What is CDH?

Congenital diaphragmatic hernia (CDH) is a condition that develops before birth. Children with CDH have a hole in their diaphragm, the wide, flat muscle that separates the chest from the abdominal cavity and is important for breathing. The hole in the diaphragm allows some of the contents of the abdomen, such as the stomach, part of the intestines, and liver, to move up into the chest. These abdominal organs occupy space in the chest and prevent the lungs from growing to a normal size before birth. Growth of both lungs can be affected, but the lung on the same side of the hole in the diaphragm is usually smaller. When the lung is smaller than it should be, it is called pulmonary (lung) hypoplasia.

What is Pulmonary Hypertension (PH)?

Children with CDH also have fewer and smaller blood vessels (arteries) in their lungs. This causes high blood pressure in the lungs, known as pulmonary hypertension (PH). PH can cause problems with blood entering the lungs, which makes oxygen levels in the blood lower. PH can also affect the ability of the right side of the heart (the right ventricle) to pump blood well. PH is very common in children with CDH, especially shortly after birth, and can be more severe in children with larger diaphragmatic hernias. PH most often occurs early but can also continue over time and need longer-term treatment.
Early PH Management in Newborn CDH Patients

Children with CDH and PH require care from an experienced multidisciplinary team and skilled intensive care nursery. Almost all children with CDH will require a breathing tube and breathing machine at birth. Your child’s specialists will decide the best time for surgery to close the hole in the diaphragm, but it is typically performed as early as safely possible. Even with closure of the hole with surgery, however, the lung and PH problems must be closely monitored and will still require treatment.

There is a wide range in the severity of CDH. In the best cases, your child will do very well with surgical treatment after birth, and PH will improve and resolve in the first weeks of life. On the other hand, children with severe CDH are challenged by very small lungs and severe PH. In the most severe cases, some children will require extracorporeal membrane oxygenation (ECMO), which provides temporary support for heart and lung failure by circulating the child’s blood through a heart-lung machine.

Medications in Early CDH and PH Treatment

During the early treatment of CDH it is most important to keep the lungs working as best they can with the help of a breathing machine and oxygen. Your team will evaluate for PH frequently and make sure the heart is pumping well. There are several medications that your child’s medical team may decide to use to treat PH.

<table>
<thead>
<tr>
<th>Inhaled Nitric Oxide (iNO)</th>
<th>Milrinone</th>
<th>Prostaglandin E1 (PGE)</th>
<th>Prostaglandins</th>
</tr>
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<tbody>
<tr>
<td>An inhaled gas that goes into your child’s breathing tube that helps the blood vessels in the lungs to relax</td>
<td>Continuous medication that helps blood vessels relax and helps the heart squeeze</td>
<td>Continuous medication that is used to keep the ductus arteriosus (PDA) open to relieve pressures in the heart and lungs when they are too high</td>
<td>Used to relax the blood vessels in the lungs when PH is very severe</td>
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</table>

PH SYMPTOMS DUE TO CDH
- Hypoxemia (low blood oxygen levels)
- Tachycardia (rapid heart rate)
- Hypotension (low blood pressure)
- Tachypnea (fast breathing)
- Labored breathing or retractions (skin pulling in between or around ribs)
- Nostrils flaring and/or grunting while breathing
- Failure to thrive (growth failure or poor feeding)
Evaluation

The following tests or procedures may be ordered by your child’s medical team to diagnose and evaluate PH.

**Labwork**

- Blood gas: a blood test that measures oxygen and carbon dioxide in the lungs

- Natriuretic peptide tests (NT proBNP or BNP): a blood test that shows stress in the heart, which can be because of PH

**Imaging**

Echocardiogram (Echo): an ultrasound of the heart to help estimate what pressures are in the lungs by looking at the heart

Chest X-ray: an image of the heart, lungs, airways, blood vessels, and bones of the spine and chest

Chest CT: a more in-depth look at the lungs that can show changes in airways, blood vessels, and lung tissue

Cardiac MRI: a test performed to evaluate the structure, size, and function of the heart chambers, heart valves and flow through the major blood vessels

Lung Ventilation-Perfusion (VQ) Scan: a test that evaluates the air and blood flow patterns in the lung

**Other Studies**

- Cardiac catheterization: a procedure to directly measure the pressures in the heart and lungs, diagnose PH and/or address a problem like a congenital heart defect

- Swallow study: a test completed to see how your child is swallowing and if he/she is aspirating (when food goes “down the wrong way” in the airway)

- Electrocardiogram (EKG/ECG): a test of the electrical signal from your child’s heart

- Genetic testing: blood test to look for genetic differences that may impact your child

**Later PH Management**

After your child’s CDH repair, his/her PH is expected to improve over time as the lungs and blood vessels grow and develop. The severity of PH and how fast it improves varies between children. This depends on the how large the hole in the diaphragm was and the severity of the lung disease or related heart problems. For most children, PH improves and resolves before leaving the intensive care nursery. For others, long-term PH medications and respiratory support will be needed for many months or years. During this time, it will be very important to keep your child’s lungs and heart healthy.
**Long-Term Medications for PH**

The decision to use medications to treat PH in CDH is one that should be made by specialists trained in the use of these medications. Children with PH require careful review before medications are started, to make sure that the medications will not cause any clinical worsening. If medications are started, close monitoring is recommended. Although not FDA approved for use in this age group or type of PH, there are three classes of drugs that have been used in children with CDH.

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Medication Examples</th>
<th>Routes of Administration</th>
<th>Common Side Effects in Infants</th>
<th>Special Considerations &amp; Information</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Phosphodiesterase-5 Inhibitors</strong></td>
<td>Sildenafil (Revatio®)</td>
<td>Oral, IV (in hospital setting only)</td>
<td>May cause increased spit up/reflux, low BP in the body, mismatch between the air/blood interface in the lungs, erections in males</td>
<td>Patients can take these medications in a liquid form (suspension) or a tablet in the outpatient setting</td>
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<tr>
<td><strong>Endothelin Receptor Antagonist</strong></td>
<td>Bosentan (Tracleer®)</td>
<td>Oral</td>
<td>May cause low BP in the body, reversible liver injury, requires protection if handled while pregnant as ingestion can harm developing fetus</td>
<td>The child must be enrolled in a monitoring program (REMS) due to the liver and pregnancy toxicity concerns. Lab results must be monitored monthly.</td>
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<tr>
<td><strong>Prostacyclins</strong></td>
<td>Epoprostenol (Flolan®, Veletri®)</td>
<td>IV/inhaled (in hospital setting only)</td>
<td>Inhaled has the potential to be irritating to the lungs</td>
<td></td>
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<tr>
<td></td>
<td>Treprostinil (Remodulin®)</td>
<td>IV/Subcutaneous (SQ)</td>
<td>IV and SQ may cause low BP in the body, headache, nausea, vomiting, diarrhea. SQ may cause pain, redness, or swelling at the site of the infusion.</td>
<td>IV and SQ options require extensive training on how to prepare and deliver medications from home. These medications require a pump to infuse 24 hours a day, 7 days a week.</td>
</tr>
<tr>
<td></td>
<td>Iloprost (Ventavis®)</td>
<td>Inhaled</td>
<td>Inhaled has the potential to be irritating to the lungs</td>
<td>Frequent dosing every 2-3 hours.</td>
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Other Therapies

• Oxygen may be used to relax and help open the blood vessels in the lungs.

• Diuretics are often used to help the body get rid of extra fluid. Examples of diuretics include furosemide, bumetanide, and chlorothiazide. These can be given IV or by mouth/feeding tube.

• Bronchodilators are used for lower airway obstruction and wheezing. Examples include albuterol and levalbuterol.

• Steroids inhaled, by mouth or IV may be used to treat your child.

Long-Term Care and Follow Up

All children with CDH require long-term follow-up, and those with PH from CDH require care from several pediatric specialists, including a PH team. Some children with CDH may need long-term oxygen therapy and breathing help from machines like ventilators, even after they go home. The primary goals for children with PH from CDH are to grow and for the lungs to be as healthy as possible. This can be done by following the below recommendations:

• Making sure advancement of oral feeding is done safely without chronic aspiration, which can make PH worse. If there is a concern for aspiration (coughing or choking with feeds, changes on chest x-ray), a swallow study is recommended.

• Staying up to date on childhood immunizations, including annual vaccination and boosters for influenza (flu shot) and COVID-19, as well as Pneumovax 23 after 2 years old.

• Receiving Synagis® (palivizumab) therapy if your child qualifies. This is a monthly injection (antibodies) to protect against respiratory syncytial virus (RSV), a virus that can make infants very sick. This can be obtained for children who meet certain criteria during the first 1-2 years of life and will require your medical team to apply for it.

• Avoiding secondhand smoke in the home or other places where your child spends time. This includes cigarette smoke and vaping.

• Staying inside and wearing masks if the air quality is poor, for example wildfires or pollution.

• Taking extra caution to minimize exposures to viral illnesses. This includes avoiding individuals who are sick, good hand hygiene, and social distancing during the viral season.

• Providing close respiratory monitoring and supportive care in case of viral illness since PH can worsen in children during an acute viral illness.

• Continuing close follow up with your child’s pediatrician, pediatric surgeons, pulmonologists, gastroenterologists and/or PH team to follow growth, respiratory status, and developmental progress.

• Discussing any scheduled surgery or procedure your child may need with your PH team so they can make sure your child is safe to get anesthesia.

• Weaning of oxygen and PH medications when ready, under the guidance of your PH team. This will be done slowly, typically weaning only 1 thing at a time.