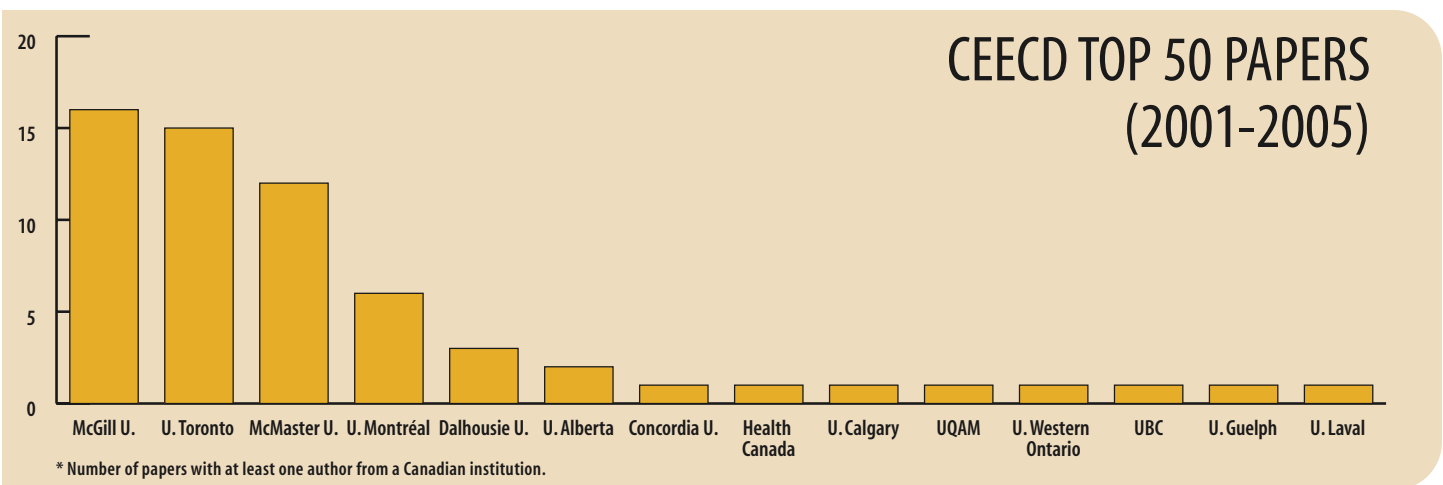
As the father of 10 children and a man with chronic health problems, Darwin was acutely aware of the importance of experiments in the field of education and health. He saw clearly that "best practices" in education and health should be the outcome of rigorous experiments. Unfortunately, these experiments were and still are extremely rare in the area of early childhood development. Still less frequent are replications of successful experiments, although they are essential so that we can find out whether the first experiment can be generalized to a different context.

Given the scarcity of such experiments, it came as quite a surprise to see that our annual Top 10 scientific articles by Canadian investigators included two experiments reporting "failures" to help parents and their children (see page 3 and page 11). The most surprising was an experiment to prevent child abuse, with a careful adaptation of a very well-known "best practice." Harriet MacMillan, who led this extremely important study, was chosen our 2005 Researcher of the Year (see page 2). The findings of this study must be taken very seriously. If this intensive "best practice" applied to abusing parents had no effect,

what are the effects of the untested interventions delivered by thousands of practitioners in the field of child abuse and neglect? The urgency of finding answers to these questions becomes even clearer when we consider that interventions have also been shown to cause harm.

This is the fifth year that we have selected 10 papers published in high-impact scientific journals by investigators who include at least one researcher working in a Canadian institution. Harriet MacMillan is our third CEECD Researcher of the Year from McMaster University (2002: Malcolm Sears; 2003: Daphne Maurer-Richard Le Grand). The other two were from McGill University: Michael Kramer (2001) and Michael Meaney (2004).

We have now chosen a total of 50 scientific papers for our annual Top 10. Each of these includes at least one author from a Canadian institution. The figure at the bottom of the page shows the distribution of authors among Canadian research institutions. For example, McGill University had at least one author on 16 of the 50 articles, the University of Toronto had 15, and McMaster University had 12. A sample of 50 over five years is probably sufficient to give a very good idea of the distribution of strength in Canadian ECD research. 🦋



# RESEARCHER UNDAUNTED BY NEGATIVE STUDY FINDINGS

by Philip Fine



DR. HARRIET MACMILLAN

*“More interventions need to be evaluated; more needs to be done to reduce the stressors on families; and support for at-risk families must be beefed up”*

**Harriet MacMillan is at a loss. The psychiatrist and pediatrician, who has successfully worked with clinical teams and written numerous papers on the subject of child maltreatment, sees that there still is no intervention proven to bring down the incidences of child physical abuse and neglect.**

She found this out the hard way. A study on nurse home visiting to families where one or more children had been exposed to child maltreatment, which MacMillan and colleagues spent years preparing, showed that parents who received visits were just as likely to re-abuse as those who had not been visited.

The news was disappointing. She expected the intervention to make a difference in lowering the rate of recurrence.

The clinician in her was especially hoping for positive results. Founding director of the Child Advocacy and Assessment Program at McMaster Children’s Hospital in Hamilton, Ontario, MacMillan wonders what she can now tell a contrite parent who arrives at her clinic. “Families ask, ‘What can we do?’ It’s hard to tell them that in some circumstances, we just don’t know.”

But MacMillan looks past disappointing results and analyzes what needs to be done in her field: “more interventions need to be evaluated; more needs to be done to reduce the stressors on families; and support for at-risk families must be beefed up,” says the principal investigator of a Canadian Institutes of Health Research team grant that is investigating the health impacts of violence across the life span.

One story stands out for her. A four-year-old boy had been referred to her after having been punched in the abdomen by his father. “He felt that he brought it on himself because he had spilled something on the

floor.” She followed the boy’s progress. Psychotherapy seemed to quell the self-blame. Living with just his mother made his home safer. When MacMillan saw him in follow-up two years later, the boy showed a marked improvement.

That case raised many questions for the researcher: Was it the psychotherapy that made a difference, or would time have healed the boy’s psychological wounds? What helps on an individual level, and what can work across the board?

And one big question remains: “Why is it that some children who are maltreated can go on to experience major difficulties in their lives, while some others don’t?”

MacMillan’s philosophy stresses stability and a safe home environment. Her desire to help children can be traced to her father, Angus MacMillan, a pediatrician who brought to the dinner table tales of unnamed patients who suffered terrible neglect. “He had a strong interest in helping disadvantaged children.” Now retired, he also felt disappointed by the results of the study. “He knows how difficult it can be to change behaviour,” she says, referring to the families whose abuse seemed to be entrenched and did not cease with an intensive program of home visits.

While she may be at a loss for the moment as to what to tell some of her families, the field of child maltreatment has certainly gained a great deal from her questions. 🦋

# NURSE VISITS FAIL TO PREVENT FURTHER CHILD ABUSE

by Philip Fine

**Is it possible to stop child maltreatment from revisiting those previously subjected to it? A recent study shows that nurse visiting programs are not as effective as anticipated in preventing the recurrence of abuse.**

**T**he study, which involved a network of public health nurses who regularly visited families with a history of abuse, showed that those who received the visits were just as likely to strike their children or abdicate their duties as families that did not receive the tailored intervention.

Harriet MacMillan, lead author of the study, says these results mean that, for children remaining in a home that is deemed high risk for recurrence of physical abuse and neglect, there is currently no intervention proven to reduce that risk.

*"This is a study that highlights how complex recurrence of physical abuse and neglect is,"* said the pediatrician and child psychiatrist at McMaster University, where the study was conducted. *"This was a very intensive program with a theoretical basis and it was not effective."*

Indeed, the study, which involved 163 families and was published last year in *The Lancet*, had years of planning behind it, with a program that saw public health nurses visiting approximately half of those families with at least one child who had suffered physical abuse or neglect. Each family in the intervention group received two years of regular visits from the practitioners, who provided them with family support, education on child development and connections to social services.

According to Susan Jack, professor in the School of Nursing at McMaster University, who is currently analyzing interviews from the study's mothers and public health

*"The earlier you get to them, the more potential there is to help families"*



nurses, the visits had seemed to be doing wonders. Mothers, by and large, appreciated the support from the nurses, who posed less of a threat than child protection workers, who had the power to take their children away. *"What mothers loved was that there was someone to listen to them. Nurses also advocated for the mothers, helping them with such things as finding housing and filling in forms for subsidized child care."* Nevertheless, the point of the study was to see whether children who had been abused were being subjected to further abuse after this intervention. According to child protection and hospital records, the intervention did not protect children from recurrence.

But the study did show something promising. Among the subgroup of families with less than three months of involvement

with the child protection agency, there was less recurrence of physical abuse for those receiving home visits compared to the control group. This was not the case for neglect.

The study shows a clear demarcation between preventing families from ever physically abusing or neglecting a child, and the greater challenge of trying to stop maltreatment that has already taken place from happening again. MacMillan and Professor Helen Thomas from the School of Nursing, had tried to take David Olds's theory of prevention further by seeing if the visits could also prevent recurrence. But entrenched abuse proves to be challenging, says MacMillan, who emphasizes the early-prevention maxim for at-risk parents: *"The earlier you get to them, the more potential there is to help families."* 🐾

Ref.: MacMillan HL, Thomas BH, Jamieson E, Walsh CA, Boyle MH, Shannon HS, Gafni A. Effectiveness of home visitation by public-health nurses in prevention of the recurrence of child physical abuse and neglect: A randomised controlled trial. *Lancet* 2005;365(9473):1786-1793.

# RESPONSIVE PARENTING MAKES ALL THE DIFFERENCE

by Alison Palkhivala

**For doubting mothers and fathers, the data are in: responsive, sensitive parenting really does matter. Mother rats that tend to their pups by licking and grooming them frequently produce adult rats that are particularly resilient to stress. In humans, this could mean that responsive, caring parenting also produces healthy, resilient offspring.**

## GOOD NURTURING IS IMPORTANT

Alain Gratton, an associate professor of medicine at McGill University, studies the long-term impact of mother rats' behaviour towards their pups, specifically with respect to the development of dopamine pathways in the prefrontal cortex of the brain, an area that plays an important role in interpreting and managing stressful situations. In human beings, this part of the brain is also known to undergo major changes throughout childhood and adolescence. Gratton and his colleagues are interested in learning about how development of the prefrontal cortex may contribute to the emergence of certain psychopathologies, such as attention deficit hyperactivity disorder (ADHD).

The investigators have found that adult male rats who were frequently nurtured by their mothers as newborns, through licking and grooming, exhibited brain development associated with resilience to stressful situations. Adult offspring of poor nurturers, on the other hand, had brain development associated with a highly emotional response to stress. *"These are generally more anxious rats,"* says Gratton.

This research may help explain why human children who receive poor maternal care appear to be more vulnerable to certain pathologies in adulthood. *"I cannot stress enough that many, many things are involved in child development,"* says Gratton. *"If a child has a difficult first few years, he*



*"All that time and effort that we put into taking care of our babies is fundamentally important"*

*might be just fine. But we do know, however, that such a history makes him more vulnerable to a whole host of psychopathologies, such as depression, drug abuse and so on."*

## PARENTING MATTERS

Megan R. Gunnar, a professor at the Institute of Child Development at the University of Minnesota, says that Gratton's research helps elucidate how parenting affects the neural systems involved in the stress response. The challenge is determining what it means to be a nurturing parent in the human world. While premature babies have been shown to respond well to simple touch and cuddling, much as baby rats benefit from licking and grooming, an older human child's needs are more complex. *"By that time, there's a well-established [parent-child] dance, so that intrusively [cuddling and touching] just won't work,"* she

says. *"It will be annoying."* The key lies in responding to babies' particular needs: cuddling them when they want cuddles, feeding them when they're hungry, or leaving them alone when they'd rather explore a new toy.

*"All that time and effort that we put into taking care of our babies is fundamentally important for helping them to establish normal, healthy patterns of brain development,"* says Gunnar. By extension, therefore, if there are *"disturbances in babies that make those relationships harder to establish, you should maybe get some help because there's a lot that can be done if you get in there early. And you shouldn't beat yourself up if everything's not working out right."* In fact, other research findings from Gratton suggest that damage done early on from a poor nurturing environment can be turned around with enriched care later in life. 🐾

Ref.: Zhang TY, Chrétien P, Meaney MJ, Gratton A. Influence of naturally occurring variations in maternal care on prepulse inhibition of acoustic startle and the medial prefrontal cortical dopamine response to stress in adult rats. *Journal of Neuroscience* 2005;25(6):1493-1502.

# TAKING “YOU ARE WHAT YOU EAT” TO THE NEXT LEVEL

by Alison Palkhivala

**While early childhood experiences can have a profound impact on later development, some of the damage done by a neglectful environment may be turned around by improving that environment later in life. It could even be as simple as optimizing your diet.**

## SUBTLE ENVIRONMENTAL CUES AFFECT GENE EXPRESSION AT ANY AGE

Moshe Szyf, professor in the Department of Pharmacology and Therapeutics, Michael Meaney, professor in the Department of Psychiatry, both at McGill University, as well as Ian Weaver, doctoral student, and their team have already shown that baby rats who receive plenty of nurturing licks and grooming from their mothers handle stressful situations later in life far better than those who receive little of this nurturing care. They also showed that this effect occurs because the mother's care actually causes neurochemical changes in the brain, and these changes affect how the rat pup's genes are expressed.

Szyf, Meaney and colleagues have now added to this research by demonstrating that injecting the amino acid methionine into the brains of adult rats can undo the effects of early nurturing care they received from their mothers. This means, says Szyf, that *“the gene expression programming that we have early in life, although highly stable, is also plastic to a certain extent. Things that happen later in life do count, and they can have implications in humans.”*

## COULD DIET AFFECT GENE EXPRESSION?

Methionine is commonly found in everyday foods, and changing the amount of methionine in the diet of humans has already been shown to affect behaviour. *“This research indicates that diet can affect you at any time, using the same mechanisms that occur in early childhood, which is the mechanism of reprogramming gene expression. ... You eat certain food, you reprogram genes in a certain*

*way, and that effect will remain long after whatever food you ate is gone,”* says Szyf.

Arturas Petronis, a research scientist at the Centre for Addiction and Mental Health and an associate professor at the University of Toronto, is an expert in epigenetics, the study of long-term change in gene expression programming that occurs without change in the gene sequence itself. He says that this research is *“revolutionary”* in that it shows for the first time that something as subtle as maternal nurturing can actually affect the body on a molecular level, having an impact on the way genes are expressed, and subsequent behaviour, for years to come.

## SCIENTIFIC SHORT CUT

An important implication of this latest study on the effects of methionine, Petronis says, is that researchers can now investigate the impact of the environment on behaviour by looking directly at the cellular changes they are known to create — a “short cut,” if you will, around complex epidemiologic studies that typically make it difficult to tease apart the effects of different components of the environment. This can dramatically simplify research into any disease — from Alzheimer's disease to cancer to schizophrenia — that arises as the result of a complex interaction between a person's genetic makeup and the environment in which the person lives.

Szyf is already conducting research with aggressive and non-aggressive children, looking for genetic markers that distinguish the two groups. If researchers can find such markers, and these markers prove to be reversible, aggressive behaviour might one day be treated with something as simple as a nutritional supplement. 🦋



*“The gene expression programming that we have early in life, although highly stable, is also plastic to a certain extent”*

Ref.: Weaver ICG, Champagne FA, Brown SE, Dymov S, Sharma S, Meaney MJ, Szyf M. Reversal of maternal programming of stress responses in adult offspring through methyl supplementation: Altering epigenetic marking later in life. *Journal of Neuroscience* 2005;25(47):11045-11054.

# WHAT DOES THAT TODDLER THINK YOU'RE THINKING?

by Philip Fine

**Kris Onishi has long wanted to know when children begin to understand that other people's thoughts are not the same as their own.**

The research literature on the subject left the McGill University professor puzzled. Experiments conducted by others in the field had come to a conclusion on the age at which this development takes place, having set up conditions where children watch someone looking in the wrong place for an object, with its location known by the child. Those researchers found that four-year-olds understood that the other person held an idea that was different from their own – but not three-year-olds.

The psychologist's intuition told her otherwise. Onishi suspected that children

three or younger are capable of knowing another person could have a different take on a situation and even recognizing that others could be mistaken – what's known in psychology as having a false belief. *"Say it's raining this morning. It stops. The child notices it's stopped raining but Mom does not. Mom grabs the umbrella."* She says the child would make sense of that action based on a false belief.

To try to demonstrate that this cognitive change begins to develop earlier, Onishi and U.S. colleague Renée Baillargeon designed an experiment that was similar to

those done on the older children, but removed the language aspect. The subjects came to the child-friendly lab and watched an actor hide a toy in a box. Then the toy would move from one box to another. The actor would sometimes be watching from a window behind the boxes, at other times closing the window and hiding her face behind it, so that the child was the only one who saw the toy go into the box. When the toy was switched without the actor knowing it, the child would know something that the actor did not.

The experiment supported her intuition. When the actor went looking for a toy in what the child knew was the wrong place based on the actor's knowledge, the study's subjects repeatedly spent longer periods looking at the events, suggesting surprise at the unexpected actions. *"One of the key points of the study is that the infant's surprise doesn't depend on the true location of the toy, but only on the infant's idea about the actor's knowledge or belief about the location of the toy."*

Onishi says the experiment shows that young children appeal to what other people are thinking in order to make sense of their actions. The results also point to a theory that children begin to acquire the building blocks of empathy at an early age.

That point is not lost on Isabelle Vinet, who conducts training at the Centre de Psycho-Éducation du Québec and who has worked with children with behavioural problems. She says many people who teach young kids would welcome the study's findings. *"We usually won't think of working on certain problem-solving strategies with children under the age of four, mainly because we don't think they're able to consider other people's perspective,"* said Vinet.

Onishi's study noted that using non-verbal tasks to peer into the thoughts of those who have difficulty communicating could open new avenues to detecting autism in children. 🦋

*"Young children appeal to what other people are thinking in order to make sense of their actions"*



Ref.: Onishi KH, Baillargeon R. Do 15-month-old infants understand false beliefs? *Science* 2005;308(5719):255-258.

# BOUNCING BABIES TO THE BEAT OF LANGUAGE

by Alison Palkhivala

**We tend to think of music appreciation as being all about how we hear, but new research shows that the experience of rhythm and music is far more complex than just hearing a pattern of sounds. Laurel Trainor has demonstrated how the senses work together in young babies to form their experience of rhythm and music.**

## WHY BABIES LOVE RHYTHM AND MOVEMENT

Whether in their fathers' arms or still in their mothers' bellies, babies experience a great deal of rhythmic movement, and any parent will tell you that quiet humming and rocking will soothe a baby, while lively singing and bouncing can make a cranky baby attentive and happy. This natural connection between movement and sound, evidenced in adults by the need to groove to a favourite tune, *"suggests that there are multisensory connections between the auditory system and the movement system,"* says Trainor, director of the McMaster Institute for Music and the Mind and a professor in the Department of Psychology, Neuroscience, and Behaviour.

To see how early these multisensory connections come into play, Trainor and her team had babies listen to an ambiguous rhythm with no accents while half of them were bounced on every second beat, as in a march, and half on every third beat, as in a waltz. The babies later preferred to listen to the rhythm with auditory accents as in a march or auditory accents as in a waltz, depending on how they had been bounced. This means, says Trainor, that *"there are multisensory connections very early in life between movement systems and auditory systems. Not only does auditory stimulation make us move, but the opposite is true as well: The way that we move actually affects what we hear."*

## COMBINING RHYTHM AND MOVEMENT IS GOOD FOR BABIES

According to Trainor, these findings suggest that giving infants stimulation that combines both sound and movement, such as bouncing them on your knee while singing to them, is not only pleasurable but could be beneficial. Fortunately, this is something most parents do already. *"We don't have any evidence that doing anything other than what parents do naturally is going to have a huge effect,"* she says. *"My advice to parents is always that what comes naturally is usually the best thing."*

## THE LANGUAGE CONNECTION

According to Tim Griffiths, professor of Cognitive Neurology at the Newcastle University Medical School in England, the development of rhythm perception may follow a pattern similar to the pattern of language perception. Both require the integrated action of several senses although, on the surface, both seem to be all about sound and hearing.

Trainor's findings, says Griffiths, could have important implications for understanding how young children learn to understand and use the rhythm of sounds we call language. It also opens the doors to new methods of helping children who are experiencing difficulty with language acquisition. If the development of language is dependent on more than one sense, then it is possible that input to one sense can



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make up for lack of input to another. For instance, perhaps movement exercises that replicate language rhythm could facilitate language development in children who are hard of hearing or who have developmental disorders, such as autism, associated with language difficulties.

Trainor is conducting a follow-up study to see if taking infants to a music and movement program will have an impact on their development. 🐾

Ref.: Phillips-Silver J, Trainor LJ. Feeling the beat: Movement influences infant rhythm perception. *Science* 2005;308(5727):1430.

# BABIES WALK LIKE ANIMALS

by Tracey Arial

**When held above a split-belt treadmill that enabled the speed and direction of stepping in each leg to vary, infants between the ages of five months and one year maintained coordinated walking by changing the speed of stepping, by taking extra steps with one leg or by moving one leg forward and the other backward.**

**T**he results were even more impressive than researchers had hoped. *“One belt can go very fast and one can go slow — up to a 22-fold difference — and they still walk quite well,”* says Jaynie Yang, the lead author on the study. *“They take two or three steps on the fast belt to each one on the slow belt. Even so, they still maintain coordination so that only one leg is off the ground at a time. The same thing has been shown in insects and cats and dogs. Our control of walking isn’t that different from quadrupeds.”*

The study included 45 infants between the ages of five and 11.8 months who were tested at the Department of Physical Therapy at the University of Alberta in Edmonton. Researchers wanted to find out whether human walking compares to that of four-legged animals, like cats and dogs, in that the pattern generators (groups of nerve cells) for each leg function autonomously while interacting with each other for coordination. Infants make ideal test subjects because their volition isn’t yet capable of overriding the behaviour of their pattern generators.

*“In infants under one, the response is mostly automatic,”* says Yang. *“It’s one of the few ways that we can look at how the spinal cord and brain stem control walking behaviour in humans.”*

Researchers plan to study babies with brain injuries to determine whether they have the same early stepping capability.

*“In the long term, this work could have implications in retraining”*



*“As the brain develops and exerts more control over the spinal circuitry, it becomes less and less autonomous,”* says Yang. *“Maybe people depend on the brain for walking more than other animals. In the long term, this work could have implications in retraining. For example, we might be able to harness this stepping ability by training.”*

Possibilities in retraining give Tina Del Duca, who heads the physical therapy department at Sainte-Justine University Hospital Center in Montreal, hope for child-

ren under the age of five who suffer major trauma injuries from motor vehicle accidents, falls and abuse. Del Duca isn’t treating children with head or spinal cord injuries at the moment, but says that they can be devastating for families. *“This study shows that the automatic reflex for stepping that occurs in babies at birth still occurs when they are almost a year old. If it continues as they grow, perhaps we can use functional muscular stimulation (FMS) or other treatments to help injured children walk again.”* 🐾

Ref.: Yang JF, Lamont EV, Pang MYC. Split-belt treadmill stepping in infants suggests autonomous pattern generators for the left and right leg in humans. *Journal of Neuroscience* 2005;25(29):6869-6876.

# COOLCAP CAN IMPROVE BRAIN DAMAGE OUTCOMES AT BIRTH

by Tracey Arial

**Permanent neurological problems related to encephalopathy can sometimes be lessened, and occasionally eliminated, by cooling the heads of affected newborns for 72 hours, says a recent study in *The Lancet*.**

**E**ncephalopathy — abnormal brain function — occurs in one to two babies of every thousand births. Twisted cords, weak placentas or contractions that are too strong can all cause such damage. Some babies get into trouble weeks before birth. Until this study, there was no treatment for brain injuries that usually cause death, cerebral palsy or intellectual disability by 18 months of age. Even infants who aren't handicapped can experience learning problems as they grow up.

With a new protocol that uses hypothermia to treat affected babies, Alistair Jan Gunn, senior author on the study and a Canadian researcher at the University of Auckland in New Zealand, who played a central role in designing the trial, says, "For every six babies who are treated on current criteria, one extra baby will live without severe handicap. Hypothermia works! It is not a magic bullet, it has very tight requirements and its potential is constrained in several real and now reasonably understood ways, but there is no doubt that it makes a real difference, and it is the first treatment ever to do so."

Doctors from the authorized hospitals provided researchers with data from 234 babies who suffered from encephalopathy when they were born. The babies all had signs of distress, such as low Apgar scores or the need for prolonged resuscitation, and abnormal aEEG readings. Many experienced seizures, while others fell into stupors or comas.

Almost half of the babies received standard care and became the control group.

The other 116 babies were treated with a specialized cooling cap within the first six hours of their lives. The babies were cooled to body temperatures between 34 and 35 degrees for 72 hours and were then slowly warmed to normal.

About a third of the babies died. The remaining babies have been given complete examinations, including a full assessment of motor skills and movement, every six months. In Edmonton, the clinic, run by Dr. Charlene M. Robertson, follows 20 babies from the study and another 10 who have been treated under the protocol.

Researchers like Robertson found that cooling did little for the most severely dam-

aged infants. With others, however, the levels of handicap were significantly lower in cooled babies than in control babies. Some healed completely.

"The outcome of the babies that were cooled is better than the outcome of the other babies," said Edmonton doctor Abraham Peliowski, Director of NICUs in the Gray Nuns and Misericordia hospitals and Senior Neonatologist at the Royal Alexandra Hospital, one of 25 hospitals in Canada, New Zealand, the United Kingdom and the United States authorized to use the cooling cap. "Hypothermia is the only form of treatment for these babies that has proven to do anything, even if it's not perfectly effective." 🐼



*"For every six babies who are treated on current criteria, one extra baby will live without severe handicap"*

PHOTO: REPRODUCED BY PARENTAL PERMISSION, DR. DURAND, OAKLAND

Ref.: Gluckman PD, Wyatt JS, Azzopardi D, Ballard R, Edwards AD, Ferriero DM, Polin RA, Robertson CM, Thoresen M, Whitelaw A, Gunn AJ. Selective head cooling with mild systemic hypothermia after neonatal encephalopathy: Multicentre randomised trial. *Lancet* 2005;365(9460):663-670.

# NEW HOPE FOR BABIES WITH KRABBE'S DISEASE

by Eve Krakow

**A recent study shows that a cord-blood transplant performed soon after birth can not only save the child's life, but also significantly limit the progression of the disease.**



*"So what this study means is a chance for children to have a life, a future"*

**K**rabbe's disease is a very rare neurological disorder resulting from an enzyme deficiency. Symptoms appear in the first few months of life, when the infants do not progress as they should. Affected infants deteriorate rapidly and usually die before they reach the age of 18 months.

In the study, 11 infants were diagnosed prenatally or shortly after birth and underwent the transplantation of umbilical-cord blood within the first few weeks of life. These were cases where the parents had already had a child with Krabbe's disease, so they knew they were carriers. Fourteen more infants who were diagnosed between four and nine months of age, once symptoms appeared, also received transplants.

The 11 children who received the transplants as newborns (before the appearance of symptoms) have all survived and made phenomenal progress. *"We changed the nature of the disease,"* said Dr. Martin Champagne, medical director of the hematopoietic stem cell transplant program at the Sainte-Justine University Hospital Center in Montreal. *"After the transplantation, we looked at the children's ability to acquire developmental landmarks. Many still had mild to severe impairments in gross motor function, but they had age-appropriate cognitive function and language skills."*

Champagne said there had been some previous attempts with bone marrow transplants, but that it usually takes too long to find a match: 70% of children lack a suitable donor in their family. As well, donors who are family members are likely to be carriers of the disease, and researchers fear that

stem cells from carriers would not be as effective in regenerating the missing enzyme. Cord blood, however, is readily available, and donors do not have to be related.

Micki Gartzke's daughter died of Krabbe's disease at two years of age. Gartzke is now the Director of Education and Awareness for Hunter's Hope, a U.S. foundation that seeks to increase public awareness about Krabbe's disease and improve early detection and treatment.

*"One of the children in this study was born about 10 days before my daughter,"* she said. *"He came from a case index family, so he was diagnosed early and received the treatment. He goes to school now. My daughter has been buried in her grave for quite some time. So what this study means is a chance for children to have a life, a future."*

Gartzke has met most of the 11 children who received the transplants as newborns. *"Some can run around, others need assistance with mobility and speech, but they're all there, they're all smiling, and they all know what's going on."*

Unfortunately, of the children who received the transplants later because of the late diagnosis, some have died, while others are living with extreme difficulties. This is why Hunter's Hope is working with researchers and health officials to have Krabbe's disease included in universal newborn screening.

Dr. Champagne says the study could lead to treatment for other diseases, too. *"The role of stem-cell transplants in many genetic diseases is not well established. This can be seen as a model to consider intervention very early on, before the onset of symptoms."* 🐾

Ref.: Escolar ML, Poe MD, Provenzale JM, Richards KC, Allison J, Wood S, Wenger DA, Pietryga D, Wall D, Champagne M, Morse R, Krivit W, Kurtzberg J. Transplantation of umbilical-cord blood in babies with infantile Krabbe's disease. *New England Journal of Medicine* 2005;352(20):2069-2081.

# NEW STUDY MAY LIMIT INTERVENTIONS PERFORMED ON PREGNANT WOMEN

by Eve Krakow

**A large, multi-centre trial has concluded that amnioinfusion — the process whereby a saline solution is introduced into the amniotic cavity — does not prevent meconium aspiration syndrome, suggesting that factors other than meconium may be contributing to this problem.**

**M**econium aspiration syndrome is a disorder of pulmonary function, believed to occur when the baby passes stool (meconium) before birth. Because the baby can aspirate amniotic fluid while in the uterus or at the first breath, meconium can get into the baby's airways. This can obstruct the airway or cause irritation to the lungs, leading to respiratory distress at birth or interfering with the transition to independent cardiovascular circulation. In some cases, it can result in neurological damage, or even death. About 5% of pregnant women have thick meconium staining of the amniotic fluid, and about 5% of these babies develop meconium aspiration syndrome.

A systematic review of previous trials had suggested that amnioinfusion might reduce the risk of meconium aspiration. However, these studies had small sample sizes. *"There had been no large multi-centre randomized control trials conducted in settings with standard obstetrical care,"* explained William Fraser, Canada research chair in perinatal epidemiology at the Université de Montréal.

Fraser led an international study that involved 1,998 pregnant women in 56 centres in 13 countries who had thick meconium staining of the amniotic fluid. Half the women were assigned to amnioinfusion, and half received standard care. The difference in results between the two groups was not statistically significant. The study therefore reversed the observations of the meta-

analysis, concluding that amnioinfusion does not reduce the risk of meconium aspiration syndrome.

For pregnant women, this could mean avoiding an unnecessary intervention. *"While this finding will not improve the outcome for the baby, it will limit our interventions,"* said Dr. Bruno Piedboeuf, neonatologist at the Centre hospitalier universitaire de Québec. This is important, since any intervention that involves putting in a catheter can have adverse side effects. *"We try to practise evidence-based medicine, but too often, our practices are based on small clinical trials, or sometimes just case reports,"* Piedboeuf added. *"This study is important because it shows that what was believed to be a very good practice did not change anything."*

The study also suggests that what is called meconium aspiration syndrome may actually be the result of several other factors. Traditionally, chest X-rays are used to diagnose the syndrome, yet researchers found a poor correlation between chest X-ray findings and the clinical status of the baby. *"The babies could be clinically quite sick, but the chest X-ray abnormality was not necessarily severe,"* Fraser explained. *"This suggests that there may be more going on in this syndrome than simply aspiration of the meconium."*

One possibility is that these babies are already vulnerable from other intrauterine stresses. *"More and more, we think that whatever stresses are making the baby pass meconium may be what is affecting the other*



*"This study is important because it shows that what was believed to be a very good practice did not change anything"*

*systems in the baby,"* said Piedboeuf. *"Meconium is just one element of the picture. We need to focus on why the baby is passing meconium. Intuitively, this is what we have been doing, and I think that is why outcomes of meconium aspiration syndrome have improved in the last 20 years."* 🐾

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# CHILDREN'S HEARING INITIATIVE OFFERS MODEL FOR PEACE-BUILDING

by Philip Fine

**Harvey Skinner has seen small miracles take place between Arabs and Israelis. While the miracles are not of biblical proportions, they're big enough to give him hope that the Middle East is very capable of conducting peace-building dialogue.**

Skinner, chair of the Department of Public Health Sciences at the University of Toronto, is research director at the Canada International Scientific Exchange Program (CISEPO), an organization that entered the conflict region using public health initiatives and the promise of scientific exchanges. Its results could offer inspiration to high-ranking peace negotiators.

In 1995, the office of the late King Hussein of Jordan invited CISEPO's founding chair,

Arnold Noyek, to come up with an initiative to foster collaboration between Arabs and Israelis. The organization used a high incidence of hereditary hearing loss shared by Jordanians and Israelis to begin a project providing audiology tests for infants.

In the initial project, 17,000 Arab and Israeli newborn babies were assessed and habilitated for hearing loss. The group's work now involves testing more than 130,000 infants in the underserved communities of Jordan and the Palestinian territories and fills a void in regional conflict resolution by establishing itself long-term, walking softly over the political cracks.

"Hearing is fundamental in the development of language," says Skinner, who believes that regional conflict is "disastrous" for early childhood development and that the damage can take generations to undo.

Since its 1998 brokering of the Middle East Association for Managing Hearing Loss (MEHA), CISEPO has celebrated many milestones. There have been scholarly exchanges between Canada, Israel and Jordan, joint Israeli-Palestinian publications and several symposiums. In 2003, an Arab and Israeli surgical exchange was set up, and in 2004 cochlear implant surgery equipment purchases in Jordan became government-supported. To date, more than 145,000 infants have been hearing screened and habilitated and the program has expanded to youth health promotion, maternal nutrition and eLearning initiatives.

In chaotic regions like the Middle East, Skinner says that peace-building starts with small steps and — ironically enough for a group that built its work on hearing loss — it also requires good listening skills. 🦏

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