RettEd Q&A: Respiratory Issues in Rett Syndrome

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Attendee Questions	Response	
Breathing Irregularities		
Why is breathing so funny when our girls/ boys wake up, almost as if startled?	A behavioral arousal can trigger breathing abnormalities in Rett syndrome. A person goes through stages of sleep and particularly if aroused from a deep sleep state (REM) may be more disoriented or startled. This can trigger the irregular breathing.	
Could she address the stereotypical breathing abnormalities such as gasping and breath holding and how they play a part in respiratory illness?	You may observe breathing abnormalities like breath holding and hyperventilation more with the stress of an acute respiratory illness. Breath holding and hyperventilation do not directly cause respiratory illness. If a person has difficulty with swallowing and has these breathing episodes while trying to eat or drink, aspiration could occur which can cause respiratory symptoms. If one has very shallow breathing, especially when there is more mucus from acute infection, it may be more likely to build up in the lower lungs causing airway obstruction and atelectasis (collapse of some air sacs).	
Is there any evidence (even anecdotal) that breathing patterns change in Rett patients over time?	Frequent breath-holding and hyperventilation has been reported to become less evident with increasing age though it is not certain whether this could be that families are used to the irregular breathing and don't report it as much or that it is the people who live longer who are less symptomatic.	Reference 1

Does hyperventilation cause long-term problems with any organs?	There has been some suggestion that breath holding may affect cardiac function and lead to prolonged QT syndrome (which is when the electrical signal moves too slowly in the heart). The irregular breathing episodes may cause dizziness, reduce mental focus, reduced coordination, complicating even basic tasks like eating and drinking.	
Can hyperventilation cause lung collapse?	It is not likely that hyperventilation causes lung collapse (atelectasis) which is usually from mucus plugging. Shallow breathing together with ineffective cough can contribute. Immobility (such as after spine surgery) and respiratory infections causing increased mucus result in much higher risk.	
If a 32 year-old Rett woman has not had major irregular breathing, what is the likelihood that it will begin at some point?	Breathing irregularity typically starts in early childhood. A large survey of 413 Rett families found 63.8% started breath holding by 5 years of age and 50.8% hyperventilation. Mutation type did not influence age of onset. Breath holding was more common than hyperventilation and 41% had both. Typically breathing abnormalities are more severe during wakefulness compared to sleep and are worsened by behavioral arousal.	Reference 1
•My granddaughter was placed on Topamax by her Rett Specialist in the hopes that it would decrease her hyperventilating. It has but I am curious to know if there are any other medications that would normalize her breathing pattern?	There are no current medicines that can 'normalize' breathing. Several medicines have been tried in severe cases of breath holding with limited research on benefit: • Buspirone (BusPar®) mild anti-anxiety drug • (serotonin agonist as well) • Magnesium sulfate – used as well for constipation • Opioid antagonists	

	• Naltrexone • Nalaxone • Desipramine –anti-depressant The STARS clinical research study is currently enrolling subjects to test the investigational medication sarizotan to see if it may help reduce the frequency and severity of irregular breathing episodes in people with Rett syndrome. For more information go to https://www.rettstars.com	
Sleep Problems		
Very interested in the sleep patterns	Sleep patterns can be irregular in Rett syndrome and sleep disturbances affect 80 percent or more of patients. More parents of Rett patients report sleep related problems than of some other conditions. They can have delayed sleep onset and awakenings in the night with disruptive behaviors. They can have shortened night sleep time and increased sleep during the day. It appears that older Rett patients sleep more during the day than younger Rett patients perhaps due to circadian rhythm dysfunction and/or experiencing nighttime sleep problems like insomnia, sleep disordered breathing. All of these patterns are frustrating for caregivers as well. They have reduced REM sleep. Breath holding, central and/or obstructive apnea episodes can be seen. All people generally breathe more shallowly during sleep, but this may be more significant with Rett syndrome and lead to hypoventilation.	
Is sleep apnea common with Rett syndrome?	Exact frequency not known but higher than healthy peers. Not observed in all Rett patients. Can be a problem with obesity.	

	Sometimes develops with use of a vagal nerve stimulator for seizure control.	
How does sleep apnea play a part in respiratory illness?	Poor sleep quality from sleep apnea may lead to daytime fatigue and contribute to impaired cough clearance and weakness but sleep apnea does not directly result in respiratory infections.	
Our daughter, who is 48, has no significant breathing issues as noted here. She does, however sleep at night 11-12 hours. Sometimes her sleep is disturbed and is having sort of a night terror. She calms quickly and falls back to sleep. However, she seems to be taking increased catnaps, as she has gotten older. Therefore, in total she is sleeping about 14-15 hours a day. Should we be concerned? Any recommendations?	As above, people with Rett syndrome can have disrupted sleep and sleep problems. A healthy adult should get 7-8 hours of uninterrupted sleep so her need for more sleep likely reflects the disruptions. As noted above, older Rett patients sleep more during the day than younger Rett patients perhaps due to circadian rhythm dysfunction and/or experiencing nighttime sleep problems like insomnia, sleep disordered breathing. If she has obstructive sleep apnea that can affect how well rested, she is and lead to daytime sleepiness. If she has snoring, could consider having a sleep study. Could consider talking with a sleep specialist about potential therapy to help with night terrors but can see irregular sleep in Rett syndrome.	
My daughter wears a bipap at night for obstructive sleep apnea, with a nasal mask. However, she does have some challenges with closing her mouth due to jaw position. Do you have any suggestions? I have seen mouth guards (not sure of the term) on the market to wear at night, would something like this	Having one's mouth open when using a nasal mask for PAP therapy (CPAP or bias) does lead to more leak and less positive pressure to keep the airway open. At times, one compensates for this leak with adjusting the pressure settings. Some people have tried adding a chinstrap or using a full-face mask. The concern with these strategies if the patient cannot take it off in the event of vomiting, he or she could choke. In these cases, you may need to have a night nurse or attendant	Oral appliances in Sleep apnea and PAP therapy in Children fact sheets can be found at www.thoracic.org/patients

work?	available. Oral appliances for obstructive sleep apnea work in some mild cases, but would likely not be useful in a Rett patient.	
Can you please discuss the ramifications of Metabolic Acidosis for our children?	Abnormal breathing could cause respiratory alkalosis (over breathing with low carbon dioxide levels and high pH) or respiratory acidosis (hypoventilation with high carbon dioxide levels and low pH). Metabolic acidosis might occur in some situations such as poorly controlled diabetes or with a kidney problem. If a person has metabolic acidosis, the lungs try to compensate by breathing faster to blow off more carbon dioxide that could reduce the acid load in the body. Talk with your Rett specialist about when metabolic acidosis might occur. Any state of acidosis is not healthy for one's body.	
Looking for any treatment suggestions for dyspnea and aerophagia.	Air swallowing and air bloat are often worse when individuals are distressed. Anxiolytic medications may reduce this in some individuals. Having a GT allows one to vent the stomach to reduce the amount of swallowed air that has built up.	
Can aerophagia cause problems such as frequent vomiting after feeding?	Swallowing excessive air (aerophagia) can distend the stomach and may contribute to feeding intolerance. Vomiting after feeds can be caused by gastroesophageal reflux and people with Rett syndrome are also know to have esophageal and gastric dysmotility. A gastroenterologist familiar with Rett syndrome can offer ideas for helping with gut motility and aerophagia.	
My adult with Rett most typically has pulmonary events around illnesses with heavy and aggressive mucus.	Pulmozyme® (dornase alfa) is a medication that was developed for use with cystic fibrosis (CF) in which there is abnormally thick mucus from impaired cell function. Mucus can	

Do you ever treat with Pulmozyme? When, if ever, might Pulmozyme be an effective treatment? Do you use it therapeutically or prophylactically?	be thick with infections in anyone but is not the same as that seen in CF. However, clinical trials of its use in patients without CF have not shown similar benefit and its use is not FDA approved for non-CF patients. Its benefit may be limited and it is a very expensive drug as well. Instead, I would consider use of inhaled hypertonic saline (3% or 7%) or N-acetylcysteine to try to thin secretions to make it easier to cough up.	
Very interested in the cough inability and mucus issues	Impaired airway clearance refers to the reduced or Inability to cough out mucus well. All young children do not cough as well as adults and do not usually spit out mucus. Swallowing mucus is okay – as long as it is out of the lungs. However, mucus that is stuck in the lower airways can lead to obstruction with difficulty breathing, atelectasis and can become a good place for infection to take hold. Scoliosis can affect mechanics of breathing and cough. Muscle weakness and poor tone makes cough weaker as well. Immobility limits movement of mucus up the airways.	
•Hopefully you will explain signs of what to watch for. Then what steps to take. (for respiratory problems)	Signs and symptoms of concern for a serious breathing problem include: • Increased work of breathing – sustained increased respiratory rate, retractions, distress suggesting an acute illness • Frequent generalized cyanosis (blue spells) or syncope (passing out) • Chest congestion and/or chronic cough • Snoring and obstructive apnea noted with sleep	

When my daughter has aspiration pneumonia, her breathing becomes very rapid (over 100 respirations/minute). Is this strictly a pulmonary issue or is this her compromised autonomic system reacting to her respiratory illness?	The child's age is not given, breathing 100 times per minute is never normal. Younger children breathe faster than older children or adults. Dysautonomia in Rett syndrome caused increased sympathetic tone could stimulate fast breathing. Hyperventilation is brought on by stress or agitation and if the child has pneumonia this may plan a role. If the lungs are now working well and particularly if there are signs of increased work of breathing, the fast breathing is likely mainly from lung problem. Low oxygen levels or high carbon dioxide due to inadequate ventilation should trigger one to breathe faster. Very fast shallow breathing may not be very effective however.	
I'm new to this. My 17 year old was just dx with Rett. My question is she doesn't have a good cough reflex at all and does not get mucus out through cough. She does however gag and vomit ALOT. Like daily. Especially in the mornings, she gags and usually vomits. Anything known that might help that? Is that normal with the inability to cough? In addition, is it normal when gagging vomiting to not have the "lean forward" reflex that you or I would have? She usually goes rigid and leans back. I always worry because she gets choked and doesn't give breath in these moments	Gastroesophageal reflux (GER) and gut motility issues are common in Rett syndrome. Reflux events result in vomiting and can cause gagging and abnormal posturing due to heartburn or choking sensation. Perhaps her rigidity and posture reflect an acid reflux episode. This could trigger a breath-holding event as well. Having an impaired cough reflex is a problem in this situation as well as there is more risk of aspiration. Coughing in the morning may reflect shallow breathing and decreased movement causing a build up of mucus that then needs to clear out when awakening. If one swallows a lot of mucus, it might upset the stomach causing vomiting. However, if one has regular vomiting I would look into GI related causes. Keeping a diary and videotaping an episode if possible may be helpful to share with your Rett or GI specialist. There are medications to treat GER and gut motility.	

•Should all dental sedation be hospital based even if patient does not have significant breathing issues?	You would need to discuss with your child's primary Rett specialist and anesthesiologist about how it is safe for your child to be sedated and what monitoring is advised. The healthcare provider doing the sedation needs to be familiar with Rett syndrome and the irregular breathing patterns that can occur as these can occur during recovery. Close monitoring of oxygen levels and ventilation are important. Reactions may be unpredictable but if the child does not have breathing problems at baseline, the risk is lower.	
My daughter (19yrs) has recently started to exhibit dystonia - in her jaw - especially while eating. Could this be related to breathing/swallowing issues? Any suggestions?	One cause of jaw problems can be bruxism – teeth grinding which is very common in Rett patients. It could cause pain in jaws. Dystonia occurs in more than 50% of Rett patients and can affect various muscle groups. In the throat and jaw, it can contribute to swallowing problems though usually the tone of the muscles in the throat are more of a factor. Upper airway tone affects breathing and risk of airway obstruction. Jaw clinching could perhaps impair cough clearance as well.	
My 8-year old daughter that has been on a ventilator for the last 40 months, and sprinting for 8 hours a day now, it is a good sign that she might be getting off the ventilator sometime. Her CO2 levels and everything is ok. My daughter started with 5 minutes a day and now she is at 8 hours. I had to ask the pulmonologist not to stop the sprinting when she falls sleep	Some children can be off ventilatory support during the day but still require some assistance with sleep due to shallow breathing with hypoventilation and/or obstructive apnea. Sometimes stepping down from full support to more limited CPAP/Pressure Support when not off the vent can be another means of transition in the weaning process. Sometimes a person can do well for a few days but if not breathing deeply enough or clearing secretions can develop atelectasis that will result in need for oxygen or some ventilatory support again.	

since due to Rett Syndrome her sleeping patterns are very irregular and she falls sleep sometimes 5 minutes after the sprint starts. After asking the Doctor to all the Resp Therapists to continue the sprinting even if she falls sleep, my daughter has been doing really good and we have been increasing 15 minutes a week (1 hour a month). I just wanted to know your opinion my 8-year old daughter that has been on a ventilator for the last 40 months, and sprinting for 8 hours a day now, it is a good sign that she might be getting off the ventilator sometime. Her CO2 levels and everything is ok. just wanted to know your opinion	Obviously, a new acute respiratory infection can also set back progress in weaning. I agree that if she is doing well with weaning a plan for continued withdrawal of support is reasonable to try.	

References:

1. Mackay J et al, Autonomic breathing abnormalities in Rett syndrome: Caregiver perspectives in an international database study, J Neurodevelomental disorders 2017; 9:15.