PMD Family Support
Inspiring Hope

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2015 Leukodystrophy Awareness Month Facts

September 1, 2015
Pelizaeus-Merzbacher Disease (PMD) was named for two Dr's that did early research on the disease. Dr Friedrich Pelizaeus a Neurologist (1851-1942) & Dr Ludwig Merzbacher (1875-1942) a Neuropathologist.

September 2, 2015
PMD is a Leukodystrophy a disorder that affects the white matter of the brain. Leuko meaning white, dys meaning lack of & throph meaning growth, in other words lack of myelin.

September 3, 2015
PMD is a caused by a mutation in the Proteolipid Protein (PLP) Gene.

September 4, 2015
PMD males are very amazing individuals. Although they may be very limited in their physical abilities and speech they are very smart.

September 5, 2015
PMD is a dysmyelinating disease, verses a demyelinating one. Meaning the myelin is never properly formed instead of being destroyed.

September 6, 2015
The PLP gene is located on the X chromosome so, generally, only males who inherit the abnormal PLP gene from their carrier mothers are affected.

September 7, 2015
PMD is present at conception although symptoms may not become obvious right away.

September 8, 2015
Generally the 1st symptom of PMD is a shaking, rocking, dancing movement of the eyes called nystagmus, it is usually noticed between birth and 3 months of age.

September 9, 2015
The types of PLP gene mutations that cause PMD are generally point mutations & duplications. With a point mutation one specific amino acid is changed to another. Duplication mutations, the most common type of mutation, can cause a part of the gene or even the whole gene to be duplicated or even triplicated. There seems to be no consistent correlation between mutations and the severity of the disease.

September 10, 2015
Life expectancies for males with PMD varies greatly, as it does for everyone. But the information given in some of the literature is very grim, stating life expectancies may be from a few months to possibly the first decade (10 yrs). We know of many PMD males still living into their 20's, 30's, 40's, 50's & 60's.

September 11, 2015
There are less than 1200 cases of PMD diagnosed worldwide. There may be others who have PMD who are misdiagnosed. Many PMD males are labeled Cerebral Palsy until a second child is born into a family with similar symptoms, or until a Dr with some knowledge of PMD suggested the child be tested for it.

September 12, 2015
The Annual PMD Family Support Conference is held each year in Indianapolis, IN. It is hosted by Patti & George Daviau & the gracious Drs from Riley Children's Hospital who volunteer their services. I know this is not an actual PMD fact, but it is where all the "real" experts on PMD meet!

September 13, 2015
Having PMD does not exempt our children from having other conditions too. For example meconium aspiration, diabetes, cleft lip/palette, autism, cerebral palsy, etc.. Some things may be excluded, ignored or attributed to PMD when they may have no connection to this disease.

September 14, 2015
PMD & SPG2 are two different diseases, but both have mutations of the PLP1 gene.

They are at two opposite ends of the spectrum as far as the severity of the diseases. Generally at the high end PMD males talk, feed themselves, maneuver their own manual or electric wheelchair & become toilet trained. It is generally inherited from carrier mothers to their sons.

Generally at the high end of SPG2, also known as Spastic Paraparesis. Males may show some muscle weakness, they generally walk with a somewhat spastic gait & have variable bladder disturbances. The inheritance mode for SPG2 may be x-linked, autosomal dominate, or recessive. Because they are able to live a more "normal" life they will likely have children of their own. The mode of inheritance will determine how they may pass the disease to their children.

September 15, 2015
PMLD OR PMDL (Pelizaeus Merzbacher Like Disease/ Pelizaeus Merzbacher Disease Like) are terms used to describe diseases that are like PMD. The patients, many times females, may have some symptoms like nystagmus & delayed myelin, but generally don't have a PLP1 mutation. Occasionally a PLP1 mutation may be identified but the significance is not clear. It may indicate that a female is a carrier of PMD and her symptoms may or may not be related to PMD. When associated with a male it generally means he has a clinical presentation of PMD but a mutation of the PLP1 gene was not identified. This may be because he doesn't have one & thus does not have PMD or it may be that the mutation was not identified.

September 16, 2015
Testing for PMD focuses on the PLP1 gene. The testing cannot be done by just any lab and the results should not be given by anyone unfamiliar with what the results mean. One of the hardest facts for families to accept is that a negative result for PMD does not guarantee the child does not have PMD, but a positive result is definitely positive. Negative may just mean they didn't find a previously identified mutation. When a Dr or Genetic Counselor says this is a new, first-time, previously unseen mutation, it is not as rare as that may sound. Mutations are unique to individual families. If your child is the first diagnosed member of your family and they find a point mutation that would be a new, unique mutation. But if there is another family with that same mutation you are likely related. I know this is all confusing, but cracking the genetics of humans is a very complex process & as much as we know there is much more that we don't.

September 17, 2015
The nerves of the central nervous system (brain & spinal cord) that send & receive impulses are

covered by an insulation called myelin. This myelin wraps around the axons & allows the impulses to get from neuron to neuron. In PMD the myelin is patchy, or missing. If we think of the nerves like an electrical wire with the insulation stripped off in places we get an idea what happens with PMD. With a poorly insulated wire the electricity may sometimes make it from the switch to the light bulb, but because of the stripped off insulation the electricity can jump to other wires causing shorts, sparking, etc. In PMD the nerve impulse to move your hand may get crossed to another nerve causing you to move your leg, or to just short out & go no where.

September 18, 2015
Because of the defective myelin in PMD patients tests like the BAER & EEG used to test brain waves don't read the nerve impulses properly. This is why many PMD newborns fail the initial hearing test & why things that look clinically like a seizure don't register as such. Because the eye is an extension of the brain Drs sometimes interpret the optic nerve pallor (paleness) as actual optic nerve atropy & assume the PMD child is blind. Drs have to rely strongly on their own observations & the reports of the parent & less on the technology when dealing with PMD children. In today's society people expect immediate, definite answers & because of that Drs try to accommodate those expectations & in doing so they sometimes give erroneous information. Just because professionals tell you your child is severe to profoundly retarded, deaf, blind, etc. never stop encouraging them & stimulating their senses, if you never put anything in you can't expect to get anything back. PMD children do make progress in their development, not as quickly as their peers but in their own time.

September 19, 2015
The 1st test many PMD children get is an MRI, which isn't a very effective test for myelin disorders. But it is an effective test for diagnosing things like brain tumors, malformations, etc.. Since the brains of newborns aren't myelinated an MRI done in early infancy can be misleading, especially if interpreted by someone with limited knowledge reading them. The only definitive test for PMD is the molecular analysis of the PLP1 gene (blood test).

September 20, 2015
Many times we hear there has never been anyone in our family with any type of genetic disorder. Genetic mutations must start somewhere. Life starts with 2 cells that join & then divide & multiply creating thousands of copies. If we think about the human body making those copies like copies in a copy machine we must realize that it isn't like placing a page (gene) on the copier & pressing the number of copies needed. It is place page 1 on the machine, make 1 copy, remove, place that new page on the copier, make 1 copy, remove, and repeat thousands of times. So if when placing a page on the copier it gets turned, or a corner gets folded every copy from that point will then be mutated.

September 21, 2015
PMD is sometimes referred to as a progressive disease, but because the myelin in PMD patients is never properly formed, instead of being actively destroyed it is not exactly progressive. PMD males may lose skills & abilities as they grow & mature, or as a result of recurrent illnesses and/or muscular skeletal changes. But unlike other diseases like Adrenal Leukodystrophy, Crabbes Disease, Multiple Sclerosis, etc. PMD is not progressive.

September 22, 2015
PMD is an X-linked recessive disorder, meaning it is passed from mothers to their sons. When a male inherits the defective X chromosome from his Mother he will have PMD. Because females have 2 X Chromosomes they generally do not have symptoms, their good X balances the defective X. Females who are carriers of PMD have a 50/50 chance of having a daughter who is a carrier of PMD & a 50/50 chance of having a son affected with PMD. Meaning that she has a 1 in 4 chance of having a son affected with PMD. This is the same with each pregnancy. Having a son affected with PMD does not increase or decrease her chance of having another affected son. If a PMD male should have children, the X-linked recessive inheritance would dictate that none of his sons would be affected but

all of his daughters would be carriers.

September 23, 2015
Although the human brain is formed before birth, the myelination of the central nervous system begins at birth and continues rapidly through the first 2 yrs of life. It is believed myelin formation continues to occur until about age 30... Because the nerves of "normal" newborns are not fully myelinated at birth, PMD infants may not look any different at birth & even an MRI done in early infancy may appear "normal". As the myelin begins to form in a baby without PMD & they begin to develop eye, head, hand & trunk control, the differences become more obvious.

September 24, 2015
Myelin is the insulation that covers the nerves. It wraps around the nerves sort of like a jelly roll, protecting the nerves & allowing the impulses to travel properly from the brain to the rest of the body. In PMD it is the nerves of the central nervous system (the brain & spinal cord) that are not properly myelinated, the peripheral nerves are generally not affected.

September 25, 2015
PMD spells... In infancy many PMD males exhibit symptoms that may first appear as colic (inconsolable crying, drawing up of the legs, extension & arching of the back, facial grimacing, eye twitching/fluttering), the episodes may last a few seconds, to several minutes. Because no one gets any sleep Drs may try things like anti gas medications, or melatonin, but if any relief is found it is generally short lived. By this time someone may be thinking this could be a seizure. But since an EEG doesn't detect this as seizure activity, most Drs then begin to address it more seriously as a GI issue. Most PMD infants will show some type of reflux, whether there is a connection to the "spell" or true reflux, is not really clear. They may sometimes respond to medications that reduce the stomach acid. But the low muscle tone likely plays into the situation too. These spells seem to continue off & on with no rhyme or reason. These spells are also sometimes diagnosed as infantile spasms, or night terrors because they seem to happen more at night, or when the child has been sleeping for a while. At this point Drs may try some anticonvulsant medications & the spells seem to respond to these medications. Drugs like Dilantin, Valporic Acid (Depakene) & especially Tregretol seem to work best. These drugs also seem to have an added benefit in that they may help with some of the spasticity/ tightness the boys have. Are they seizures, are they autonomic events, or what? It is not clearly understood, but making them stop makes everyone's life a lot happier. As the guys get a little older there seems to be another form of spell, again what are they... with the lack of myelin who really knows. These spells are generally more like a fainting episode. They seem to happen when they are in a stander, in their chair for an extended period of time, when they get too hot, or perhaps when they are experiencing pain. Which may not register "normally" because of the myelin issue. They generally get fussy, sweaty, clammy, flushed & then sort of melt, get very pale, breathing becomes very slow, blood pressure drops & they faint. When placed in a full reclining position, or with their feet higher than their heart they quickly recover. I would suspect the low muscle tone also plays into this. As they get longer, it takes longer to pump the blood back up to the brain when they are more upright thus making them more prone to fainting. Although it is extremely scary to see the color wash out of their face & lips & see their heart rate & blood pressure drop, but this is what happens to anyone who faints. There are no real treatments that I am aware of to "fix" these spells. It is basically watching them, making frequent position changes & keeping them cool & hydrated. I believe all our PMD guys teater on the edge of dehydration & if they get a little over heated, run a little fever, or run late eating it can easily push them over their limit & cause an issue.

September 26, 2015
There are currently no proven treatments for PMD. Treatment is limited to treating symptoms as they arise. Stimulating sight & hearing in infancy is important in allowing the PMD kiddos to develop to their fullest potential. Good nutritional & respiratory health can enhance their quality of life but not prevent all problems. Early physical & occupational therapy can help delay physical problems

like scoliosis & contractures. But despite the best efforts problems will arise. Their limited physical abilities make them more prone to these types of problems & no amount of therapy can prevent them all. When given the opportunity to explore their environment & do things in their own way most PMD males will amaze those around them with their ingenuity. There are currently some research projects focusing on stem cell, bone marrow transplants, I am not aware of any proven results from these treatments. As modern science & technology are making significant advancements we don't know what future may hold for our PMD kids.

September 27, 2015

Pulmonary complications associated with PMD are similar to other CNS disorders. Poor oral motor skills, decreased laryngeal control, decreased control of thoracic & respiratory muscles. These issues put them at risk of aspiration which can lead to recurrent pneumonias. Treatments for the oral motor issues may include thickened feedings, G-tube, chest physiotherapy, medications to reduce acid reflux & oral secretions as well as oral suctioning. The decreased laryngeal control may result in upper airway obstruction issues like stridor & sleep apnea. Treatments may include supplemental oxygen, cpap/bipap, cardiac apnea monitoring, tracheostomy. Decreased thoracic muscle control may result in issues like scoliosis & may restrict lung function, making them more prone to respiratory issues like low lung volumes, recurrent pneumonias & atelectasis. Treatment may include bracing or spinal surgery. The decreased control of the muscles responsible for breathing can result in things like ineffective cough & recurrent or persistent pneumonias. The treatment for these conditions may include percussion & postural drainage, nebulizer treatments, antibiotics, supplemental oxygen, cough assist vest, cpap/bipap or tracheostomy.

September 28, 2015

There are many GI problems that are common in PMD males things like; poor oral motor skills that result in difficulty sucking, swallowing & chewing. These problems create their own difficulties & contribute to others. They are also more prone to acid reflux, delayed stomach emptying, abnormal/delayed motility & issues associated with these problems. These issues are likely associated with their poor muscle tone. The swallowing issues can lead to aspiration & pneumonia. The delayed stomach emptying & motility issues contribute to things like constipation, vomiting, failure to thrive, etc. The treatments for these issues are the same as for other problems associated with PMD... symptomatic, meaning they treat the issues as they arise. Thickened foods & liquids can help reduce vomiting & aspiration. Gtube feedings can reduce aspiration risk. Small frequent feedings, medications to block acids & speed motility can aid in reducing reflux, vomiting, constipation & discomfort. Sometimes a fundoplication is done at the same time as a gtube, but it can result in other undesired issues such as bloat, dumping syndrome & retching, which can cause the procedure to be undone. Sometimes a g-j-tube maybe needed to bypass the stomach for awhile to let things rest. In severe cases TPN may also be used to get over a severe episode. Most issues resolve given time & effort. As always caring for our PMD guys is a challenge, but they are also such a blessing!

September 29, 2015

PMD males all make progress in their development, although that progress may be very slow. Even those with the most severe form of PMD make progress. They learn & develop is their own unique ways. When given the freedom & opportunity to try, they find ways to do things that seem impossible considering their physical limitations. Even those unable to do much physically find ways to interact with toys, electronics & siblings & peers. Those same individuals who are unable to do much physically find ways to communicate with those around them, those who take the time to "listen". Communication can be in the form of facial expressions or words but it is obvious that they understand much more than they can generally express. Those with more physical abilities find ways to maneuver their bodies in ways to do what they want, or need, to do. It is not impossible to see some PMD males who find ways to actually control electric wheelchairs, video games and/or other games or electronic devices. Many males who speak prefer to speak themselves instead of trying to communicate with computers or vocal assistive devices. Even those who have severe athetoid-type

movements, tremors or ataxia seem to find ways to use their abnormal movements to do things they want. Always allow your child to try to do things, don't discourage them because a Dr says they can't, or hinder them because a therapist says he should not be allowed to do something "his way". We know they won't develop "normally" but they should be given the opportunity to develop in their own way. Don't set their goals so high that they never achieve them, set them low enough that they can & then move the bar up as they do. Several small achievements are better than one failure. If they don't achieve a goal, don't become too discouraged, make a new one! Most PMD males who can speak don't mourn for the things that their parents consider important, things like walking, running, becoming a successful businessman, etc. They appreciate everything in life, are happy with who they are & love with pure unconditional love. Step back & watch them as they teach us about living & enjoying life!

September 30, 2015

*My final PMD fact for the month is on PMD Family Support. This is a project that started in 1984, with my family meeting with the Drs from Riley Children's Hospital & the IU School of Medicine Department of Medical & Molecular Genetics & 3 families I had met with PMD sons of their own. This meeting started the research that identified the PMD mutation in my family & sparked the testing that can now diagnose others. It was during this PMD family meeting that the idea of an official PMD Family Support Conference was born. Our first conference was held in 1990 & has been held here in Indpls, IN every year since. In 2014 PMD Family Support became an official non- profit organization. We have always been a 100% volunteer group & our mission is PMD family support & PMD awareness. The PMD Family Support Conference is a family oriented conference where parents can bring their PMD child/children, siblings, grandparents, aunts, uncles & others to meet with other families who actually have children with the same diagnosis. The Drs provide exams & confirmation of diagnosis when necessary. They educate the families about PMD & the issues the children face. All this education & information is sprinkled in among lots of family friendly, fun activities. It is always our goal to make the PMD Family Support Conference a positive, happy, upbeat event. Many families make this conference a family vacation & come year after year. If you would like to help support this conference you may make a tax deductible donation to PMD Family Support through our web page***PMDFamilySupport.com*** *or mail to PMD Family Support 525 S Harris Ave, Indpls., IN 46222*