



## BREATHING PROBLEMS IN POMPE DISEASE

Many infants, children, and adults with Pompe disease have early signs of breathing problems that can become more serious as muscles get weaker. These problems may develop slowly or come on suddenly, depending on the stage or the severity of your disease. This handout describes the most common breathing problems and how they can be managed. It also explains what steps should be taken to maintain or restore lung function in an emergency or if you ever need surgery.



### **Q: Why do people with Pompe disease develop breathing problems?**

**A:** Pompe disease weakens the diaphragm. The diaphragm is a dome-shaped muscle, which separates the chest from the abdominal cavity. There are four sets of muscles that control the respiratory system. The four sets of muscles are the diaphragm, the intercostal muscles, the abdominal muscles, and the accessory muscles. These four sets of muscles play a major role in breathing. When they get weaker, it can be hard to breathe deeply enough to fill your lungs with air and expel carbon dioxide (CO<sub>2</sub>). This causes CO<sub>2</sub> to build up in your blood, making you feel bad and affecting your overall health. The medical term for this condition is **respiratory insufficiency**.

As Pompe disease progresses, the muscles can weaken leading to low lung volumes, blood gas abnormalities, sleep-disordered breathing, and an impaired cough. If your cough is not strong enough to clear your airways of mucus, it can lead to lung infections and other health problems.

There can be a progressive loss of pulmonary function with Pompe disease, especially in those without treatment. In a 2006 review<sup>Ref 1</sup>, approximately 60% of patients with late-onset Pompe disease were found to have a mild reduction in ability to breathe deeply with reduced airflow in and out of the lungs. Although the pattern of muscle weakness is variable, a rough connection has been observed between measures of pulmonary function and muscle weakness, particularly in the lower extremities.

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Weakness of the diaphragm can be an early and major finding in Pompe disease and respiratory failure often develops while patients are still able to walk; for some patients it may even be the initial clinical manifestation of the disease. Diaphragm weakness may be characterized by a decrease in the vital capacity (VC) while the patient is in the supine (lying down with the face up) versus the sitting position. Objective assessment of pulmonary function in infants is technically difficult, thus complete pulmonary evaluation may require the additional assessment of clinical factors such as daytime energy-level and degree of fatigability (i.e., the ability to feed without developing increased work of breathing).

### **Q: What is respiratory insufficiency (pulmonary insufficiency)?**

**A:** Respiratory Insufficiency is the condition in which the lungs cannot take in sufficient oxygen or push out sufficient CO<sub>2</sub> to meet the needs of the cells of the body. It is also called pulmonary insufficiency. If not treated properly, this can lead to respiratory failure. Respiratory failure describes inadequate gas exchange by the respiratory system, with the result that arterial oxygen and/or carbon dioxide levels cannot be maintained within their normal ranges. If not treated in time, this may lead to death.

### **Q: What are the signs and symptoms of breathing problems in a person diagnosed with Pompe disease?**

**A:** There are many signs and symptoms of respiratory insufficiency, the breathing problem caused by reduced air flow into the lungs. These include:

#### **Impact on Daily Activities:**

- Having a hard time concentrating or staying alert.
- Marked decline in performance (for example, doing poorly in gym class or needing more time to complete tasks at work).
- Feeling short of breath when at rest or after physical effort or exercise.
- Loss of appetite or desire to eat.

#### **Sleep Problems:**

- Being very tired or sleepy during the day
- Having trouble falling asleep or staying asleep
- Frequent nightmares

#### **Other Problems:**

- Anxiety
- Depression
- Morning headaches
- Weak sneezing and coughing
- Using muscles in the neck and spine to help with breathing.

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Having one or more of these symptoms does not always mean you have a breathing problem. Becoming aware of symptoms that make it hard to function during the day or sleep soundly at night can help you take steps to manage them.

### **Q: How often should you have an evaluation of respiratory function?**

**A:** If a patient has respiratory difficulties assessment of the respiratory status should be done on a regular basis as recommended by a specialist. Symptoms reviewed include a cough, the presence of wheezing or shortness of breath, exercise tolerance, energy level, degree of fatigue, and in infants, their ability to feed. Physical examination may focus on the respiratory rate, the use of accessory muscles of respiration, adequacy of air exchange, and quality of the patient's cough.

Spirometry (the measuring of breath) is the most common pulmonary function test (PFT), measuring lung function, specifically the measurement of the amount (volume) and/or speed (flow) of air that can be inhaled and exhaled.

In late onset patients, pulmonary function tests may include measurement of vital capacity (VC), and forced expiratory volume in 1 second (FEV1). Maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) measurements may aid in evaluating respiratory muscle weakness. Diaphragm weakness can be further evaluated by measurement of the supine (lying down with the face up) vital capacity.

For infantile onset disease, spirometry is not an option and infant pulmonary function testing may require sedation, which is not advisable. When available, measurement of crying vital capacity (CVC) can give reproducible measurements of the infant's vital capacity. Negative inspiratory flow measurement (NIFM), a parameter similar to the MIP, gives a measurement of inspiratory muscle strength.

Gas exchange may be evaluated in people diagnosed with Pompe disease to assess for the development of respiratory failure. Pulse oximetry is a non-invasive method allowing the monitoring of the oxygenation of a patient's hemoglobin and capnography may routinely be performed. It is done by the use of a finger pulse oximeter.

Hemoglobin in the blood is what transports oxygen from the lungs to the rest of the body (i.e. the tissues) where it releases the oxygen for cell use.

Capnography is the monitoring of the concentration or partial pressure of carbon dioxide (CO<sub>2</sub>) in the respiratory gases. It's main development has been as a monitoring tool for use during anesthesia and intensive care.

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### **Q: Can weak abdominal muscles and diaphragm impair a cough?**

**A:** Weakness in the muscles can impaired cough which may results in retained secretions and an inability to clear both the normal volume of pulmonary secretions as well as those associated with acute infections. This weakness may thereby predispose the person diagnosed with Pompe disease to develop atelectasis (a complete or partial collapse of a lung) and pneumonia.

### **Q: What kind of therapy can help stretch out the lungs and chest muscles and make it easier to cough?**

**A:** The following therapies can help stretch out the lungs and chest muscles and make it easier to cough:

- **Air Stacking:** Air stacking occurs when a person takes a breath and holds it, and then taking a second breath on top of that and trying to hold that, and putting as much air into the lungs as possible. An ambu bag (which has a mask that fits over the mouth and nose and a flexible bag that forces air into the lungs when it's squeezed) can be used to stack air in a person.
- **Manually Assisted Cough:** This form of assisted coughing involves insufflating the patient with a deep breath and then using either an abdominal thrust or a thoracic squeeze to augment the patient's own cough. The deep insufflations (blowing air into the lungs) allows the elastic recoil of the lungs and chest wall to aid in the expiration, while an abdominal thrust or thoracic squeeze aids in the expulsive phase (and, to a lesser extent, the compressive phase). Manually assisted cough relies on the ability of the patient to keep the glottis closed.
- **Mechanical Insufflator-Exsufflator (Cough Assist):** A mechanical insufflator-exsufflator is a noninvasive therapy that safely and consistently removes secretions in people with an ineffective ability to cough. A mechanical insufflator-exsufflator clears secretions by gradually applying a positive pressure to the airway, and then rapidly shifting to negative pressure. The rapid shift in pressure produces a high expiratory flow, simulating a natural cough.

### **Risk of infection:**

When you have a cold or bronchitis, a weak cough increases your risk for developing pneumonia. Pneumonia is a disease that causes inflammation of the lungs due to the invasion of a virus or bacteria and the resulting buildup of fluid in the lungs. Symptoms include fever, chills, cough, and difficulty breathing. Pulmonary infections should be treated aggressively to avoid complications.

If someone has acute respiratory failure or develops a respiratory infection that is too

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hard to treat, it may be necessary to make an incision (or cut) in the skin and insert a breathing tube into the windpipe to maintain ventilation. This surgical procedure is called a **tracheostomy**. Most people with Pompe disease should be able to get the respiratory support they need by using a combination of noninvasive therapies (therapies that use masks or a mouthpiece and do not require surgery). Sometimes, a breathing tube that is inserted during an illness can later be removed. It is vital for people with breathing problems to be under the care of a pulmonologist or a respiratory therapist so that respiratory support can be started in time to avoid emergency situations.

### **Q: How often should I have a routine evaluation of sleep respiratory function?**

**A:** All patients with Pompe disease should speak with their treating specialist about the need to undertake, if symptoms are present, a review of their sleep. This may include in some cases a sleep study (polysomnography). Alternative studies such as pulse oximetry and/or capnography are insufficient to assess for sleep disordered breathing, though they may be used to assess for nocturnal hypoxia or hypoventilation, respectively. Oximetry alone is not a sufficient screening modality for the assessment of sleep disordered breathing.

Hypoxia is a pathological condition in which the body as a whole (generalized hypoxia) or a region of the body (tissue hypoxia) is deprived of adequate oxygen supply.

Hypoventilation is too shallow or too slow breathing, which does not meet the needs of the body. If a person hypo ventilates, the body's carbon dioxide level rises, which results in too little oxygen in the blood. Hyperventilation (or over breathing) is the state of breathing faster and/or deeper than normal.

### **Q: What does sleep disordered breathing mean?**

**A:** Sleep disordered breathing is often present in people diagnosed with Pompe disease with respiratory muscle weakness. Decrease in upper airway tone, especially during REM (rapid eye movement) sleep, may further compromise ventilation. Nocturnal (occurring during the night) hypoventilation commonly precedes daytime respiratory failure.

In people diagnosed with late onset Pompe disease, sleep disordered breathing may occur while the upright vital capacity is only moderately abnormal due to the disproportionate diaphragmatic involvement. Pompe patients may also have an impaired ability to compensate for any obstructive sleep apnea that may be present leading to worsened hypercapnia (too much CO<sub>2</sub> in the blood) and hypoxemia (decreased partial pressure of oxygen in blood). In infantile Pompe disease, sleep disordered breathing may develop before the patients report symptoms.

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### **Q: How can you tell if you have problems with sleep apnea?**

**A:** Sleep apnea is a sleep disorder characterized by pauses in breathing during sleep. Each episode lasts long enough so that one or more breaths are missed, and such episodes occur repeatedly throughout sleep. The standard definition of any apneic event includes a minimum 10 second interval between breaths, with either a neurological arousal (a 3-second or greater shift in EEG frequency), a drop in the blood oxygen level (desaturation) of 3-4% or greater, or both arousal and desaturation. Sleep apnea is diagnosed with an overnight sleep test called a polysomnogram, or a "sleep study".

### **Q: Is there a list of pulmonary recommendations that may be followed by a person diagnosed with Pompe disease and having respiratory difficulties?**

**A:** The following is a list of pulmonary recommendations:

- Clinical assessment of respiratory status should be performed on a regular basis.
- When feasible, assessment of pulmonary function and gas exchange should be performed at diagnosis, at regular visits, and with changes in patients' clinical condition.
- Chest radiographs may be requested where clinically indicated.
- Maximizing clearance of airway secretions may be routinely performed.
- Patients should discuss with their specialist changes in respiratory function during sleep if the patient experiences changes of daytime sleepiness, unexplained fatigue or has observed apneas during sleep.
- All pulmonary infections should be aggressively managed.

### **Q: What kinds of therapy may help people with breathing problems?**

**A:** Mechanical ventilation helps people with Pompe disease manage breathing problems by sending air to the lungs. The use of machines (known as ventilators) can greatly improve the quality of life for children and adults with respiratory insufficiency.

At first, non-invasive ventilatory support therapy may only be needed at night to help maintain normal airflow while sleeping. A portable machine is used to supply a steady stream of air through a mask that fits over the nose or over the nose and mouth. Mouth pieces can be used to provide breathing support during the day as well if required.

**Types of ventilators most often used by people diagnosed with Pompe disease:**

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- **BiPAP/VPAP Ventilators:** BiPAP (Bi-level Positive Airway Pressure). The BiPAP aids oxygenation and ventilation in cases of sleep apnea or ventilatory muscle fatigue. It has also been applied to prevent the more invasive procedures of intubation or tracheostomy. With bi-level pressure ventilation, the machine pushes air into the lungs at a constant pressure. It then drops down to a lower pressure to allow breathing out.
- **Volume Ventilators:** Volume ventilation delivers a set volume, rather than a set pressure, of air to the lungs, with each “breath.” Volume-cycled ventilators can deliver higher volumes and higher pressures of air than the maximum possible with BiPAP ventilators.
- **CPAP Ventilator:** CPAP (Continuous Positive Airway Pressure) is a method of taking positive pressure and applying it inside the throat in order to keep it from collapsing while you are sleeping. CPAP usually does not give people with weak breathing muscles the kind of respiratory support they really need. CPAP should only be used by people with Pompe disease in rare cases to treat sleep apnea. In general, it can be said that CPAP should not be used by people diagnosed with Pompe disease.

### **Q: How to improve the comfort of a BiPapp/VPAP ventilator**

**A:** A Heated humidification option may be recommended that warms the air in the ventilator and provides enough moisture to prevent mucus dehydration.

### **Q: Some people may experience difficulties with ventilator humidifiers at night because the ventilator hose fills up with water condensation. Why does this happen?**

**A:** This condensation is called "rainout." If your room is cold, the warmed, humidified air hits the colder room temperature and cools. When air cools, the amount of humidity (water vapor) that it can hold is reduced, which causes the humidity to "rain out." The amount of water air can carry varies with temperature: warmer air can carry more water while cold air can carry less. As warm air becomes cooler (ie, overnight), it has less capacity to carry water, so water condenses and forms droplets.

### **Several ways to deal with rainout:**

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- Try turning down the humidity level
- Raise the temperature of the bedroom at night to lessen the difference between the room temperature and the humidifier—make sure that the bedroom window is closed.
- Run the air tubing beneath blankets to keep it warm.
- Cover the tube with aluminum foil or some type of insulation such as a tubing wrap. The goal is to keep the tube and its air warm
- Select a different model of ventilator with a heated hose.

### **Q: What is heated humidification?**

**A:** Heated humidification in the ventilator breathing circuit warms the air and provides enough moisture to prevent mucus dehydration.

### **Q: I am scheduled to have a surgical procedure, and there is a chance that I will need general anesthesia. What steps should I take to help prevent breathing problems or lung infections?**

**A:** If a surgery requires general anesthesia, you should alert the medical team *ahead of time* that you will need extra support to help you breathe and cough when you come out of surgery. Make it clear what option you want. Some people with Pompe disease prefer to have noninvasive ventilation (such as a BiPAP ventilator and cough-assist machine). Others feel that invasive ventilation (such as a breathing tube inserted into your throat) is more effective. Family members who will be helping you through the recovery period will need to learn how to use this equipment. A respiratory therapist can provide the necessary training. You will also want to inform the surgical team if you are already using a ventilator so that a plan can be worked out in advance to handle your anesthesia needs as smoothly as possible. It is a good idea to bring your own ventilator into the hospital with you and you should discuss this with your doctor and anesthesiologist.

### **Q: What do I need to tell healthcare providers about using oxygen?**

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**A:** Healthcare providers may not be aware that it is inadvisable to give oxygen to people with Pompe disease who are having trouble breathing. It can be dangerous and should only be used with knowledge and with caution in a controlled environment when needed. Remember that breathing problems in Pompe disease are caused by weak muscles not by lung disease. In fact, most Pompe patients have healthy lungs. Instead of helping you breathe more deeply, the rush of oxygen shuts down your natural urge to breathe. The level of CO<sub>2</sub> in your blood goes way up and puts you at risk for respiratory failure. This can be avoided by giving you ventilation therapy that restores deep breathing. To protect yourself in an emergency, you may want to wear a medical-alert bracelet or carry written instructions from your pulmonologist or respiratory specialist. Oxygen may only be used in the hospital when you also suffer from a lung disease like pneumonia or to provide comfort in the late stages of Pompe disease.

### **Where to Learn More: Please see the More Information section**

Ref 1

Pompe disease diagnosis and management guideline

Genetics in Medicine

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