Classic Infantile-Onset Pompe Disease (IOPD)

Classic IOPD *without* Treatment

Classic infantile-onset Pompe disease (IOPD) is the most severe form of the disease. It usually appears in infancy, during the first few months of life. It gets worse quickly. Some signs are:

- enlarged heart, abnormal heartbeat.
- muscle weakness.
- poor muscle tone. Babies look “floppy” and cannot hold their heads up.
- trouble with breathing, feeding, and hearing.
- Lung and other respiratory infections.

An enlarged heart cannot work as it should. It is a classic sign of IOPD. As the baby’s condition progresses, breathing gets difficult and muscle weakness gets worse. Babies may never be able to sit, crawl, or stand. The tongue and liver are enlarged. Babies have a hard time sucking and swallowing. They may not gain weight or grow at the expected rate (this is called failure to thrive). Then, as their condition continues to decline, the heart muscle gets weaker and weaker which causes heart and breathing failure.

Without treatment, the natural course of Classic IOPD leads to death usually in the first year of life. However, there is good news. This does NOT have to be your baby’s fate. There is a treatment for Pompe. With treatment, the natural history of Pompe disease for Classic IOPD babies has changed. Please see the next section.
Learn more from these references:

- Baby’s First Test- Pompe https://www.babysfirsttest.org/newborn-screening/conditions/pompe
- Kishnani, P. S., Hwu, W., Mandel, H., et al (2006). A retrospective, multinational, multicenter study on the natural history of infantile-onset Pompe disease. The Journal of Pediatrics 148.5: 671-676.
- Hahn A, Schänzer A. Long-term outcome and unmet needs in infantile-onset Pompe disease. Ann Transl Med 2019;7(13):283

Classic IOPD *with* Treatment

Treatment with enzyme replacement therapy (ERT) and other supportive therapies can change the natural course of Classic IOPD. With treatment, babies have an improved quality of life. They have a better chance of growing into adults.

ERT is proven to decrease the size of a baby’s enlarged heart, which means that the heart can work better. Breathing can then become easier. And many babies develop their motor skills like sitting and standing. However, babies are likely to continue to have medical challenges, and will require treatment for their entire lives. In addition, they may need one or more supportive therapies.

Supportive Therapy

- Physical therapy helps babies gain muscle strength as they grow. Infants, children, and teens can develop motor skills meant for their ages like crawling, running, and playing ball.
- Respiratory therapy is needed for lung infections and breathing problems. Babies may need to use a machine to help them breathe.
- Dietary therapy is needed for babies who have trouble feeding. They may need special diets to grow and develop. Some babies may need a feeding tube.
- Therapies for speech, hearing, learning, and other challenges may be needed.

It takes a team of the family, doctors, and therapists to care for a baby with IOPD. Babies will have different medical care and therapy needs. Their needs will change as they grow. Changes will also come as more is learned about Classic IOPD. Be assured that research continues to find better treatments. The AMDA is actively involved in supporting this research.

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How Does ERT Work?

ERT replaces the GAA enzyme that is missing in the body. The ERT GAA enzyme is made in the laboratory. It is given through the baby's vein into the bloodstream. ERT is done on a regular schedule for life.

ERT works well for some babies but not as well for others. Babies who start ERT early do better. Another factor in how well ERT works is a baby's CRIM status. **C**ross-**R**eactive **I**mmunological **M**aterial or CRIM is a measure of GAA enzyme made naturally in a baby's body. Lab tests can determine a baby's CRIM.

CRIM-negative
Babies who do not make any GAA enzyme are CRIM-negative. They have a strong immune response against ERT, which affects how well it can work. Their bodies treat the lab-made GAA enzyme in ERT as a threat. Their bodies then make antibodies to fight the GAA enzyme. However, there are medicines to help decrease this immune response against ERT. There is also on-going research to change the course of disease. Early treatment can make a big difference in the lives of these babies.

CRIM-positive
Babies whose gene mutations cause them to make GAA that doesn't work at all (inactive) are CRIM-positive. In general, these babies do better on ERT than CRIM-negative. With proper support and disease management, they do much better than the natural history. There are babies on treatment since birth who are thriving decades later.

Effects of IOPD and ERT

ERT helps babies with IOPD live longer. But at all ages, there are medical challenges with multiple body systems. These challenges are different for each person. Some of this has to do with when ERT is started and how well it works. Also, new symptoms may occur as people age.

Some individuals with IOPD continue to have heart problems with enlarged hearts and irregular heartbeats. If that happens, they need to be seen by the cardiologist regularly.

It is difficult to regain lost strength, even with ERT. As babies grow, they may face new challenges during childhood and adolescence. However, with proper support and treatment, Classic IOPD patients have much better outcomes than patients who are not treated.

Breathing in and out may be a challenge due to weak breathing muscles. People with IOPD are at high risk for lung and other respiratory infections. They may need to use machines to help them cough normally and to breathe.

Babies may also experience speech and hearing problems. However, speech therapy can help. There is a high chance of hearing loss in Classic IOPD patients. Hearing aids may be needed.

Swallowing may continue to be a problem and there may be other digestive issues. These should be followed carefully.

There is emerging research that the white matter in the brains of IOPD patients may also be affected, but further research is needed.

AMDA Resources

A diagnosis of Classic IOPD may be overwhelming. The AMDA's goal is that no family will ever be alone when questions and needs arise. **There is hope for the future. We are here to help.** We have many resources and programs to support families and patients. Two important resources are:

Patient Advocate: The AMDA's Patient Advocate, Marsha Zimmerman, is a registered nurse. She has been working as a Pompe Patient Advocate since 2001. She has experience assisting families with everything from access to therapy to disease education and tips for communicating with medical professionals. She also provides emotional support. Whatever questions or issues you may have, Marsha Zimmerman can help. Her email address is: marsha.zimmerman@amda-pompe.org

Mentor Program: This program puts families and patients in touch with other people who have been through similar experiences. AMDA volunteer mentors from the Pompe community are available to help in dealing with a new diagnosis. They can share experiences, feelings, and resources related to Pompe disease. Reach out to Morgan.Burroughs@amda-pompe.org or through links on the website: www.amda-pompe.org

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