

IN THE NEWS

Wendy Macklin is the grandmother of a beautiful three year old girl with Rett syndrome. Wendy wrote a wonderful piece called "A grandmother's story" describing her thoughts and perspectives in relation to her little granddaughter growing and developing but also being diagnosed with Rett syndrome. Her piece was published in the West Australian newspaper in March 2014. Here is the link:

<http://aussierett.org.au/latest-news/>

Jenny and Helen also wrote a piece in The Conversation giving an overview about scoliosis. Here is the link: <http://theconversation.com/explainer-everything-you-need-to-know-about-scoliosis-28409>



The booklet on the management of gastrointestinal disorders is available on our website (<http://aussierett.org.au/resources/guidelines-reports-and-books/>). We can also send you more hard copies if you prefer.



December 2014 - ISSUE SEVENTEEN

NEWSLETTER OF THE AUSTRALIAN RETT SYNDROME STUDY

AussieRett Christmas Newsletter 2014

Welcome

We would like to wish you a very Merry Christmas and a Happy New Year from Helen, Jenny and the team at the Australian Rett Syndrome study. We would also like to wish you and your loved ones a safe, joyous and relaxing holiday season.

This newsletter features a short report on this year's Rett Syndrome Conference in Washington DC and describes recent studies on spinal fusion, gallbladder function, and gastrostomy feeding in girls with Rett syndrome.

Thank you

Again, we have many wonderful people to thank this year who have made the Australian Rett syndrome study possible. Thank you to the families, children and adults with Rett syndrome, for your continued interest and support of our research through your participation and commitment to the study. We would like to thank all of the members of the Parent Consumer Reference Group for their input and contribution to Rett syndrome research. Thank you also to the clinicians who support our research. Finally we would like to thank and acknowledge students who work with us. Anna Urbanowicz and Amanda Jefferson have been working on their PhD and hope to complete during 2015. Eloise Wilson and Leon Lor each have completed Honours projects. Thomas Horne has commenced Honours and will complete his project next year.

In particular, we would like to thank the wonderful families and supporters who have raised important funds to keep the Australian Rett Syndrome Database going. We have a growing list of friends and supporters and are overwhelmed with the support provided to us. Many families and friends have grouped together to fundraise for us and everybody had fun along the way. Thank you to everybody, but we would particularly like to mention:

- Teresa Pracilio, Caroline Fitzpatrick, Narelle Read, Gillian Iannuci, Kristy Pearson, Jessica Markou, Melanie Kennelly, Rebecca Watson in Western Australia.
- Rokeby Dental surgery in Western Australia
- The Diddy family in New South Wales
- The Klingner Family in South Australia
- The Brown Family in New South Wales
- The Macklin Family in ACT/New South Wales

Thank you all so much. We are all the more determined to make a difference for those affected by Rett syndrome.

We also welcome visits from families from around Australia if you are visiting Perth. This year we met up with Molly Beggs and Jet Thomas. It was lovely to catch up.

Jet from Queensland (top photo) and Molly from Victoria (bottom photo) each travelled in Australia this year and visited us at the Telethon Kids Institute when in Perth. Really fabulous to catch up!



Keep in touch with AussieRett CONNECT

Every AussieRett family helps to improve our knowledge and research into Rett syndrome. Please let us know if your contact details change. We don't want to lose you! If you would like to make a contribution to the next AussieRett CONNECT, please contact:

AussieRett

PO Box 855, WEST PERTH WA 6872
Email: aussie.rett@telethonkids.org.au
Web: aussierett.org.au
Mobile: 0419 956 946
Phone: 08 9489 7774/7790

2014 Publications

The following papers and book chapters written by members of the AussieRett team have been published or accepted for publication in 2014. You can read snapshots of these papers on our website under 'Our Research', or copies of full papers can be obtained by emailing the team at aussierett@icmr.uwa.edu.au.

1. Downs J, Wong K, Ravikumara M, Ellaway C, Elliott E, Christodoulou J, Jacoby P, Leonard H. Experience of gastrostomy using a quality care framework: the example of Rett syndrome, Medicine (in press).
2. Urbanowicz A, Downs J, Girdler S, Ciccone N, Leonard H. Language abilities of girls with Rett syndrome are influenced by MECP2 mutation type, American Journal of Medical Genetics Part A (in press).
3. Wong K, Leonard H, Jacoby P, Ellaway C, Downs J. The trajectories of sleep disturbances in Rett syndrome. Journal of Sleep Research. 2014, 14 Sept. [Epub ahead of print]
4. Anderson A, Wong K, Jacoby P, Downs J, Leonard H. Twenty years of surveillance in Rett syndrome: What does this tell us? Orphanet Journal of Rare Diseases. 2014;9:87.
5. Downs J, Torode I, Ellaway C, Jacoby P, Bunting C, Wong K, Christodoulou J, Leonard H. Family satisfaction following spinal fusion in Rett syndrome, Developmental Neurorehabilitation. 2014; April 11. [Epub ahead of print]
6. Urbanowicz A, Leonard H, Girdler S, Ciccone N, Downs J. The perspectives of mothers on the communication abilities of their daughter with Rett syndrome, Developmental Neurorehabilitation. 2014, 24 Feb. [Epub ahead of print]
7. Freilinger M, Bohm M, Lanator I, Vergesslich-Rothschild K, Huber W-D, Anderson A, Wong K, Baikie G, Ravikumara M, Downs J, Leonard H. Prevalence, clinical investigation and management of gallbladder disease in Rett syndrome, Developmental Medicine and Child Neurology. 2014;56(8):756-762. .
8. Baikie G, Madhur R, Downs J, Nasseem N, Wong K, Percy A, Lane J, Weiss B, Ellaway C, Bathgate K, Leonard H. Guidance in the management of gastroesophageal reflux, constipation and abdominal bloating in Rett syndrome, Journal of Pediatric Gastroenterology and Nutrition. 2014;58(2):244-51.
9. Andrews J, Leonard H, Hammond G, Girdler S, Rajapaksa R, Bathgate K, Downs J. Community participation for girls and women living with Rett syndrome. Disability and Rehabilitation. 2014;36(11):894-899.

Shenzhen, China

Laboratory studies have found that mice with a *MECP2* mutation develop better motor skills if their environment is enriched, possibly due to the physical activity which then causes the brain to produce Brain Derived Neurotrophic Factor (BDNF) proteins. BDNF is important for nerve cell growth and maturity. For Rett syndrome, therapies such as physiotherapy should be more effective when implemented intensively at an early age due to brain plasticity and also potentially due to more production of BDNF proteins. However, available research cannot tell us the precise benefits of intensive early interventions.

Jenny and Helen have developed relationships with families and clinicians in Shenzhen, China and worked with them earlier this year to run a pilot study testing an intensive therapy program. A pilot study is a practice study to learn how best to manage all the different aspects that need to be properly run in a larger study. Four young girls participated in the 7 week pilot program and each made some gains in relation to their motor abilities and their general wellbeing. This is encouraging and sets the scene for a larger study.

Jenny and Helen are now working with the team in China to find funding for a larger study of approximately 18 girls to participate in a 9 month intensive therapy intervention period.



Some of our studies in 2014

QUALITY OF LIFE

We have asked the families of twenty-two girls with Rett syndrome in interviews to talk about their daughter's life experiences (e.g. social inclusion) - to identify aspects of their lives that are most important. Parents shared many beautiful, deeply heartfelt stories of different life events that continue to help foster what they feel is a good quality of life for their daughter. These interviews are allowing us to develop a state-of-the-art measure of quality of life. This measure will help in identifying your daughter's needs and also the value of services that she receives. It will also be an important outcome measure for future clinical trials.

SCOLIOSIS

Some girls develop a severe scoliosis and spinal fusion may be recommended as management. This can be a difficult time for families when making the decision about whether to proceed with the surgery. In our 2011 questionnaire, we included questions on how families felt about the different aspects of the hospital management. The majority of families were very satisfied with their daughter's surgery and hospital care, especially when the staff were experienced and proactive and took family perspectives into account when making decisions. Many families were pleased with their daughter's straighter posture, her health and comfort, and greater ease of sitting, dressing and transfers. Most families said that they would consent to spinal fusion if faced with the same situation again.

GASTROSTOMY

Approximately one quarter of families in the Australian Rett syndrome population currently report using a gastrostomy. A gastrostomy can be used for all feeds, some feeds, just for medications or for venting excess air from the stomach. In our 2011 questionnaire, we included questions about families' satisfaction with gastrostomy surgery and the hospital care. Again, many families expressed their satisfaction with the gastrostomy procedure. They also reported improvements in their daughter's health and reduced family stress and burden during daily care activities.

GALL BLADDER

We used information in our Australian database together with information from our international database InterRett to investigate gall bladder disorders in Rett syndrome. Whilst gall bladder problems are relatively rare, they occur more commonly in Rett syndrome than in girls of similar ages in the general population. This may be because the muscles in the gall bladder are weaker and there is less efficient emptying. Gallbladder disease should be considered as a possible cause of abdominal pain in Rett Syndrome.

13th Rett Syndrome Symposium and Family Conference, June 2014, Washington DC, United States

Helen and Jenny attended these two conferences that were organised by Rettsyndrome.org, the new name for the International Rett Syndrome Foundation. They were held consecutively giving opportunity for scientists and clinicians to attend both of the conferences. Here are some of the main points that were discussed.

There were many presentations on how the MeCP2 protein (produced by the *MECP2* gene) actually functions. There is now a much clearer understanding of how MeCP2 works differently in different parts of the brain. In some parts of the brain, MeCP2 is too active and in other parts, it is not active enough. This gives some explanation as to why we might see too much activity in some functions such as breathing abnormalities and lower levels of functioning in other aspects such as in the motor and communication domains.

One group of researchers found the MeCP2 protein in nerve cells of the gastrointestinal system in a mouse model, giving some explanation as to why gastrointestinal problems occur so commonly in girls and women with Rett syndrome. Previous studies have only looked at MeCP2 in brain tissue.

There were many presentations on experiments that aimed to manipulate the biochemical pathways and reduce symptoms. For example, one laboratory reported their progress on making genetic alterations to the *MECP2* gene and another laboratory was testing ways of incorporating the BDNF protein into tiny nanoparticles that could be easier to absorb by the brain. It was encouraging to hear of experiments getting positive results in mouse models.

Most mouse studies are now using female mice and therefore advances will be more directly applicable to girls and women with Rett syndrome.

However, the *MECP2* gene is extraordinarily complex and it works in so many different biochemical pathways that our knowledge is still extremely limited. And most of the experimental ideas are not yet ready to be tested in humans. There is still much research to do to find the medicines likely to have the best chances of helping. With any potential new medication, the safety for the girls and women with Rett syndrome remains the number one consideration.



Two treatments that have previously been the topic of a lot of laboratory research and is now being tested in girls and women with Rett syndrome is IGF-1 and the related compound NNZ-2566.

1. IGF-1 is a growth factor hormone that helped with neurological function in the laboratory studies and is now being tested at the Boston Children's Hospital. It is given by sub-cutaneous injection daily. The first small safety study has now been completed and IGF-1 was well tolerated. Recruitment has now ongoing for a larger and longer study of 2 to 10 year old girls.

2. NNZ-2566 is a medicine that is very similar to IGF-1 but can be taken orally. Its safety is currently being tested in 3 centres in the US – Houston, Alabama and Minnesota. This first study recruited adults with Rett syndrome and has now been completed. There has been a recent press release and NNZ-2566 is believed to be safe and the preliminary results are encouraging. For more information, see <http://www.neurenpharma.com/IRM/Company/ShowPage.aspx/PDFs/1448-10000000/NeurensuccessfulinRettsyndromePhase2trial>

Another small trial is testing the safety of the drug Capoxone that has been used for adults with multiple sclerosis. This study is being conducted in both New York and Israel and is in the very early stages.

There was a lot of discussion about plasticity of the brain with the view that favourable opportunities for practice and learning have potential to enhance the learning of skills. An environment that is "enriched" and is full of opportunities for motor learning and practice, communication and social interaction is believed to allow optimal development for girls and women with Rett syndrome.

Together with a spinal surgeon from the US, Jenny presented to families (mainly from the US) on scoliosis. The information provided by families across Australia in AussieRett was the basis for the presentation, highlighting the value of every small piece of information that is contained in the database. We currently have several projects on scoliosis and look forward to sharing those findings.