Respiratory Care in Lysosomal Disorders

Dr. Ozlem Goker-Alpan:

Hello, everyone. I would like to welcome everyone to this year's last CME presentation, and the third of the CME quarterly series on lysosomal disorders. It is my pleasure to welcome our guest speaker, Dr. John Bach.

As an introduction, I would like to first start with the lysosomal disorders that present as pulmonary diseases, so we're going to be covering the pulmonary manifestations of lysosomal diseases. The main topic is how to assess patients, monitor, and to manage and treat the bonds that come with that pulmonary disorder. So the reason that pulmonary system is not too much in mention is because pulmonary system is not majorly primarily involved in lysosomal disorders. So when you go to the textbooks or Google whether the pulmonary system is primarily involved, we actually came into mostly the sphingolipidoses.

So as presented as interstitial lung disease when you get an X-ray, it is typical is basically in ground-glass appearance in a child or in an unsuspecting adult. So if you want to do a differential diagnosis with this x-ray and for a patient who is suspected lysosomal disorders, then the primary diseases that we are going to be looking into are Gaucher disease, this is the neuropathic Gaucher disease more prominently. There's Niemann-Pick A/B, Farber disease, and Fabry disease. Actually, Fabry disease can present as interstitial lung disease, not as a primary manifestation, but obviously as a comorbidity.

The second scenario is the lungs are normal. However, there is lung disease secondary to the involvement of the muscles of the respiratory system that includes the diaphragm, which is a big muscle, and also other accessory respiratory muscles. The third way, how the airway and respiratory system is involved, so basically the soft tissue infiltration accompanied by limited chest mobility, and mucopolysaccharidosis is the prime example for that. If you want to dig into a little bit more into pulmonary interstitial disease and the pathophysiology of that, actually, this x-ray appearance by pathology is accompanied by infiltrative or inflammatory cells invading the tissue in the upper side that you are seeing the CT scan. That is actually very pathognomonic for interstitial lung disease even though the X-ray is not doing the justice. Actually, you are seeing this hazy appearance.

In the postmortem studies, you can see the immune cells, which is the Gaucher cells here in the perivascular space, in the interstitium, and rarely at the alveolar space. Actually, that is probably the terminal event in a patient with Gaucher disease. When we talk about the secondary pulmonary involvement, so basically, this is the complication of the disorder. So obviously, hepatosplenomegaly or having a huge liver and spleen will decrease the vital capacity of the lungs. So even though lungs are normal, you can get restricted pattern in a breathing test. Obviously, similarly, spines like progressive kyphoscoliosis that occurs in Gaucher disease or in MPSs, also the chest deformities, pectus carinatum or excavatum, actually can give the restricted pattern on the PFTs. And obviously, secondary cardiac disease that occurs in Fabry disease, MPSs, and similarly recurrent infections and aspirations can give rise to chronic lung disease. More rarely, we can actually evaluate the patient for pulmonary hypertension as in type 1 Gaucher disease or due to chronic respiratory failure in patients with Pompe disease.

So even though we don't usually deal with a patient on a respiratory support, meaning as a geneticist I am, but it is not uncommon for the patients to be on ventilatory support and even have tracheotomies, which any disorder that has a progressive neurological disease and that includes Gaucher disease, Tay-Sachs, so on and so forth, and when there is central apnea stridor or laryngeal dysfunction like in

Gaucher disease or there is a progressive diaphragmatic or accessory respiratory muscle dysfunction like in Pompe disease.

So I don't want to actually have the audience take more time, and I would like to go ahead and introduce Dr. Bach, who is a leader in helping patients with varied neuromuscular diseases to breathe effectively. Dr. Bach has received his medical degree from the College of Medicine and Dentistry of New Jersey and had extensive training in pulmonary rehabilitation and non-invasive mechanical ventilation. He's currently a professor of physical medicine and rehabilitation at Rutgers New Jersey Medical School, as well as a professor of neurology and medical director at the Center for Non-invasive Mechanical Ventilation. So he has authored more than 200 publications on the respiratory issues in both lysosomal and neuromuscular disorders. He also has seven books on neuromuscular pulmonary rehabilitation and non-invasive mechanical ventilation. Today, Dr. Bach is going to share some of his experiences in helping people with neuromuscular condition like Pompe disease lead breathable lives. Thank you. Thank you, Dr. Bach. The podium is yours.

Dr. John Bach

That’s a wonderful introduction. A really wonderful introduction to this because I'm going to explain that it's extremely important to distinguish people with intrinsic lung disease from people who have potentially normal lungs but have muscle weakness and people with airways disease and also people with upper motor neuron disease, and you'll understand why as we get into this. I have no conflicts of interest to declare, and you're going to also learn something that nobody ever needs a tracheostomy tube for being too weak to breathe, and we'll go over this.

Now, I'm not going to spend time on the basics of lysosomal storage diseases. I guess I could say that technically, Gaucher is the most common at one in 40,000. It's estimated that there's one in 7,000 of the population that has these conditions, but some of the conditions, as you said, affect the lungs intrinsically and others, basically the diaphragm and the respiratory muscles.

Now, I have my most experience with Pompe disease. I've got 14 basically adult-onset Pompe patients and several with Morquio so that's where my experience lies. I'm going to want to talk about the respiratory management of these patients. I'm sure you all know how to make the diagnoses at this point. I will tell you that several of my Pompe patients had been diagnosed with limb-girdle muscular dystrophy, and it turned out that they did not have that. One of the first indications that there was something funny going on with the diagnosis was the fact they couldn't breathe lying on their backs, so it's classical for all of my, basically, adult-onset Pompe patients that we initially expected this or to search for it because the patients could not breathe lying on their backs. The reason they couldn't, their vital capacities went down drastically when they lie on their backs because their diaphragm was weak, and this is not recognized by pulmonary function testing.

Pulmonary function testing is virtually useless for the diagnosis of any muscle weakness condition. The vital capacity when you're sitting is not nearly as important as the vital capacity when you're lying down. The difference between the two should not be more than 7%, but when patients get short of breath lying on their backs, the difference can be as much as 80%, and this is completely missed by pulmonary function testing. Likewise, I'm going to tell you that sleep studies are not important either. I have 3,000 patients on non-invasive ventilatory support. I haven't had to order polysomnograms on any of them, and I'll explain to you why, and you'll understand before this is finished.

Yeah, so one in 40,000 Gaucher's disease. Pompe was described in 1932, acid alpha-glucosidase deficiency, but you know all of this. Okay. You will learn how to prevent ventilatory or respiratory failure and any need to resort to tracheostomies for lysosomal storage disorders that are not predominantly intrinsic in nature, which I have never seen one that was. You can have infiltrative disease in Gaucher

and Fabry's and so on, but the primary problem has usually been muscle weakness from the diaphragm, infiltration of the diaphragm and other respiratory muscles.

So what I like to do is describe the Pompe's and other neuromuscular conditions in terms of type 1 through type 3 or type 4. I got this idea from SMA because children with spinal muscular atrophy type 1 never sit, and they usually stop breathing during sleep between five and eight months of age because their muscles are week. They also have paradoxical breathing, whereas their diaphragm goes down, their belly goes out, but their chest wall sinks in. That's paradoxical breathing.

Now, I can tell you right now, with Pompe disease, infantile Pompe disease, or any neuromuscular condition where there's paradoxical breathing, if you do not reverse the paradoxing during sleep by placing the patient on ventilatory support settings to reverse the paradoxing, the lungs will not grow, and the patient is going to die pretty soon. They need ventilatory support settings to rest their muscles overnight so that they're stronger during the day, but also to reverse paradoxing. Now, I consider type 2 disease to be, well, in SMA, it's children who can never sit, but in any infants with congenital myopathies, Pompe, or anything else, you have children who cannot sit. I'm sorry. With type 1, they don't sit. With type 2, they can sit independently.

However, there's type 2A and 2B depending on if they have paradoxical breathing or not, so in other words, any child with any neuromuscular condition with severe muscle weakness who has paradoxical breathing. Now, in the case of SMA, it's all type 1s, and it's half, literally 50% of type 2s, they have paradoxical breathing. They need to be on nighttime ventilatory support to expand their lungs and reverse the paradoxing or their prognosis. Now, with type 2B disease, the patients don't have paradoxing and they usually do not need ventilators overnight. With all these types, including type 3 where children can walk for a period of time as occurs with childhood-onset Pompe disease, even when these kids have the type 3 condition, their cough flows may be ineffective. So for example, there are children with type 2B and type 3 neuromuscular conditions, including Pompe, who do not need ventilators except when they're sick. When they're sick, they need non-invasive ventilatory support 24 hours a day for the time that they're sick.

Now, the problem in the United States is it's very difficult to do this because the insurance companies often want three or four days to approve a ventilator, but of course, these kids get short of breath without the ventilator and without what was called a CoughAssist for mechanical insufflation-exsufflation, which I will describe. And so, they go to the emergency room. Now, when they go to the emergency room, when you or I or anybody goes to the emergency room with any respiratory symptoms, the first thing that is done is that we're given oxygen, but that does not solve the problem. The oxygen saturation is going down not because of hypoxic respiratory disease. It's going down because the patient's not able to clear their secretions and ventilate their lungs to a normal CO2. That's usually what the problem is, and it's only worsened by getting oxygen.

So the first thing that people taking care of lysosomal storage disorders need to understand is you need to distinguish if the primary symptomatic problem is from intrinsic lung disease, which frankly, I have never seen, although I'm sure it exists and is usually perhaps cared for by pulmonologists, or if the problem is predominantly muscular, in which case giving oxygen is pretty much the worst thing you could do until you actually intubate the patient. So again, in children, whether they can sit or walk or not, if they have a neuromuscular condition where it prevents them from running, if a child can run, they probably have adequate cough flows, but the cough flows in type 1 and type 2A disease are essentially zero, and a mild cold will cause pneumonia for that reason. In type 2B disease and type 3 disease, the cough flows are not ideal. Some kids can get over colds without getting pneumonia, but it's extremely difficult and all these kids should have access to mechanical insufflation-exsufflation.

Now, let's go on. This is a child with Pompe disease. You see that head lag. This child has severe paradoxical breathing. Now, enzyme replacement therapy in infants with Pompe disease that I have seen work. They can triple the life expectancy, but usually, these kids die from heart failure even at one or two years of age. We can prevent respiratory deaths 100% of the time by doing what we do, but in infantile Pompe, we cannot prevent cardiac deaths. In contrast with adults with Pompe, usually, their hearts are not significantly affected at all, and they can go into cor pulmonale from bad pulmonary management. So that's another system.

So this is a type 1 condition, and how we ventilated these children before nasal interfaces were on the market was by taking Hudson CPAP prongs, putting them through the nasal bridge of a CPAP mask, the foam that you see here to seal the nostrils, and ventilate the child's lungs to expand them to reverse the paradoxing. This provides full ventilatory support for when the child needs it or the adult needs it for that matter, we'll go into that, and also rests the muscles overnight. BiPAP doesn't do this because for decades, BiPAP was prescribed at spans of four to six, which is... Well, we'll talk about that in a minute.

The other thing that you're going to learn is that nobody ever needs to be trached for being too weak to breathe. That includes children with SMA type 1 and infantile-onset Pompe disease, of which this child, for example, was intubated at 17 days of age, totally unweanable, in ventilatory failure at 17 days of age. He failed two extubation attempts, and the doctors wanted to trach him, but the mother knew about us, so told the doctors to call me, and I explained how to extubate this child. But basically, what they tried to do is extubate the child to oxygen and BiPAP, and that's a good way to fail.

We extubate the child to full non-invasive nasal ventilatory support like you see here. And this child, they succeeded, which is remarkable because most of the time critical care doctors don't want to hear anything about this. They just want to trach the kid and send them to an LTAC or to another institution so that the complications that will eventually kill the child are not their problem. So harshly put, but it's honestly true. So anyway, this child was successfully extubated and eventually came off the ventilator and was able to sit with enzyme replacement therapy.

Signs and symptoms of infantile-onset Pompe disease as I think you know, basically it's cardiopulmonary is why these children die. And like I said, we can't do so much for the heart, but we can prevent respiratory problems. Now, this is a patient with Morquio. I believe he's 32 years old, one of our patients with Morquio, and his history is really very interesting because it's really typical. I considered him to have neuromuscular condition type 3 because he was able to walk until he was two... Let me see, when he's two and a half... He was born in 1984. He was floppy at birth, diagnosed by biopsy, his skin fibroblast. In 1990, at the age of six, he got pneumonia, was hospitalized and intubated, unweanable, transferred to us to be extubated. That happened again two years later when he was eight. So in other words, he was hospitalized locally in New York State. He would've been trached and he would've died from...

52 over 80% of patients on trach ventilation with neuromuscular weakness die because of the trach tube, not directly because of their neuromuscular condition. This is kind of amazing when you think about it, and it's very different from lung disease because when a person presents to a doctor with COPD and their FEV ones, their forced expiratory volume in one second, is 750 or less. Their five-year prognosis for survival is only 30%. That's worse than many cancers. So if they get trached, they often don't die from the trach tube. But I have patients now on 24-hour non-invasive ventilatory support since coming out of our lungs in 1954, 70 years of continuous ventilatory support with no ability to breathe whatsoever and no tracheostomy tube.

I have 18 patients with spinal muscular atrophy type 1, zero vital capacity. They are 18 to 30 years old with no muscle movement whatsoever, no muscles above or below the neck, yet they don't have trach tubes. You cannot get weaker than that. It is impossible to get weaker. The only thing they can move is

an eye, and one of them can move an eye and the eyelid. Others cannot even open their eyelids. You have to open the eyelid and ask them yes or no left and right. They can't move their tongue a millimeter. They don't have a finger. They don't have even trace muscle movement, and yet, I have three of them over 30 years old now like this, and the only way they can communicate is with the eye movement through their computer. So if that's the case, nobody with Morquio or any lysosomal storage disorder that causes muscle weakness should ever need a tracheostomy tube, and they won't need it if they come to us. I'll tell you right now.

In fact, I guarantee to my patients the first time I see them that you'll never need a trach tube and don't let any doctor convince you to get one because it'll probably kill you. And quite frankly, that's the case. So, what was done was the child was extubated successfully to 18 centimeters of water pressure. Inspiratory pressure's 18 and zero and did fine. Oh, this is the Morquio patient. We extubated him to full ventilatory support. Now, if you or I need general anesthesia and we go to an anesthesiologist, and we say to them, "Well, while we're under with a neuro paralyzing agent, we essentially have zero vital capacity. And how do you ventilate my lungs? If you give me a normal tidal volume, what pressure do you need to give me?"

They'll tell you 17 to 20, 22 centimeters of water. So obviously, that's what you need to rest your muscles and to give you a full breath if you cannot breathe at all. Or they could, of course, give you five or 600 milliliters of air, which will create a back pressure of 18 centimeters of water. It basically comes out the same. So why in heaven's name when a patient is intubated or trached and if you look at the PIPs, the positive inspiratory pressures on the ventilator, they're 18 to 20 centimeters of water. Why do critical care doctors extubate these unweanable or these very, very weak patients to a BiPAP of 8 and 4 or 10 and 5, which is a pressure support of five? And then when they fail the extubations, say that, "Well, NIV didn't work, so we had to trach them." This is absolute nonsense.

Non-invasive ventilation is having a ceiling fan in a hot room or using CPAP, which is a continuous flow of air, which is a pneumatic splint to keep the airway open, so you could use your muscles to breathe. But if the problem is that your muscles are too weak for normal ventilation, the CPAP is completely useless, yet it's called non-invasive ventilation.

In 1990, because there were so many people overweight who couldn't really breathe and who had obesity hypoventilation, but when they increase the CPAP to 20 or 30 centimeters of water, it's like breathing in a tornado, they developed BiPAP. BiPAP, you get the air when you inhale at a higher flow than the air stopping you from exhaling. However, the only way to ventilate severely morbidly obese patients, 400-pound patients, to a normal CO2 is not with the pressure support of 18 to 20, but with an inspiratory pressure of 35 to 55 centimeters of water, which means that if you give them EPAP of, say, 10, you've got to increase the IPAP by that amount to get the CO2 normal. And it's not true that patients should be breathing with CO2s of 60. They're only going to go into cor pulmonale and die from heart failure.

We ventilate 400-pound patients here without trach tubes. We even take their trach tubes out when they have them on pressures of about 35 to 40 centimeters of inspiratory PIP, positive inspiratory pressures, to normal C02s, get them off of oxygen, and they never need trach tubes. So with lysosomal storage disease, you don't need pressures of 30 or 40 or 50 centimeters of water unless there's severe restriction on the lungs. Now, is there a limit to how you can use non-invasive ventilatory support settings? Well, we do use them on patients with restrictive lung disease from severe scoliosis and morbid obesity to pressures of 40 centimeters of water. However, if you're extubating somebody and you need pressures like that, there tends to be a lot of leak and sometimes, well, difficulty training patients how to use non-invasive ventilation when their lungs are that stiff.

I guess I'm getting off of the subject of this patient here. All right, so he was transferred twice to us because he is unweanable and intubated. We extubated him. We've had him on nighttime ventilation since he was six years old. He had scoliosis surgery when he was 14. We extubated him to full ventilatory support, which was a bi-level of 22 and 4 for a pressure support of 18, 22 minus 4. In January of 2004, his vital capacities were varying from 580 to actually about 1,000 now that we do sitting and lying down. Lying down was lower. In July of 2015, somebody put him on BiPAP. He was doing so well. He didn't come to see us for a few years. He was on a BiPAP of 12 and 8 with an AHI of 77. We, of course, stopped that and put them back on 22 and 4. Now, normally, we switch patients to active circuits, so we could shut off the EPAP, and I'll tell you why very soon.

But on 22 and 4, his apnea-hypopnea index became zero. He was getting full pressure ventilation and was doing very well with normal blood gases day and night. He started replacement therapy in December of 2015. Now interestingly, even though he got to require ventilator use day and night, every night and for many periods during the day till he was actually using it most of the day, and even though his vital capacity has not gone up tremendously since he began replacement therapy, his vital capacities have improved a little bit. He no longer needs to use the vent during the day, and his manual muscle testing is slightly better.

I am totally convinced, as I am with some of my adult patients, that the replacement therapy has been very beneficial for him. His left ventricular ejection fractions are normal. He has an AV block, some mitral thickening, but oh, interestingly too, with the replacement therapy, he lost the ability to walk at the age of two and a half. But then four years after starting replacement therapy, he started walking again and he has been walking ever since. He can still take some steps. So that's one of our several Morquio patients, and he's bright. He does have hearing deficit and seizures, so he's sort of a classic Morquio individual.

Well, again, it's cardiac and pulmonary that we're concerned about. Of course with lysosomal storage diseases, the GI tract can be involved, the spleen, but you know all of this, and I don't really want to go into that, enzyme replacement therapy. Okay, so now, this is crucial. One of the questions asked was about what pulmonologists need to do about this or need to know. The fact of the matter is pulmonologists treat lung disease, they don't treat muscles. When they try to wean people in critical care units, they do it by synchronized, intermittent mandatory ventilation and decreasing pressure support, which means that the patient never gets full rest. It's like lifting weights at 70% of your maximum capacity and never resting your muscles. When you treat muscles like I do, if you want to make them stronger, you've got to rest them and exercise them, not continually use them at sub maximum capacity levels. That can just make them weaker. So pulmonologists really end up traching all these patients because when they're unweanable, they think they need to be extubated to a trach tube. That is never the case.

So number one, you got to distinguish the patient with ventilatory pump failure who cannot cough effectively or breathe to a normal CO2 and from muscle weakness like these diagnoses I have here, including morbid obesity, chest wall disease, spinal cord injury, and so on, where there's an increased work of breathing from upper motor neuron diseases. Now, what do I mean by that? I mean people with traumatic brain injury, stroke, cerebral palsy, Lou Gehrig's disease, ALS. When you have upper motor neuron disease, the upper airway tends to close. So on babies with type 1 neuromuscular disease, when I use mechanical in-exsufflation on them at 50 to 60 centimeters of pressure, mechanical in-exsufflation is like a vacuum cleaner. It delivers a deep breath, but then the pressure drops from plus 50 or 60 centimeters of water to minus 50 or 60 centimeters of water. And I use these pressures on infants as well as on adults.

I know what you're thinking. Aren't you afraid of barrel trauma? It doesn't happen. The way we use it, it just doesn't, and the pressures in the lungs are not 60 centimeters of water. But at any rate, when you use those pressures like applying a vacuum cleaner to the airway, non-invasive suctioning, it creates 10 liters a second of flow to bring secretions up from the right and left airways. Now, if you suction through a trach tube or a translaryngeal tube, up to 92% of the time, you don't get the left main stem bronchus. It goes into the right airway because of anatomical reasons. The tube just goes in, down the trachea, into the right airways, which is why over 80% of pneumonias in these patients are in the left lung. When you use mechanical in-exsufflation at effective settings like 60 to minus 60, it clears both the left and right airways and prevents pneumonia and allows us to extubate unweanable people because we can get their secretions out.

So because of the availability of mechanical in-exsufflation, because we extubate to full ventilatory support settings, which you can do with BiPAP, but it's not been done until recently with volume-targeted BiPAP, but even with that, it's not usually used optimally, no one needs a trach tube for being too weak to breathe from ventilatory pump failure. Proposition two, as I've mentioned, muscle strengthening requires rest and exercise, and you don't do this with SIMV, PAV, low span bi-level, CPAP, or oxygen. In fact, oxygen is actually harmful for these patients, and it's counterproductive and it's no substitute for non-invasive ventilatory support settings or mechanical insufflation-exsufflation. Number three, it's easier to extubate ventilator unweanable patients, even patients with no respiratory muscles whatsoever, than to remove the trach tubes of patients who are unweanable. But we've done that, too.

Just last year, we removed the trach tube of a 28-year-old with spinal muscular atrophy type 1, who's been 24-hour dependent on nasal ventilation since eight months of age, was trached as an emergency at the age of 28. Six months later, he wanted the trach out, and we removed it even though he doesn't have any muscle movement above or below the neck anywhere except the use of one eye and the eyelid, and he wanted it removed in his house. I have more faith in his nurse and his mother than a lot of other people. So we actually removed the trach tube in his house. I'm not recommending this to anyone else now. I make that clear. It's better to do this gradually. First of all, remove the trach tubes of patients who only use them overnight than patients who need them overnight and some periods during the day, and eventually like us, you should be able to remove the trach tubes of anybody who's 24-hour vent dependent and who should never have gotten them in the first place.

So what is NIV? As I mentioned, NIV is CPAP and BiPAP. It's usually not provided at full ventilatory support settings. The EPAP is bad for people with healthy lungs. It's fine if you're a neonate. It can help them. It can help people with COPD. It can help perhaps people on trach ventilation with no subglottic pressures. But EPAP is not only not helpful, it's a little bit harmful for patients with ventilatory pump failure. Why? It increases intrathoracic pressure, it increases sensitivity of the myocardium to sympathetic stimulation and arrhythmias, decreases cardiac preload, stroke volumes and output, causes ventilator auto cycling, disrupts sleep. It increases the risk of reflux and aspiration. It prevents active lung volume recruitment to maintain pulmonary compliance, to increase voice volume and cough flows, and it is uncomfortable. That was published by Dr. Crescimanno on bulbar ALS patients in 2016, and she's right.

The EPAP is actually counterproductive, and the only reason it's being used is because doctors can bill for polysomnogram and for titrating away apneas and hypopneas that are completely useless because if you put the patient on non-invasive ventilatory support settings, there is no obstruction to the airway that will prevent the air from ventilating the lungs, and exhalation is passive. Now what do I mean by that? We published a paper last year on morbidly obese people for whom CPAP of 30 centimeters of water was not normalizing their CO2. Their CO2s were 60 to 80. What we did was we turned off the EPAP and we put them on an active circuit and ventilated them at 35 to 55 centimeters of water pressure to a normal CO2, turned off the O2, and they no longer had obstructive apneas because a

pressure of 50 centimeters is going to get past the obstruction, and the exhalation is passive. So again, these patients don't need EPAP. Is it harmful for them? Slightly, but it's also uncomfortable. There's some more reasons why the EPAP is not useful.

So what is non-invasive ventilatory support settings? Okay, again, as I said, you can use high-span BiPAP at greater than 16 centimeters of water spans, generally 18 to 20. You can use intermittent positive pressure ventilatory support at a pressure assist-control ventilation of about 20 centimeters of water, or you could use volume assist-control ventilation. Now, for adolescents and adults, I usually set a range of 650 to 1400 or 1500 milliliters. When the patients are sleeping, their brains control how much of that air they take with every insufflation, with every breath, and it ventilates them to usually a normal CO2, normal oxygen saturation. And like I said, well, and that's how we do it for like 3000 patients at this point. I try to avoid BiPAP. Sometimes the patients actually get used to EPAP of four, but I usually get my patients off of it and onto non-invasive ventilatory support settings.

In 1952, they did not have iron lungs in Denmark, so they started putting patients in trach tubes in patients. But in the Rancho Los Amigos in 1953, Dr. Affeldt said the therapists and the patients were using the tubing from a Zephyr device and putting it by the patient's mouth and the patients was getting deep breaths and stopped going into iron lungs. And he said, "The mouthpiece, you just hang it by the patients. They grip it with their lips when they want it, and when they don't want it, they let it go. It's just too simple. I don't know why we didn't think of this a long time ago." My mentor, Dr. Augusta Alba in 1957 took 257 patients out of iron lungs, gave them a mouthpiece, used ventilatory support settings, which were pressures of 20 to 25 centimeters of water. There was no EPAP or PEEP on those Bantam ventilators. I published this in 1993. In 1969, Dr. Alba began to remove the trach tubes of unweanable spinal cord patients and put them on mouthpiece ventilation day and night.

In 1981, I was the first person to use nasal non-invasive ventilatory support, and I started putting it on patients in 1984. We started extubating unweanable patients to it in 1988 after Jack Emerson gave me his In-Exsufflator, the prototype of his CoughAssist or his mechanical insufflator-exsufflator. And then 60 years after John Affeldt described mouthpiece ventilatory support, Respironics put a mouthpiece ventilatory support mode on their Trilogy ventilator. So doctors take a lot of time to learn things. In this case, it was 60 years. This is one of my patients who's 79 years old on 24-hour mouthpiece ventilation since 1954. She used the lip seal overnight, and some patients still use these lip seals, although most patients prefer nasal ventilatory support. In 1981, there was no CPAP mask available. I took Foley catheters, put them in my nostrils, inflated the balloons, hooked myself up to a Monnal D ventilator, ventilated my lungs, but I didn't think it would work overnight. I thought the air would go through the nose and out the mouth.

1984, this girl with under 200 milliliters of vital capacity, I was able to ventilate with nasal ventilatory support. That year, CPAP mask came on the market. We used them. We taped the holes shut to use an active circuit because you need to use non-vented interfaces when you use an active circuit and you don't want EPAP, and that's what we did with her. Two years later, we extubated this MS patient who was unweanable. Her vital capacity had decreased to 250 milliliters. She hadn't slept in three days. I put her on nasal ventilatory support like this. After three days of not sleeping and being anxious, she immediately fell asleep. Her vital capacity was 250. I was giving her 900 milliliters through this mask, and I put a spirometer at the exhalation valve. She was exhaling back 750 milliliters of the 900 I was giving her. In the morning, her vital capacity was 100 milliliters. I asked her why she was still using the nasal ventilation, and she said, "Because I can't breathe without it."

She responded to ACTH treatments, and four days later, her vital capacity was a liter and a half, and she came off the vent and went back home. So then I started thinking to myself... By the way, her mouth never closed, so I got a flashlight. I looked through her mouth, and I saw that the air was going through

the nose, pushing the soft palate against the back of the tongue, sealing off the oral pharynx, and she was getting almost all the air I was giving her, maintaining normal ventilation throughout sleep and normal oxygen saturation. So then I thought to myself, "What about my patients with zero vital capacity on mask, on lip seal ventilation at night?" I convinced two of them to let me watch them all night and to use nasal mask like this, and they never desaturated. In fact, the two of them never opened their mouths. They maintained, with zero vital capacity, normal ventilation all night long. But then I asked them if they wanted to continue nasal ventilation. They said, "No, I want to go back to my lip seal, my mouthpiece ventilation."

In 1988, two of my patients put a request in the newspapers for somebody to put the Cofflator back on the market. The Cofflator is mechanical in-exsufflation. It gives you a deep breath and the pressure drops to basically minus 55 centimeters of water, which is how it was used in the 1950s and '60s. Patients who had these things would never give them up because they knew that this was what was saving them from ever needing a trach tube and going into respiratory failure. We started using it. This was a 72-year-old woman spinal cord injured, less than 200 milliliters of vital capacity, who was intubated. We extubated her, used this machine on her to clear her secretions, and managed her by non-invasive ventilation, and that's her. We extubated her to mouthpiece ventilation to nasal ventilation. We let her choose what she wanted to use. She used the mouthpiece during the day and nasal at night and went home and never got a trach, never had airway secretions because she never was intubated long enough to actually develop them very much.

Now, this is a 54-year-old with Duchenne muscular dystrophy who's been on 24-hour ventilatory support for 30 years. He's never been to a hospital, and he's been married for 30 years and that's his wife of 30 years. This was taken at their 25th wedding anniversary in 2018. I have four Duchenne patients over 50 years old and over 100 over 40. None of them have trach tubes. I tell them on first visit they will never need a trach tube and don't ever let a doctor convince them to get one or anyone in their family to put one in them. ALS patient, 24-hour nasal ventilation. Okay, fundamental principles to learn. Nobody ever needs a trach, as I mentioned. You must distinguish simple... Okay. Ventilatory pump failure is when the patient cannot maintain the CO2 and the CO2 goes up, and the CO2 can go up long before the oxygen saturation goes below normal, which is 95%. However, the CO2 can be normal and the saturation go down during colds when there are airway secretions or RSV or COVID. That is not a reason to think that they need a trach tube.

First, you need to ventilate them noninvasively, which in emergency rooms could be done with high-span BiPAP, although it's certainly not ideal, but you need to use the CoughAssist or the mechanical in-exsufflation to try to get their saturation back to normal without giving them oxygen. If you're going to give these patients oxygen, they usually cycle downwards to the point where they stop breathing. Their CO2 goes through the roof. A CO2 of 50 can go to 180 in 20 minutes, and the pH drop to 6.9 and the patient then gets intubated. Then, when they're intubated, the doctors never shut off the oxygen. They think they're unweanable and need to be trached. Nobody, even if they are unweanable, needs to be trached, so that's what you got to understand.

The big problem for people with Pompe and other neuromuscular disease is, like I said before, how do they get access to non-invasive ventilatory support when they're sick? How do they get access to a CoughAssist when they're sick? If their cough flows are over 270 liters a minute, they're not likely to need it when they're sick. But you've got to measure the cough flows and understand this. Babies typically get exsufflation flows with the CoughAssist of 50 to 70 liters a minute, which is little, which is why they end up getting intubated once a year when they have paradoxical breathing. After the age of five, and they're able to cooperate with the CoughAssist, hospitalization rate is two per 50 years, and after the age of 10, it's two per 100 years, even for patients with zero vital capacity and no muscle

movement at all because they're able to use the CoughAssist effectively to get flows of almost 400 liters a minute.

Again, your critical care doctors do not understand this. Your neurologists don't understand it, and your pulmonologists don't understand it. In fact, your physiatrist don't understand it. By the way, it's not just the necks of people with lysosomal storage disease, any of you who have an elderly family member, 85 years old, let's say. Do you know that women lose 1.2% of their vital capacity per year from the age of 20? Men lose 1% a year. By the time you're 85, you're down to less than half of what you had when you were young. Then, you get a bronchitis or a kidney stone. You go to a hospital and what do they do? They give you nothing to eat because they want to do imaging or surgeries. They wake you up all night to check vital signs and you lie in a hospital bed. You lose 1 to 3% of vital capacity per day.

After a week or two, your 85-year-old is going to get short breath. Do they give you a mouthpiece with a ventilator delivering deep breaths or through the nose? No. They stick a tube through the nose or mouth into the airway, hook you up to the vent, knock you out, and then tell the family, "Well, your grandma had a good long life. She wouldn't want to live on a respirator with a tube to her neck, but we could put one there, or we could give her oxygen and morphine," which is a palliative death. They never tell you we could extubate her to a nasal ventilatory support and use the CoughAssist. They never tell you that. And frankly, not too many people are anxious to learn it. Okay. So you need specifically trained respiratory therapists who know how to set people up on non-invasive ventilatory support.

By the way, in New Jersey and in New York, we can get ventilators and CoughAssist to our patients within an hour or two because the home care companies here, all of the therapists are trained by a therapist I've been working with since 1983. By the way, that's 1983, not 1883. And he trains all the therapists for the company, and the company knows that we have to get them what they need within an hour or two, or they end up in the hospital with a tube down their throats. So your local clinics need to be able to provide this knowledge to the local clinicians, and you've got to try to find someone who's idealistic enough to spend the time to learn it, to maybe read a chapter or two from my book and save people's necks and lives. But it's not easy to find because doctors are very busy clicking on computers, and medicine in the United States is strictly a business. The consumers are the third party payers, not the patients. Those are the ones you have to please.

Airway tubes can be removed only when the oxygen saturation is normal in room air even if the patient can't breathe at all. So in other words, we use the CoughAssist through the translarygeal tube to clear the secretions and normalize the oxygen saturation. With no supplemental oxygen and the saturation being 95 or more and the patient fully alert, we extubate them to full non-invasive ventilatory support. That's how we do it. It's not rocket science. It works 100% of the time, but nobody else in the United States does what we do. Literally, nobody else does it. It's just amazing. It also turns off the hypoxic drive to breathe and causes the CO2 to go up. I think I've already been talking quite a long time here. Someone will have to sort of bring me to the end if I'm running out of time.

Dr. Ozlem Goker-Alpan:

Exactly. Dr. Bach, we really appreciate this fantastic talk with the wonderful pictures, and this is the second time I'm listening to you. Every time I listen to you, I am amazed. I mean, you are actually that is touching something that is very rarely known by the physicians who take care of these patients. Obviously, Pompe disease is a little bit different with the muscle weakness. So I am not seeing any in the Q and A. I have two quick questions for the people who are still around. So what is the intercurrent management of the respiratory infections in patients with Pompe disease? So let's say that this is an actually adult patient who is in the complication phase with very little forced vital capacity less than 30. I

mean, they are usually kept in BiPAP, so when would you switch them to non-invasive ventilation? When is the time?

Dr. John Bach:

No, no, it's not non-invasive ventilation. It's non-invasive ventilatory support, which you can do with BiPAP-

Dr. Ozlem Goker-Alpan:

Yep. Okay. So you can do what-

Dr. John Bach:

... but the span has got to be at least 18, and you cannot take a breath and get another volume and another volume because it's pressure limited. So you can't get the deep breaths you need to increase your cough flows or to call for help or to keep your lungs compliant. You see, BiPAP can be used at ventilatory support settings, and if you do volume-targeted BiPAP and set the volume at 500 or 600, you're giving full ventilatory support, but you can turn the EPAP off. The EPAP causes reflux and aspiration and other problems, and you cannot stack volumes to get deep breaths to cough. You see? So BiPAP can be used, but it's far from ideal. The CoughAssist is even more important because that's what keeps the airways clear and the oxygen saturation's normal. The worst thing is when the patients are given oxygen for respiratory symptoms when their muscles are weak. The CO2 can go up by 150 and the patients then get intubated, and the doctors think they need to be trached. And that's what happens everywhere except here and on the centers in BreatheNVS.com.

Dr. Ozlem Goker-Alpan:

Okay. I'm going to switch the gears a little bit. Actually, I have two questions in the chat box, and I did have actually a similar question, so we're switching gears from the neuromuscular disorder. But these babies with Gaucher disease or other sphingolipidoses, they have a neurological involvement like central apnea associated with interstitial lung disease. So it is a pretty common scenario is they get a central apnea or paradoxical neuronal spasm. They get intubated, and then they do have a viral illness, and they fail to get extubated. Actually, I have lived this through multiple times, and they end up getting tracheostomies. So basically what is the-

Dr. John Bach:

No, no. See, this is not necessary. No, it's not necessary. Look, if you cannot get the oxygen saturation to 95% or more in room air, so in other words, if their baseline is a normal saturation without getting oxygen at home, this means their lung tissue is healthy, and their airways are reasonably clear. Now, when they get a cold, the saturations go down because of the airway secretions. If they don't have CoughAssist, they get pneumonia. When they get pneumonia and they're intubated, they get weak. But if you use the CoughAssist through the tube and clear the secretions, they will go back to their baseline saturation before they went to the hospital. Now, if their lung disease is so severe that that baseline saturation was in the 80s and you can't get them back to 95 or more, they may need a trach tube because their lungs are severely diseased. I have never seen that.

Dr. Ozlem Goker-Alpan:

Yeah, it is very unlikely actually, so the next string of questions, I assume, from a mother who says that they're putting our 22-month old Gaucher type 2, 3 on BiPAP at night. So basically, are you saying not to

do it? I mean, we do recommend BiPAPs at night, especially when they have central apnea, but do you have any other recommendation?

Dr. John Bach:

No, no. Well, look, you're not going to teach the local doctors or therapists what we do here in the Tri-State area. But understand this, if the child has paradoxical breathing sleeping when he's not using the machine, then you need to use the machine at settings that will reverse that so that the lungs grow. Now, that would be 22 and 4. What they do is they titrate away the apneas and hypopneas on polysomnograms without normalizing the carbon dioxide or without reversing the paradoxing. See, that's the problem. They don't rest their muscles fully during sleep to get optimal energy during the day. I'm not saying you have to be off the BiPAP, but if the settings are less than a precious support or what we call a span of 16 to 20, then the settings are not optimal, especially if there's paradoxing. If there's paradoxing, you need to reverse that and have the chest expand with the stomach when the child is sleeping or the lungs won't grow.

When a child cries, what happens? The chest and the belly go way out. That's what's promoting growth of the lungs. If you don't do that by using an adequate inspiratory pressure, the lungs won't grow. Okay? So I'm not saying take everybody off a BiPAP because the insurance companies will want an explanation, and it'll be a tremendous amount of work, but reverse the paradoxing, use settings that rest the muscles, which is like 18 centimeters of pressure support, which is like 20 and 4 or 22 and 4. And the EPAP should be the absolute minimum, two, three, or four, depending on the machine that they have. On the Astral, you can get an EPAP of two, on the Trilogy or Evo, an EPAP of four. On BiPAP machines, usually can lower it below four. The four is not good. It can increase reflux and aspiration and all of this, but you can't turn it off unless you go to an active circuit with a non-vented [inaudible 00:55:43]. It's a little technical.

By the way, my book is also on Kindle, so if people want to read it on Kindle, they can do that, but the doctors are not going to do it. So you see, it's a little bit technical. If the patient is within 500 miles of here, they should bring the patient here. And if the patient is intubated, I strongly recommend against permitting a trach because I'll tell you right now, once that trach goes in, that patient will never breathe again almost certainly, almost certainly. When that patient's unweanable on trach ventilation and we take the trach out, if the vital capacity is over 50 milliliters in an infant, they wean. If it's over 250 in adult, they wean. But you have to have over a liter of vital capacity to wean from trach ventilation when you have a trach tube. Okay, so don't let the doctor stick a tube through your neck.

Dr. Ozlem Goker-Alpan:

We try to

Dr. John Bach:

No, no, no. It's not a question of trying. They cannot do it unless the patients consent. Don't-

Dr. Ozlem Goker-Alpan:

So I have one last question before we go. So this CoughAssist machine, I looked it up really quickly while you were giving your lectures. So can it be used without the patient getting intubated or is it only-

Dr. John Bach:

Of course.

Dr. Ozlem Goker-Alpan:

How can we use that? Can we just explain it a little bit?

Dr. John Bach:

Yes, very important. When patients are too weak to breathe and they're intubated, we make their lungs healthy by using the CoughAssist through the tube. Then, I will not extubate a child who doesn't have the strength in his arms to use it independently unless there's a family member there to use it up to every 15 to 30 minutes for the first 36 hours after extubation to non-invasive ventilatory support. So understand what I'm saying. The hospitals give excuses. We can't do this because we don't let the families in the ICU. Even during COVID, our hospital here knew that to extubate these patients without a trach tube, I had to have a care provider there after the extubation every time there was a mucus plug that caused the saturation to go down, the family member used the CoughAssist to bring it up so that the child didn't have to be re-intubated or the adult didn't have to be re-intubated.

So I'm sorry I didn't mention that, but that's critical to have access to this machine to clear the airways to prevent reintubate. You get reintubated not normally because you're too weak to breathe but because you can't cough, and the secretions build up and because like I said, when you suction, you never get the left side.

Dr. Ozlem Goker-Alpan:

Absolutely.

Dr. John Bach:

Yeah, but the doctors don't do this.

Dr. Ozlem Goker-Alpan:

And then you traumatize the airway too, which actually promotes the more swelling of the airway.

Dr. John Bach:

Right.

Dr. Ozlem Goker-Alpan:

So one last question from that parent is it looks like they have a CoughAssist at home, and obviously, the child is not on a ventilator or anything like that during daytime.

Dr. John Bach:

Oh, good. Good.

Dr. Ozlem Goker-Alpan:

Should we be using every day as a matter of preventing? The reason is these children with the neurologic disorders, they do have actually a lot of secretions, multiple reasons. They cannot clear their secretions. They can't swallow, so on, so forth. So what would you actually recommend to this family?

Dr. John Bach:

Well, first of all, anytime the child must not be receiving any oxygen. That makes the oximeter useless and is very dangerous in terms of eventually causing cor pulmonale and hypercapnia. So if the saturation goes below 95 and you think it's secretions, of course you have to use the CoughAssist. Now, there's two reasons for using this thing. One is for lung volume recruitment, but for that, you only need the positive pressure. There's no harm in giving negative pressure, but the important thing is to give it while the child is inhaling, if the child is too young to cooperate with it, to get full chest expansion so the lungs grow. That should be done at least three times a day, 10, 15 times each time. The other reason for using it is, as the mom is saying, to clear the secretions. Then, you've got to use it as often as necessary.

I'm telling you, my moms use it 10 to 15 times a day when the children are healthy but have no bulbar muscles. When they're aspirating secretions, they use it 10 to 15 times a day. So there's no harm in over... You can't overuse it. The more you use it, the better. You don't use it like a respiratory therapy technique, every six hours, hit the chest or every eight hours, give a nebulizer. No. You need to use it whenever the patient's got secretions to be cleared or for lung volume recruitment several times a day.

Dr. Ozlem Goker-Alpan:

Okay. All right. So we can-

Dr. John Bach:

By the way, you've got to use it at 50 to 60 centimeters of water. None of this crap 20 to 30 centimeters of water. Okay?

Dr**. Ozlem Goker-Alpan:**

Okay**.** All right, so everybody has your, actually, contact information. You may be getting a lot of calls and patients. Actually, I do have few patients in New Jersey area that I am very interested actually for them to see you. So we thank you a lot, and it was our ultimate pleasure to have you here. We wish you and everyone who is here happy holidays and a happy 2024. Thank you.