Diagnosis questions

What is Rett Syndrome and what causes it?

Rett Syndrome is a neurological or brain disorder which most often affects apparently healthy little girls around the age of 6-18 months. Early signs are autism like behaviours with the loss of speech and hand use. Your daughter might stop playing or interacting normally. Onset can be sudden or more subtle, where you can't quite remember the last time she waved or said a word. She may have unusual hand movements when she is awake; in Rett Syndrome, hands are usually clasped or held together in the middle of her body (midline) or she may wring them together or move them from hand to mouth. She may have other problems, such as strange breathing patterns, screaming episodes or sleep disturbances.

Rett Syndrome is named after Austrian doctor, Andreas Rett, who first identified the condition in 1966. It is as common as Huntington's Disease, although not very well known and occurs in 1:10,000 live female births. The condition is most often caused by mutations or faults in the gene *MECP2*. This gene is on the X chromosome which is why the condition most often affects girls.

There are four stages of Rett Syndrome. The condition is not degenerative as it was once thought to be. Degenerative means that there is progressive deterioration of nerve cells, leading to cell death; this does not occur in Rett Syndrome. The condition does however, usually follow a path of progression, where skills such as speech, hand use and mobility are lost. Most girls do not speak at all. Some have a few words. Some are left with some hand use. Some girls never walk, some girls learn to walk and lose it later and a few keep walking. There is currently no way to predict the severity of these different symptoms.

Does she have brain damage?

Girls with Rett Syndrome do not have structural brain damage. In the UK, they are often assumed to have severe learning disabilities. Any human who cannot use their hands, speak or move freely is going to have trouble convincing others of their understanding. As more research into the underlying causes and mechanisms of the disorder are coming to light, it is more apparent that the cognitive abilities of people with Rett Syndrome have been underestimated for decades and that standard intelligence testing, even testing typically used for people with disabilities is not appropriate for people with Rett and does not accurately reflect their understanding.

Will she end up in a wheelchair?

Some girls with Rett Syndrome never walk. Some walk and lose their mobility at a later stage or slowly over time and a few keep walking throughout their lives. Rett Syndrome is a condition that will progress slowly throughout your child's life. However, the speed at which Rett syndrome progresses in a given child and the severity of symptoms can vary.

What can I do to help her?

Children with Rett Syndrome usually have a variety of health issues that need intervention. A large part of helping her will involve managing her condition at home.

- Your child might have difficulty sleeping which is difficult for you too. Help with sleep issues can be found here.
- Many children with Rett have trouble gaining weight. To avoid malnutrition, it's important to monitor your child's food and caloric intake to make sure she is getting adequate nutrients. Remember to talk to your child's doctor about any medications or special diets that you're considering, even if they're termed "natural" or "herbal." This should alert them to developing symptoms. Some medications, herbal therapies, vitamin supplements or special diets might also be unsafe for your child, and some can be harmful if they're not used properly.
- Children with Rett Syndrome are at increased risk for aspiration. Aspiration is when you breathe food or fluids into your lungs. This can cause chest infections which are dangerous for people with Rett of all ages. You can find more information about this on our aspiration fact sheet here.

It's important that your child sees specialists to help maintain and develop skills where possible:

- Occupational therapy may help maintain or even develop your child's hand use and help her deal with sensory input from her environment.
- Physiotherapy will help her maintain and develop her gross motor skills and mobility where possible
- Speech therapy will help your child find ways to express herself.
- Rett UK have a communication project and run regional workshops and coffee mornings to support people with Rett Syndrome and their families with communication.

- Rett UK also run a network for Speech and Language Therapists (SaLT) who are working with children and adults with Rett which you may wish to connect your local SaLT to.

My daughter has Rett Syndrome. Should I have pre-natal testing when I have another baby?

In 99.5% of cases, Rett Syndrome is caused by a spontaneous mutation in a single sperm. This means that in most cases, even if you have a daughter with Rett already, you are only as likely as anyone else to have a daughter with Rett Syndrome.

On rare occasions, the mutation comes from the mother's eggs. This could happen for either of the following reasons:

The mother's eggs could have the mutation, known as germline mosaicism. Any children would have a 50% chance of inheriting the gene.

The mother has the mutation in every cell but due to favourable x-inactivation, she does not have Rett symptoms herself. Again, any children would have a 50% chance of inheriting the gene.

The risk to siblings depends upon the genetic status of the parents. When the mother of an affected individual is found to have the *MECP2* mutation identified in her affected child, the risk to siblings of inheriting the mutation is 50%.

Some parents chose to be tested to see if they carry the same *MECP2* mutation as their daughter themselves, before undergoing amniocentesis or chorionic villus sampling (CVS) as the risk of having another child with Rett, is much lower than the risk associated with these procedures.If a mutation is not identified in a parent, the risk to siblings is low. However, germline mosaicism cannot be excluded.

What will my daughter's life expectancy be?

Rett Syndrome is not a fatal condition. It was once thought that girls with Rett Syndrome would live at most into their 20’s, but recent research shows that with adequate health care, people with Rett Syndrome can live into their 50’s.

Is there a cure?

There are currently no FDA or EMA approved treatments for Rett Syndrome. Medicine can offer only supportive measures: feeding tubes, orthopaedic braces and surgeries and seizure medications which are often ineffective. Several potential treatments for individual symptoms are currently in clinical trials.

In 2007, Rett Syndrome was demonstrated to be reversible in mice, even in mice in the late stages of the disease, providing proof of concept that Rett Syndrome is a potentially curable condition. In 2013, researchers funded by Reverse Rett were able to reverse Rett in mice using Gene Therapy techniques. A human clinical trial of Gene Therapy is due to start in early 2019.

If there has ever been a good time to be diagnosed with Rett, this time is now. There is much to be hopeful about in terms of both emerging treatments for symptoms and an all out cure.

Please register your child on the **UK Rett Syndrome Patient Registry** so that we can contact you directly as and when we have information to share re upcoming clinical trials and other research opportunities.

If you would like to do something to make a difference to the effort to bring about treatments and a cure faster, please get in touch: enquiries@reverserett.org.uk