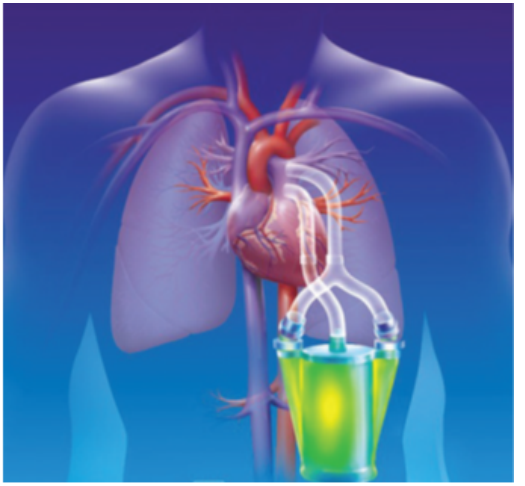
Transforming Respiratory Care through Technology



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One Woman's Journey with COPD

"It's not fun!" declares Barbara when speaking about the chronic obstructive pulmonary disease (COPD) she has struggled with for the past ten years. Barb, a retired computer expert for Mitre Corporation, had looked forward to continuing to work from her home seasonally, but spending the warmer months fulfilling a lifelong dream "traveling and seeing the world." She also planned, had even bought the equipment, to hike in the nearby woods to photograph wild life. Out the window went those dreams when her COPD kicked in, leaving her exhausted and listless each day. Instead, she has had to pursue more sedentary interests: writing, especially poetry, painting, drawing in charcoal, and playing computer games.

Barbara relates that her COPD diagnosis came in segments. She had long suffered from asthma, and, more recently, from mild emphysema, but it wasn't until she moved to Ithaca about 20 years ago that a pulmonologist put all the pieces together and diagnosed her with COPD. "You have the triple whammy - asthma, emphysema and COPD," he told her. Now, Barb finds that she can only walk short distances or stand for brief periods of time before she is out of breath. She fears catching a cold or the flu, and now COVID, because she knows that if she contracts any of these infections she will land in the hospital fighting for breath.

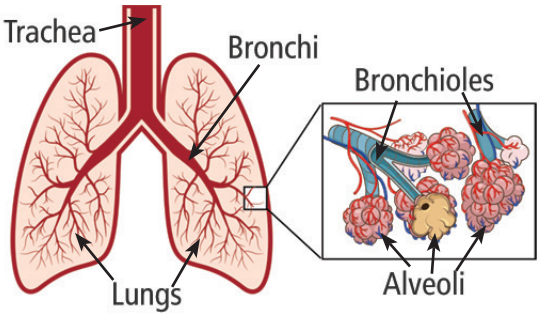
"The disease is emotionally devastating," Barb admits. She knows that it is progressive. It has already affected her heart, causing atrial fibrillation (AFib), a quivering or irregular heartbeat (arrhythmia) that can lead to blood clots, stroke, heart failure and other heart-related complications. She fears the day when she will be more debilitated, not able to drive, having to rely on a walker, and, eventually, having to move into assisted care. Already using oxygen at night, Barb recognizes that her future with COPD is not bright. Nevertheless, with true grit, she presses on, exercising as much as she is able, and enjoying the beauty of each day and each hour.

The Respiratory System

Within seconds after an infant is born, a miracle occurs. The infant breathes in his or her first breath of fresh air. Its fetal respiratory system, developing over the past nine months, and practicing to prepare for its first real breath after birth by moving tracheal fluid through its organs, begins to seal off and collapse. The infant's asymmetrical lungs spring into action. With its first breath, life outside the womb begins.

Human Respiratory System

Lungs are the only internal organs in the human body that are constantly exposed to the external environment because they process air. Air is inhaled into a respiratory system that includes the nose, trachea, and two bronchi trunks with their branching bronchioles. These constitute the passageway for air to reach the lungs which house three hundred million, spongy, fibrous connective tissue alveoli (air sacs) that are encompassed by a network of one-cell-thick walled capillaries. The capillaries have one essential function – to deliver blood into close proximity of fresh air. Here the the carbon dioxide carried in each of the 300,0000,000 hemoglobin particles of each red blood cell exchange places with the oxygen molecules lodged on the moist inner surfaces of the alveoli. With normal breathing, these alveoli fill and empty carrying life-enabling oxygen to every cell in the body.



Human Respiratory System showing bronchi, broncioles, and alveoli

Humans inhale and exhale 15,000 times a day during

The Respiratory System cont.

normal activity. This translates into 12-14 breaths each minute, or 2,100 to 2,400 gallons of air every day. At rest, the lungs fill with approximately one half a quart of air with each breath. During strenuous activity the lungs can take in up to six to seven quarts of air with each breath. A racing athlete's breathing can triple the normal resting rate to more than 42 breaths per minute.

Any infection or disease that obstructs or inhibits our normal breathing pattern limits our ability to get life-sustaining oxygen into our cells for metabolism and eliminate its carbon dioxide waste product. Many bacterial diseases such as Tuberculosis (TB) that once were fatal can now be treated with antibiotics. Others continue to plague us, but new technological advances are continually striving to find cures and ameliorate the symptoms of these diseases.

Chronic Respiratory Diseases

Chronic respiratory diseases are categorized into obstructive diseases and restrictive diseases. Depending on a patient's diagnosis, they likely fall into one of these two categories which will specify their symptoms, treatment options, and overall lifetime impact.

Chronic Obstructive Respiratory Diseases

Obstructive respiratory diseases affect the lower airways known as bronchioles and alveoli. Bronchioles are small airways that pass air into the microscopic alveoli. These air sacs are covered by tiny blood vessels which allow for gas exchange between carbon dioxide and oxygen within the capillaries to occur. Although these areas of the lungs are extremely small they account for 98.8% of the

Overview of Respiratory Diseases cont.

total lung volume, creating an overwhelming percentage of lung space that may be affected by disease. When this process is affected, patients are likely to experience difficulty breathing, shortness of breath, consistent cough, and thick mucus production. Additional swelling in these airways is common, permitting airway collapse to occur easily, ultimately trapping air within the alveoli air sacs. This air trapping makes it impossible for the patient to fully exhale and, overtime, causes an increase in air left behind within the alveoli. This obstructive process makes it more difficult for the patient to breathe, especially during times of activity, when their respiratory rate increases and the time for exhalation becomes shorter.

Example of air trapping identified on chest Xray. Normal lung fields take up 10 ribs. An obstructive disease patient's lung can easily surpass that due to air trapping within the alveoli.

Common obstructive lung diseases include asthma and cystic fibrosis as well as COPD, which incorporates emphysema and chronic bronchitis. Causes of these diseases include inhalation damage from tobacco smoke or exposure to other hazardous lung irritants. Familial genetics play an important role in cystic fibrosis and asthma, but has also been linked to COPD patients who have never had any substantial irritant or smoke exposure. COPD remains the most common obstructive respiratory disease with 251 million cases recorded globally according to the World Health Organization.

Diagnosis

Diagnosis of obstructive respiratory disease requires the care of a physician and the completion of pulmonary function testing, known as spirometry. Disease progression is imminent and will progress

Overview of Respiratory Diseases cont.

differently for each patient. Treatment typically includes pulmonary medications such as bronchodilators to maintain airway patency as well as inhaled corticosteroids to decrease inflammation. Eventually, the dosage and frequency of these may increase to help battle a patient's breathlessness. Additionally, if a patient's blood oxygen content drops, the use of supplemental oxygen will be required and is a common form of treatment for moderate to severe obstructive respiratory disease.

Lungs of COPD patient

This disease process will begin to affect the patient in everyday activities, such as holding a conversation and walking to the restroom. The burden of disability associated with a specific disease or disorder can be measured in units called disability-adjusted life years (DALYs). DALYs represent the total number of years lost to illness, disability, or premature death within a given population and help the medical community compare the burden of different disorders to one another. According to the World Health Organization, respiratory diseases account for more than 10% of all DALYs and are second only to cardiovascular diseases, including stroke.

Eventually, obstructive respiratory diseases become difficult to manage and treating the patient's primary symptoms require advanced modalities such as different forms of mechanical ventilation which require hospital admission. In severe end-stage cases of obstructive lung disease, the patient may be faced with the option of single or double lung transplant.

Overview of Respiratory Diseases cont.

Chronic Restrictive Respiratory Diseases

The second category relating to chronic respiratory diseases is restrictive lung disease. Compared to our obstructive patients where exhaling completely is difficult, restrictive patients struggle taking a deep breath and fully expanding their lungs. This process can be due to several factors which can be further categorized into intrinsic and extrinsic restrictive lung disease.

Extrinsic restrictive disorders include changes to the chest wall, pleura, and respiratory muscles which together work cohesively to allow for full lung expansion. When any of these are compromised, so is effective ventilation. Examples include scoliosis, neuromuscular diseases, obesity, and pleural effusions. Thankfully, several extrinsic restrictive disorders can be treated and cured with a number of surgical procedures or lifestyle changes.

Unfortunately, intrinsic disorders develop within the lung tissues itself, making treatment a more complex issue. Common disorders include pulmonary fibrosis, interstitial lung disease, and sarcoidosis. Collectively, these disorders cause scarring and inflammation of the lung parenchyma, resulting in decreased lung air volumes and the patient's inability to take a full deep breath.

Example of pulmonary fibrosis chest x-ray with decreased lung volume and collapse within the left lung base.

Unconsciously, we are consistently increasing our lung volumes through the day. Whether it be a cough, yawn, or sigh, our body automatically regulates this process to maintain a specific level of lung volume. This ensures that our alveoli, or tiny air sacs, remain inflated and equipped for continuous gas exchange between oxygen and carbon dioxide and the capillaries in the lung. Patient who are suffering from restrictive lung diseases may attempt to increase their lung volumes. However, the disease process has made it nearly impossible. As a result,

Overview of Respiratory Diseases cont.

atelectasis occurs – a condition in which the airways or air sacs in the lung collapse or do not expand properly, reducing the number of areas in which gas exchange can take place. This pathophysiology makes hypoxemia, or low oxygen levels, a main complication in these patients.

Treatment

Treatment for restrictive lung diseases vary depending on the expected etiology. For years patients diagnosed with idiopathic pulmonary fibrosis have been treated with immunosuppression. However, new anti-fibrotic drugs are gaining popularity as they have been clinically shown to decrease disease progression. Other treatment options include steroid therapy to diminish inflammation, as well was oxygen therapy to increase blood oxygen levels.

Restrictive diseases account for a fifth of all pulmonary diseases, leaving obstructive disorders with the majority. Restrictive diseases will quickly compromise a patient's daily activities and affect their quality of life. Expensive drug therapies and oxygen requirements pile on a large cost burden in addition to the decreased ability to work. Frequent hospitalizations and advanced treatment modalities are common and cause a significant amount of stress to patients and their families.

The causes of restrictive lung diseases are not as well defined compared to their obstructive counterparts. Idiopathic pulmonary fibrosis, for example, comes from an unknown etiology. Additionally, interstitial lung disease is an umbrella term for numerous diseases that cause scarring of the lungs which can include causes such as genetics, certain medical treatments such as chemotherapy, or exposure to hazards.

Prognosis

Prognosis of restrictive respiratory diseases vary significantly depending on the cause. As mentioned earlier, extrinsic restrictive diseases can have very high success rates after a variety of surgical procedures or significant weight loss. Intrinsic restrictive diseases are, unfortunately, not as hopeful. Patients diagnosed with idiopathic pulmonary fibrosis have a median survival of three to five years after diagnosis. Acute interstitial pneumonia has a very grave prognosis of 70% mortality within three months' time. Lung transplant options remain open to end stage restrictive lung disease patients.

Overview of Respiratory Diseases cont.

Acute Respiratory Failure

Inflamed lungs indicative of acute respiratory distress syndrome (ARDS).

The reality for many living with chronic respiratory diseases is that they learn to adapt and adjust their lifestyle based on their disease, as not many pulmonary diseases have a cure. Treatment is limited to supportive care and diminishing the effects of the disease's symptoms. Many of these patients require a cocktail of inhaled medications along with other oral medications and supplemental oxygen use. Unfortunately, there are times when these supportive therapies are not enough. As these diseases progress it is common for patients to suffer from extreme shortness of breath. In these moments, the emergency room is the only place to obtain relief, requiring acute respiratory care services. This can range from medications such as high dose IV steroids and inhaled bronchodilators, or formal respiratory support such as high-flow nasal cannula, non-invasive mechanical ventilation, and even intubation requiring the use of a mechanical ventilator. However, in this patient population, intubation is actively avoided. Evidence suggests that patients with acute exacerbations have an increased mortality when mechanically ventilated compared to treatment with other forms of support.

In severe cases of acute respiratory failure, the most advanced treatments may be offered to select patients whose acute situation is caused by an underlying chronic respiratory disease. Extracorporeal membrane oxygenation (ECMO) is a form of cardio-pulmonary bypass that can be offered in the intensive care environment. Although this therapy has now been around for decades, it is relatively new in the adult population and requires extensive training. It is associated with a cohort of risks. In recent years another form of extracorporeal support, extracorporeal carbon dioxide removal (ECCOR2) has shown promise for these patients. When compared to ECMO, ECCOR2 is more effective at eliminating carbon dioxide, one of the key signs of respiratory failure and what these patient struggle with the most. Additionally, ECCOR2 can provide support with lower current flow rates and easier venous access. This state-of-the-art method has allowed patients to remain awake and alert avoiding intubation and mechanical ventilation.

Overview of Respiratory Diseases cont.

COVID-19 and Extracorporeal Support

As COVID-19 was spreading and claiming hundreds of thousands of lives, it was also testing the boundaries of extracorporeal support. As a respiratory virus, COVID-19 highlighted pulmonary medicine to the entire world and has stretched the knowledge, resources, and experts to the max in defining exactly what support is possible.

As mentioned previously, extracorporeal membrane oxygenation (ECMO) is a lifesaving therapy for any severe respiratory disease. ECMO takes over the function of the lungs and/or heart to promote rest and limit further damage from conventional therapies. ECMO has been implemented in hundreds of hospitals around the world over the last two decades with the guidance and knowledge from the Extracorporeal Life Support Organization (ELSO), an organization dedicated to improving extracorporeal support. ELSO routinely provides education support, staffing guidelines, and a large registry database for collection of data.

Courageously, ELSO lead the ECMO community to evidence-based medicine when COVID-19 began, instituting a number of webinars to spread information around the world. Additionally, a live registry became available on their website to track the use and success of ECMO with COVID-19 patients. To date over 4,500 COVID patients have been treated with ECMO around the world.

As this number continues to climb, it has underscored the necessity of extracorporeal support. Hospitals have had to make difficult decisions regarding staffing and extra resources to be able to make ECMO support a realistic therapy for their communities. Prior to the coronavirus, the ECMO community had already seen huge growth from 150 ELSO registered ECMO centers in 2009 to 463 centers by 2019. Not surprisingly, the number of ECMO runs also drastically increased from 2,800 in 2009 to just shy of 16,000 ECMO runs in 2019. Extracorporeal support was at its peak in 2019 and, after the role it has played throughout this global pandemic, will continue to be an area of momentum in the development of new technologies and therapies.

Overview of Respiratory Diseases cont.

Extracorporeal Support Comparison

Extracorporeal support has a variety of mechanisms that can be used independently or in conjunction with one another. They range from minimally invasive or invasive mechanical ventilation (MV) to carbon dioxide (CO_2) removal via $ECCO_2R$, to extracorporeal membrane oxygenation (ECMO) with VA ECMO for acute, reversible cardiac and respiratory failure, or VV ECMO for patients with respiratory failure alone, who are unresponsive to conventional medical or pharmacologic management.

	MV	$ECCO_2R$	VV ECMO	VA ECMO
CARE SETTING				
Standard ICU	✔	✔		
ECMO Center	✔	✔	✔	✔
Patient Transport	✔		✔	✔
MECHANICAL FUNCTION				
Lung Function Support	✔	✔	✔	✔
Blood Oxygenation Support			✔	✔
Carbopn Dioxide Removal Support		✔	✔	✔
Cardiac Support				✔
REQUIRES INVASIVE ELEMENTS				
Intubation or Tracheal Cannulation	✔			
Venous Cannulation		✔	✔	
Venous and Arterial Cannulation				✔
POTENTIAL RISKS				
Ventilator Associated Pneumonia (VAP)	✔			
Ventilator Induced Lung Injury (VILI)	✔			
Bleeding		✔	✔	✔
Thrombosis		✔	✔	✔
Infection	✔	✔	✔	✔
Failure to Wean	✔	✔	✔	✔
Circuit Malfunction/Loss of Support		✔	✔	✔

Table 1: Comparison of mechanisms for extracorporeal support.

Spotlight on Novel Respiratory Technologies

Hemolung RAS

Patient connected to Hemolung RAS

ALung Technologies, Inc., a Pittsburgh, PA based medical technology company has developed an innovative system to effectively treat acute respiratory failure without over reliance on ventilators. Hemolung RAS, short for "Respiratory Assist System," was granted FDA Emergency Use Authorization (EUA) in April 2020 for treatment of COVID-19 and is also being studied in a large, randomized controlled clinical trial in patients with severe exacerbations of chronic obstructive pulmonary disease (COPD).

In these cases, high levels of carbon dioxide can result in respiratory failure and the need for life saving measures. For many patients, the only option has been intubation and invasive mechanical ventilation. Unfortunately, mechanical ventilation can be accompanied by harmful side effects, and in-hospital mortality remains as high as 30%.

Hemolung RAS Cartridge

This is where ALung's technology comes into play. Hemolung RAS allows carbon dioxide to be removed from the blood independently of the lungs and can be used as a supplement to mechanical ventilation. When used in combination with mechanical ventilation, the use of the Hemolung RAS can facilitate lung protective ventilation, reducing the risks of ventilator-induced lung injury, and/or accelerate weaning off the mechanical ventilator. The process involves low flow veno-venous extracorporeal carbon dioxide removal, or ECCO2R. An integrated centrifugal pump moves the patient's blood through an extracorporeal circuit attached percutaneously to the femoral or jugular vein. Carbon dioxide is removed through a uniquely designed filtration cartridge surrounding the pump to allow for a simple all in one device. To avoid coagulation, the filtration cartridge contains siloxane coated

Spotlight on Novel Respiratory Technologies cont.

Hemolung RAS cont.

polypropylene fibers and a heparin coating. Blood flow and carbon dioxide removal are carefully measured using in-built transit-time ultrasound flow measurement technology and nondispersive infrared carbon dioxide analyzer technology, respectively. These values are then displayed real time on the Hemolung controller for easy monitoring of the patient.

The Hemolung RAS removes 25% – 50% of basal metabolic CO_2 production at circuit blood flows of 350-550 mL/min. The Hemolung has been used to treat more than 1,000 patients world-wide, primarily in Europe. In one recent case at Ochsner/ LSU Academic Medical Center in Shreveport, Louisiana, a severely hypercapnic patient with COVID-19 was treated with Hemolung RAS. The extracorporeal CO_2 removal capabilities of the Hemolung enabled delivery of lung protective ventilation, and resulted in a significant correction of $PaCO_2$, and normalization of pH without the complexities associated with ECMO. It was concluded that without this technology being available at the site, the patient would likely not have survived.

ALung continues their US clinical trial in anticipation of full FDA clearance in 2021, and is already hard at work developing the next generation of artificial lungs.

Spotlight on Novel Respiratory Technologies cont.

LifeSPARC®

LifeSPARC® is LivaNova's next-generation ACS (Advanced Circulatory Support) system that greatly simplifies temporary cardiopulmonary bypass. The mission of the team developing LifeSPARC® was to save and improve the lives of critically ill patients by providing an easy-to-use, effective life support platform - - and by all indications, it's been "mission accomplished."

The LifeSPARC® system features a lightweight controller which is half the size of the previous generation and has a 2-hour battery backup. It can be easily removed from the docking station for in-hospital transport. The LifeSPARC® pump is a non-pulsatile centrifugal pump that benefits from a magnetic pivot bearing to rotate the impeller, with flow output of 8 LPM with selective cannulation. A nearly 40% increase in power over the legacy TandemHeart system, delivering more powerful support for the patients in greatest need.

Accompanying LifeSPARC® is The TandemLung Oxygenator® (TLO), which has been designed to satisfy the growing demand for a durable membrane lung that is streamlined for swift and simple priming, initialization, and management. The TLO was born of a design inspired by the MC3 Biolung, which had been studied and validated in chronic respiratory failure modeling. The evolution of the TLO was intended to optimize gas exchange in ambulatory populations, with aspirations for bridge-to-transplant and/or discharged patient populations to benefit from supplemental gas exchange. The device is supplied with sufficient surface area, and blood:gas flow properties to optimize oxygen and carbon dioxide flux in an adult.

Some of the features which make LifeSPARC® so simple to use are:

- Rapid and repeatable priming capability to deploy therapy at the time and place of need
- Four specialized, ready-to-deploy kits that enable a variety of cannulation strategies
- On-patient sterile disposables that enable short circuits, patient mobility, and ambulation
- A single platform for LV, RV, VV, and VA support to reduce costs and simplify training

Spotlight on Novel Respiratory Technologies cont.

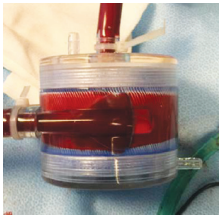
LifeSPARC cont.

LivaNova's LifeSPARC® system provides temporary support for emergent respiratory patients across multiple hospital settings. Engineers designed LifeSPARC® so that it is simple enough to be used by new practitioners, but powerful enough for expert-level centers. Typically, ECMO can only be performed in highly technical ECMO centers. Today, just 4.9% of all US-based community hospitals offer advanced respiratory support capability. LifeSPARC® may enable mid-tier hospitals to emulate the most successful centers in the U.S. Additionally, lower per-procedure costs and supportive reim-bursement (in the USA) provide strong economic support to escalate therapy when appropriate.

The COVID-19 pandemic has shed light on the need for more extracorporeal circulatory support options for patients requiring acute respiratory support. LifeSPARC® is an important step in making advanced life support available to more patients in more hospitals around the world. As observed by Dr. David Baran, System Director for Advanced Heart Failure Transplant and Mechani-cal Circulatory Support at Sentara Heart Hospital in Norfolk, VA, LifeSPARC® allows for "many more patients to have access to this higher level of support for the first time."

Spotlight on Novel Respiratory Technologies cont.

Pediatric MLung



Pediatric MLung

Although pediatric lung transplantation has been an option for treatment of end-stage lung failure (ESLF) in children since the 1990s, there are less than 100 pediatric lung transplants reported to the Registry of the International Society of Heart and Lung Transplantation each year. With limited donor availability, one in five children with end-stage lung failure succumb to their disease while awaiting transplant. Even with those that survive, the long-term success of pediatric lung transplant is limited not only by the availability of donor organs, but by debilitation from chronic disease, impaired mucus clearance, infection from immunosuppression drugs, and other late complications, such as chronic lung allograft dysfunction.

Hollow fiber oxygenators or artificial lungs (ALs) used in adult ESLF patients are bulky and do not lend themselves to children who need a wearable pulmonary support as a bridge-to-transplant therapy. To fill this need, Joseph Potkay, PhD, and his team of researchers at the Extracorporeal Life Support Lab, University of Michigan, in Ann Arbor, MI have designed, fabricated, and tested a more efficient smaller, paracorporeal, pumpless artificial lung, the Pediatric MLung, specifically for children awaiting lung transplant. Its requirements are to:

- Supplement pulmonary function of the diseased native lungs;
- Facilitate ambulation during bridge to transplant or as destination therapy;
- Eliminate the need for a mechanical pump in order to make it portable and reduce blood trauma;
- Allow the patient to be extubated to avoid ventilator-associated events;
- Allow support outside of the intensive care unit (ICU) and perhaps outside the hospital.

To relieve pulmonary arterial hypertension, provide pulmonary support, reduce ventilator-associated injury, and allow for more effective therapy for ESLF pediatric patients awaiting transplant, the Pediatric MLung has a dual-inlet hollow fiber design based on concentric gating, and a low resistance fiber mat to keep the pressure drop low while maintaining adequate gas exchange capability.

The components of the Pediatric MLung include five outer housing parts, inner and outer fiber bundles, a liquid curing ("potting") silicone to separate the blood and sweep gas, a gate insert, a blood outlet, and end caps. The fiber bundles are packed between the outer housing, gate insert, and blood outlet.

Spotlight on Novel Respiratory Technologies cont.

Pediatric MLung cont.

Two thirds of the total membrane is in the outer bundle, and one third is in the smaller inner bundle. The potting is applied to the ends of the fiber bundle as a liquid to fill in the tight spaces in between fibers. The potting then hardens at room temperature to form a barrier between the blood and gas phases to prevent blood leakage or the formation of air emboli in the blood.

The MLung is attached via a pulmonary artery (PA) to left atrium (LA), which yields several advantages. First, it is attached in parallel to the native lung, so that the high pressure in the right ventricle (RV) is relieved due to the availability of a flow path of lower resistance. Secondly, the PA–LA configuration provides a pressure gradient for blood flow, so that a blood pump is not required.

The next step for this work will be implantation of the device in a chronic sheep model to demonstrate long-term pulmonary support. It is hoped that this research may someday provide a solution for pediatric ESLF patients as they await lung transplantation, which would provide those children and their families reassurance and the gift of time.

What's Ahead

Breath is Life! To breathe is to live. It's as simple as that. With millions of people all over the world suffering from respiratory illnesses, ongoing challenges include: how do we prevent more respiratory illness, how can the treatment and management of patients with respiratory diseases be improved, and what technologies and strategies are emerging to improve respiratory care and serve as bridges to transplant.

Challenge: Improved Prevention

A campaign entitled "Healthy Lungs for Life" raises awareness of the importance of healthy lungs. It aims to speak not only to those already afflicted by respiratory conditions, but also to those who may be affected in the future. To achieve and maintain healthy lungs, the campaign focuses on one global objective: breathing clean air, as well as three healthy personal lifestyle choices: not smoking, staying active, and being vaccinated.

Air Pollution: According to the World Health Organization (WHO), air pollution accounts for one in eight deaths annually. Pollution from particulate matter, pathogens, smoke, and dangerous gases in the atmosphere affects the entire spectrum of the population from unborn babies to the very elderly. Short-term exposure to air pollution can cause or increase respiratory symptoms, and, when extended, can reduce life expectancy, affect lung development, increase asthma, and lead to other lung and heart diseases. 2020 marked the 50th anniversary of the Clean Air Act. Although this landmark law has driven dramatic improvements in air quality in the United States, too many cities still saw their year-round levels of particle pollution increase, the number of days when particle pollution (soot), soared to often unprecedented levels, and more days when ground-level ozone (smog) reached unhealthy levels. High ozone days and spikes in particle pollution put millions of people at risk for respiratory diseases. The 2020 "State of the Air" report notes that nearly half the population of the United States — about 150 million people, live in counties with unhealthy ozone or particle pollution levels. Although we may personally have little control over the air we breathe, learning more about our air quality and lobbying and working for less pollution can help protect our environment and ourselves.

Three lifestyle choices also serve to prevent or mitigate respiratory illnesses.

What's Ahead cont.

Challenge: Improved Prevention cont.

Do not smoke! The single most important step one can take to improve one's lung and overall health is not to smoke. In the United States, tobacco use remains the leading cause of preventable death and disease, killing close to half a million people each year, accounting for more than 480,000 deaths every year, or 1 of every 5 deaths. When one quits smoking, the body begins to feel its benefits immediately. One has more energy, feels younger, and coughs less. One's quality of life improves as the time without tobacco increases.

Regular physical activity improves the health for all ages, including those with lung conditions. Regular exercise increases the strength and function of muscles, making them work more efficiently. As muscle strength increases, the amount of air you need to breathe in and out for any given exercise is reduced. Regular activity also improves one's circulation and strengthens the heart while decreasing the risk of developing other conditions such as stroke, heart disease, and depression.

Placing band aid over vaccination site

Vaccination offers general protection from a number of different diseases and helps keep the lungs healthy. Those with lung or other health conditions can be at a higher risk from lung infections such as pneumonia, influenza, and whooping cough.

The Crossroads of Emerging Technology, Improved Management, and Patient Quality of Life

Depending on the severity of a respiratory illness, treatment can be relatively straight forward or exceedingly complex, demanding significant pharmacological therapy as well as mechanical ventilation support. In dire cases patients are placed on extracorporeal membrane oxygenation (ECMO) support with an artificial lung (oxygenator). For a select few, single or double lung transplants become the last resort.

What's Ahead cont.

While there aren't complete cures in our future for most respiratory diseases, we can expect to continue making positive strides towards managing those diseases. Advancements are being made with pharmacological therapies, including the delivery of medications through inhaled aerosol or nebulized delivery systems that provide effective doses of an agent while minimizing or wholly avoiding systemic side effects. As technology becomes more sophisticated, Respiratory Therapists (RT's) and nurses who work alongside doctors will require more sophisticated training. Clinicians and care teams will also spend more of their time managing patients remotely as wearable and home-based devices feed important clinical data to the cloud, including data from digital spirometers and asthma monitors, portable oxygen usage, and artificial lung performance.

Respiratory therapist setting machine.

The demand for technologies that can assist an injured or recently transplanted lung or completely replace the native will increase. An estimated 150,000 Americans experience lung failure each year according to the National Heart, Lung, and Blood Institute. About a third die, and those who survive often suffer permanent respiratory problems.

More than 2,000 people are currently waiting for a lung transplant. While lung transplantation remains a final destination therapy for lung failure, severely limited donor organ availability has created a demand for alternative management, including development of artificial lungs, either as a bridge to lung transplantation or as a true destination therapy. Such devices should ideally allow for ambulation in chronic or acute respiratory failure. The continuous progress in the development of bioartificial lungs includes tissue engineering advances that could repair, restore, replace, or regenerate lungs.

Organ Transplants
from Jan 1, 1998 to Dec. 31st 2020 (UNOS)

Kidney	492,576
Liver	181,976
Heart	79,562
Lung	43,585
Kidney/ Pancreas	25,445
Pancreas	9,029
Heart/Lung	1,363

What's in the Future cont.

The Crossroads of Emerging Technology, Improved Management and Patient Quality of Life cont.

Cell-therapy offers one of the most innovative strategies for unmanageable respiratory diseases. Their use in acute respiratory distress syndrome (ARDS) is an exciting clinical prospect. Research into mesenchymal stem cell (MSC) therapy has been shown in animal models of sepsis to reduce markers of inflammation and the incidence/severity of ARDS.

Ultimately, the future looks bright for respiratory care. Technology will allow patients to recover from acute events sooner and avoid future hospitalizations, which should greatly reduce the economic burden of respiratory disease. Patient life expectancies are likely to increase, and most importantly, quality of life will be improved as patients are more able to live normal lives and, like Barbara, treasure the beauty of each day and hour.

Appendix: Glossary of Respiratory Terms

Alung Technologies, Inc.: a medical technology company that developed the Hemolung RAS (Respiratory Assist System), an innovative system to effectively treat acute respiratory failure without overreliance on ventilators.)

Alveoli: Tiny air sacs within the lungs where the exchange of oxygen and carbon dioxide takes place.

American Lung Association: A leading organization that works to save lives by improving lung health and preventing lung disease through education, advocacy, and research.

American Thoracic Society (ATS): An international society with more than 16,000 members dedicated to advancing the clinical and scientific understanding of pulmonary diseases, critical illnesses, and sleep-related breathing disorders.

Apnoea: Absence of breathing. Brief periods of apnoea occur during sleep, caused by either by an anatomical obstruction in the upper airway or by a failure of respiratory drive.

ARDS (Acute Respiratory Disease Syndrome): A severe, often fatal medical condition characterized by widespread inflammation in the lungs. Occurs when fluid builds up in the alveoli in the lungs that deprives the body of oxygen.

Asthma: A common, chronic respiratory condition that causes difficulty breathing due to inflammation of the airways. Symptoms include dry cough, wheezing, chest tightness, and shortness of breath. Usually, asthma begins during childhood and progresses into adulthood. However, some people in their 60s, 70s, and 80s can get adult onset asthma.

Atelectasis: A complete or partial collapse of the entire lung or lobe of the lung. It occurs when the alveoli within the lung become deflated or possibly filled with alveolar fluid. Atelectasis is one of the most common respiratory complications after surgery.

Avian Flu H5N1 (Bird flu): An illness caused by the Influenza-A virus. Symptoms include fever, difficulty breathing, diarrhea, headache, body aches, confusion, sore throat, and runny nose; possibly life threatening. People infected with bird flu have often been in close contact with sick birds and their droppings, or in direct contact with someone already infected with the bird flu virus. Treatment: antiviral medications and hospitalization for breathing support and oxygen administration. A vaccine is available.

BioLung: A totally implantable artificial lung.

Blood Gas: A test that measures levels of venous and arterial oxygen, cabon dioxide, hematocrit, pH, bicarbonate, calcium, sodium, potassium, glucose, creatinine, and lactate. These are drawn usually every hour, and help guide the flow rate of the pump and gas settings on the oxygenator.

Bronchitis: A condition where the bronchi become inflamed. It is sometimes called a chest cold. The lungs swell and produce mucus, which brings on coughing fits. Symptoms include fatigue, mild body aches, headaches, sore throat, and watery eyes.

- **Acute:** An infection from a virus or bacteria; treated with antibiotics. Can last from five days to three weeks. Symptoms subside once the infection has resolved.
- **Chronic:** Bronchitis that lasts at least three months over two consecutive years. A form of COPD demonstrated by a chronic cough of mucus, especially in the morning. Smoking is the most common cause, but dust, allergens, and toxic gases can also cause and contribute to it.

Bronchoconstriction: Constriction of the airways due to contraction of the smooth muscle in the airway wall.

Bronchodilatation: Expanding or stretching of the airways due to relaxation of the smooth muscle in the airway wall, for instance in response to a bronchodilator.

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Bronchodilator therapy: Medication that opens the bronchi airways.

Chest Tube: A tube that is placed through the chest wall into the space between the lung and chest wall to drain air or fluid. Used to reinflate a collapsed lung (pneumothorax) or to drain fluid.

Chest X-Ray: A fast and painless imaging test that uses certain electromagnetic waves to create pictures of the structures in and around your chest.

Chronic Obstructive Pulmonary Disease (COPD):
An umbrella term that encompasses several irreversible,. progressive respiratory illnesses that cause breathlessness, or the inability to exhale normally. Symptoms include shortness of breath, and normally cough up sputum (mucus from the lungs), especially in the morning. COPD is the third leading cause of death in the U.S.

Congenital diaphragmatic hernia (CDH): In newborns, the abdominal contents herniate through the diaphragm into the heart and lung space, limiting breathing and cardiac output.

Common Cold (Head Cold): Common upper respiratory infection is usually caused by one of the 57 types of adenovirus. Symptoms include runny nose, sore throat, and headache, and swelling of the lymph nodes. Nearly 250 different viruses can lead to a cold. Scientists have not yet been able to develop a cold vaccine to protect against all of these viruses.

Computed tomography (CT): A medical imaging technique that uses computer-processed combinations of multiple X-ray measurements taken from different angles to produce tomographic images of a body.

Coronavirus Infections: A common virus that causes an infection in your nose, sinuses, or upper throat. The seven known coronavirus infections that make people sick range from mild to severe, depending on the virus type. This virus family is known to infect various animals, and is also known to mutate easily. Sometimes coronavirus types that infect animals (including bats, civet cats, and camels) mutate to infect humans, and can have deadly consequencess. The common cold is a mild-to-moderate coronavirus infection. Worldwide, people get sick from the four coronavirus types that cause milder infections every day. But three types—the ones that cause SARS, MERS, and COVID-19 (SARS-CoV-2)—have the potential to be fatal, and each of these has led to a significant global outbreak.

COVID-19 (SARS-CoV-2): Life threatening coronavirus first identified in humans in 2019 and spread resulting in 2020 worldwide pandemic. Primary symptoms include cough, shortness of breath, and fever. Spreads through droplets released when an infected person coughs, sneezes, or talks and spreads mainly between persons who are in close contact with one another (within about 6 feet). Vaccines became available in 2020-2021.

SARS (Severe Acute Respiratory Syndrome): Severe viral respiratory infection caused by coronavirus SARS-CoV. Symptoms include fever, chills, muscle pain, shortness of breath, headache, and diarrhea. Most SARS patients develop pneumonia. Treatment usually requires oxygen and possibly mechanical ventilation. A SARS virus outbreak began in China in 2003 and spread worldwide, infecting over 8,000 people before it was contained. Since 2004, there have been no known SARS virus cases reported.

MERS (Middle East Respiratory Syndrome)
Caused by coronavirus MERS-CoV and first reported in Saudi Arabia in 2012. Symptoms can cause a fever above 100.4°F (38°C) with chills or shivering, sore throat, coughing up blood, difficulty breathing, vomiting, abdominal pain, diarrhea, and muscle aches. Treatment usually includes oxygen supplementation and possible mechanical ventilation.

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Cystic Fibrosis/Bronchiectasis: A genetic respiratory disease caused by a defective gene that creates thick and sticky mucus that clogs up tubes and passageways. This mucus causes repeat, and dangerous, lung infections, as well as obstructions in the pancreas that prevent important enzymes from breaking down nutrients for the body. Symptoms of cystic fibrosis include salty-tasting skin, chronic coughing, frequent lung infections, a poor growth rate in children, and development of bronchiectasis or bronchiectasis, a condition in which patients develop abnormally dilated bronchial tubes. This allows mucus to pool, causing frequent respiratory tract infections, wheezing, and shortness of breath.

Delivered Blood Flow: Volume flow in mL/min that is acutally delivered to a patient as measured by the ELSA Monitor.

Diffusion: The movement of a substance from an area of high concentration (pressure) to an area of low concentration (pressure). Transfer of oxygen and carbon dioxide between the alveoli and capillaries in the lungs occur by diffusion.

Disability-adjusted life years (DALYs): Represent the total number of years lost to illness, disability or premature death within a given population. DALYs help the medical community compare the burden of disability associated with different disorders.

Dyspnoea: The subjective sensation of difficulty in breathing.

ECLS: Extracorporeal Life Support: A common alternative term for extracorporeal membrane oxygenation (ECMO), that intends to differentiate a circuit with an oxygenator to a circuit without one. While ECLS is more descriptive, ECMO is still the most common collective term for both types of support.

ECCO$_2$R: A device designed to remove carbon dioxide (CO2) from the lungs. Unlike extracorporeal membrane oxygen (ECMO), it does not provide significant oxygenation. The device consists of a drainage cannula placed in a large central vein or artery, a membrane lung (artificial gas exchanger), and a return cannula into the venous system.

ECMO (Extracorporeal Membrane Oxygenation): Traditional term associated with use of prolonged extracorporeal cardiopulmonary bypass, usually via extrathoracic cannulation, in patients with acute, reversible cardiac or respiratory failure who are unresponsive to conventional medical or pharmacologic management.

- Extracorporeal: outside the body
- Membrane: a type of artificial lung
- Oxygenation: the process of getting oxygen into the blood

ECMO Flow: The amount of blood measured in cc per minute that travels through the ECMO circuit. The amount of flow relates to how much support the patient is receiving.

ELSA (Extracorporeal Life Support Assurance) Monitor: A Flowmeter developed, manufactured, and marketed by Transonic that measures delivered blood flow, recirculation and oxygenator blood volumes during ECMO.

Edema: Swelling of tissues due to excess fluid.

Emphysema: A form of COPD where sufferers have trouble exhaling air from their lungs. It can lead to respiratory failure and the need for extra oxygen to meet breathing needs. Emphysema is usually caused by smoking that damages the alveoli in the lungs to a point where they can no longer repair themselves. It evolves slowly over the years, and there is no cure. However, those who quit smoking are more likely to see the disease's progression slow.

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Enterovirus (Non-polio): A group of common viruses transmitted through person-to-person contact that cause 10 to 15 million infections annually; usually nothing more than the common cold with fever, runny nose, sneezing, mouth blisters, and body and muscle aches. Other symptoms include skin (enterovirus) rash, trouble breathing, and wheezing. Some non-polio enteroviruses have caused large outbreaks of hand, foot, and mouth disease worldwide.

European Respiratory Society (ERS): Founded in 1990, ERS is a non-profit organization which focuses on the field of respiratory medicine.

Extrapulmonary: Outside or not related to the lungs.

Fibrosis: The formation of fibrous scar tissue where this would not normally occur, often in response to an insult or as part of a repair process.

Flu: A seasonal, acute, and contagious respiratory illness caused by influenza A or B viruses and is most dangerous to children, seniors, and those with weakened immune systems. The flu spreads through droplets created anytime an infected person sneezes or talks. Symptoms include fever, chills, throat pain, runny or stuffy nose, muscle or body aches, headaches, and fatigue. Flu symptoms in children may also include vomiting and diarrhea. Adult flu complications can include bacterial pneumonia, ear infection, sinus infection, dehydration, and worsening of chronic medical conditions, such as congestive heart failure, asthma, or diabetes.

Forced expiratory volume in 1 second (FEV1): The maximum amount of air a subject can exhale in the first second of forceful expiration following an inspiration to total lung capacity

Forced vital capacity (FVC): The maximum volume of air a subject can exhale in total following an inspiration to total lung capacity.

Forum of International Respiratory Societies (FIRS): Composed of the world's leading international respiratory societies, the goal of the FIRS is to unify and enhance efforts to improve lung health throughout the world.

Haemoptysis: Blood or blood-staining in expectorated (coughed up) sputum.

Hemoglobin particles: A red protein molecule comprising four subunits, each containing an iron atom bound to a heme group that is responsible for transporting oxygen in the blood of vertebrates. 300 million hemoglobin particles are found in one human red blood cell.

Hemolung RAS (Respiratory Assist System): An innovative system developed by Alung Technologies, Inc. to effectively treat acute respiratory failure without overreliance on ventilators.

Herd Effect (Herd or Community Immunity): The effect whereby vaccination of a significant proportion of individuals in a population has a protective effect on even non-vaccinated individuals because they are less likely to come into contact with an infected person.

Hypoxaemia: An insufficient level of oxygen in the blood.

Iatrogenic: A disease such as an infection or injury caused by medical treatment.

Idiopathic: Any disease with an unknown cause or mechanism of apparent spontaneous origin.

Histoplasmosis: A lung disease caused by an infection from a fungus, Histoplasma capsulatum, that results from inhaling airborne spores of the fungus. It is common in the Ohio and Mississippi River valleys and in soil contaminated by bird, chicken or bat droppings.

Idiopathic pulmonary fibrosis (IPF): A rare and serious irreversible lung disease.

Intertstitial lung diseases (IID): Also called diffuse parenchymal lung diseases, ILD generally presents with breathlessness due to impaired gas exchange as a consequence of widespread inflammation and/or

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fibrosis of the alveolar walls. There are more than 300 different conditions included among the total number of ILDs. Some of these diseases, such as sarcoidosis and ILD associated with connective tissue disease (CTD), also affect other organs and this may determine the prognosis to a greater extent than the lung dysfunction.

Intubation: A procedure performed to hook someone up to a ventilator when they are unable to breathe by themselves. Ventilators have different settings a respiratory therapist adjusts for each patient based on the level to which their breathing is compromised.

Lung Cancer: DNA mutations in the lungs cause irregular cells to multiply and create an uncontrolled growth of abnormal cells, or a tumor that interferes with normal lung functions. Difficult to detect, the cancer most often develops in the main part of the lungs near the air sacs. Symptoms include chronic coughing, changes in voice, harsh breathing sounds and coughing up blood. Risk factors include smoking, radon exposure, workplace exposure, including asbestos and diesel fumes, secondhand smoke, air pollution and radiation exposure from frequent CT scans of the chest.

Meconium Aspiration: Before or shortly after birth, a baby may inspire meconium, which is very detrimental to the lungs, reducing oxygen exchange, and is often fatal. ECMO is useful in its treatment.

Membrane Oxygenator: An artificial lung. Carbon dioxide is removed and oxygen is added.

National Heart, Lung and Blood Institute: The third largest division of the National Institutes of Health. It's mission is to provide global leadership for a research, training, and education program to promote the prevention and treatment of heart, lung, and blood disorders and enhance the health of all individuals so that they can live longer and more fulfilling lives.

Oxygenate: To combine or supply with oxygen. When oxygen enters the blood, as in the lungs, the oxygen molecules attached to hemoglob molecules in each red blood cell to traverse the circulatory system via this arterial blood and diffuse into each cell in the body to fuel metabolism.

Oxygenated (arterial) Blood: Blood that is high in oxygen, delivering it to the tissues of the body.

Oxygenator: An artificial lung that adds oxygen and removes carbon dioxide from the blood as it passes through. The oxygenator is divided into two separate chambers by a semipermeable membrane. The venous blood enters the oxygenator and travels along one side of the membrane termed the blood side. Fresh sweep gas is delivered to the other side termed the gas side. Gas exchange (oxygen uptake and carbon dioxide elimination) takes place across the membrane.

Oxygenator Blood Volume: Volume of blood actively flowing through an oxygenator in an ECMO circuit, as measured by the ELSA Monitor.

Pack-year: A measure of how much someone has smoked during their lifetime; 1 pack-year is equivalent to an average of 1 pack of 20 cigarettes per day for 1 year, i.e. 7305 cigarettes; despite its name, the pack-year is independent of time: the 7305 cigarettes can be smoked across any period

Pediatric MLung: A wearable, pumpless artificial lung conceived, designed, and fabricated at the University of Michigan for children with end-stage lung failure as a bridge to transplant.

Persistent fetal circulation (persistent pulmonary hypertension [PPHN]): Advanced difficulty in breathing and circulation in a newborn. Develops when the lungs cannot maintain respiratory needs. When a child is born, the circulation must change from fetal to newborn circulation, allowing the blood to pass through the lungs to be oxygenated. If this fails to occur, the blood continues to circulate as it did in the fetal state, and the child's body does not get enough oxygen.

Pleural Effusion: A buildup of fluid between the lung and the chest wall (the pleural space). Two types: transudate and exudate. Causes of transudate pleural

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effusion include congestive heart failure, kidney failure, and cirrhosis. Exudate pleural effusion can be caused by malignancy (cancer) or lung infection. Symptoms include chest pain, pain when breathing, difficulty breathing, and cough. Treatment includes a procedure to remove the fluid, which allows the lung to re-expand, allowing the patient to breathe better. The fluid is then tested to determine what's causing it and a treatment plan is formed.

Pneumonia: Common lung disease of the air sacs caused by a bacteria, virus or fungus infection.

Bacterial Pneumonia: caused by bacterial infection. Treatment: antibiotics are highly effective so long as the bacteria are not resistant to the antibiotics. Bacterial pneumonias, except for tuberculosis, are not very contagious. Walking pneumonia is used to describe a mild form of bacterial pneumonia.

Viral Pneumonia: caused by Influenza A or B ("the flu"), respiratory syncytial virus (RSV), parainfluenza, and adenovirus. Worldwide, viral pneumonia is the leading cause of death among children younger than 5 years old. Caused by infectious microbes, viral pneumonia is contagious. Symptoms include spit up phlegm and experience fever, chills, shortness of breath, fatigue, muscle aches, headache, sweating, clammy skin, and confusion (especially in the elderly).

Proning: Placement on the stomach to help recruit (open up) different areas of the lungs.

Platelets: Cells in the blood that help in the clotting ability of the blood.

Pneumothorax: An accumulation of air between the lung and the chest wall that causes the lung to collapse.

Pulmonary rehabilitation: a supervised exercise program for sufferers of COPD.

QALY (Quality-Adjusted Life-Year): A similar concept to DALY, but expressed in terms of quality of life gained following an intervention, rather than lost to disease or disability

Respiratory Disease: A disease that affects the lungs and other parts of the respiratory system. Symptoms include breathlessness (inability to exhale normally), cough, and collection of mucus. May be caused by infection, by smoking tobacco, or by breathing in secondhand tobacco smoke, radon, asbestos, or other forms of air pollution.

Upper respiratory infections: Affect the upper respiratory tract including the nose, sinuses, and throat, include the common cold (head cold), the mild flu, tonsillitis, laryngitis, and sinus infection; most common symptom is a cough; others can include stuffy or runny nose, sore throat, sneezing, achy muscles, and headache.

Lower Respiratory Infection: Found in the lungs or breathing airways; caused by viral infections like the severe flu or bacterial infections like tuberculosis; symptoms include a severe cough that may produce mucus (phlegm), cause shortness of breath, chest tightness, and wheezing when exhaling.

Acute: A sudden condition in which breathing is difficult and the oxygen levels in the blood abruptly drop lower than normal.

Chronic: lasting over an extended period of time.

Obstructive Lung Disease: Disease causing shortness of breath due to difficulty exhaling all the air from the lungs. Because of damage to the lungs or narrowing of the airways inside the lungs, exhaled air comes out more slowly than normal. At the end of a full exhalation, an abnormally high amount of air may still linger in the lungs.

Restrictive Lung Disease: Disease where people cannot fully fill their lungs with air. Restrictive lung disease most often results from a condition causing stiffness in the lungs themselves. In other cases, stiffness of the chest wall, weak muscles, or damaged nerves may cause the restriction in lung expansion. Condition causing restrictive lung disease include interstitial lung disease, such as idiopathic pulmonary fibrosis.

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Respiratory Distress: Distress at birth, or shortly after, when a child may encounter difficulty breathing. This may be caused by immature lungs or foreign material present in the lungs.

Respiratory System (Human): A system that delivers air into the lungs to exchange oxygen and carbon dioxide with the circulation to sustain life. It includes the following: the nasal passage (nose, sinuses, mouth); larynx or voice box; pharyx or throat that connects the nose and mouth to the trachea (via the larynx) and esophagus; trachea or windpipe; bronchi (two air passageways from the trachea and branching out like a tree to multiple smaller broncioles); broncioles; lungs; alveoli; diaphragm and pleural cavity (the area between the chest wall and the lungs).

Respiratory Therapy: A specialized health care field where practitioners are trained in pulmonary medicine in order to work therapeutically with people suffering from pulmonary disease.

- **Respiratory Therapists (RT):** Certified medical professionals who specializes in providing healthcare for your lungs. They have advanced knowledge of high-tech equipment, such as mechanical ventilators.

Rhinovirus: Viruses that commonly cause upper respiratory tract infections, like the common cold.

Sensitivity: Refers to the proportion of cases (people with a disease) that will be detected by a diagnostic test.

Specificity: Refers to the proportion of people without the disease who will have a negative diagnostic test.

Spirometry: A method of testing lung function by using a spirometer to measure the flow rate and volume of air exhaled over time and using the information to calculate various indices such as FEV1 and FVC.

Stridor: A monophonic, low-pitched sound accompanying breathing; if heard during inspiration, its presence suggests significant narrowing of the upper airway (larynx or extrathoracic trachea).

Sputum: Mucus from the lungs.

Surfactant: A slippery fluid that lines the lungs, and keeps the sticky surface from adhering to itself, It renders the alveoli unreachable during breathing. Premature babies often do not have enough of this to keep their lungs from collapsing.

Swine Flu (H1N1): A respiratory illness in humans, cats, dogs, monkeys, and others caused by the Influenza-A virus. Named because the viruses that causes swine flu (H1N1v viruses) show genetic similarities to viruses that infect pigs. Symptoms include fever, throat pain, a general feeling of being unwell (malaise), headache, chills, muscle pain, joint pain, vomiting and diarrhea. Usually, spread from person to person though sneezing or kissing. A swine flu vaccine is available either as a "killed virus" shot or as a "live attenuated virus" nasal spray.

Thrombosis: Clotting of blood within a blood vessel, potentially causing infarction (tissue death).

Total Lung Capacity: The volume of gas in the lungs after a subject has inhaled as much as he or she is able.

Triple Therapy: A corticosteroid to reduce airway swelling, a long-acting beta-agonist to relax the muscles around the airway, and an anticholinergic drug to widen the large airways combined in one inhaler. It was approved by the FDA in 2017.

Tuberculosis (TB): A bacterial disease caused by Mycobacterium tuberculosis, an organism belonging to the M. tuberculosis complex, which also includes other genetically related mycobacteria. TB is an important clinical and public health problem worldwide. Although its incidence and prevalence have declined notably in high-income countries over the past century, they have increased in low- and middle-income countries, owing to the emergence of strains resistant to several antimycobacterial drugs and to co-infection with HIV/AIDS.

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Unoxygenated (venous) blood: Blood that has delivered most of its oxygen to the tissues of the body and is lower in oxygen.

Ventilation: methods to get air into a person's lungs:
Invasive Mechanical (IMV): In invasive ventilation, air is delivered via a tube that is inserted into the trachea through the mouth or sometimes the nose.
Non-invasive Mechanical (NMV): NIV creates positive airway pressure and gives a push behind each breath to assist in expelling carbon dioxide from the body. A noninvasive ventilator uses no tubes, instead delivering oxygen using a tight fitting mask attached over the patient's mouth and nose and held in place with straps. Some masks are designed to cover the nose only and are known as nasal masks. Another noninvasive option is a hood which encloses the entire head versus a mask covering the nose and/or mouth. None of these delivery options requires physical "invasion" of the patient's body, thus the term: noninvasive.

Vital Capacity: The maximun volume of air that can be expired in a single breath after full inspiration (or inspired after full expiration), irrespective of the time taken.

Volutrauma: Injury to the lung caused by excessive distension.

Wheeze: A musical, polyphonic, high-pitched sound which indicates narrowing of the airways; heard most commonly during expiration, e.g. in individuals with asthma or COPD.

Ventilator: A breathing machine that delivers oxygen, pressure and a rate of breathing to the patient by a breathing tube. Also known as a respirator.

Whooping Cough (Pertussis): Caused by the Bordetella pertussis bacterium. Symptoms include uncontrollable, violent coughing that can make it difficult to breathe. The whooping sound comes from a sick person sucking in air after a coughing fit. Can be life-threatening. The pertussis vaccine helps prevent the spread of infection of whooping cough in infants and others.

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