**Common and Chronic Pediatric Pulmonary Diseases**

## Asthma

## Overview

Asthma is a chronic lung disease affecting people of all ages. It is caused by inflammation and muscle tightening around the airways, which makes it harder to breathe.

Symptoms can include coughing, wheezing, shortness of breath and chest tightness. These symptoms can be mild or severe and can come and go over time.

Although asthma can be a serious condition, it can be managed with the right treatment. People with symptoms of asthma should speak to a health professional.

**Key Facts**

* Asthma is a major non communicable disease (NCD), affecting both children and adults, and is the most common chronic disease among children.
* Inflammation and narrowing of the small airways in the lungs cause asthma symptoms, which can be any combination of cough, wheeze, shortness of breath, and chest tightness.
* Asthma affected an estimated 262 million people in 2019 (1) and caused 455 000 deaths.
* Inhaled medication can control asthma symptoms and allow people with asthma to lead a normal, active life.
* Avoiding asthma triggers can also help to reduce asthma symptoms.
* Most asthma-related deaths occur in low- and lower-middle-income countries, where under-diagnosis and under-treatment is a challenge.
* WHO is committed to improving the diagnosis, treatment and monitoring of asthma to reduce the global burden of NCDs and make progress towards universal health coverage.

## Impact

Asthma is often under-diagnosed and under-treated, particularly in low- and middle- income countries.

People with under-treated asthma can suffer sleep disturbance, tiredness during the day, and poor concentration. Asthma sufferers and their families may miss school and work, with financial impact on the family and wider community. If symptoms are severe, people with asthma may need to receive emergency health care and they may be admitted to hospital for treatment and monitoring. In the most severe cases, asthma can lead to death.

## Symptoms

Symptoms of asthma can vary from person to person. Symptoms sometimes get significantly worse. This is known as an asthma attack. Symptoms are often worse at night or during exercise.

Common symptoms of asthma include:

* a persistent cough, especially at night
* wheezing when exhaling and sometimes when inhaling
* shortness of breath or difficulty breathing, sometimes even when resting
* chest tightness, making it difficult to breathe deeply.

Some people will have worse symptoms when they have a cold or during changes in the weather. Other triggers can include dust, smoke, fumes, grass and tree pollen, animal fur and feathers, strong soaps and perfume.

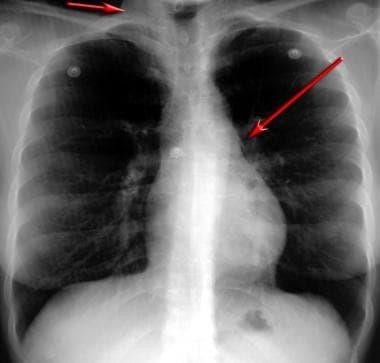
Symptoms can be caused by other conditions as well. People with symptoms should talk to a healthcare provider.

## Diagnosis

Chest radiographic imaging is an important tool in the examination of patients with an exacerbation of [asthma,](https://emedicine.medscape.com/article/296301-overview) but patients should not be left waiting in the treatment room for a radiograph before treatment.Chest radiography is the initial imaging evaluation in most individuals with symptoms of asthma. The value of chest radiography is in revealing complications or alternative causes of wheezing in the diagnosis of asthma and its exacerbations. It usually is more useful in the initial diagnosis of bronchial asthma than in the detection of exacerbations, although it is valuable in excluding complications such as pneumonia and asthma mimics, even during exacerbations.

Significant advancements have been made in a number of imaging techniques used for evaluating patients with asthma. CT utilizes specific airway and lung density measurements to identify severity of disease and pathology, hyperpolarized gases are used as MRI contrast media to identify small airway disease, and positron emission tomography (PET) can help identify and target lung inflammation.

(See the images below.)



Posteroanterior chest radiograph demonstrates a pneumomediastinum in bronchial asthma. Mediastinal air is noted adjacent to the anteroposterior window and airtrapping extends to the neck, especially on the right side.



Lateral chest radiograph demonstrates a pneumomediastinum in bronchial asthma. Air is noted anterior to the trachea (same patient as in the previous image).

Although bronchial thickening, hyperinflation, and focal atelectasis suggest asthma when they are present, chest radiographs obtained during asthma exacerbations can demonstrate normal findings, which reduce its sensitivity as a diagnostic tool. Similarly, identical findings may be observed with chronic

## Causes

Many factors have been linked to an increased risk of developing asthma, although it is often difficult to find a single, direct cause.

* Asthma is more likely if other family members also have asthma – particularly a close relative, such as a parent or sibling.
* Asthma is more likely in people who have other allergic conditions, such as eczema and rhinitis (hay fever).
* Urbanization is associated with increased asthma prevalence, probably due to multiple lifestyle factors.
* Events in early life affect the developing lungs and can increase the risk of asthma. These include low birth weight, prematurity, exposure to tobacco smoke and other sources of air pollution, as well as viral respiratory infections.
* Exposure to a range of environmental allergens and irritants are also thought to increase the risk of asthma, including indoor and outdoor air pollution, house dust mites, moulds, and occupational exposure to chemicals, fumes or dust.
* Children and adults who are overweight or obese are at a greater risk of asthma.

## Treatment

Asthma cannot be cured but there are several treatments available. The most common treatment is to use an inhaler, which delivers medication directly to the lungs.

Inhalers can help control the disease and enable people with asthma to enjoy a normal, active life.

There are two main types of inhaler:

* bronchodilators (such as salbutamol), that open the air passages and relieve symptoms; and
* steroids (such as beclometasone) that reduce inflammation in the air passages, which improves asthma symptoms and reduces the risk of severe asthma attacks and death.

People with asthma may need to use their inhaler every day. Their treatment will depend on the frequency of symptoms and the types of inhalers available.

Using an inhaler can be difficult, especially for children and during emergency situations. Using a spacer device makes it easier to use an aerosol inhaler. This helps the medicine to reach the lungs more easily. A spacer is a plastic container with a mouthpiece or mask at one end and a hole for the inhaler in the other. A homemade spacer, made from a 500ml plastic bottle, can be as effective as commercially manufactured spacers.

Access to inhalers is a problem in many countries. In 2021, bronchodilators were available in public primary health care facilities in half of low- and low-middle income countries, and steroid inhalers available in one third.

It is also important to raise community awareness to reduce the myths and stigma associated with asthma in some settings.

## Self-care

People with asthma and their families need education to understand more about their asthma. This includes their treatment options, triggers to avoid, and how to manage their symptoms at home.

It is important for people with asthma to know how to increase their treatment when their symptoms are worsening to avoid a serious attack. Healthcare providers may give an asthma action plan to help people with asthma to take greater control of their treatment.

## WHO response

Asthma is included in the WHO Global Action Plan for the Prevention and Control of NCDs and the United Nations 2030 Agenda for Sustainable Development.

WHO is taking action to extend diagnosis of and treatment for asthma in a number of ways.

The WHO Package of Essential Noncommunicable Disease Interventions (PEN) was developed to help improve NCD management in primary health care in low-resource settings. PEN includes protocols for the assessment, diagnosis and management of chronic respiratory diseases (asthma and chronic obstructive pulmonary disease), and modules on healthy lifestyle counselling, including tobacco cessation and self-care.

Reducing tobacco smoke exposure is important for both primary prevention of asthma and disease management. The Framework Convention on Tobacco Control is enabling progress in this area as are WHO initiatives such as MPOWER and mTobacco Cessation.

Air pollution is an important risk factor for asthma, causing new cases and making existing disease worse. WHO has developed training for health care workers on air pollution which highlights this link and offers practical advice to reduce and mitigate exposure.

The Global Alliance against Chronic Respiratory Diseases (GARD) contributes to WHO’s work to prevent and control chronic respiratory diseases. GARD is a voluntary alliance of national and international organizations and agencies from many countries committed to the vision of a world where all people breathe freely.

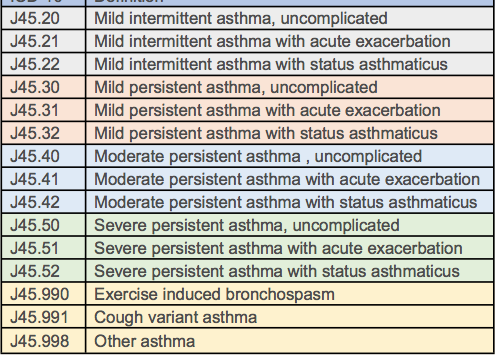
### Procedure Explanation and Clinical guidelines

Guidelines Summary

The following organizations have issued guidelines for the management of asthma:

* National Asthma Education and Prevention Program (NAEPP)
* Veteran’s Administration/Department of Defense (VA/DoD)
* The Global Asthma Network (GAN)
* Global Initiative for Asthma (GINA)
* Japanese Society of Allergology (JSA)
* European Respiratory Society/American Thoracic Society (ERS/ATS)

## Clinical code:



### References

>>>[Global burden of 369 diseases and injuries in 204 countries and territories, 1990–](https://www.thelancet.com/gbd/summaries) [2019: a systematic analysis for the Global Burden of Disease Study 2019.](https://www.thelancet.com/gbd/summaries) Lancet. 2020;396(10258):1204-22.

>>><https://www.who.int/news-room/fact-sheets/detail/asthma.>

>>><https://nycreach.org/2019/01/using-icd-10-asthma-severity-codes/.>

# Cystic Fibrosis

## Medical code:

* **E84.0:** Cystic fibrosis with pulmonary manifestations.
* **E84.1:** Cystic fibrosis with intestinal manifestations.
* **E84.8:** Cystic fibrosis with other manifestations.
* **E84.9:** Cystic fibrosis, unspecified.

## Disease and Descriptions

Cystic fibrosis (CF) is the most common, fatal genetic disease in the United States. About 30,000 people in the United States have the disease. CF causes the body to produce thick, sticky mucus that clogs the lungs, leads to infection, and blocks the pancreas, which stops digestive enzymes from reaching the intestine where they are required in order to digest food.

#### What do we know about heredity and cystic fibrosis?

Mutations in a single gene - the Cystic Fibrosis Transmembrane Regulator (CFTR) gene - causes CF. The gene was discovered in 1989. Since then, more than 900 mutations of this single gene have been identified. In normal cells, the CFTR protein acts as a channel that allows cells to release chloride and other ions. But in people with CF, this protein is defective and the cells do not release the chloride. The result is an improper salt balance in the cells and thick, sticky mucus. Researchers are focusing on ways to cure CF by correcting the defective gene, or correcting the defective protein.

Gene Therapy Research Offers Promise of a Cure for Cystic Fibrosis

Gene therapy offers great promise for life-saving treatment for CF patients since it targets the cause of CF rather than just treating symptoms. Gene therapy for CF had its start in 1990, when scientists successfully corrected faulty CFTR genes by adding normal copies of the gene to laboratory cell cultures.

In 1993, the first experimental gene therapy treatment was given to a patient with CF. Researchers modified a common cold virus to act as a delivery vehicle - or "vector"- carrying the normal genes to the CFTR cells in the airways of the lung.

Subsequent studies have tested other methods of gene delivery, such as fat capsules, synthetic vectors, nose drops or drizzling cells down a flexible tube to CFTR cells lining the airways of lungs. Researchers are now testing aerosol delivery using nebulizers.

But finding the best delivery system for transporting normal CFTR genes is only one problem that scientists must solve to develop an effective treatment for CF. Scientists must also determine the life span of affected lung cells, identify the "parent cells" that produce CFTR cells, find out how long treatment should last and how often it needs to be repeated.

The first cystic fibrosis gene therapy experiments have involved lung cells because these cells are readily accessible and because lung damage is the most common, life-threatening problem in CF patients. But scientists hope that the technologies being developed for lung cells will be adapted to treat other organs affected by CF.

Genetic Research May Lead to New Drugs to Treat Cystic Fibrosis

Another research breakthrough offers a promising approach to treating cystic fibrosis. Researchers at the University of Washington's Genome Center and at PathoGenesis Corporation have completed a genetic map for the *Pseudomonas aeruginosa* bacterium.

This bacterium is the most common cause of chronic and fatal lung infections for people with CF. Scientists hope to use their knowledge of this bacterium's genetic sequence to develop innovative drugs for treating infections caused by *P. aeruginosa.*

Gene Database Speeds Research

As the amount of information about CF grows, scientists have recognized the need to share their research findings. To facilitate this sharing of information, the Cystic Fibrosis Foundation funds **[Cystic Fibrosis Foundation Therapeutics](http://www.cff.org/research/CFFT/)** (CFFT) located at The University of North Carolina Chapel Hill. The center is becoming a repository for data derived from gene expression studies. By pooling information, researchers hope to accelerate the process of finding a cure for CF.

#### Is there a test for the cystic fibrosis gene?

CF has a variety of symptoms, including very salty-tasting skin, a persistent cough and excessive appetite but poor weight gain. The "sweat test" - which measures the amount of salt in sweat - is the standard diagnostic test for those with symptoms. A high salt level indicates CF.

But one in 31 Americans - more than 10 million people - are symptom-less carriers of the defective CF gene and can pass on the defective gene to their children. To develop CF, a child must inherit a defective gene from both parents. If both parents are carriers, there is a 25 percent chance that each child they conceive will have CF, and a 50 percent chance that the child will be a carrier.

The purpose of carrier testing - a laboratory test done on a sample of blood or saliva

- is to see if a couple is at risk for giving birth to a child with CF. Carrier testing is not infallible. It cannot detect all of the CF gene mutations. In rare cases, a person can have a normal test result and still be a CF carrier.

If both parents are carriers, they may want to consult with a genetic counselor for help in deciding whether to conceive or whether to have a fetus tested for CF.

Prenatal testing for CF can be done around the 11th week of pregnancy using chorionic villi sampling (CVS). This involves removing a tiny piece of the placenta.

Or, the fetus can be tested with amniocentesis, around the 16th week of pregnancy. In this procedure, a needle is used to take amniotic fluid surrounding the baby for testing. Since CF cannot be treated before birth, the purpose of prenatal testing is to prepare parents to care for a baby with special health needs, or to make a decision about terminating the pregnancy.

**Symptoms**

In the U.S., because of newborn screening, cystic fibrosis can be diagnosed within the first month of life, before symptoms develop. But people born before newborn screening became available may not be diagnosed until the symptoms of CF show up.

CF symptoms vary, depending on which organs are affected and how severe the condition is. Even in the same person, symptoms may worsen or get better at different times. Some people may not have symptoms until their teenage years or adulthood.

People who are not diagnosed until adulthood usually have milder symptoms and are more likely to have symptoms that aren't typical. These may include repeated bouts of an inflamed pancreas called pancreatitis, infertility and repeated bouts of pneumonia.

People with CF have a higher than usual level of salt in their sweat. Parents often can taste the salt when they kiss their children. Most of the other symptoms of CF affect the respiratory system and digestive system.

##### Respiratory symptoms

In cystic fibrosis, the lungs are most commonly affected. The thick and sticky mucus that happens with CF clogs the tubes that carry air in and out of the lungs. This can cause symptoms such as:

* A cough that won't go away and brings up thick mucus.
* A squeaking sound when breathing called wheezing.
* Limited ability to do physical activity before tiring.
* Repeated lung infections.
* Irritated and swollen nasal passages or a stuffy nose.
* Repeated sinus infections.

##### Digestive symptoms

The thick mucus caused by cystic fibrosis can block tubes that carry digestive enzymes from the pancreas to the small intestine. Without these digestive enzymes, the intestines can't completely take in and use the nutrients in food. The result is often:

* Foul-smelling, greasy stools.
* Poor weight gain and growth.
* Blocked intestines, which is more likely to happen in newborns.
* Ongoing or severe constipation. Straining often while trying to pass stool can cause part of the rectum to stick out of the anus. This is called a rectal prolapse.

##### When to see a doctor

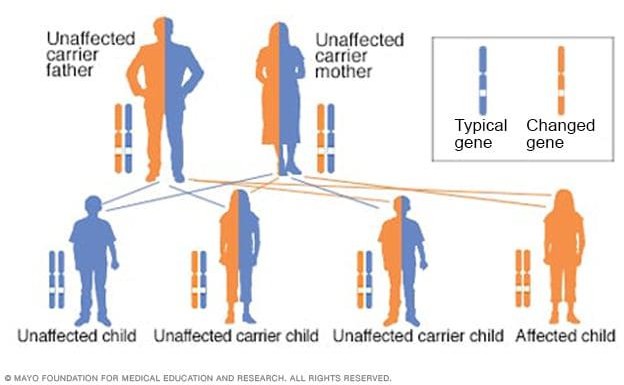
If you or your child has symptoms of cystic fibrosis — or if someone in your family has CF

— talk with your healthcare professional about testing for the condition. Make an appointment with a doctor who has skills and experience in treating CF.

CF requires regular follow-up with your healthcare professional, at least every three months. Call your healthcare professional if you have new or worsening symptoms, such as more mucus than usual or a change in the mucus color, lack of energy, weight loss, or severe constipation.

Get medical care right away if you're coughing up blood, have chest pain or trouble breathing, or have severe stomach pain and bloating.

**Causes**

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**Autosomal recessive inheritance pattern**

In cystic fibrosis, a change in a gene causes problems with the protein that controls the movement of salt and water in and out of cells. This gene is the cystic fibrosis transmembrane conductance regulator (CFTR) gene. It affects the cells that make mucus, sweat and digestive juices. When the CFTR protein doesn't work as it should, the result is thick, sticky mucus in the respiratory, digestive and reproductive systems, as well as extra salt in sweat.

Changes in the CFTR gene that cause CF are divided into several different groups based on the problems they cause. Different groups of gene changes affect how much CFTR protein is made and how well it works.

To have cystic fibrosis, children must get one copy of the changed CFTR gene from each parent. If children get only one copy, they won't develop CF. But they will be carriers and could pass the changed gene to their own children. People who are carriers may have no symptoms of CF or a few mild symptoms.

##### Risk factors

Because cystic fibrosis is a condition passed down in families, family history is a risk factor. CF occurs in all races, but it's most common in white people of Northern European ancestry. Because it's less common in people who are Black, Hispanic, Middle Eastern, Native American or Asian, this might lead to a much later diagnosis.

A late diagnosis may cause worse health issues. Early and effective treatment can improve your quality of life, prevent complications and help you live longer. If you're a person of color and have symptoms that could be CF, talk to your healthcare professional so that you can get tested for CF.

##### Complications

Complications of cystic fibrosis can affect the respiratory, digestive and reproductive systems, as well as other organs.

##### Respiratory system complications

* **Damaged airways.** Cystic fibrosis is one of the leading causes of damaged airways, a long-term lung condition called bronchiectasis. Bronchiectasis results in widening and

scarring of the airways. This makes it harder to move air in and out of the lungs and clear mucus from the airways.

* **Ongoing infections.** Thick mucus in the lungs and sinuses makes a place for bacteria and fungi to live and grow. Sinus infections, bronchitis or pneumonia are common and may happen repeatedly. Infections with bacteria that don't respond to antibiotics and are difficult to treat is common too.
* **Growths in the nose.** Because the lining inside the nose is irritated and swollen, it can develop soft, fleshy growths called nasal polyps.
* **Coughing up blood.** Bronchiectasis can occur next to blood vessels in the lungs. The combination of airway damage and infection can result in coughing up blood. Often this is only a small amount of blood, but rarely it can be life-threatening.
* **Collapsed lung.** Also called pneumothorax, this condition happens when air leaks into the space that separates the lungs from the chest wall. This causes part or all of a lung to collapse. Collapsed lung is more common in adults with CF. Collapsed lung can cause sudden chest pain and trouble breathing. People often have a bubbling feeling in the chest.
* **Respiratory failure.** Over time, CF can damage lung tissue so badly that it no longer works. Lung function usually worsens slowly over time and can become life- threatening. Respiratory failure is the most common cause of death with CF.
* **Bouts of worsening symptoms.** People with CF may experience times when respiratory symptoms are worse than usual. These are called exacerbations (eg-zas- er-bay-shuns). Symptoms may include coughing with more mucus than usual and trouble breathing. Low energy and weight loss also are common during exacerbations. Exacerbations are treated with antibiotics. Sometimes treatment can be given at home, but a stay in the hospital may be needed.

##### Digestive system complications

* **Poor nutrition.** Thick mucus can block the tubes that carry digestive enzymes from the pancreas to the intestines. Without these enzymes, the body can't take in and use protein, fats or fat-soluble vitamins and can't get enough nutrients. This can result in delayed growth and weight loss. An inflamed pancreas, a condition called pancreatitis, is common.
* **Diabetes.** The pancreas makes insulin, which the body needs to use sugar. Cystic fibrosis raises the risk of diabetes. About 20% of teenagers and up to 50% of adults with CF develop diabetes.
* **Liver disease.** The tube that carries bile from the liver and gallbladder to the small intestine may become blocked and inflamed. This can lead to liver problems, such as jaundice, fatty liver disease and cirrhosis, and sometimes gallstones.
* **Intestinal obstruction.** Intestinal blockage can happen to people with CF at all ages. Sometimes, a condition in which a section of the intestine slides inside another nearby section of the intestine, like a collapsible telescope, also can happen.
* **Distal intestinal obstruction syndrome (DIOS).** DIOS is partial or complete blockage where the small intestine meets the large intestine. DIOS requires treatment right away.

##### Reproductive system complications

* **Infertility in men.** Almost all men with cystic fibrosis are not fertile. The tube that connects the testicles and prostate gland, called the vas deferens, is either blocked with mucus or missing entirely. Sperm is still made in the testicles even though it can't pass into the semen made by the prostate gland. Certain fertility treatments and surgical procedures sometimes make it possible for men with CF to become biological parents.
* **Lower fertility in women.** Although women with CF may be less fertile than other women, it's possible for them to conceive and to have successful pregnancies. Still, pregnancy can worsen the symptoms of CF. Talk with your healthcare professional about the risks.

##### Other complications

* **Thinning of the bones.** Cystic fibrosis raises the risk of developing a dangerous thinning of bones called osteoporosis. Joint pain, arthritis and muscle pain also may occur.
* **Out of balance electrolytes and dehydration.** CF causes saltier sweat, so the balance of minerals in the blood may be upset. This raises the risk for dehydration, especially with exercise or in hot weather. Symptoms of dehydration include a fast heartbeat, extreme tiredness, weakness and low blood pressure.
* **Gastroesophageal reflux disease (GERD).** Stomach acid repeatedly flows back up into the tube connecting the mouth and stomach, called the esophagus. This backwash is known as acid reflux, and it can irritate the lining of the esophagus.
* **Mental health conditions.** Having an ongoing medical condition that has no cure may cause fear, depression and anxiety.
* **Higher risk of digestive tract cancer.** The risk of cancer of the esophagus, stomach, small and large bowel, liver, and pancreas is higher in people with cystic fibrosis. Regular colorectal cancer screening should begin at age 40.

##### Prevention

If you or your partner have close relatives with cystic fibrosis, you both may choose to have genetic testing before having children. Testing done in a lab on a sample of blood can help find out your risk of having a child with CF.

If you're already pregnant and the genetic test shows that your baby may be at risk of CF, your healthcare professional can do other tests on your unborn child.

Genetic testing isn't for everyone. Before you decide to be tested, talk with a genetic counselor about the mental health impact the test results might have.

##### Newborn screening and diagnosis

Every state in the U.S. now routinely screens newborns for cystic fibrosis. Early diagnosis means that treatment can begin right away. Testing can include:

* **Newborn screening.** In this screening test, a healthcare professional takes a few drops of blood from the baby's heel. A lab checks the blood sample for higher levels than expected of a chemical called immunoreactive trypsinogen (IRT). IRT is released by the pancreas and may suggest CF. A newborn's IRT levels also may be high because of premature birth or a stressful delivery. For that reason, other tests may be needed to confirm a diagnosis of cystic fibrosis.
* **Sweat test.** To check if a baby has CF, a sweat test is done once the baby is at least 2 weeks old. A chemical that causes the skin to sweat is put on a small area of skin. Then the sweat is collected to test it and see if it's saltier than typical. Testing done at a care center accredited by the Cystic Fibrosis Foundation helps ensure results that can be trusted.
* **Genetic testing.** Healthcare professionals also may recommend genetic testing to look for specific changes on the gene responsible for CF. Genetic testing may be used along with IRT levels to confirm the diagnosis.

##### Testing of older children and adults

Cystic fibrosis tests may be recommended for older children and adults who weren't screened at birth. Your healthcare professional may suggest genetic and sweat tests for CF if you have repeated bouts of an inflamed pancreas, nasal polyps, chronic sinus infections, lung infections, bronchiectasis or male infertility.

## Treatment

There is no cure for cystic fibrosis, but treatment can ease symptoms, lessen complications and improve quality of life. Close monitoring and early, aggressive intervention is recommended to slow the worsening of CF over time. This can lead to a longer life.

Managing CF is complicated, so it's best to get treatment at a center with a multispecialty team of doctors and other healthcare professionals trained in CF. They can evaluate and treat your condition.

The goals of treatment include:

* Preventing and controlling infections that occur in the lungs.
* Removing and loosening mucus from the lungs.
* Treating and preventing intestinal blockage.
* Getting enough nutrition.

##### Medicines

Options include:

* Medicines that target gene changes and improve how the CFTR protein works. These are called cystic fibrosis transmembrane conductance regulator (CTFR) modulators.
* Antibiotics to treat and prevent lung infections.
* Anti-inflammatory medicines to lessen swelling in the airways in the lungs.
* Mucus-thinning medicines, such as hypertonic saline, to help cough up mucus. This can improve lung function.
* Medicines breathed into the lungs called bronchodilators. These can help keep airways open by relaxing the muscles around the bronchial tubes.
* Pancreatic enzyme capsules taken by mouth to help the digestive tract take in and use nutrients.
* Stool softeners to prevent constipation or bowel obstruction.
* Acid-reducing medicines to help pancreatic enzymes work better.
* Specific medicines for diabetes or liver disease, when needed.

##### Medicines that target genes

For those with cystic fibrosis who have certain gene changes, cystic fibrosis transmembrane conductance regulator (CFTR) modulators may help. About 90% of people with CF may be helped by using these medicines. Gene testing is needed to find out which specific gene change you have and if a CFTR modulator may work for you.

CFTR modulators are newer medicines that many experts think are a breakthrough in the treatment of CF. The medicines help the CFTR protein work better. This can make lung function better, help digestion and weight, and lessen the amount of salt in sweat.

The U.S. Food and Drug Administration (FDA) has approved these CFTR modulators for treating CF in people with specific changes in the CFTR gene:

* The newest combination medicine with elexacaftor, ivacaftor and tezacaftor (Trikafta) is approved for people age 2 years and older. Trikafta has been shown to be the most effective CFTR modulator.
* The combination medicine with ivacaftor and tezacaftor (Symdeko) is approved for people age 6 years and older.
* The combination medicine with ivacaftor and lumacaftor (Orkambi) is approved for people who are age 1 year and older.
* Ivacaftor (Kalydeco) is approved for people who are 1 month and older.

Your healthcare professional may do liver function tests and eye exams before prescribing these medicines. While taking these medicines, you'll likely need testing on a regular basis to check for side effects such as liver function changes and clouding of the eye lenses called cataracts. Ask your healthcare professional and pharmacist for information on possible side effects and what to watch for.

Keep regular follow-up appointments so your healthcare professional can monitor you while taking these medicines. Tell your healthcare professional about any side effects that you have.

### A respiratory therapist with a person wearing a vest for vest therapyAirway clearance techniques

##### Vest therapy

Using a personalized approach, a Mayo Clinic respiratory therapist discusses inflatable vest therapy with an adult who has cystic fibrosis.

Airway clearance techniques, also called chest physical therapy, can help get rid of mucus blocking the airways. It also can help to lessen infection and inflammation in the airways. Airway clearance techniques loosen the thick mucus in the lungs, making it easier to cough up.

Airway clearing techniques are usually done several times a day. Different techniques, and often more than one method, can be used to loosen and remove mucus.

* Clapping with cupped hands on the front and back of the chest. This is a common technique.
* Special breathing and coughing activities.
* Mechanical devices, such as a tube that you blow into, and a machine that pulses air into the lungs called a vibrating vest.
* Vigorous exercise.

Your healthcare professional can give you instructions on the airway clearance techniques that are best for you and how often you should do them.

##### Pulmonary rehabilitation

Your healthcare professional may recommend a long-term program called pulmonary rehabilitation. The program may improve your lung function and your overall well-being. Pulmonary rehabilitation is usually done on an outpatient basis and may include:

* Physical exercise that may improve your condition.
* Breathing techniques that may help loosen mucus and make breathing easier.
* Dietary counseling.
* Mental health counseling and support.
* Education about your condition.

### Surgery and other treatments

Options for certain conditions caused by cystic fibrosis include:

* **Nasal and sinus surgery.** Surgery can remove nasal polyps that get in the way of breathing. Sinus surgery may be done to treat repeated or long-term sinusitis.
* **Oxygen therapy.** If there isn't enough oxygen in your blood, you may need supplemental oxygen. You can get this extra oxygen to your lungs through a mask or through plastic tubing with tips that fit into your nose. These attach to an oxygen tank. Lightweight, portable units that you take with you can help you be more mobile. Oxygen therapy may prevent high blood pressure in the lungs, a condition called pulmonary hypertension.
* **Noninvasive ventilation.** Typically used while sleeping, noninvasive ventilation uses a nose or mouth mask to give positive pressure in the airway and lungs when breathing in. It's often used along with oxygen therapy. Noninvasive ventilation can increase air exchange in the lungs and lessen the work of breathing. The treatment also may help with airway clearance.
* **Feeding tube.** CF interferes with digestion, so you can't take in and use nutrients from food very well. A feeding tube delivers extra nutrition. This may be a short-term tube placed through your nose and guided to your stomach. Or the tube may be surgically placed in the stomach through a small cut in the skin on your belly. A feeding tube gives extra calories during the day or night and does not keep you from eating by mouth.
* **Bowel surgery.** If a blockage happens in the intestines, you may need surgery to remove it. If part of an intestine folds inside a nearby section of intestine, you may need surgery.
* **Lung transplant.** If you have severe breathing problems or life-threatening lung complications, or if antibiotics no longer work to treat lung infections, a lung transplant may be an option. Because bacteria line the airways in diseases such as CF that cause permanent widening of the large airways, both lungs need to be replaced.

Cystic fibrosis does not recur in transplanted lungs. But other complications linked with CF, such as sinus infections, diabetes, pancreas conditions and osteoporosis, can still happen after a lung transplant.

* **Liver transplant.** For severe CF-related liver disease, such as cirrhosis, liver transplant may be an option. In some people, a liver transplant may be done together with lung or pancreas transplants.

## Procedure explanations and clinical guidelines

The diagnosis of cystic fibrosis is based on clinical signs and symptoms consistent with the disease and objective evidence of cystic fibrosis transmembrane conductance regulator (CFTR) dysfunction.

The Cystic Fibrosis Foundation assembled a group of 32 CF diagnosis experts from 10 countries to revise prior diagnostic criteria.

The discussion generated specific consensus statements voted on by conference participants. The statements that met the threshold of 80 percent agreement were enacted.

## Question and Answer

* + How is cystic fibrosis diagnosed?

A sweat test checks for high levels of chloride in your sweat. The sweat test is the standard test for diagnosing cystic fibrosis. It may be used if you or your child has symptoms that could indicate cystic fibrosis, or to confirm a positive diagnosis from a screening of your newborn.15 Nov 2024

## Doctor-patient conversation

* + What sparked your interest and focus on cystic fibrosis care? How long have you been in CF care?

PF: I had the great fortune to go to the University of North Carolina at Chapel Hill (UNC) for my pulmonary and critical care fellowship and that is where I was first exposed to CF patients and their care. It was there that I discovered my interest in CF, or should I say, that CF found me. It was the broad clinical impact, affecting so much of the body, and the very

cool science that was happening at the time that drew me in. The patients and families really pulled me in, too, as they were so motivated to know about their health and how to make it better; that is what drove my enthusiasm to engage in clinical research. So, I started in 1990, and have been engaged ever since.

* + What have been the most significant changes to witness in CF care, as a physician?

PF: While it is easy to focus on the newer [medications](https://www.cff.org/Life-With-CF/Treatments-and-Therapies/Medications/) and their impact, what has been most significant is the approach we, as a community, take to delivering care, and the CF Foundation has played a key role in this. The development of adult programs, transition from a pediatric life into adulthood, transparency of our data, sharing among centers, the concept of a team approach including [engaging patients and families](https://www.cff.org/Get-Involved/Connect/Community-Voice/) in care and [research](https://www.cff.org/Get-Involved/Connect/Community-Voice/" \l "section3) [design](https://www.cff.org/Get-Involved/Connect/Community-Voice/" \l "section3) -- these represent cultural changes in how we provide care, and they have been transformational.

SF: In the past, since there wasn't a high demand for adult CF programs, I think adults were left to manage their CF care on their own in many ways. Now, thanks to so many revolutionary discoveries, we have been able to shift thinking from ways to treat CF symptoms for a while, to actually helping people with CF plan out their lives. You are so right when you say that the programs implemented by the CF Foundation are invaluable. In addition, the internet makes these programs accessible to everyone and creates a way for CF patients to interact with each other and not feel so isolated. This shift within the CF community continues to draw us closer than ever before.

* + What have you found to be the most helpful element in building a rapport with patients, especially those who may be newly transitioning from pediatric to adult clinic?

PF: Spending time with them.

Time is the most valuable commodity, especially as the medical world keeps getting busier. Spending time is key to listening and learning about a person, what drives them, what holds them back.

One thing I have learned from patients who have been coming to an academic program where they are exposed to trainees, getting asked the same questions over and over -- why should they share of themselves if the clinician doesn't seem to really care? So, I try to teach our young clinicians to make the time, pull up a chair and listen, engage in a conversation rather than an interrogation. Walk into the room; don't just stand at the door. Acknowledge everyone in the room. Simple stuff really.

SF: I have had many moments in my life feeling like I was being spoken “at” rather than being spoken “to,” so this really resonates with me. I remember feeling somewhat intimidated when it came time for me to transition to an adult clinic. A lot of people made it sound as though it was going to be this huge emotional cut-off. However, I have truly enjoyed attending adult clinic more than pediatric clinic because, as you said, the personnel at [MUSC](https://www.cff.org/ccd/Disclaimer?returnUrl=%2Fccd%2FProgramMeasureSummaries%3FprogramNumber%3D209) take time to have a conversation and make me feel like an equal. The MUSC personnel renewed my interest in my health and gave me a feeling of confidence going into appointments. I now know that no matter who I am seeing, I will be able to have a productive and engaging discussion and leave feeling like I'm ready to conquer the issues at hand. I always feel like my team has my back, which is imperative to leading a happy life with CF.

* + Balancing the demands of life and cystic fibrosis treatments is challenging. What is your approach to partnering with patients to help them pursue their life goals while maintaining their health?

PF: We have spent years developing tools for patients to use, but this is done with the assumption that everyone wants the same thing. I have learned from our patients that they all have different ways in which they learn and want to communicate. Some text, others email, while others will talk on the phone. So, we need to find out [what works best for each](https://www.cff.org/Life-With-CF/Treatments-and-Therapies/Treatment-Plan/Partnering-With-Your-Care-Team/) [person.](https://www.cff.org/Life-With-CF/Treatments-and-Therapies/Treatment-Plan/Partnering-With-Your-Care-Team/) Also, we bring so much to the clinic that it gets overwhelming; it is just too much information and perhaps the patient and their family don't leave with what we had hoped to deliver. We try to focus what happens in clinic to what we perceive is the greatest issue (with feedback from the patient, of course). But, since we still value the whole of what we bring as a team, we have increasingly tried to increase interactions using telemedicine or other approaches.

SF: I appreciate that you and your team take time to figure out what method of communication each patient will respond to best and I sincerely appreciate that they do always respond! Also, you are absolutely correct in saying that sometimes clinic can feel like information overload, especially if you're going into it not feeling well. Having alternative ways for patients to access information -- such as telemedicine or a patient portal -- is super helpful.

Many patients feel insecure about sharing information with their care team out of a fear of judgement, such as missing treatments or practices that may adversely affect their health. How does that affect the care you are able to provide and what is your approach to helping patients feel comfortable in sharing that information.

PF: I understand this very well, and since we keep tracking numbers (i.e., weight, lung function) it is hard not to feel judged. Much like the angst of taking tests in school, how do we not worry about the results and how they will be interpreted.

I tell my patients from the very start that I will never yell at them. I am greedy and want the best for them, but my goal is not to see how much therapy they can do, but to find out what works best for them. And the only way we get there is to sort it out together.

I also acknowledge that I am not the one taking the meds or [doing the therapies,](https://www.cff.org/Life-With-CF/Treatments-and-Therapies/Treatment-Plan/Managing-Your-Treatment-Plan/) and I know I ask (or recommend) a lot. I have learned a lot from my patients. They teach me things that I can use with others, so sharing with me is a way to help themselves as well as others.

SF: I know from my own experiences and through chatting with other CF friends, “number anxiety” is very real and seems to be common amongst a lot of us. We all acknowledge that numbers can tell a story and it's the easiest way to see trends for a patient. However, as you said, it can be hard not to feel judged or like you've done something wrong if the numbers don't add up because we, as patients, tend to put a lot of pressure on ourselves regarding numbers. When they're up, it's exhilarating; when they're down or unchanged, it's emotionally draining. Hearing professionals give credence to our anxiety is comforting and makes the testing experience a little easier knowing that whatever the outcome is, we won't be made to feel like we've done something wrong or haven't done enough. I remember when I first started coming to MUSC how impressed and relieved I was at the fact that when somebody would come into the room they didn't immediately start talking numbers. It made the entire clinic experience a lot less taxing since I could go in knowing that whatever the outcome was, we could collaborate and figure out a plan of action.

* + Do you have any tips or advice for patients on how they could achieve a more open and honest relationship with their team?

PF: For a clinician to do their best, they must be up to speed with the best information, so the patient must trust their clinician. However, trust is earned. If the patient feels the clinician has not earned that trust, they need to let them know. The clinician needs to accept that this is a [partnership](https://www.cff.org/Care/Partnerships-for-Sustaining-Daily-Care/The-Partnerships-for-Sustaining-Daily-Care-Initiative/); the clinician serves many roles (i.e., diagnostician, prescriber, coach, etc.) but cannot do it effectively if the patient doesn't share, contribute, and provide feedback.

SF: I concur. Withholding information is doing not only your team, but yourself a disservice because it makes it difficult to treat the underlying issues. However, medical settings can be daunting places and it can sometimes evoke panic when it comes time to actually talk with your doctor. That being said, as you pointed out, it does work both ways. If your doctor

hasn't taken the time to make you feel like they're listening and that they see you as a person and not a number, it can create a vicious cycle of just saying anything to get out of there as soon as possible. I think clinicians and patients alike can learn that the key element of long-term care is honest communication but -- to achieve that -- you have to be willing to let your guard down a little and acknowledge that we are all just people trying to do our best.

* + Finally, what is the most rewarding aspect of your job?

PF: It is a privilege that I get to do this job. The mere fact that my patients trust me with this job is enough. Seeing them thrive, enjoy personal successes (school, job, travel, family) is gravy.

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# Bronchopulmonary dysplasia(BPD)(Chronic lung disease of prematurity).

### Disease Descriptions

What is Bronchopulmonary Dysplasia (BPD) / Chronic Lung Disease of Prematurity? Bronchopulmonary dysplasia (BPD) is a breathing disorder in premature infants where the infants' lungs become irritated and do not develop normally. It occurs most often in low- weight infants born more than two months early.

Bronchopulmonary dysplasia is also known as:

* + Chronic lung disease of prematurity
  + Chronic lung disease
  + Neonatal chronic lung disease
  + Respiratory insufficiency

BPD is often seen in infants with respiratory distress syndrome (RDS). This breathing disorder is common in babies, born too early, whose lungs have not fully grown.

As many as 10,000 babies each year in the United States could develop BPD.

Bronchopulmonary dysplasia can be mild, moderate or severe. While breathing difficulties improve, babies with BPD are often in the hospital and need a lot of care. Many children struggle with illnesses, especially during the first two years of life. BPD may also cause asthma-like symptoms like cough and wheezing throughout childhood.

What are the Causes of Bronchopulmonary Dysplasia?

BPD develops because babies born too early have lungs that are not fully developed and are at risk of damage and swelling. Premature babies often need oxygen and/or other types of breathing support, such as ventilators, which can cause damage such as scarring. Some babies may get infections such as pneumonia, which can worsen swelling as well. The blood vessels in the lungs may also be underdeveloped, which can cause issues with the heart. All of these things can lead to BPD.

## Signs and Symptoms

Signs and symptoms of bronchopulmonary dysplasia include:

* + Breathing that is fast or difficult
  + Shortness of breath
  + Pauses in breathing that last for a few seconds (apnea)
  + Nostrils flare while breathing
  + Grunting while breathing
  + Wheezing
  + Skin pulling in between the ribs or collar bones (retractions)
  + Bluish color of the skin (cyanosis) – due to low oxygen levels in the blood

## Diagnosis

Most infants are diagnosed when they are already in the hospital. To diagnose this disorder, your child’s care team will consider:

* + Your baby’s symptoms
  + How premature your baby is
  + Your baby’s need for oxygen after a certain age They may also use the following tests:
  + [Chest X-ray,](https://www.cincinnatichildrens.org/patients/child/encyclopedia/diagnostic/chest-x-ray) [CT scan](https://www.cincinnatichildrens.org/health/c/ct-scan) or [MRI](https://www.cincinnatichildrens.org/health/m/mri) – to see if the lungs are growing as they should
  + Blood test – to look at oxygen and carbon dioxide levels in the blood
  + Tests to look for infection
  + [Echocardiogram (echo)](https://www.cincinnatichildrens.org/health/e/echo) – an ultrasound test to view the heart and find out if a heart problem is causing your baby’s breathing trouble
  + Pulse-oximetry- to continuously look at oxygen levels in the blood

## Treatment

Your care team will use treatments to limit damage to your baby’s lungs. The goal with treatment is to allow your child’s lungs to heal and grow. Treatment for this chronic lung disease of prematurity can include:

* + Oxygen
  + Mechanical ventilator (breathing machine) – your child still needs a ventilator by their due date, they may need a tracheostomy (a surgically placed breathing tube) to promote better development
  + Nutrition therapy – to make sure your baby is getting enough nutrition to grow properly. Some babies will need a g-tube (gastrostomy tube) to allow nutrition to go through a tube directly into the stomach
  + Developmental therapies – Speech, physical and occupational therapies help make sure your child is developing as expected
  + Medicines
    - Bronchodilators – to improve flow of air through the lungs
    - Diuretics – to reduce extra fluid o Antibiotics – to control infections and prevent pneumonia
    - Steroids – to decrease swelling in the lungs
    - Pulmonary Vasodilators - to improve blood flow to the lungs Your child’s care team will adjust treatments over time as needed.

**What is the Long-Term Outlook for Infants with Bronchopulmonary Dysplasia?** Babies with this disorder heal and grow at different rates. They usually get better over time. Most babies with BPD spend several weeks to several months in the

hospital’s [Newborn Intensive Care Unit (NICU).](https://www.cincinnatichildrens.org/service/n/nicu)

After leaving the hospital, your child will need to see many specialists to support their lungs, growth, development and possibly the heart. These check-ups will be very frequent initially and space out as your child grows and matures.

Some babies go home without needing any more treatment. Others may need medicine, extra oxygen or breathing machine, or a special diet at home

Children who had bronchopulmonary dysplasia as infants have a higher risk for certain types of breathing problems. This includes asthma, sleep apnea and respiratory infections.

##### Related Disorders / Conditions

Related disorders or conditions include:

* + Respiratory distress syndrome (RDS)
  + [Pulmonary hypertension](https://www.cincinnatichildrens.org/patients/child/encyclopedia/diseases/pulmonary-hypertension)
  + Retinopathy of prematurity (ROP)
  + Intraventricular hemorrhage (IVH)
  + Necrotizing enterocolitis (NEC)

##### What are the risk factors?

Those at greatest risk for developing bronchopulmonary dysplasia are infants who:

* + Are born more than 2 months early
  + Have a birth weight less than 2.2 pounds
  + Have respiratory distress syndrome
  + Have a history of pneumonia or other infections

##### What are possible long-term complications?

Children and adults who had bronchopulmonary dysplasia as infants may experience any of the following as they grow:

* + Health problems after leaving the hospital that involve oxygen therapy or breathing support
  + Higher risk for colds, flu and other infections
  + Trouble swallowing
  + Delayed growth and development, especially in the first two years after birth
  + Breathing problems as a child and adult

## Procedure explanation and clinical guidelines:

Procedure Explanation and Clinical Guidelines for BPD Management

##### Respiratory Support

1. Oxygen supplementation: Target saturations vary by phase:

Early/Evolving BPD: SpO2 target of 87–93% to balance oxygenation with risk of oxygen toxicity.

Established BPD: Target SpO2 92–96% to prevent pulmonary hypertension.

Weaning from mechanical ventilation and supplemental oxygen should be done as early and cautiously as possible to minimize lung injury.

Non-invasive ventilation (NIPPV, CPAP, HFNC) is often used in evolving and established BPD to reduce invasive ventilation time.

Gentle ventilation strategies are emphasized to avoid further lung damage.

##### Pharmacotherapy

* + Diuretics (chlorothiazide, spironolactone, furosemide): Used to transiently improve pulmonary compliance by reducing pulmonary edema. Chlorothiazide is preferred long- term due to fewer side effects, while furosemide is limited due to risks like osteoporosis.

Caffeine: Recommended early to improve extubation success and reduce BPD incidence.

Corticosteroids:

Systemic steroids (dexamethasone, prednisolone) may help in weaning from ventilation and oxygen but require cautious use due to potential side effects.

Inhaled corticosteroids (e.g., budesonide) have shown short-term oxygenation improvements; recent trials indicate potential reduction in BPD incidence though with some concerns about mortality risk.

May reduce BPD risk when administered intramuscularly in early phases.

Vitamin A:

##### Nutritional Support

High-calorie nutritional supplementation is critical to support lung growth and increased energy demands from work of breathing.

Typically, caloric intake aims for with protein 3.5–4 g/kg/day.

150 kcal/kg/day

Fluid restriction to about 120–140 mL/kg/day is common to limit pulmonary congestion. Monitoring of hydration and electrolytes is essential during diuretic therapy.

1. Monitoring and Assessment

Regular assessment with chest X-rays, blood gases (to monitor CO2 retention), and echocardiography (to screen for pulmonary hypertension) is recommended, especially prior to discharge.

Question:

Swallowing function evaluation (e.g., modified barium swallow study) is important if aspiration risk is suspected.

1. Discharge Planning and Follow-up

A multidisciplinary team including neonatologists, nursing, dietitians, therapists, and social workers should collaborate for discharge planning.

Preparing caregivers with training on oxygen and ventilator equipment use at home is necessary.

Early intervention follow-up, pulmonology, and feeding clinics should be arranged.

Home environment assessment and equipment needs must be addressed before discharge.

**Question and Answer:**

What is Bronchopulmonary Dysplasia (BPD) and what are its causes, symptoms, and long-term effects?

Answer:

Bronchopulmonary Dysplasia (BPD) is a chronic lung disease primarily affecting premature infants, especially those who have required prolonged oxygen therapy or mechanical ventilation after birth. It results from lung injury caused by inflammation and scarring due to oxygen exposure and mechanical ventilation. This damage disrupts the normal development of the tiny air sacs (alveoli) and blood vessels in the lungs, leading to impaired lung function.

**Causes and Risk Factors:**

Prematurity, particularly infants born before 28 weeks gestation, and low birth weight (under 1500 grams) are major risk factors.

The condition is caused by lung injury from mechanical ventilation and long-term oxygen therapy used in respiratory support of immature lungs.

Additional contributors include respiratory infections, congenital lung malformations, exposure to secondhand smoke, poor prenatal care, and possibly genetic predisposition.

Male infants and multiples (twins, triplets) have a higher incidence.

**Symptoms:**

Breathing difficulties such as rapid breathing, nasal flaring, grunting, chest retractions, and dependency on supplemental oxygen or ventilators.

Feeding difficulties and poor growth may also be present.

Long-Term Effects:

Many infants improve over time, but some may suffer chronic respiratory problems including susceptibility to lung infections, asthma-like symptoms, and pulmonary hypertension (high blood pressure in the lungs).

Developmental delays in motor and cognitive skills can also occur as a consequence of prolonged illness and oxygen deprivation.

Severe BPD may lead to heart complications such as heart failure.

While BPD is a serious condition, advances in neonatal care have improved survival and quality of life. Many children with BPD eventually require less respiratory support as their lungs grow and develop.

## Doctor-Patient conversation

Hello, I want to talk with you about your baby’s lung condition called *bronchopulmonary dysplasia*, or BPD. It is a chronic lung disease that often happens in babies born prematurely and who needed help with breathing using oxygen or a ventilator soon after birth.

Doctor:

What caused this condition in my baby?

Parent:

BPD happens because the baby’s lungs are not fully developed yet, and the treatments needed to help them breathe, like oxygen support or mechanical ventilation, can sometimes cause some lung injury or inflammation. This injury interferes with how the lungs grow and heal, leading to longer term breathing problems.

Doctor:

What does this mean for my baby’s care?

Parent:

Managing BPD is a team effort. We focus on helping your baby breathe as comfortably as possible while supporting lung growth. We may use gentle breathing support like nasal CPAP or ventilators when needed, and monitor oxygen levels carefully to avoid further lung injury. Medications such as diuretics, bronchodilators, or sometimes steroids may be prescribed to reduce lung swelling and improve breathing. Nutrition is very important too, as your baby needs extra calories to grow stronger.

Doctor:

Will my baby be in pain? How do you keep them comfortable?

Parent:

Babies with BPD sometimes become uncomfortable, especially with tubes or procedures, but the NICU team carefully manages pain and discomfort. We use gentle handling, swaddling, and when necessary, medicine to keep your baby calm and comfortable. Your presence also helps soothe your baby a lot.

Doctor:

What is the outlook for my baby? Will this get better?

Parent:

Many babies with BPD gradually improve as their lungs develop. However, some may have ongoing breathing problems and require oxygen at home for a time. It’s important to have regular follow-ups with specialists who understand BPD. We will help support your family through this journey, providing education and resources. Though the road can be challenging, many children with BPD grow and thrive.

Doctor:

If I have concerns or questions, who do I contact?

Parent:

You’ll have a dedicated BPD team including doctors, nurses, and therapists. You can always ask questions during rounds or reach out by phone or email. It’s important to write down any questions you have before visits, and remember you are a vital part of your baby’s care team.

Doctor:

This conversation represents the kind of clear, empathetic communication emphasized by specialized BPD programs and clinical guidelines, aiming to empower families and ensure comprehensive care.

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# Primary Ciliary Dyskinesia

## Medical code:

The primary medical codes for Primary Ciliary Dyskinesia (PCD) are as follows:

|  |  |  |
| --- | --- | --- |
| **Coding System** | **Code(s)** | **Description** |
| **ICD-10** | Q34.8 | Other specified congenital malformations of respiratory system; often used for PCD |
| **ICD-10**  **(alternative)** | Q89.3 | Other congenital malformation syndromes affecting multiple systems; also referenced for PCD |
| **ICD-11** | LA75.Y | Other specified structural abnormalities of the lungs, including Primary ciliary dyskinesia |
| **ICD-11**  **(alternative)** | CB40.0 | Ciliary dyskinesia, encompassing primary and secondary forms |
| **ORPHA code** | 244 | Rare disease classification for PCD |
| **OMIM** | Multiple entries, including 620032, 244400, 242650, among others | Genetic reference codes related to PCD |

|  |  |  |
| --- | --- | --- |
| **Coding System** | **Code(s)** | **Description** |
| **MedDRA** | 10069713 | Medical dictionary code for PCD |
| **UMLS** | C4551720 | Unified Medical Language System code for PCD |

## Disease Description

Primary ciliary dyskinesia is a disorder characterized by chronic respiratory tract infections, abnormally positioned internal organs, and the inability to have children (infertility). The signs and symptoms of this condition are caused by abnormal cilia and [flagella.](https://medlineplus.gov/images/PX000184_PRESENTATION.jpeg) Cilia are microscopic, finger-like projections that stick out from the surface of cells. They are found in the linings of the airway, the reproductive system, and other organs and tissues. Flagella are tail-like structures, similar to cilia, that propel sperm cells forward. In the respiratory tract, cilia move back and forth in a coordinated way to move mucus towards the throat. This movement of mucus helps to eliminate fluid, bacteria, and particles from the lungs. Most babies with primary ciliary dyskinesia experience breathing problems at birth, which suggests that cilia play an important role in clearing fetal fluid from the lungs. Beginning in early childhood, affected individuals develop frequent respiratory tract infections. Without properly functioning cilia in the airway, bacteria remain in the respiratory tract and cause infection. People with primary ciliary dyskinesia also have year-round nasal congestion and a chronic cough. Chronic respiratory tract infections can result in a condition called bronchiectasis, which damages the passages, called bronchi, leading from the windpipe to the lungs and can cause life-threatening breathing problems.

Some individuals with primary ciliary dyskinesia have abnormally placed organs within their chest and abdomen. These abnormalities arise early in embryonic development when the differences between the left and right sides of the body are established. About 50 percent of people with primary ciliary dyskinesia have a mirror-image reversal of their internal organs (situs inversus totalis). For example, in these individuals the heart is on the right side of the body instead of on the left. Situs inversus totalis does not cause any apparent health problems. When someone with primary ciliary dyskinesia has situs inversus totalis, they are often said to have Kartagener syndrome.

Approximately 12 percent of people with primary ciliary dyskinesia have a condition known as [heterotaxy syndrome](https://medlineplus.gov/genetics/condition/heterotaxy-syndrome/) or situs ambiguus, which is characterized by abnormalities

of the heart, liver, intestines, or spleen. These organs may be structurally abnormal or improperly positioned. In addition, affected individuals may lack a spleen (asplenia) or have multiple spleens (polysplenia). Heterotaxy syndrome results from problems establishing the left and right sides of the body during embryonic development. The severity of heterotaxy varies widely among affected individuals.

Primary ciliary dyskinesia can also lead to infertility. Vigorous movements of the flagella are necessary to propel the sperm cells forward to the female egg cell. Because their sperm do not move properly, males with primary ciliary dyskinesia are usually unable to father children. Infertility occurs in some affected females and is likely due to abnormal cilia in the fallopian tubes.

Another feature of primary ciliary dyskinesia is recurrent ear infections (otitis media), especially in young children. Otitis media can lead to permanent hearing loss if untreated. The ear infections are likely related to abnormal cilia within the inner ear.

Rarely, individuals with primary ciliary dyskinesia have an accumulation of fluid in the brain (hydrocephalus), likely due to abnormal cilia in the brain.

## Symptoms

Babies born with primary ciliary dyskinesia (PCD) may have [respiratory distress](https://www.nhlbi.nih.gov/health/respiratory-distress-syndrome) within the first day after birth, while other people may go through life without knowing that they have the disease.

PCD affects mainly the sinuses, ears, and lungs. One sign that you might have PCD is if you have chronic (ongoing) infections, such as a wet cough and constant nasal congestion, in one or more of these areas. You may often get sinus infections and middle ear infections.

##### Symptoms in the body include:

* Both men and women may have fertility problems, or difficulty having children.
* About half of all people who have PCD have Kartagener’s syndrome, a rare condition that includes situs inversus (internal organs in a mirror image of their normal positions).

##### Symptoms in the sinuses include:

* Chronic (long-term) nasal congestion
* Runny nose with mucus and pus discharge
* Chronic sinus infections
* Nasal polyps

##### Symptoms in the ears include:

* Chronic middle ear infections
* Hearing loss

##### Symptoms in the lungs include:

* Chronic cough
* Respiratory distress (breathing problems) in newborns
* [Pneumonia](https://www.nhlbi.nih.gov/health/pneumonia) that goes away and comes back often
* [Atelectasis](https://www.nhlbi.nih.gov/health/primary-ciliary-dyskinesia/symptoms)
* [Bronchiectasis](https://www.nhlbi.nih.gov/health/bronchiectasis)

##### How serious are the symptoms?

The symptoms of PCD and how serious they are can vary from person to person. A person who has the disease may have serious sinus, ear, or lung infections. If the disease is mild, it may not show up until the teen or adult years.

Your symptoms may also vary over time. Sometimes you may have few symptoms. Other times, your symptoms may become more serious.

Some people who have PCD have breathing problems when they are born and need [extra](https://www.nhlbi.nih.gov/health/primary-ciliary-dyskinesia/treatment) [oxygen](https://www.nhlbi.nih.gov/health/primary-ciliary-dyskinesia/treatment) for several days. Afterward, airway infections are common.

[Diagnosing PCD](https://www.nhlbi.nih.gov/health/primary-ciliary-dyskinesia/diagnosis) in children can be hard. This is because some PCD symptoms — such as ear infections, chronic cough, and runny nose — are common in children, even if they don’t have PCD. Also, the disease may be confused with another condition, such as [cystic fibrosis.](https://www.nhlbi.nih.gov/health/cystic-fibrosis)

A correct and early diagnosis of PCD is very important. It will allow you or your child to get the proper [treatment](https://www.nhlbi.nih.gov/health/primary-ciliary-dyskinesia/treatment) to keep your airways and lungs as healthy as possible. An early diagnosis and proper treatment can also prevent or delay ongoing and long-term lung damage.

When to call a healthcare provider

Make sure to report new or worsening symptoms, such as increased coughing, to your provider (or your child’s provider) right away. This will allow them to find out whether you have an infection and what’s causing it. Your provider can then prescribe medicine to prevent the infection from worsening.

## Diagnosis

Your healthcare provider or your child’s provider will diagnose primary ciliary dyskinesia (PCD) based on your [symptoms,](https://www.nhlbi.nih.gov/health/primary-ciliary-dyskinesia/symptoms) [family history,](https://www.nhlbi.nih.gov/health/primary-ciliary-dyskinesia/causes) and test results.

Genetic testing

Researchers have found many [genes](https://www.nhlbi.nih.gov/health/primary-ciliary-dyskinesia/diagnosis) associated with PCD. Genetic testing can show whether you have faulty genes linked to the disease.

Genetic testing is done using a blood sample. The sample is taken from a vein in your body using a needle. The blood sample is checked at a special genetic testing laboratory (lab).

Couples who are planning to have children and know that they are at risk of having a child with PCD may want to meet with a genetic counselor. A genetic counselor can answer questions about the risk and explain the choices that are available.

Electron microscopy

Your healthcare provider can use a special microscope, called an electron microscope, to look at samples of your airway cilia. This test can show whether there are any problems with the structure of your cilia or how they are working.

An ear, nose, and throat (ENT) specialist or a pulmonologist (a doctor who specializes in treating conditions affecting the respiratory system, including the lungs) will take samples of your cilia. The provider will brush the inside of your nose to remove some cells from your airways. However, this test doesn’t give a final diagnosis.

Other tests

Sometimes healthcare providers use one or more of the following tests to help diagnose PCD. Some of these tests are less complex than genetic testing and electron microscopy, and they can be done in a provider’s office.

Based on your test results, your provider may recommend a more complex test.

* **Ear, nose and throat tests:** Because ear and sinus symptoms are common in PCD, tests focused on those areas can determine if you have hearing loss or loss of your sense of smell. Exams could include pressure testing to check the eardrum for fluid buildup.
* **[Lung function tests](https://www.nhlbi.nih.gov/health/lung-tests):** These are a group of tests that evaluate how well the lungs work by measuring lung volume, rates of flow, and gas exchange. Lung function may be lower in people living with PCD than in those not living with the disease.
* **Nasal nitric oxide measurement:** This test measures the level of nitric oxide (a gas) when you breathe out. In people who have PCD, the level of nitric oxide is very low compared with normal levels. The reason for this is currently unknown.
* **Video microscopy:** For this test, a pulmonologist brushes the inside of your nose to get a sample of cilia. Then he or she looks at the cilia under a microscope to see how they move. Abnormal movement of the cilia may be a sign of PCD.
* **Radiolabeled particles:** For this test, you breathe in tiny particles that have a small, safe amount of radiation attached to them. Your provider will test how well your cilia can move the particles. If your lungs remove the particles more slowly than normal, your cilia may not be working well. This could be a sign of PCD.
* **Semen analysis:** This test is used for adult men. In men, PCD can affect cilia-like structures that help sperm cells move. As a result, men who have PCD may have fertility problems. For this test, a sample of semen is checked under a microscope. Sperm that don’t look normal or a low sperm count may be signs of PCD.
* **[Chest computerized tomography (CT) or other imaging](https://www.nhlbi.nih.gov/health/lung-tests):** This test checks for structural changes in the lung as a result of chronic infections. A thorough physical exam, followed by an [X-ray of the chest](https://www.nhlbi.nih.gov/health/lung-tests) and abdomen and [echocardiography,](https://www.nhlbi.nih.gov/health/heart-tests) will also identify most cases of situs inversus.

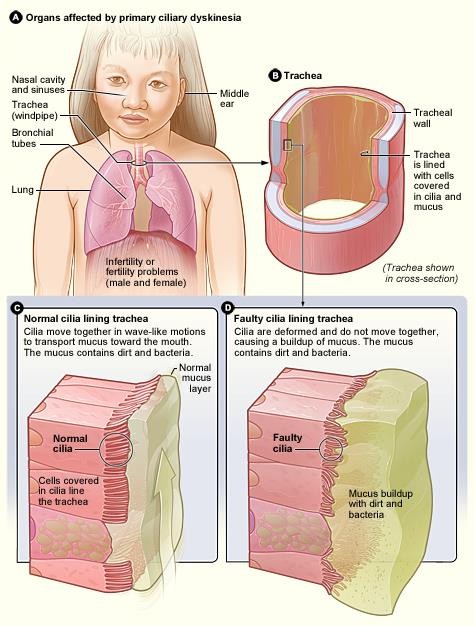
Your provider also might want to do tests to rule out diseases and disorders that have symptoms similar to those of PCD. For example, you may have tests to rule out [cystic](https://www.nhlbi.nih.gov/health/cystic-fibrosis) [fibrosis](https://www.nhlbi.nih.gov/health/cystic-fibrosis) or immune disorders.

## Causes

Primary ciliary dyskinesia (PCD) is a rare, inherited disease. “Inherited” means the disease is passed from parents to children through genes. With PCD, this process is very complex. Researchers are still learning how the disease is inherited and which genes are involved.

Generally, a child must inherit faulty [genes](https://www.nhlbi.nih.gov/health/primary-ciliary-dyskinesia/causes) from both parents to have PCD. These genes affect how cilia grow and work. Cilia are tiny, hairlike structures that line the airways.

Faulty genes may cause the cilia to be the wrong size or shape or move in the wrong way. Sometimes the cilia are missing altogether. If the cilia don’t work well, bacteria stay in your airways. This can cause breathing problems, infections, and other disorders.



*Figure A shows the organs that primary ciliary dyskinesia can affect. Figure B shows a cross-section of the trachea (windpipe). Figure C shows a closeup view of normal cilia lining the trachea. The cilia move together in wavelike motions to transport mucus toward the mouth. Figure D shows a closeup view of faulty cilia lining the trachea. The cilia are deformed and do not move together, causing a buildup of mucus.*

If a child inherits a faulty gene (or genes) from only one parent, the child may be a “PCD carrier.” Carriers usually have no [symptoms](https://www.nhlbi.nih.gov/health/primary-ciliary-dyskinesia/symptoms) of PCD. However, carriers can pass faulty PCD genes on to their children.

## Treatment

Unfortunately, no treatment is available yet to fix faulty airway cilia, which are the tiny, hairlike structures that line the airways. Treatments for primary ciliary dyskinesia (PCD) focus on which symptoms and complications you have.

The main goals of treating PCD are to:

* Control and treat lung, sinus, and ear infections
* Remove trapped mucus from the lungs and airways

Your healthcare team

You may have several providers caring for you besides your primary healthcare provider.

* An **ear, nose, and throat (ENT)** specialist may help [diagnose](https://www.nhlbi.nih.gov/health/primary-ciliary-dyskinesia/diagnosis) and treat PCD. If a child has chronic sinus or ear infections, an ENT specialist may be involved in the child’s care.
* A **pulmonologist** may help diagnose or treat lung problems related to PCD. This type of doctor specializes in diagnosing and treating lung diseases and conditions. Most people who have PCD have lung problems at some point in their lives.

##### Treatments for breathing and lung problems

Standard treatments for breathing and lung problems are chest physical therapy (CPT), exercise, and medicines.

One of the main goals of these treatments is to get you to cough. Coughing clears mucus from the airways, which is important for people who have PCD. For this reason, your provider may also advise you to avoid medicines that suppress coughing.

##### Chest physical therapy

CPT is also called chest clapping or percussion. It involves pounding your chest and back over and over with your hands or a device to loosen the mucus from your lungs so that you can cough it up.

You might sit down or lie on your stomach with your head down while you do CPT. Gravity can help drain the mucus from your lungs.

Some people who perform CPT find it hard or uncomfortable to do. Several devices have been made to help with CPT, such as:

* An electric chest clapper, known as a mechanical percussor
* An inflatable therapy vest that uses high-frequency airwaves that forces the mucus deep in your lungs toward your upper airways so you can cough it up
* A small handheld breathing device that causes vibrations to dislodge the mucus
* A mask that creates vibrations to help break the mucus loose from your airway walls

Breathing techniques also may help dislodge mucus so you can cough it up. These techniques include forcing out a couple of short breaths or deeper breaths and then doing relaxed breathing. This may help loosen the mucus in your lungs and open your airways.

##### Exercise

Aerobic exercise that makes you breathe harder helps loosen the mucus in your airways so you can cough it up. Exercise also helps improve your overall physical condition.

Talk with your healthcare provider about what types and amounts of exercise are safe for you or your child.

##### Medicines

If you have PCD, your provider may prescribe antibiotics, bronchodilators, or anti- inflammatory medicines. These medicines help treat lung infections, open up the airways, and reduce swelling.

* **Antibiotics** are the main treatment to prevent or treat lung infections. Oral antibiotics are often used to treat mild lung infections. For serious or hard-to-treat infections, you may be given intravenous (IV) antibiotics through a tube inserted into a vein. To help decide which antibiotics you need, your provider may send mucus samples to a pathologist. The pathologist will try to find out which bacteria are causing the infection. Side effects of antibiotics depend on which antibiotic is used but may include diarrhea; problems with your hearing, balance, kidneys; or low white blood cell counts.
* **Bronchodilators** help open the airways by relaxing the muscles around them. You inhale these medicines. Often, they’re taken just before CPT to help clear mucus from your lungs. You may also take bronchodilators before inhaling other medicines into your lungs. Side effects can include trembling in the hands, headache, dizziness, and nausea.
* **Anti-inflammatory medicines** can help reduce swelling in your airways that’s caused by ongoing infections. These medicines may be inhaled or taken by mouth. Side effects can include mainly gastrointestinal symptoms, such as abdominal pain, nausea, vomiting, and diarrhea.

##### Treatments for sinus and ear infections

To treat infections, your healthcare provider may recommend saline nasal washes and anti- inflammatory nasal sprays. If these treatments aren’t enough, you may need medicines, such as antibiotics. If antibiotics don’t work, surgery may be an option.

Tympanostomy is a procedure in which small tubes are inserted into the eardrums to help drain mucus from the ears. This procedure may help children who have hearing problems caused by PCD.

Nasal or sinus surgery may help drain the sinuses and provide short-term relief of symptoms. However, the long-term benefits of this treatment are unclear.

##### Treatments for advanced lung disease

People who have PCD may develop a serious lung condition called [bronchiectasis.](https://www.nhlbi.nih.gov/health/bronchiectasis) This condition often is treated with medicines, hydration (drinking plenty of fluids), and CPT. If you have serious lung damage from bronchiectasis, you may need surgery to remove part of the lung.

Rarely, and when other treatments haven’t worked, [lung transplant](https://www.nhlbi.nih.gov/health/lung-treatments) may be an option for serious lung disease. A lung transplant is surgery to remove the damaged lung and replace it with a healthy lung from a deceased donor.

## Procedure Explanation and clinical guidelines

Procedure Explanation for Diagnosis:

##### Clinical Assessment:

Consider PCD in patients with key clinical features such as chronic upper and lower respiratory tract infections, neonatal respiratory distress, chronic wet cough, recurrent otitis media, and laterality defects like situs inversus.

Patients typically present symptoms early, often within the first 6 months of life.

##### Diagnostic Testing:

The reference standard diagnosis combines:

**Transmission Electron Microscopy (TEM):** Examines ciliary ultrastructure for defects. Though historically considered "gold standard," TEM misses about 30% of cases due to normal ultrastructure in some patients.

**Genetic Testing:** Identification of biallelic pathogenic variants in known PCD-related genes can confirm diagnosis.

Additional tests to improve diagnostic accuracy include:

**Nasal Nitric Oxide (nNO) Measurement:** Markedly low nNO levels are a sensitive and non-invasive screening tool for patients older than 5 years.

**High-Speed Video Microscopy (HSVM):** Assesses ciliary beat pattern and frequency but is technically demanding and less widely available.

**Immunofluorescence (IF) Microscopy:** Detects absence or alteration of specific ciliary proteins.

##### Other investigations:

Imaging such as chest CT scans to detect structural lung changes.

Consider abdominal and cardiac ultrasounds to identify laterality defects or congenital heart disease associated with PCD.

## Diagnosis

Diagnosis requires exclusion of other conditions like cystic fibrosis and immunodeficiencies.

At least one hallmark clinical feature plus positive results from TEM, genetic testing, or other confirmatory tests are required for definite diagnosis.

When diagnosis is uncertain, use combination testing and clinical judgment to guide.

### Clinical Guidelines for Management

##### Monitoring:

Regular respiratory assessment, including pulmonary function tests and sputum cultures 2–4 times per year.

Chest imaging every 2–4 years or as needed.

Otolaryngology evaluations 1–2 times per year in children for ear and sinus involvement, including audiology assessments.

Periodic testing for non-tuberculous mycobacteria and allergic bronchopulmonary aspergillosis based on symptoms.

## Treatment Principles

Aggressive airway clearance with physiotherapy to enhance mucus removal. Prompt and targeted antibiotics to manage respiratory infections.

Management of complications such as bronchiectasis and hearing loss.

Multidisciplinary approach involving pulmonologists, ENT specialists, and genetic counselors.

##### AdditionalConsiderations:

Evaluate for organ laterality abnormalities and congenital heart defects. Genetic counseling for affected families.

Lung transplantation in advanced cases may be considered.

Clinical guidelines stress that no single test suffices and diagnosis should be confirmed with a combination of tests interpreted in the clinical context. Guidelines also highlight the importance of routine monitoring and supportive care to manage chronic complications.

## Question and Answer

Question: What is Primary Ciliary Dyskinesia (PCD), and how is it diagnosed and managed?

Answer: Primary Ciliary Dyskinesia (PCD) is a rare, inherited autosomal recessive disorder caused by defects in the structure or function of motile cilia and flagella. These defective cilia lead to impaired mucociliary clearance, resulting in chronic upper and lower respiratory tract infections, fertility problems, and laterality defects such as situs inversus in about 50% of cases (known as Kartagener syndrome).

## Doctor-Patient conversation

**Doctor:** Good morning. I reviewed your symptoms of a persistent wet cough, frequent sinus infections, and the chest X-ray findings. I want to discuss a potential diagnosis called Primary Ciliary Dyskinesia or PCD. Are you familiar with it?

**Patient:** No, I haven’t heard of PCD before. What is it exactly?

**Doctor:** PCD is a rare inherited disorder where tiny hair-like structures called cilia, which normally help clear mucus and debris from your airways, don’t work properly. Because of this, mucus builds up and causes frequent lung and sinus infections, as well as problems with hearing and sometimes fertility. About half of people with PCD also have their internal organs reversed in position, known as situs inversus.

**Patient:** How do you confirm if I have this condition?

**Doctor:** Diagnosis is a bit complex. First, we look closely at the symptoms you’ve described, including your history of respiratory infections and any other related problems. To confirm PCD definitively, we usually perform a combination of tests:

* Measuring nasal nitric oxide, which is abnormally low in PCD patients.
* Taking a sample of the cells lining your nose or throat to examine the cilia under an electron microscope to look for structural defects.
* Genetic testing to identify mutations known to cause PCD.
* Sometimes, we use high-speed video microscopy to analyze cilia movement. Since PCD is rare, these tests are done in specialized centers.

**Patient:** What will happen if I do have PCD?

**Doctor:** Early diagnosis really helps. Although there's no cure for PCD, management focuses on preventing lung damage and controlling infections. This includes regular airway clearance physiotherapy to help clear mucus, prompt use of antibiotics when infections occur, regular ENT assessments to monitor and manage ear and sinus problems, and lifestyle adjustments to reduce infection risk.

We will also monitor your lung function over time to adjust treatments as needed.

**Patient:** Is this something I would need to be checked for regularly?

**Doctor:** Absolutely. We recommend regular follow-ups—usually annually or more often if needed—with a multidisciplinary team including specialists in respiratory medicine, ENT, physiotherapy, and audiology. This team approach helps manage all aspects of the disease and maintains your lung and ear health, improving quality of life.

**Patient:** What about my family? Could they have this too?

**Doctor:** PCD is inherited in an autosomal recessive pattern. This means both parents carry one copy of the mutated gene, so your siblings or children may need evaluation, especially if they have similar symptoms. Genetic counseling is useful for you and your family.

**Patient:** Thank you, doctor. What are the next steps?

**Doctor:** I will arrange for you to have nasal nitric oxide testing and refer you to a specialized PCD center for further diagnostic tests. Meanwhile, keeping track of your symptoms, staying hydrated, and avoiding respiratory irritants will be helpful.

This conversation reflects the key clinical features, diagnostic approach, multidisciplinary management, and genetic counseling recommended by the NHS England PCD Management Service and international guidelines (ERS, ATS).

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# Chronic Cough

## Medical code:

Coding use: R05.3 should be used as the primary code unless an underlying condition is identified, in which case the code for that condition takes precedence and R05.3 is secondary.

## Disease Description

A chronic cough is a cough that lasts eight weeks or longer in adults, or four weeks in children. A chronic cough is more than just annoying. It can interrupt your sleep and leave you feeling very tired. Severe cases of chronic cough can cause vomiting and lightheadedness, and even break a rib.

The most common causes are tobacco use and asthma. Other common causes include fluid that drips from the nose down the back of the throat, called postnasal drip, and the backward flow of stomach acid into the tube that connects the throat to the stomach, called acid reflux. Fortunately, chronic cough usually goes away once the underlying issue is treated.

## Symptoms

A chronic cough can occur with other symptoms, including:

* A runny or stuffy nose.
* A feeling of liquid running down the back of your throat, also known as postnasal drip.
* Clearing your throat a lot.
* Sore throat.
* Hoarseness.
* Wheezing and shortness of breath.
* Heartburn or a sour taste in your mouth.
* In rare cases, coughing up blood.

##### When to see a doctor

See your healthcare professional if you have a cough that lasts for weeks, especially one that brings up sputum or blood, disturbs your sleep, or affects school or work.

## Causes

A cough that happens once in a while is common. It helps clear irritants and mucus from your lungs and prevents infection. But a cough that lasts for weeks is usually due to a health concern. Many times, more than one health concern causes the cough.

Most cases of chronic cough are due to these causes, which can occur alone or together:

* **Postnasal drip.** When your nose or sinuses produce extra mucus, it can drip down the back of your throat and cause you to cough. This condition also is called upper airway cough syndrome.
* **Asthma.** An asthma-related cough may come and go with the seasons. It may appear after an upper respiratory tract infection. Or it can get worse when you're exposed to cold air or certain chemicals or fragrances. In one type of asthma known as cough- variant asthma, a cough is the main symptom.
* **Gastroesophageal reflux disease.** In this common condition, also called GERD, stomach acid flows back into the tube that connects your stomach and throat. This tube is also known as your esophagus. The constant irritation can lead to chronic coughing. Then the coughing can make GERD worse, creating a vicious cycle.
* **Infections.** A cough can last long after other symptoms of pneumonia, flu, a cold or another infection of the upper respiratory tract have gone away. A common cause of a chronic cough in adults — but one that often isn't recognized — is whooping cough, also known as pertussis. Chronic cough also can occur with fungal infections of the lung, as well as tuberculosis infection, also called TB, or lung infection with nontuberculous mycobacteria, also called NTM. NTM is found in soil, water and dust.
* **Chronic obstructive pulmonary disease (COPD).** Also called COPD, this is a lifelong inflammatory lung disease that limits airflow from the lungs. COPD includes chronic bronchitis and emphysema. Chronic bronchitis can cause a cough that brings up colored sputum. Emphysema causes shortness of breath and damages the air sacs in the lungs, also known as alveoli. Most people with COPD are current or former smokers.
* **Blood pressure drugs.** Angiotensin-converting enzyme inhibitors, also called ACE inhibitors, which are commonly prescribed for high blood pressure and heart failure, are known to cause chronic cough in some people.

Less commonly, chronic cough may be caused by:

* Aspiration — when food or other items are swallowed or inhaled and go into the lungs.
* Bronchiectasis — widened and damaged airways that slowly lose the ability to clear out mucus.
* Bronchiolitis — an infection that causes swelling, irritation and buildup of mucus in the small airways of the lung.
* Cystic fibrosis — a genetic disorder that affects the lungs, digestive system and other organs.
* Idiopathic pulmonary fibrosis — gradual damage and scarring of the lungs due to a cause that isn't known.
* Lung cancer — cancer that starts in the lungs, including non-small cell lung cancer and small cell lung cancer.
* Nonasthmatic eosinophilic bronchitis — when airways are inflamed but asthma is not the cause.
* Sarcoidosis — groups of inflamed cells that form lumps or nodules in different parts of the body but most often in the lungs.

### Risk factors

Being a current or former smoker is one of the leading risk factors for chronic cough. Exposure to a lot of secondhand smoke also can lead to coughing and lung damage.

##### Complications

Having a cough that doesn't stop can be very tiring. Coughing can cause various concerns, including:

* Sleep disruption.
* Headache.
* Dizziness.
* Vomiting.
* Sweating a lot.
* Unintended bladder loss, also known as urinary incontinence.
* Broken ribs.
* Passing out, also known as syncope.

## Diagnosis

Your healthcare professional asks about your medical history and does a physical exam. A thorough medical history and physical exam can give important clues about a chronic cough. Your health professional also may order tests to look for the cause of your chronic cough.

But many health professionals start treatment for one of the common causes of chronic cough rather than ordering expensive tests. If the treatment doesn't work, you may be tested for less common causes.

##### Imaging tests

* **X-rays.** Although a routine chest X-ray won't reveal the most common reasons for a cough — postnasal drip, acid reflux, tobacco use or asthma — it may be used to check for lung cancer, pneumonia and other lung diseases. An X-ray of your sinuses may reveal evidence of a sinus infection.
* **Computerized tomography scans.** These scans also are called CT scans. They may be used to check your lungs for conditions that may produce chronic cough or your sinus cavities for pockets of infection.

### Person using a spirometerLung function tests

##### Spirometer

These simple, noninvasive tests, such as spirometry, are used to diagnose asthma

and COPD. They measure how much air your lungs can hold and how fast you can exhale. Your healthcare professional may request an asthma challenge test. This test checks how well you can breathe before and after inhaling the drug methacholine (Provocholine).

##### Lab tests

If the mucus that you cough up is colored, your healthcare professional may want to test a sample of it for bacteria.

##### Scope tests

If your healthcare professional can't find the cause of your cough, special scope tests may be used to look for possible causes. These tests may include:

* **Bronchoscopy.** A bronchoscope is a thin, flexible tube that has a light and camera attached to it. Your health professional can look at your lungs and air passages. A biopsy also can be taken from the inside lining of your airway, also known as the mucosa, to look for anything unusual. A biopsy is a procedure to remove a sample of tissue for testing in a lab.
* **Rhinoscopy.** Using a fiberoptic scope, also known as a rhinoscope, your health professional can view your nasal passageways, sinuses and upper airway.

##### Children

A chest X-ray and spirometry, at a minimum, are usually ordered to find the cause of a chronic cough in children.

## Treatment

Finding out what's causing a chronic cough is very important to effective treatment. In many cases, more than one underlying condition may be causing your chronic cough.

If you smoke, your healthcare professional likely will talk with you about your readiness to quit and give you advice on how to achieve this goal. If you're taking an ACE inhibitor medicine, your health professional may switch you to another medicine that doesn't have cough as a side effect.

Medicines used to treat chronic cough may include:

* **Antihistamines, corticosteroids and decongestants.** These medicines are standard treatment for allergies and postnasal drip.
* **Inhaled asthma medicines.** The most effective treatments for asthma-related cough are corticosteroids and bronchodilators. They reduce inflammation and open up your airways.
* **Antibiotics.** If a bacterial, fungal or mycobacterial infection is causing your chronic cough, your healthcare professional may prescribe antibiotic medicines for the infection.
* **Acid blockers.** When lifestyle changes don't take care of acid reflux, you may be treated with medicines that block acid production. Some people need surgery to resolve the problem.

##### Medicine to reduce coughing

Your healthcare professional works to find the cause of your cough and the best treatment for you. During that time, your healthcare professional also may prescribe a medicine to reduce coughing, called a cough suppressant. Cough suppressants are not recommended for children.

Cough and cold medicines available without a prescription treat the symptoms of coughs and colds — not the underlying disease. Research suggests that these medicines don't work any better than no medicine at all. These medicines are not recommended for children because of potentially serious side effects, including fatal overdoses in children younger than 2 years old.

Don't use over-the-counter cough and cold medicines, except for fever reducers and pain relievers, to treat coughs and colds in children younger than 6 years old. Also, avoid use of these medicines for children younger than 12 years old. Check with your healthcare professional for guidance.

## Procedure explanations and clinical guideline:

Procedure Explanations and Clinical Guidelines for Chronic Cough

##### Initial Assessment

* + Take a detailed medical history and physical examination focusing on cough characteristics, associated symptoms, medication use (notably ACE inhibitors), smoking, and potential environmental exposures.
  + Perform a two-view chest X-ray early to exclude serious lung diseases such as cancer, tuberculosis, bronchiectasis, pneumonia, or structural abnormalities.
  + Laboratory blood tests (CBC, CRP, total IgE) and sputum analysis for infection (Gram stain and culture) may be warranted based on presentation.

##### Targeted Diagnostic Testing Based on Clinical Suspicion

**Asthma**: Conduct spirometry with bronchodilator reversibility testing; if needed, perform bronchoprovocation (methacholine challenge) and measure fractional exhaled nitric oxide or sputum/blood eosinophils to confirm or rule out asthma and NAEB.

**UACS/Allergic Rhinitis or Sinusitis**: Trial treatment with antihistamines, nasal corticosteroids, or decongestants; sinus CT or allergy testing can be used if diagnosis is unclear.

**GERD**: Initiate proton pump inhibitor (PPI) therapy for patients with typical reflux symptoms; if refractory, consider 24-hour esophageal pH and impedance monitoring or endoscopy to confirm diagnosis.

**Infectious Causes**: If productive cough or suspected infection, sputum culture and specialized tests like bronchoscopy with bronchoalveolar lavage may be indicated, especially in children or immunocompromised adults.

Further Advanced Investigations if Diagnosis is Unclear or Common Causes Are: Excluded

* + High-resolution chest CT to detect bronchiectasis, interstitial lung diseases, foreign bodies, or anatomical abnormalities.
  + Bronchoscopy for direct airway visualization and biopsy if malignancy or endobronchial pathology is suspected.
  + ENT evaluation with nasendoscopy or sinus imaging for upper airway causes like vocal cord dysfunction or chronic sinusitis.
  + Screening for rare causes such as alpha-1 antitrypsin deficiency (serum levels), iron deficiency, and obstructive sleep apnea (polysomnography).

##### Therapeutic Trials

Therapy directed against the suspected cause is often initiated before exhaustive testing: Asthma: Inhaled corticosteroids and bronchodilators.

UACS: Nasal steroids, antihistamines. GERD: PPIs and lifestyle modifications.

If patients use ACE inhibitors, discontinuation or substitution with other antihypertensives should be considered prior to pursuing further invasive investigations.

##### Management Algorithm

* + Start with ruling out serious lung pathology via chest X-ray.
  + Use clinical history and examination to prioritize testing or trials towards the four common causes.
  + If no improvement is seen, proceed with specialized testing like bronchoscopy, CT, or 24-hour reflux studies.
  + Refer to pulmonary, ENT, or speech pathology specialists as needed, especially for complex or refractory cases.

**Pediatric Considerations**

In children, chest X-ray and spirometry are foundational.

Additional considerations include protracted bacterial bronchitis (diagnosed by bronchoscopy and lavage), aspiration, cystic fibrosis, and congenital abnormalities.

## Question and Answer:

**Question:** What are the procedures and clinical guidelines for managing and treating chronic cough?

**Answer:** Managing chronic cough (lasting eight weeks or more in adults) involves a stepwise clinical approach focused on identifying and treating underlying causes, combined with supportive lifestyle and behavioral strategies.

## Diagnostic Procedures

##### Initial Evaluation:

Comprehensive medical history and physical exam to identify cough characteristics, triggers, and potential causes such as smoking, medication use (especially ACE inhibitors), or exposure to irritants.

is strongly recommended for all patients to exclude serious diseases like lung cancer, pneumonia, or tuberculosis.

Chest X-ray

Pulmonary function tests (spirometry) to detect asthma or chronic obstructive pulmonary disease.

##### Targeted Testing:

If asthma is suspected, perform bronchodilator reversibility testing or bronchoprovocation. For upper airway cough syndrome (postnasal drip/allergies), consider sinus imaging or allergy tests and trials of antihistamines or nasal steroids.

For suspected gastroesophageal reflux disease (GERD), empiric proton pump inhibitor therapy may be started; further tests like 24-hour pH monitoring if symptoms persist.

Sputum cultures or bronchoscopy may be necessary if infection or less common causes are suspected.

##### Advanced Investigations:

Chest CT scan for structural lung diseases if initial tests are inconclusive. ENT evaluation for vocal cord dysfunction or sinus pathology.

Specialist referrals (pulmonologist, allergist, gastroenterologist) as needed.

## Treatment Guidelines

##### Address underlying causes:

Asthma: inhaled corticosteroids and bronchodilators. Allergies/postnasal drip: antihistamines, nasal corticosteroids.

GERD: lifestyle changes plus acid-blocking medications or surgery if needed. Infections: appropriate antibiotics or antifungal therapy.

Medication-induced cough (e.g., ACE inhibitors): switch to alternative drugs.

##### Behavioral and Supportive Therapies:

Behavior modification therapy by speech and language therapists includes cough suppression techniques, vocal hygiene, and counseling to control symptoms and reduce triggers.

Lifestyle changes: quitting smoking, avoiding irritants (tobacco smoke, pollution, dust), staying hydrated, using humidifiers, and throat soothing with honey or candy (excluding young children).

## Symptom management:

Cough suppressants are generally not recommended, especially in children, due to limited benefit and potential risks.

Ongoing communication with healthcare providers is vital, particularly for chronic refractory cough when no clear cause is found

## Prevention and Patient Education

* Avoid smoking and smoke exposure.
* Manage comorbid conditions like asthma and GERD effectively.
* Practice good hygiene and vaccinations (e.g., influenza, pertussis) to reduce respiratory infections.

## Doctor-Patient conversations

**Doctor:** “So, you’ve had this cough for about two months now. Can you tell me if it tends to be worse at certain times, like when you lie down or after meals?”

**Patient:** “Yes, it gets worse at night, especially when I’m lying flat.”

**Doctor:** “That’s helpful to know. Do you also experience any heartburn or sour taste in your mouth?”

**Patient:** “Actually, yes, sometimes I feel a burning sensation in my chest.”

**Doctor:** “Okay, that might suggest reflux could be contributing. I’d like to explore a few more things related to your cough, including any medications you’re taking.”

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# Recurrent respiratory infections and pneumonia

## Medical code:

Recurrent respiratory tract infections without pneumonia are coded differently, generally under upper respiratory tract infection codes (e.g., J06.9 for acute unspecified upper respiratory infection

## Disease Description

Recurrent respiratory infections are common in adults. However, frequently recurring infections can also be a sign of an underlying medical condition.

Respiratory infections involve the [upper respiratory tract,](https://www.verywellhealth.com/upper-respiratory-infection-overview-4582263) [lower respiratory tract,](https://www.verywellhealth.com/what-is-a-lower-respiratory-infection-770644) or both. They can be caused by viruses, bacteria, and fungi and include the common cold, [sinusitis,](https://www.verywellhealth.com/sinus-infection-overview-83143) [pneumonia,](https://www.verywellhealth.com/types-of-pneumonia-5121133) or [bronchitis.](https://www.verywellhealth.com/bronchitis-causes-and-risk-factors-4164112)

Some healthy adults can get respiratory infections yearly. More frequent respiratory infections may be caused by increased levels of exposure, underlying lung disease, anatomical or structural problems in the airways, and immune system disorders.

This article discusses recurrent respiratory infections in adults. It explains possible reasons why you keep getting upper respiratory infections and when to see your healthcare provider.

##### Risk Factors for Recurrent Respiratory Infections

Recurrent respiratory infections in adults occur when exposure to infectious organisms exceeds the immune system's ability to fight them. They can be caused by an anatomical problem or a weak immune system (immunodeficiency).

Factors that increase the likelihood of recurrent respiratory infections in adults include:1

* Increased exposure to infectious organisms, such as through living or working in a crowded environment or working in a daycare or school with young children
* Smoking or secondhand smoke exposure
* Winter months
* Dry mucous membranes
* Allergies to dust, pollen, molds, and more
* Sleep deprivation
* Lung diseases (such as bronchiectasis due to repeated respiratory infections in childhood)
* Difficulty swallowing

##### Anatomic Problems

Anatomic or structural problems in the airways are the most common cause of otherwise unexplained recurrent respiratory infections in adults. This includes a wide range of conditions that may be congenital (present from birth) or acquired. Examples include:

##### Structural Abnormalities

In the upper airways, abnormalities such as [nasal polyps](https://www.verywellhealth.com/nasal-polyps-83137) or a [deviated septum](https://www.verywellhealth.com/what-causes-a-deviated-septum-7852960) can lead to chronic nasal/sinus infections.

Abnormalities of the [bronchi](https://www.verywellhealth.com/what-is-the-bronchus-structure-function-and-conditions-2249066) (the airways that leave the trachea and enter the lungs), such as congenital hypoplasia, can likewise lead to repeated lower respiratory tract infections.

##### Tumors

Tumors such as [lung cancer](https://www.verywellhealth.com/lung-cancer-symptoms-4014389) are a far too common cause of recurrent respiratory infections in adults, and many people are treated for several lower respiratory tract infections before the diagnosis is made.

This is particularly true in never smokers, as lung cancer is not usually high on a healthcare provider's radar screen. That said, lung cancer is relatively common in lifelong never smokers, and the incidence is increasing.2 Other tumors may also lead to repeated infections.

##### Foreign Bodies

Foreign bodies in the nasal passages are not common in adults (unlike children), but foreign bodies in the lower airways of adults sometimes lead to repeated infections. Unlike large foreign bodies that lead to choking and can be life-threatening, people often have no recollection of inhaling smaller foreign bodies.

Symptoms such as recurrent pneumonia may occur for months or years before the diagnosis is made. The exact frequency is unknown, but bronchial foreign bodies are found in 0.2% to 0.33% of all bronchoscopies. The most frequent finding is organic matter, such as pieces of bones or seeds.

##### Aspiration

Aspiration (breathing contents from the mouth/esophagus/stomach into the lungs) is a relatively common cause of repeated infections.4 It is more common in people who have seizure disorders, other neurological conditions, or alcohol and/or drug abuse.

##### Lung Diseases

Conditions such as bronchiectasis (dilating of the airways) are an important cause of repeated infections and may not be diagnosed until several infections have occurred. Other diseases that may lead to repeated infections include allergic bronchopulmonary aspergillosis and pulmonary vasculitis.

##### Cystic Fibrosis

While [cystic fibrosis](https://www.verywellhealth.com/cystic-fibrosis-4014739) is most often diagnosed in childhood, it is sometimes diagnosed in early adulthood or even later.5 Common symptoms include recurrent respiratory infections, and a prompt diagnosis is critical to improve survival.

##### Acid Reflux

[Gastroesophageal reflux disease (GERD)](https://www.verywellhealth.com/symptoms-of-gerd-1742343) can lead to a chronic cough and repeated respiratory infections, but it is easily overlooked as a potential cause. Other abnormalities associated with infections may include Zenker's diverticulum (an outpouching in the region where the lower throat connects with the esophagus) and achalasia (a rare swallowing disorder that affects the esophagus).

##### Alpha-1-Antitrypsin (AAT) Deficiency

Alpha-1-antitrypsin deficiency is a relatively common hereditary condition affecting roughly 1 in 1,500 to 3,500 people of European ancestry. As a cause of COPD as well as liver disease in some people, it often presents with recurrent respiratory infections between the ages of 20 and 50.6

While the condition cannot be cured, careful monitoring (and enzyme replacement therapy in those who have severe disease) may prevent complications such as severe COPD. AAT deficiency is also a risk factor for lung cancer, and being aware of the diagnosis could be important in lung cancer screening.

##### Primary Immunodeficiency

Primary immunodeficiency disorders are not common, but researchers are learning they are more common than previously thought and are thought to be underdiagnosed. Population studies suggest 1 in 1,200 adults is affected by an immunodeficiency disorder that predisposes them to repeated infections.

Often considered a condition that presents in childhood, around 60% of immunodeficiency disorders remain undiagnosed until adulthood.

There are well over 200 different disorders that include:

* Antibody disorders
* T cell disorders
* Combined B cell/T cell disorders
* Phagocyte disorders
* Complement disorders

That said, a few, in particular, are more commonly discovered in adults who are experiencing repeated respiratory infections.

##### Selective IgA Deficiency

[Selective IgA deficiency](https://www.verywellhealth.com/immunoglobulin-a-deficiency-82726) is estimated to affect roughly one in 143 to one in 965 people (primarily Caucasians) and often goes undiagnosed. It is more commonly found in people who have celiac disease and/or allergies, and it often presents with either repeated respiratory or digestive tract symptoms.

There is no specific treatment for the disorder, but using antibiotics for infection and occasionally immunoglobulins are options. People who have IgA deficiency are also more likely to develop an autoimmune disease such as lupus.

##### Combined Variable Immune Deficiency (CVID)

CVID is characterized by low IgA levels, as with IgA deficiency, but also includes low IgG levels and sometimes low IgM levels. It is less common, affecting roughly one in 30,000 people, but the frequency can vary considerably with geography. It is often diagnosed in people in their 20s and 30s who present with repeated bacterial infections involving the lungs, sinuses, and ears.

Roughly 25% of people with CVID also have an autoimmune condition. Treatment is important to reduce chronic lung damage and includes regular immunoglobulin (gammaglobulin given either IV or IM) as well as the judicious use of antibiotics to treat infections. A high index of suspicion is important, as there is an average delay of four years between symptoms and the diagnosis.

##### Anti-Polysaccharide Antibody Deficiency (SPAD)

A 2017 small study postulated that specific anti-polysaccharide antibody deficiency may be linked with recurrent respiratory infections in the elderly, and it found an increased prevalence among those who experienced these infections. Rather than a congenital condition, they theorized it may be an acquired deficiency.

While the significance of this isn't yet clear, it is another reminder that primary immunodeficiency needs to be considered when other reasons for recurrent infections aren't apparent.

##### Other Disorders

There are many other primary immunodeficiency disorders, such as IgG subclass deficiencies and more, that may not be diagnosed until adulthood. Since the evaluation for these conditions is highly specialized, an immunology consult is usually recommended if there is any suspicion.

##### Secondary Immunodeficiency

Secondary immunodeficiency is a relatively common cause of recurrent respiratory infections in adults and refers to an immunodeficiency related to another medical condition. There are many conditions that could impact the immune system, including:

* Infections such as HIV, Epstein-Barr virus (EBV), and cytomegalovirus (CMV)
* Medications such as chemotherapy, chronic corticosteroid therapy, and immunosuppressive drugs
* Cancers, especially blood-related cancers such as [chronic lymphocytic leukemia](https://www.verywellhealth.com/chronic-lymphocytic-leukemia-7551732) and non-Hodgkin lymphoma
* Plasma cell dyscrasias
* Nephrotic syndrome
* Malabsorption

##### When to See a Healthcare Provider

The American Academy of Allergy and Immunology provides a list of criteria that should raise suspicion of an underlying cause, such as primary immunodeficiency disorder.

Some of these related specifically to recurrent respiratory infections include:

* Do you need antibiotic treatment more than two times each year?
* Have you had pneumonia twice (at any time)?
* Have you had any unusual or difficult-to-treat infections?
* Have you required preventive antibiotics to reduce the number of infections you are having?
* Have you required multiple courses of antibiotics (or intravenous antibiotics) to get rid of an infection?
* Have you had more than three episodes of sinusitis in one year, or do you have chronic sinusitis?
* Have you had more than four ear infections in one year?
* Have you had a very severe infection that began as a common infection?
* Do you have a family history of primary immunodeficiency disorders? (Most people with these do not have a family history.)
* Do you have enlarged lymph nodes (swollen glands) or an enlarged spleen?
* Have you had any recurrent deep abscesses of your skin or other organs?
* Do you have a history of any autoimmune diseases, including autoimmune thyroiditis?

Other questions that are important to ask include:

* Do you or did you ever smoke?
* Have you experienced any weight loss without trying?
* Did you have repeated respiratory infections as a child?
* Have you ever choked?

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| --- | --- |
| **Symptom-diagnosis mapping** | in the context of respiratory infections like pneumonia |
| involves linking clinical symptoms to their corresponding diagnostic codes, primarily ICD-  10 codes. This mapping ensures accurate medical record-keeping, billing, and epidemiological tracking.  Here is a concise mapping of common symptoms to pneumonia-related diagnoses and their  ICD-10 codes: | |

|  |  |  |
| --- | --- | --- |
| **Symptom** | **Possible Diagnosis** | **ICD-10 Code(s)** |
| Fever, cough, sputum production | Pneumonia, unspecified organism | J18.9 (Pneumonia, unspecified organism) |
| Sudden onset of localized chest pain, cough with sputum | Lobar pneumonia, unspecified organism | J18.1 |
| Bronchitis-like cough with patchy infiltrates on X-ray | Bronchopneumonia, unspecified organism | J18.0 |
| Viral pneumonia symptoms (fever, cough, malaise) | Viral pneumonia due to specific viruses (e.g., adenovirus, RSV) | J12.0 (Adenoviral), J12.1 (RSV), J12.2 (Parainfluenza), J12.82 (COVID-19) |
| Recurrent respiratory | Personal history of recurrent | Z87.01 (History of recurrent |

|  |  |  |
| --- | --- | --- |
| **Symptom** | **Possible Diagnosis** | **ICD-10 Code(s)** |
| infections with pneumonia | pneumonia | pneumonia) |
| Bacterial cause known (e.g., Streptococcus pneumoniae) | Bacterial pneumonia from specific pathogens | B953 (Strep. pneumoniae as cause), J15.9 (Bacterial pneumonia, unspecified) |
| Chronic cough (>8 weeks) | May indicate underlying chronic respiratory disease | R05.3 (Chronic cough) |

**Key points:**

* ICD-10 codes for pneumonia distinguish by organism (bacterial, viral, fungal) and specificity; for example, J18.9 is used for unspecified pneumonia, while J12.- covers viral pneumonia due to identified viruses.
* Symptoms like cough, fever, chest pain, and sputum production classically point to pneumonia but require clinical confirmation and sometimes microbiologic testing to assign precise diagnosis codes.

Chronic or recurrent respiratory symptoms may map to history codes or underlying chronic lung conditions.

This symptom-diagnosis mapping model guides clinicians and coders in aligning presenting symptoms to the correct ICD-10 diagnosis codes for respiratory infections, improving documentation accuracy and patient care continuity.

## Symptoms

The signs and symptoms of pneumonia vary from mild to severe, depending on factors such as the type of germ causing the infection, and your age and overall health. Mild signs and symptoms often are similar to those of a cold or flu, but they last longer.

Signs and symptoms of pneumonia may include:

* Chest pain when you breathe or cough
* Confusion or changes in mental awareness (in adults age 65 and older)
* Cough, which may produce phlegm
* Fatigue
* Fever, sweating and shaking chills
* Lower than normal body temperature (in adults older than age 65 and people with weak immune systems)
* Nausea, vomiting or diarrhea
* Shortness of breath

Newborns and infants may not show any sign of the infection. Or they may vomit, have a fever and cough, appear restless or tired and without energy, or have difficulty breathing and eating.

###### When to see a doctor

See your doctor if you have difficulty breathing, chest pain, persistent fever of 102 F (39 C) or higher, or persistent cough, especially if you're coughing up pus.

It's especially important that people in these high-risk groups see a doctor:

* Adults older than age 65
* Children younger than age 2 with signs and symptoms
* People with an underlying health condition or weakened immune system
* People receiving chemotherapy or taking medication that suppresses the immune system

For some older adults and people with heart failure or chronic lung problems, pneumonia can quickly become a life-threatening condition.

## Causes

Many germs can cause pneumonia. The most common are bacteria and viruses in the air we breathe. Your body usually prevents these germs from infecting your lungs. But sometimes these germs can overpower your immune system, even if your health is generally good.

Pneumonia is classified according to the types of germs that cause it and where you got the infection.

###### Community-acquired pneumonia

Community-acquired pneumonia is the most common type of pneumonia. It occurs outside of hospitals or other health care facilities. It may be caused by:

* **Bacteria.** The most common cause of bacterial pneumonia in the U.S. is Streptococcus pneumoniae. This type of pneumonia can occur on its own or after you've had a cold or the flu. It may affect one part (lobe) of the lung, a condition called lobar pneumonia.
* **Bacteria-like organisms.** Mycoplasma pneumoniae also can cause pneumonia. It typically produces milder symptoms than do other types of pneumonia. Walking pneumonia is an informal name given to this type of pneumonia, which typically isn't severe enough to require bed rest.
* **Fungi.** This type of pneumonia is most common in people with chronic health problems or weakened immune systems, and in people who have inhaled large doses of the organisms. The fungi that cause it can be found in soil or bird droppings and vary depending upon geographic location.
* **Viruses, including COVID-19.** Some of the viruses that cause colds and the flu can cause pneumonia. Viruses are the most common cause of pneumonia in children younger than 5 years. Viral pneumonia is usually mild. But in some cases it can become very serious. Coronavirus 2019 (COVID-19) may cause pneumonia, which can become severe.

###### Hospital-acquired pneumonia

Some people catch pneumonia during a hospital stay for another illness. Hospital-acquired pneumonia can be serious because the bacteria causing it may be more resistant to antibiotics and because the people who get it are already sick. People who are on breathing machines (ventilators), often used in intensive care units, are at higher risk of this type of pneumonia.

###### Health care-acquired pneumonia

Health care-acquired pneumonia is a bacterial infection that occurs in people who live in long-term care facilities or who receive care in outpatient clinics, including kidney dialysis centers. Like hospital-acquired pneumonia, health care-acquired pneumonia can be caused by bacteria that are more resistant to antibiotics.

###### Aspiration pneumonia

Aspiration pneumonia occurs when you inhale food, drink, vomit or saliva into your lungs. Aspiration is more likely if something disturbs your normal gag reflex, such as a brain injury or swallowing problem, or excessive use of alcohol or drugs.

##### Risk factors

Pneumonia can affect anyone. But the two age groups at highest risk are:

* Children who are 2 years old or younger
* People who are age 65 or older Other risk factors include:
* **Being hospitalized.** You're at greater risk of pneumonia if you're in a hospital intensive care unit, especially if you're on a machine that helps you breathe (a ventilator).
* **Chronic disease.** You're more likely to get pneumonia if you have asthma, chronic obstructive pulmonary disease (COPD) or heart disease.
* **Smoking.** Smoking damages your body's natural defenses against the bacteria and viruses that cause pneumonia.
* **Weakened or suppressed immune system.** People who have HIV/AIDS, who've had an organ transplant, or who receive chemotherapy or long-term steroids are at risk.

##### Complications

Even with treatment, some people with pneumonia, especially those in high-risk groups, may experience complications, including:

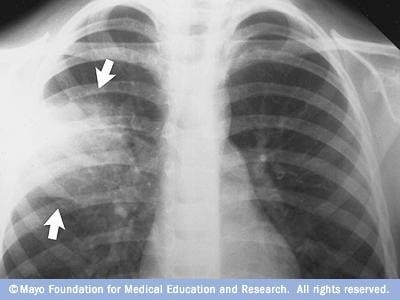
* **Bacteria in the bloodstream (bacteremia).** Bacteria that enter the bloodstream from your lungs can spread the infection to other organs, potentially causing organ failure.
* **Difficulty breathing.** If your pneumonia is severe or you have chronic underlying lung diseases, you may have trouble breathing in enough oxygen. You may need to be hospitalized and use a breathing machine (ventilator) while your lung heals.
* **Fluid accumulation around the lungs (pleural effusion).** Pneumonia may cause fluid to build up in the thin space between layers of tissue that line the lungs and chest cavity (pleura). If the fluid becomes infected, you may need to have it drained through a chest tube or removed with surgery.
* **Lung abscess.** An abscess occurs if pus forms in a cavity in the lung. An abscess is usually treated with antibiotics. Sometimes, surgery or drainage with a long needle or tube placed into the abscess is needed to remove the pus.

### Prevention

To help prevent pneumonia:

* **Get vaccinated.** Vaccines are available to prevent some types of pneumonia and the flu. Talk with your doctor about getting these shots. The vaccination guidelines have changed over time so make sure to review your vaccination status with your doctor even if you recall previously receiving a pneumonia vaccine.
* **Make sure children get vaccinated.** Doctors recommend a different pneumonia vaccine for children younger than age 2 and for children ages 2 to 5 years who are at particular risk of pneumococcal disease. Children who attend a group child care center should also get the vaccine. Doctors also recommend flu shots for children older than 6 months.
* **Practice good hygiene.** To protect yourself against respiratory infections that sometimes lead to pneumonia, wash your hands regularly or use an alcohol-based hand sanitizer.
* **Don't smoke.** Smoking damages your lungs' natural defenses against respiratory infections.
* **Keep your immune system strong.** Get enough sleep, exercise regularly and eat a healthy diet.

#### Diagnosis

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##### Chest X-ray showing pneumonia

Your doctor will start by asking about your medical history and doing a physical exam, including listening to your lungs with a stethoscope to check for abnormal bubbling or crackling sounds that suggest pneumonia.

If pneumonia is suspected, your doctor may recommend the following tests:

* **Blood tests.** Blood tests are used to confirm an infection and to try to identify the type of organism causing the infection. However, precise identification isn't always possible.
* **Chest X-ray.** This helps your doctor diagnose pneumonia and determine the extent and location of the infection. However, it can't tell your doctor what kind of germ is causing the pneumonia.
* **Pulse oximetry.** This measures the oxygen level in your blood. Pneumonia can prevent your lungs from moving enough oxygen into your bloodstream.
* **Sputum test.** A sample of fluid from your lungs (sputum) is taken after a deep cough and analyzed to help pinpoint the cause of the infection.

Your doctor might order additional tests if you're older than age 65, are in the hospital, or have serious symptoms or health conditions. These may include:

* **CT scan.** If your pneumonia isn't clearing as quickly as expected, your doctor may recommend a chest CT scan to obtain a more detailed image of your lungs.
* **Pleural fluid culture.** A fluid sample is taken by putting a needle between your ribs from the pleural area and analyzed to help determine the type of infection.



##### Treatment

Treatment for pneumonia involves curing the infection and preventing complications. People who have community-acquired pneumonia usually can be treated at home with medication. Although most symptoms ease in a few days or weeks, the feeling of tiredness can persist for a month or more.

Specific treatments depend on the type and severity of your pneumonia, your age and your overall health. The options include:

* **Antibiotics.** These medicines are used to treat bacterial pneumonia. It may take time to identify the type of bacteria causing your pneumonia and to choose the best antibiotic to treat it. If your symptoms don't improve, your doctor may recommend a different antibiotic.
* **Cough medicine.** This medicine may be used to calm your cough so that you can rest. Because coughing helps loosen and move fluid from your lungs, it's a good idea not to eliminate your cough completely. In addition, you should know that very few studies have looked at whether over-the-counter cough medicines lessen coughing caused by pneumonia. If you want to try a cough suppressant, use the lowest dose that helps you rest.
* **Fever reducers/pain relievers.** You may take these as needed for fever and discomfort. These include drugs such as aspirin, ibuprofen (Advil, Motrin IB, others) and acetaminophen (Tylenol, others).

##### Hospitalization

You may need to be hospitalized if:

* You are older than age 65
* You are confused about time, people or places
* Your kidney function has declined
* Your systolic blood pressure is below 90 millimeters of mercury (mm Hg) or your diastolic blood pressure is 60 mm Hg or below
* Your breathing is rapid (30 breaths or more a minute)
* You need breathing assistance
* Your temperature is below normal
* Your heart rate is below 50 or above 100

You may be admitted to the intensive care unit if you need to be placed on a breathing machine (ventilator) or if your symptoms are severe.

Children may be hospitalized if:

* They are younger than age 2 months
* They are lethargic or excessively sleepy
* They have trouble breathing
* They have low blood oxygen levels
* They appear dehydrated

refer to best practices for healthcare providers to communicate medical procedures clearly to patients, ensuring understanding, informed consent, and comfort. While the search results focus mainly on pneumonia diagnosis and treatment, general principles for explaining procedures (such as chest X-rays or sputum tests) in respiratory infections like pneumonia can be drawn from clinical standards:

**Procedure explanation guidelines**

Explain why the procedure is necessary. For example, a chest X- ray is done to confirm pneumonia and see its extent; a sputum test identifies the infecting organism.

**Start with the purpose:**

Use clear, non-technical language. For a chest X-ray, explain it’s a painless scan where the patient will stand briefly while a picture of the lungs is taken. For blood tests, mention a small needle prick to collect blood.

**A:**

**Describe the procedure simply:**

Inform about sensations, duration, positioning, and any preparation needed (e.g., deep cough for sputum collection).

**Explain what to expect:**

Emphasize the low risk (e.g., minimal radiation from X-ray), benefits of accurate diagnosis, and how results guide treatment.

**Discuss risks and benefits:**

Encourage patients to ask questions to clarify

**Address patient questions and concerns:**

doubts.

Ask patients to summarize what they understood to

**Check patient understanding:**

confirm effective communication.

Ensure that informed consent is recorded, particularly for invasive procedures like pleural fluid sampling.

**Document consent:**

In pneumonia care, these guidelines help patients understand diagnostic steps such as chest radiography, pulse oximetry, sputum tests, or more advanced tests like CT scans or thoracentesis (pleural fluid extraction) if indicated.

Effective explanation improves patient cooperation, reduces anxiety, and supports shared decision-making in diagnosis and treatment planning.

**A:**

**Q: What is pneumonia?**

Pneumonia is an infection that inflames the air sacs (alveoli) in one or both lungs. The alveoli may fill with fluid or pus, causing cough, fever, chills, and difficulty breathing.

**Q: What causes pneumonia?**

Pneumonia is most commonly caused by bacteria or viruses. Bacterial causes

include *Streptococcus pneumoniae*, while viruses include influenza and COVID-19. Fungi and other organisms are less common causes, especially in immune compromised patients.

**A:**

**A:**

**Q: What are common symptoms of pneumonia?**

Typical symptoms include cough, fever, sweating, chills, shortness of breath, chest pain, fatigue, and in some cases nausea, vomiting, or confusion especially in older adults.

**Q: How is pneumonia diagnosed?**

Diagnosis involves a medical history, physical examination (including lung auscultation), and diagnostic tests such as chest X-rays, sputum cultures, and blood tests to identify the causative organism.

**A:**

**Q: How is pneumonia treated?**

Treatment depends on the cause; bacterial pneumonia requires antibiotics, while viral

**A:**

pneumonia often resolves on its own. Supportive care includes rest, fluids, oxygen therapy if needed, and symptom relief.

**A:**

**Q: Who is at risk for pneumonia?**

Risk groups include children under 5, adults over 65, people with chronic diseases or weakened immune systems, smokers, and those recently ill with respiratory infections.

**Q: How can pneumonia be prevented?**

Vaccinations (against pneumococcus, influenza, COVID-19, Hib), good hand hygiene, avoiding smoking and exposure to smoke, healthy nutrition, and managing chronic conditions reduce pneumonia risk.

**Q: When should I see a doctor?**

Seek medical attention if you have difficulty breathing, chest pain, persistent high fever, or cough that doesn’t improve.

This Q&A structure aligns with key information from respected sources like Mayo Clinic, WHO, WebMD, and others, offering accurate, concise guidance on pneumonia.

**A:**

The doctor shares the diagnosis (like a viral RTI or pneumonia) and recommends a management plan. If antibiotics are not indicated, this is explained clearly with reasons (e.g., no signs of bacterial infection). Safety- netting advice is given on symptoms that should prompt reassessment.

**Discussing the diagnosis and treatment plan:**

If patients implicitly or explicitly expect antibiotics, the doctor uses communication techniques such as reflection, acknowledgement of seriousness, and providing symptomatic or delayed antibiotic options to maintain trust while avoiding unnecessary prescriptions

**Handling expectations and resistance:**

## References

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# Sleeping-disordered breathing, including obstructive and central apnea

## Medical code

##### [Obstructive Sleep Apnea ICD-10 Code – G47.33](https://www.zmedsolutions.net/obstructive-sleep-apnea-icd-10-code-g47-33/)

**Overview**

Sleep apnea is a potentially serious sleep disorder in which breathing repeatedly stops and starts. If you snore loudly and feel tired even after a full night's sleep, you might have sleep apnea.

The main types of sleep apnea are:

* **Obstructive sleep apnea (OSA),** which is the more common form that occurs when throat muscles relax and block the flow of air into the lungs
* **Central sleep apnea (CSA)**, which occurs when the brain doesn't send proper signals to the muscles that control breathing
* **Treatment-emergent central sleep apnea**, also known as complex sleep apnea, which happens when someone has OSA — diagnosed with a sleep study — that converts to CSA when receiving therapy for OSA

**Symptoms**

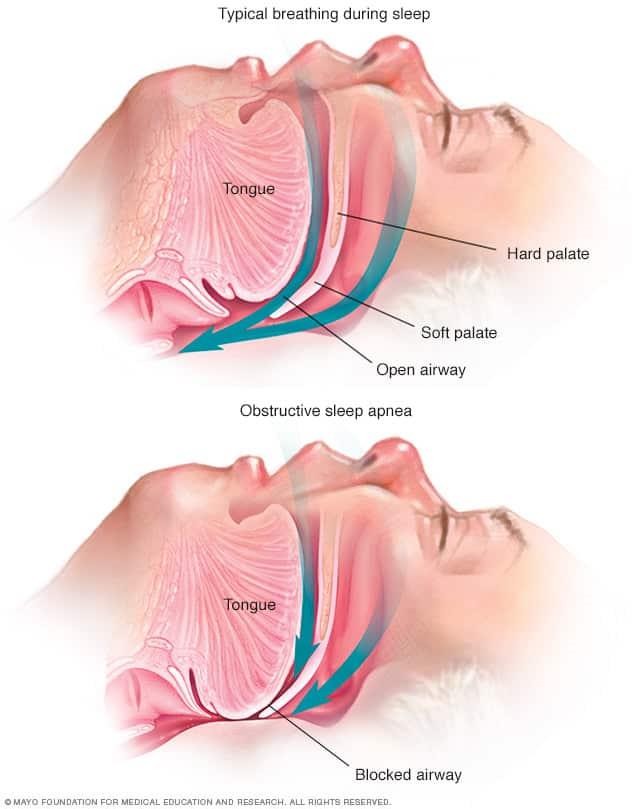
The symptoms of obstructive and central sleep apneas overlap, sometimes making it difficult to determine which type you have. The most common symptoms of obstructive and central sleep apneas include:

* Loud snoring.
* Episodes in which you stop breathing during sleep — which would be reported by another person.
* Gasping for air during sleep.
* Awakening with a dry mouth.
* Morning headache.
* Difficulty staying asleep, known as insomnia.
* Excessive daytime sleepiness, known as hypersomnia.
* Difficulty paying attention while awake.
* Irritability.

##### When to see a doctor

Loud snoring can indicate a potentially serious problem, but not everyone who has sleep apnea snores. Talk to your health care provider if you have symptoms of sleep apnea. Ask your provider about any sleep problem that leaves you fatigued, sleepy and irritable.

**Causes**

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**Obstructive sleep apnea**

This type of sleep apnea happens when the muscles in the back of the throat relax. These muscles support the soft palate, the triangular piece of tissue hanging from the soft palate called the uvula, the tonsils, the side walls of the throat and the tongue.

When the muscles relax, your airway narrows or closes as you breathe in. You can't get enough air, which can lower the oxygen level in your blood. Your brain senses that you can't breathe, and briefly wakes you so that you can reopen your airway. This awakening is usually so brief that you don't remember it.

You might snort, choke or gasp. This pattern can repeat itself 5 to 30 times or more each hour, all night. This makes it hard to reach the deep, restful phases of sleep.

**Central sleep apnea**

This less common form of sleep apnea occurs when your brain fails to send signals to your breathing muscles. This means that you make no effort to breathe for a short period. You might awaken with shortness of breath or have a difficult time getting to sleep or staying

asleep.

#### Risk factors

Sleep apnea can affect anyone, even children. But certain factors increase your risk.

##### Obstructive sleep apnea

Factors that increase the risk of this form of sleep apnea include:

* **Excess weight.** Obesity greatly increases the risk of OSA. Fat deposits around your upper airway can obstruct your breathing.
* **Neck circumference.** People with thicker necks might have narrower airways.
* **A narrowed airway.** You might have inherited a narrow throat. Tonsils or adenoids also can enlarge and block the airway, particularly in children.
* **Being male.** Men are 2 to 3 times more likely to have sleep apnea than are women. However, women increase their risk if they're overweight or if they've gone through menopause.
* **Being older.** Sleep apnea occurs significantly more often in older adults.
* **Family history.** Having family members with sleep apnea might increase your risk.
* **Use of alcohol, sedatives or tranquilizers.** These substances relax the muscles in your throat, which can worsen obstructive sleep apnea.
* **Smoking.** Smokers are three times more likely to have obstructive sleep apnea than are people who've never smoked. Smoking can increase the amount of inflammation and fluid retention in the upper airway.
* **Nasal congestion.** If you have trouble breathing through your nose — whether from an anatomical problem or allergies — you're more likely to develop obstructive sleep apnea.
* **Medical conditions.** Congestive heart failure, high blood pressure and type 2 diabetes are some of the conditions that may increase the risk of obstructive sleep apnea. Polycystic ovary syndrome, hormonal disorders, prior stroke and chronic lung diseases such as asthma also can increase risk.

##### Central sleep apnea

Risk factors for this form of sleep apnea include:

* **Being older.** Middle-aged and older people have a higher risk of central sleep apnea.
* **Being male.** Central sleep apnea is more common in men than it is in women.
* **Heart disorders.** Having congestive heart failure increases the risk.
* **Using narcotic pain medicines.** Opioid medicines, especially long-acting ones such as methadone, increase the risk of central sleep apnea.
* **Stroke.** Having had a stroke increases the risk of central sleep apnea.

#### Complications

Sleep apnea is a serious medical condition. Complications of OSA can include:

* **Daytime fatigue.** The repeated awakenings associated with sleep apnea make typical, restorative sleep impossible, in turn making severe daytime drowsiness, fatigue and irritability likely.

You might have trouble concentrating and find yourself falling asleep at work, while watching TV or even when driving. People with sleep apnea have an increased risk of motor vehicle and workplace accidents.

You might also feel quick-tempered, moody or depressed. Children and adolescents with sleep apnea might perform poorly in school or have behavior problems.

* **High blood pressure or heart problems.** Sudden drops in blood oxygen levels that occur during OSA increase blood pressure and strain the cardiovascular system. Having OSA increases your risk of high blood pressure, also known as hypertension.

OSA might also increase your risk of recurrent heart attack, stroke and irregular heartbeats, such as atrial fibrillation. If you have heart disease, multiple episodes of

low blood oxygen (hypoxia or hypoxemia) can lead to sudden death from an irregular heartbeat.

* **Type 2 diabetes.** Having sleep apnea increases your risk of developing insulin resistance and type 2 diabetes.
* **Metabolic syndrome.** This disorder, which includes high blood pressure, abnormal cholesterol levels, high blood sugar and an increased waist circumference, is linked to a higher risk of heart disease.
* **Complications with medicines and surgery.** Obstructive sleep apnea is also a concern with certain medicines and general anesthesia. People with sleep apnea might be more likely to have complications after major surgery because they're prone to breathing problems, especially when sedated and lying on their backs.

Before you have surgery, tell your doctor about your sleep apnea and how it's being treated.

* **Liver problems.** People with sleep apnea are more likely to have irregular results on liver function tests, and their livers are more likely to show signs of scarring, known as nonalcoholic fatty liver disease.
* **Sleep-deprived partners.** Loud snoring can keep anyone who sleeps nearby from getting good rest. It's common for a partner to have to go to another room, or even to another floor of the house, to be able to sleep.

Complications of CSA can include:

* **Fatigue.** The repeated awakening associated with sleep apnea makes typical, restorative sleep impossible. People with central sleep apnea often have severe fatigue, daytime drowsiness and irritability.

You might have difficulty concentrating and find yourself falling asleep at work, while watching television or even while driving.

* **Cardiovascular problems.** Sudden drops in blood oxygen levels that occur during central sleep apnea can adversely affect heart health.

If there's underlying heart disease, these repeated multiple episodes of low blood oxygen — known as hypoxia or hypoxemia — worsen prognosis and increase the risk of irregular heart rhythms.

**Diagnosis**

Your health care provider may make an evaluation based on your symptoms and a sleep history, which you can provide with help from someone who shares your bed or your household, if possible.

You're likely to be referred to a sleep disorder center. There, a sleep specialist can help you determine your need for further evaluation.

An evaluation often involves overnight monitoring of your breathing and other body functions during sleep testing at a sleep center. Home sleep testing also might be an option. Tests to detect sleep apnea include:

* **Nocturnal polysomnography.** During this test, you're hooked up to equipment that monitors your heart, lung and brain activity, breathing patterns, arm and leg movements, and blood oxygen levels while you sleep.
* **Home sleep tests.** Your health care provider might provide you with simplified tests to be used at home to diagnose sleep apnea. These tests usually measure your heart rate, blood oxygen level, airflow and breathing patterns. Your provider is more likely to recommend polysomnography in a sleep testing facility, rather than a home sleep test, if central sleep apnea is suspected.

If the results aren't typical, your provider might be able to prescribe a therapy without further testing. Portable monitoring devices sometimes miss sleep apnea. So your health care provider might still recommend polysomnography even if your first results are within the standard range.

If you have obstructive sleep apnea, your health care provider might refer you to an ear, nose and throat specialist to rule out a blockage in your nose or throat. An evaluation by a heart specialist, known as a cardiologist, or a doctor who specializes in the nervous system, called a neurologist, might be necessary to look for causes of central sleep apnea.

**Treatment**

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##### Continuous positive airway pressure (CPAP)

For milder cases of sleep apnea, your health care provider may recommend only lifestyle changes, such as losing weight or quitting smoking. You may need to change the position in which you sleep. If you have nasal allergies, your provider may recommend treatment for your allergies.

If these measures don't improve your symptoms or if your apnea is moderate to severe, a number of other treatments are available.

Certain devices can help open a blocked airway. In other cases, surgery might be necessary.

##### Therapies for OSA

* **Continuous positive airway pressure (CPAP).** If you have moderate to severe obstructive sleep apnea, you might benefit from using a machine that delivers air pressure through a mask while you sleep. With CPAP (SEE-pap), the air pressure is somewhat greater than that of the surrounding air and is just enough to keep your upper airway passages open, preventing apnea and snoring.

Although CPAP is the most common and reliable method of treating sleep apnea, some people find it cumbersome or uncomfortable. Some people give up on the CPAP machine. But with practice, most people learn to adjust the tension of the straps on the mask to obtain a comfortable and secure fit.

You might need to try more than one type of mask to find one that's comfortable. Don't stop using the CPAP machine if you have problems. Check with your health care provider to see what changes can be made to increase your comfort.

Additionally, contact your provider if you're still snoring or begin snoring again despite treatment. If your weight changes, the pressure settings of the CPAP machine might need to be adjusted.

* **Other airway pressure devices.** If using a CPAP machine continues to be a problem for you, you might be able to use a different type of airway pressure device that automatically adjusts the pressure while you're sleeping (auto-CPAP). Units that supply bilevel positive airway pressure (BPAP) also are available. These provide more pressure when you inhale and less when you exhale.
* **Oral appliances.** Another option is wearing an oral appliance designed to keep your throat open. CPAP is more reliably effective than oral appliances, but oral appliances might be easier to use. Some are designed to open your throat by bringing your jaw forward, which can sometimes relieve snoring and mild obstructive sleep apnea.

A number of devices are available from your dentist. You might need to try different devices before finding one that works for you.

Once you find the right fit, you'll need to follow up with your dentist repeatedly during the first year and then regularly after that to ensure that the fit is still good and to reassess your symptoms.

You'll likely read, hear or see TV ads about different treatments for sleep apnea. Talk with your health care provider about any treatment before you try it.

##### Surgery for OSA

Surgery may be an option for people with OSA, but usually only after other treatments have failed. Generally, at least a three-month trial of other treatment options is suggested before considering surgery. However, for a small number of people with certain jaw structure problems, surgery is a good first option.

Surgical options might include:

* **Tissue removal.** During this procedure (uvulopalatopharyngoplasty), a surgeon removes tissue from the rear of your mouth and top of the throat. Your tonsils and adenoids usually are removed as well.

This type of surgery might be successful in stopping throat structures from vibrating and causing snoring. It's less effective than CPAP and isn't considered a reliable treatment for obstructive sleep apnea.

Removing tissues in the back of the throat with radiofrequency energy (radiofrequency ablation) might be an option for those who can't tolerate CPAP or oral appliances.

* **Tissue shrinkage.** Another option is to shrink the tissue at the rear of the mouth and the back of the throat using radiofrequency ablation. This procedure might be used for mild to moderate sleep apnea. One study found this to have effects similar to that of tissue removal, but with fewer surgical risks.
* **Jaw repositioning.** In this procedure, the jaw is moved forward from the remainder of the face bones. This enlarges the space behind the tongue and soft palate, making obstruction less likely. This procedure is known as maxillomandibular advancement.
* **Implants.** Soft rods, usually made of polyester or plastic, are surgically implanted into the soft palate after numbing with a local anesthetic. More research is needed to determine how well implants work.
* **Nerve stimulation.** This requires surgery to insert a stimulator for the nerve that controls tongue movement (hypoglossal nerve). The increased stimulation helps keep the tongue in a position that keeps the airway open. More research is needed.
* **Creating a new air passageway, known as tracheostomy.** You may need this form of surgery if other treatments have failed and you have severe, life-threatening sleep apnea. In this procedure, your surgeon makes an opening in your neck and inserts a metal or plastic tube through which you breathe.

You keep the opening covered during the day. But at night you uncover it to allow air to pass in and out of your lungs, bypassing the blocked air passage in your throat.

Other types of surgery may help reduce snoring and contribute to the treatment of sleep apnea by clearing or enlarging air passages:

* Surgery to remove enlarged tonsils or adenoids.
* Weight-loss surgery, also known as bariatric surgery.

##### Therapies for CSA

* **Treatment for associated medical problems.** Possible causes of central sleep apnea include heart or neuromuscular disorders, and treating those conditions might help. Other therapies that may be used for CSA include supplemental oxygen, CPAP, BPAP, and adaptive servo-ventilation (ASV).
* **Medicine changes.** You may be prescribed medicine to help manage your breathing, such as acetazolamide. If medicines are worsening your CSA, such as opioids, your health care provider may change your medicines.
* **Supplemental oxygen.** Using supplemental oxygen while you sleep might help if you have central sleep apnea. Various forms of oxygen are available with devices to deliver oxygen to your lungs.
* **Adaptive servo-ventilation (ASV).** This more recently approved airflow device learns your typical breathing pattern and stores the information in a built-in computer. After you fall asleep, the machine uses pressure to regulate your breathing pattern and prevent pauses in your breathing.

ASV may be an option for some people with treatment-emergent central sleep apnea. However, it might not be a good choice for people with predominant central sleep apnea and advanced heart failure. And ASV is not recommended for those with severe heart failure.

**Procedure explanations and clinical guidelines**

**Uvulopalatopharyngoplasty** is a procedure to remove the uvula, tonsils, and parts of the soft palate. Doctors use small surgical instruments to excise the tissues blocking the airway, increasing its size and thereby improving airflow and reducing apnea episodes.

**Question and Answer:**

* [How is artificial intelligence being utilized to enhance the diagnosis and treatment](https://www.researchgate.net/post/How_is_artificial_intelligence_being_utilized_to_enhance_the_diagnosis_and_treatment_of_sleep_apnea?_tp=eyJjb250ZXh0Ijp7ImZpcnN0UGFnZSI6Il9kaXJlY3QiLCJwYWdlIjoiX2RpcmVjdCJ9fQ) [of sleep apnea?](https://www.researchgate.net/post/How_is_artificial_intelligence_being_utilized_to_enhance_the_diagnosis_and_treatment_of_sleep_apnea?_tp=eyJjb250ZXh0Ijp7ImZpcnN0UGFnZSI6Il9kaXJlY3QiLCJwYWdlIjoiX2RpcmVjdCJ9fQ)

AI has the potential to improve the management of sleep apnea by personalizing treatment, enhancing diagnostic accuracy, and advancing our understanding of the condition.

### Doctor-Patient conversation:

Patient: "What's the difference between obstructive and central sleep apnea?"

Doctor: "In OSA, the airway gets blocked because the muscles in the back of your throat relax and narrow or close the airway when you breathe in. This causes the characteristic snoring and pauses in breathing. In CSA, the problem is with the signals from your brain. Your brain doesn't send the correct signals to your breathing muscles, so you stop breathing, even though your airway might be open. Some people have a combination of both, called mixed or complex sleep apnea."

Patient: "So, what causes these different types of sleep apnea?"

Doctor: "OSA is often linked to factors like obesity, enlarged tonsils or tongue, and a narrow airway. It can also be hereditary. CSA, on the other hand, is often associated with other medical conditions like heart failure, stroke, or certain neurological conditions. It can also be a side effect of some medications, like opioids or sleeping pills. Sometimes, people develop CSA after starting treatment for OSA, which is called treatment-emergent central sleep apnea."

Patient: "How do we know which type I have?"

Doctor: "We'll need to do a sleep study, also known as polysomnography. This involves spending a night in a sleep lab where we monitor your breathing, brain waves, heart rate, and other bodily functions while you sleep. We'll look for patterns of apnea and hypopnea (partial blockage of the airway) to determine the type and severity of your sleep apnea."

Patient: "What are the potential consequences of not treating sleep apnea?"

Doctor: "Untreated sleep apnea can lead to a range of health problems. It can increase your risk of high blood pressure, heart disease, stroke, type 2 diabetes, and other conditions. It can also lead to daytime sleepiness, difficulty concentrating, and mood changes. In severe cases, it can even increase the risk of accidents due to excessive daytime sleepiness."

Patient: "What are the treatment options?"

Doctor: "For OSA, the most common treatment is CPAP (continuous positive airway pressure) therapy. This involves wearing a mask over your nose and/or mouth while you sleep, connected to a machine that delivers a continuous stream of air to keep your airway open. For mild cases, lifestyle changes like weight loss, avoiding alcohol before bed, or sleeping on your side might be enough. In some cases, oral appliances or surgery may be considered. For CSA, treatment often involves addressing the underlying medical condition

or adjusting medications. We may also use CPAP, but it might need to be adjusted to accommodate the specific needs of CSA."

Patient: "This all sounds a bit overwhelming. Can I learn more about it?"

Doctor: "Absolutely. We can discuss your specific situation in more detail, and I can provide you with educational materials about sleep apnea, treatment options, and resources for support groups. We'll work together to find the best approach for managing your sleep apnea."

**References**

>>><https://www.google.com/search?q=Doctor-Patient+conversation+on+sleeping->[disordered+breathing+including+obstructive+and+central+apnea&oq=Doctor-Patient+conversation+on+sleeping-](https://www.google.com/search?q=Doctor-Patient%2Bconversation%2Bon%2Bsleeping-disordered%2Bbreathing%2Bincluding%2Bobstructive%2Band%2Bcentral%2Bapnea&oq=Doctor-Patient%2Bconversation%2Bon%2Bsleeping-disordered%2Bbreathing%2Bincluding%2Bobstructive%2Band%2Bcentral%2Bapnea&gs_lcrp=EgZjaHJvbWUyBggAEEUYOdIBCTk2NDA2ajBqN6gCALACAA&sourceid=chrome&ie=UTF-8) [disordered+breathing+including+obstructive+and+central+apnea&gs\_lcrp=EgZjaHJvbWUy](https://www.google.com/search?q=Doctor-Patient%2Bconversation%2Bon%2Bsleeping-disordered%2Bbreathing%2Bincluding%2Bobstructive%2Band%2Bcentral%2Bapnea&oq=Doctor-Patient%2Bconversation%2Bon%2Bsleeping-disordered%2Bbreathing%2Bincluding%2Bobstructive%2Band%2Bcentral%2Bapnea&gs_lcrp=EgZjaHJvbWUyBggAEEUYOdIBCTk2NDA2ajBqN6gCALACAA&sourceid=chrome&ie=UTF-8) [BggAEEUYOdIBCTk2NDA2ajBqN6gCALACAA&sourceid=chrome&ie=UTF-8.](https://www.google.com/search?q=Doctor-Patient%2Bconversation%2Bon%2Bsleeping-disordered%2Bbreathing%2Bincluding%2Bobstructive%2Band%2Bcentral%2Bapnea&oq=Doctor-Patient%2Bconversation%2Bon%2Bsleeping-disordered%2Bbreathing%2Bincluding%2Bobstructive%2Band%2Bcentral%2Bapnea&gs_lcrp=EgZjaHJvbWUyBggAEEUYOdIBCTk2NDA2ajBqN6gCALACAA&sourceid=chrome&ie=UTF-8)

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>>>https:[//www.researchgate.net/topic/Sleep-Apnea.](http://www.researchgate.net/topic/Sleep-Apnea)

**BRONCHIOLITIS**

**Definition**

Bronchiolitis is a common lung infection in young children and infants. It causes swelling and irritation and a buildup of mucus in the small airways of the lung. These small airways are called bronchioles. Bronchiolitis is almost always caused by a virus.

ronchiolitis is an acute viral infection of the lower respiratory tract that occurs primarily in the very young. It is a clinical diagnosis based upon typical symptoms and signs. Bronchiolitis is generally a self-limiting illness, and management is mostly supportive.

There is some discrepancy between the use of 'bronchiolitis' in the UK and in the USA and other parts of Europe, and no universally accepted definition for such a common condition.**[1](https://patient.info/doctor/bronchiolitis-pro" \l "ref-1" \o "Kuzik BA; Maybe there is no such thing as bronchiolitis. CMAJ. 2016 Mar 15;188(5):351-4. doi: 10.1503/cmaj.150683. Epub 2016 Feb 1.)** In the UK, the term describes an illness in infants, beginning as an upper respiratory tract infection (URTI) that evolves with signs of respiratory distress, cough, wheeze, and often bilateral crepitations. In North America, bronchiolitis is used to describe a wheezing illness associated with an URTI in children up to the age of 2 years (whilst this would be described as a 'viral-induced wheeze' in the UK).**[2](https://patient.info/doctor/bronchiolitis-pro" \l "ref-2" \o "Douros K, Everard ML; Time to Say Goodbye to Bronchiolitis, Viral Wheeze, Reactive Airways Disease, Wheeze Bronchitis and All That. Front Pediatr. 2020 May 5;8:218. doi: 10.3389/fped.2020.00218. eCollection 2020.)** This causes difficulties in interpreting results of clinical trials, as the populations may display considerable heterogeneity. This article is based on UK guidelines.

**Causes**

Bronchiolitis happens when a virus infects the bronchioles, which are the smallest airways in the lungs. The infection makes the bronchioles swollen and irritated. Mucus collects in these airways, which makes it difficult for air to flow freely in and out of the lungs.

Bronchiolitis is usually caused by the respiratory syncytial virus (RSV). RSV is a common virus that infects just about every child by 2 years of age. Outbreaks of RSV infection often happen during the colder months of the year in some locations or the rainy season in others. A person can get it more than once. Bronchiolitis also can be caused by other viruses, including those that cause the flu or the common cold.

The viruses that cause bronchiolitis are easily spread. You can get them through droplets in the air when someone who is sick coughs, sneezes or talks. You also can get them by touching shared items — such as dishes, doorknobs, towels or toys — and then touching your eyes, nose or mouth.

Bronchiolitis is caused by a viral infection, most often respiratory syncytial virus (RSV). This is responsible for up to 80% of cases. Other possible viral causative agents include human metapneumovirus (hMPV), adenovirus, bocavirus, rhinovirus, and parainfluenza and influenza viruses. In some cases there may be infection with more than one virus.

* [Respiratory syncytial virus](https://my.clevelandclinic.org/health/diseases/rsv-respiratory-syncytial-virus" \t "_blank) (RSV).
* [Influenza](https://my.clevelandclinic.org/health/articles/influenza" \t "_blank) (flu) virus.
* [Adenovirus](https://my.clevelandclinic.org/health/diseases/23022-adenovirus" \t "_blank).
* [Parainfluenza](https://my.clevelandclinic.org/health/diseases/24522-parainfluenza" \t "_blank).
* [Metapneumovirus](https://my.clevelandclinic.org/health/diseases/22443-human-metapneumovirus-hmpv" \t "_blank).
* SARS-Cov-2 (the virus that causes [COVID](https://my.clevelandclinic.org/health/diseases/21214-coronavirus-covid-19" \t "_blank)).
* Bronchiolitis typically occurs in infants under the age of 2 years, peaking between the ages of 3 months and 6 months.
* It is the most common lower respiratory infection in the first year of life in the UK. Around a third of babies develop bronchiolitis before the age of 1 year, and 2-3% of infants with bronchiolitis require hospitalisation.
* In 2019/20 in England, there were 47,506 admissions for bronchiolitis.**[5](https://patient.info/doctor/bronchiolitis-pro" \l "ref-5" \o "Interactive Health Atlas of Lung conditions in England (INHALE): February 2022 update; Office for Health Improvement & Disparities, 1 February 2022.)**
* Bronchiolitis is the leading cause of hospitalisation in the under 2s in the UK.
* Peak incidence is in the winter months (October to March). There tends to be an annual 6- to 8-week epidemic where incidence peaks.
* In 2021, there was an unprecedented summertime surge in bronchiolitis cases in the UK, probably due to a very low number of cases in the prior winter (itself due to Covid-19 control measures) and resulting low levels of RSV immunity.**[6](https://patient.info/doctor/bronchiolitis-pro" \l "ref-6" \o "Bardsley M, Morbey RA, Hughes HE, et al; Epidemiology of respiratory syncytial virus in children younger than 5 years in England during the COVID-19 pandemic, measured by laboratory, clinical, and syndromic surveillance: a retrospective observational study. La)**

**Risk factors**

Bronchiolitis usually affects children under the age of 2 years. Infants younger than 3 months have the highest risk of getting bronchiolitis because their lungs and their ability to fight infections aren't yet fully developed. Rarely, adults can get bronchiolitis.

Other factors that increase the risk of bronchiolitis in infants and young children include:

* (Being born too early) Were born before 37 weeks of pregnancy.
* Having a heart or lung condition Have a congenital (present at birth) lung or heart condition.
* Having a weakened immune system. This makes it hard to fight infections.
* (Passive smoke, particularly maternal) Being around tobacco smoke.
* Contact with lots of other children, such as in a child care setting.
* (Overcrowding) Spending time in crowded places.
* (Older siblings) Having siblings who go to school or get child care services and bring home the infection.
* Nursery attendance.

**Signs & Symptoms**

For the first few days, the symptoms of bronchiolitis are much like a cold:

* Either wheeze or crackles on chest auscultation (or both)
* Either tachypnoea or chest recession (or both)
* Persistent cough
* Runny nose.
* Stuffy nose.
* Sometimes a slight fever.

Later, your child may have a week or more of working harder than usual to breathe, which may include wheezing.

Many infants with bronchiolitis also have an ear infection called otitis media.

Other typical features include fever (usually of less than 39°C) and poor feeding. Consider an alternative diagnosis such as pneumonia if temperature is higher and crackles are focal. Consider viral-induced wheeze or early-onset asthma if there is wheeze without crackles, episodic symptoms and/or a family history of atopy. These, however, are rare in children under the age of 1.

Very young babies may present with apnoea alone, with no other signs.

**Diagnosis Mapping**

Doctors will usually start with a basic physical exam when determining if a child has bronchiolitis. Additional tests may be necessary if symptoms are severe. A chest X-ray may be needed to look for signs of pneumonia. A blood test may be needed to check white blood cell count for signs of infection. A doctor may take a nose swab to test your child’s mucus in an attempt to identify the virus that is causing the infection.

Your child's health care provider can usually diagnose bronchiolitis by the symptoms and listening to your child's lungs with a stethoscope.

Tests and X-rays are not usually needed to diagnose bronchiolitis. But your child's provider may recommend tests if your child is at risk of severe bronchiolitis, if symptoms are getting worse or if the provider thinks there may be another problem.

Tests may include:

* **Chest X-ray.**A chest X-ray can show if there are signs of pneumonia.
* **Viral testing.**A sample of mucus from your child's nose can be used to test for the virus causing bronchiolitis. This is done using a swab that's gently inserted into the nose.
* **Blood tests.**Occasionally, blood tests might be used to check your child's white blood cell count. An increase in white blood cells is usually a sign that the body is fighting an infection. A blood test also can show if the level of oxygen in your child's bloodstream is low.

Your child's provider may look for symptoms of dehydration, especially if your child has been refusing to drink or eat or has been vomiting. Signs of dehydration include dry mouth and skin, extreme tiredness, and making little or no urine.

**Treatment Options**

There are no vaccines or specific treatments for bronchiolitis. Antibiotics and cold medicine are not effective in treating bronchiolitis. Most cases go away on their own and can be cared for at home.

It is key that your child drinks lots of fluids to avoid dehydration. To aid your infant’s breathing, your doctor may recommend saline nose drops. Using a suction bulb to clear your child’s nasal airways is also a simple solution. Your doctor may recommend acetaminophen if they develop a fever. About three percent of children with bronchiolitis will need to be hospitalized. Here the child may be put on humidified oxygen and receive fluids through an IV to prevent dehydration. For the most severe cases, the child may have to have a tube inserted into the windpipe to aid breathing. Most children will be sent home between 2 and 8 days in the hospital.

The management of bronchiolitis is primarily supportive, and it usually focuses on ensuring hydration, performing upper airway suctioning as needed, and monitoring for signs of respiratory failure or the need for intubation and mechanical ventilation. Infants with oxygen saturation levels below 92% in room air should receive supplemental oxygen, and continuous pulse oximetry monitoring is recommended for hospitalized patients.

Antipyretics should be administered if a fever develops. Although bronchodilators are not universally effective, a trial of aerosolized albuterol may be considered, especially for infants with severe respiratory compromise. Glucocorticoids and racemic epinephrine have not shown efficacy and are not recommended. Antibiotics should be reserved for cases with clear evidence of a superimposed infection in addition to bronchiolitis.

If an infant tests positive for influenza, oseltamivir (Tamiflu™) is recommended, particularly if administered within the first 48 hours of symptom onset. Early initiation of this antiviral improves its effectiveness and may positively impact the course of the illness. Similarly, if SARS-CoV-2 is identified, treatment with nirmatrelvir-ritonavir (Paxlovid™) can be considered. Prevention is preferred over treatment, and new tools are now available to help prevent bronchiolitis. Palivizumab (Synagis™)—a monoclonal antibody targeting the F protein of RSV—was previously recommended for high-risk infants during their first year. This product was administered monthly via intramuscular injection during RSV season but was unavailable for otherwise healthy infants in their first 3 months of life—a group that experiences a substantial burden of RSV disease cases.

Fortunately, 2 options are now available for RSV prevention—vaccination of pregnant individuals with an RSV vaccine (Abrysvo™) or administering the newer monoclonal antibody nirsevimab (Beyfortus™) to infants during their first RSV season if the birth parent did not receive an RSV vaccine. The availability of these products may vary, so clinicians should consult local guidelines for administration in case of limited supplies.

Vaccines are available for influenza and SARS-CoV-2, which, although contributing significantly to the overall burden of respiratory disease, account for only a small proportion of bronchiolitis cases. Nonetheless, the American Academy of Pediatrics and other healthcare organizations recommend age-appropriate vaccination for all infants and children to prevent these infections. For infants too young for vaccination, vaccinating household members and close contacts is essential to minimize the risk of disease transmission.

Bronchiolitis usually lasts for 1 to 2 weeks but symptoms occasionally last longer. Most children with bronchiolitis can be cared for at home with comfort measures. It's important to be alert for problems with breathing that are getting worse. For example, struggling for each breath, not being able to speak or cry because of struggling to breathe, or making grunting noises with each breath.

Because viruses cause bronchiolitis, antibiotics — which are used to treat infections caused by bacteria — don't work against viruses. Bacterial infections such as pneumonia or an ear infection can happen along with bronchiolitis. In this case, your child's health care provider may give an antibiotic for the bacterial infection.

Medicines called bronchodilators that open the airways don't seem to help bronchiolitis, so they usually aren't given. In severe cases, your child's health care provider may try a nebulized albuterol treatment to see if it helps. During this treatment, a machine creates a fine mist of medicine that your child breathes into the lungs.

Oral corticosteroid medicines and pounding on the chest to loosen mucus, a treatment called chest physiotherapy, have not been shown to be effective for bronchiolitis and are not recommended.

**Hospital care**

A small number of children may need a stay in the hospital. Your child may receive oxygen through a face mask to get enough oxygen into the blood. Your child also may get fluids through a vein to prevent dehydration. In severe cases, a tube may be guided into the windpipe to help breathing.

Do not use any of the following to treat bronchiolitis in babies or children:

* antibiotics
* hypertonic saline
* adrenaline (nebulised)
* salbutamol
* montelukast
* ipratropium bromide
* systemic or inhaled corticosteroids
* a combination of systemic corticosteroids and nebulised adrenaline

**Prevention Tips**

Because the viruses that cause bronchiolitis spread from person to person, one of the best ways to prevent infection is to wash your hands often. This is especially important before touching your baby when you have a cold, flu or other illness that can be spread. If you have any of these illnesses, wear a face mask.

If your child has bronchiolitis, keep your child at home until the illness is past to avoid spreading it to others.

To help prevent infection/Prevention tips:

* Avoiding others who are sick.
* Practicing [good handwashing](https://my.clevelandclinic.org/health/articles/simple-secret-staying-well-wash-your-hands" \t "_blank).
* Washing and sanitizing frequently touched surfaces or objects like toys.
* Not sharing cups, forks or spoons.
* **Limit contact with people who have a fever or cold.** If your child is a newborn, especially a premature newborn, avoid being around people with colds. This is especially important in the first two months of life.
* **Clean and disinfect surfaces.** Clean and disinfect surfaces and items that people often touch, such as toys and doorknobs. This is especially important if a family member is sick.
* **Wash hands often.** Frequently wash your own hands and those of your child. Wash with soap and water for at least 20 seconds. Keep an alcohol-based hand sanitizer handy to use when you're away from home. Make sure it contains at least 60% alcohol.
* **Cover coughs and sneezes.** Cover your mouth and nose with a tissue. Throw away the tissue. Then wash your hands. If soap and water aren't available, use a hand sanitizer. If you don't have a tissue, cough or sneeze into your elbow, not your hands.
* **Use your own drinking glass.** Don't share glasses with others, especially if someone in your family is ill.
* **Breastfeed, when possible.** Respiratory infections are less common in breastfed babies.

**Prognosis**

The prognosis of bronchiolitis is generally favorable, with most infants recovering within 5 to 7 days. Although some studies suggest an increased risk of asthma following bronchiolitis, only a small percentage of affected children develop asthma. A history of recurrent wheezing and a positive family history of asthma, allergies, or atopic dermatitis may increase the likelihood of asthma development in these patients in the future.

Your child may have symptoms for up to a week if they have bronchiolitis. During their illness, they may have trouble eating full meals or lose their appetite. To help your child eat when they don’t want to, try feeding them multiple small meals throughout the day instead of larger meals less often. It’s important to keep your child hydrated since they’re at a high risk of dehydration during their illness.

To alleviate your child’s symptoms, talk to their healthcare provider to see what’s safe for your child to take, like over-the-counter (OTC) medications to reduce a fever. Don’t give your child aspirin, as it can lead to [Reye’s syndrome](https://my.clevelandclinic.org/health/articles/6088-reyes-syndrome" \t "_blank).

If your child has symptoms that don’t improve after one week or get worse, contact their healthcare provider. If your child has trouble breathing, contact emergency services or visit the emergency room immediately.

Some children develop asthma as they grow if they had bronchiolitis when they were infants. While less common, some children may develop pneumonia after bronchiolitis

* Most children with bronchiolitis make a full recovery.
* The illness is typically self-limiting, lasting 3-7 days. The cough settles within three weeks in most.
* Bronchiolitis is more likely to be severe in children with chronic lung disease, who are under 3 months of age or who were born <32 weeks of gestation.
* There is an association with long-term respiratory conditions such as asthma but it is not known if there is causality.
* Death from bronchiolitis is uncommon. In England there are around 70 deaths per year due to bronchiolitis. Most deaths occur in infants younger than 6 months or in those with underlying cardiac or pulmonary disease.

**Possible Complications**

Complications of severe bronchiolitis may include:

* Low oxygen in the body.
* Pauses in breathing, which is most likely to happen in babies born too early and in babies under 2 months old.
* Not being able to drink enough liquids. This can cause dehydration, when too much body fluid is lost.
* Not being able to get the amount of oxygen needed. This is called respiratory failure.

Acute complications of bronchiolitis include:

* Aspiration
* Respiratory failure
* Apnea
* Secondary bacterial infections
* Death

Chronic complications of bronchiolitis include:

* Recurrent episodes of wheezing
* Bronchiolitis obliterans

If any of these happen, your child may need to be in the hospital. Severe respiratory failure may require that a tube be guided into the windpipe. This helps your child breathe until the infection improves.

**When To See A Doctor/ Red Flags**

If symptoms become serious, call your child's health care provider. This is especially important if your child is younger than 12 weeks old or has other risk factors for bronchiolitis — for example, being born too early, also called premature, or having a heart condition.

Get medical attention right away if your child has any of these symptoms:

* Has blue or gray skin, lips and fingernails due to low oxygen levels.
* Struggles to breathe and can't speak or cry.
* Refuses to drink enough, or breathes too fast to eat or drink.
* Breathes very fast — in infants this can be more than 60 breaths a minute — with short, shallow breaths.
* Can't breathe easily and the ribs seem to suck inward when breathing in.
* Makes wheezing sounds when breathing.
* Makes grunting noises with each breath.
* Appears slow moving, weak or very tired.
* **Signs of severity:**
  + **Significant deterioration in general condition, toxic appearance (pallor, greyish colouration)**
  + **Apnoea, cyanosis (check lips, buccal mucosa, fingernails)**
  + **Respiratory distress (nasal flaring, sternal and chest wall indrawing)**
  + **Anxiety and agitation (hypoxia), altered level of consciousness**
  + **Respiratory rate > 60/minute**
  + **Decreased signs of respiratory distress (exhaustion) and decline of respiratory rate (< 30/minute below the age of 1 year and < 20/minute below the age of 3 years). Exercise caution in interpreting these signs as indicators of clinical improvement.**
  + **SpO2 persistently < 92%**
  + **Sweats, tachycardia at rest and in the absence of fever**
  + **Silence on auscultation (severe bronchospasm)**
  + **Difficulty drinking or sucking (reduced tolerance for exertion)**

**Differential Diagnosis**

* [Viral-induced wheeze.](https://patient.info/doctor/wheezing-in-children) Consider if there is wheeze but no crackles, a history of episodic wheeze, and/or a family or personal history of atopy.
* [Pneumonia](https://patient.info/doctor/pneumonia-pro). Consider if temperature is above 39°C and there are persistent focal crackles.
* [Asthma](https://patient.info/doctor/asthma-pro).
* [Bronchitis](https://patient.info/doctor/lower-respiratory-tract-infection-in-children).
* [Pulmonary oedema](https://patient.info/doctor/acute-pulmonary-oedema).
* [Foreign body inhalation](https://patient.info/doctor/choking-and-foreign-body-airway-obstruction-fbao).
* [Oesophageal reflux](https://patient.info/doctor/childhood-gastro-oesophageal-reflux-pro).
* [Aspiration](https://patient.info/doctor/aspiration-pneumonia-pro).
* [Cystic fibrosis](https://patient.info/doctor/cystic-fibrosis-pro).
* [Kartagener's syndrome](https://patient.info/doctor/kartageners-syndrome).
* [Tracheomalacia](https://patient.info/doctor/stridor)/bronchomalacia.
* [Pneumothorax](https://patient.info/doctor/pneumothorax-pro).

Drug Information / Side Effects

No Specific antoviral drug

**Bronchodilators**

Bronchodilators are frequently tried in infants presenting with wheezing due to bronchiolitis because of its similarity to asthma. Their routine use is controversial. Despite many randomized, controlled trials (RCT), no consistent benefit has been demonstrated. It is probably sensible to give a brief trial of bronchodilators to patients with bronchiolitis while the effect is carefully monitored, but their use should be continued only if clinical improvement can be documented by objective endpoints.

**Albuterol**

A number of small RCTs have evaluated the effectiveness of albuterol in the treatment of acute bronchiolitis, with conflicting results. A double-blind, placebo-controlled trial evaluated the efficacy of nebulized albuterol in the treatment of infants aged 0–24 months with wheezing ([Schweich et al 1992](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b54-tcrm-4-895)). Twenty-five infants were randomized to receive nebulized albuterol or saline placebo. The infants were assessed after each treatment for wheeze, retractions score, respiratory rate, heart rate, and pulse oximetry. In this study, the authors were able to demonstrate significant improvement in the wheeze and oxygenation scores of those infants that received albuterol, while no significant difference in the heart rate and respiratory rate were noted. These findings are supported by a Canadian double-blind, placebo-controlled trial that evaluated 40 infants between 6 weeks and 24 months of age with a first episode of wheezing and signs and symptoms of bronchiolitis ([Schuh et al 1990](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b52-tcrm-4-895)). Improvements were demonstrated in oxygenation and work of breathing after two doses of albuterol. A criticism of both of these studies is that the patients were not followed over time, and no effect was demonstrated in improved resolution of symptoms or in length of stay (LOS). In fact, several other studies have shown opposite results, suggesting that albuterol offers no consistent improvement in patients with bronchiolitis.

[Gadomski et al (1994)](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b22-tcrm-4-895) evaluated 88 infants with the first episode of wheezing in an emergency department setting. The subjects were randomized to receive two nebulized albuterol or nebulized placebo treatments 30 minutes apart or a single dose of oral albuterol or saline placebo. The investigators measured respiratory rate, heart rate, clinical scores, oxygen saturations and level of wakefulness. No significant difference was demonstrated among the four groups. [Klassen et al (1991)](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b35-tcrm-4-895) demonstrated a short-term improvement in clinical scores 30 minutes after a single albuterol treatment; however no difference was demonstrated 60 minutes after the treatment. There was no difference between the two groups when oxygenation was compared.

Inpatient trials have also failed to demonstrate benefit in patients receiving nebulized albuterol. A small RCT evaluated 52 hospitalized infants with moderately severe acute viral bronchiolitis ([Dobson et al 1998](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b17-tcrm-4-895)). There was no improvement in oxygenation, time to meet discharge criteria, or length of stay. A 1992 meta-analysis of 8 clinical trials examined several outcomes ([Flores and Horwitz 1997](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b20-tcrm-4-895)). The analysis was unable to demonstrate any impact on the hospitalization rate or respiratory rate. The authors did find a statistically significant, but clinically insignificant, improvement in oxygen saturation and heart rate. They concluded that evidence for the efficacy of β2-agonist therapy in bronchiolitis is lacking.

In summary, albuterol has not been shown to consistently reduce the duration or severity of illness or length of hospital stay, and so cannot be recommended for routine care of the patient with bronchiolitis. A carefully monitored trial in individual patients may be warranted, with discontinuation of therapy if no improvement is noted. Animal model studies suggesting that single-isomer preparations like levalbuterol may have a better anti-inflammatory effect than racemic albuterol in RSV-infected airways ([Auais et al 2005](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b3-tcrm-4-895)) have yet to be confirmed in clinical trials.

**Racemic epinephrine**

As with albuterol, the use of nebulized racemic epinephrine is controversial. No strong evidence exists to support its routine use; nevertheless, it is frequently used in wheezing infants with bronchiolitis. In a small, placebo-controlled, randomized trial, [Kristjansson et al (1993)](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b36-tcrm-4-895) demonstrated an improvement in oxygen saturations at 30, 45 and 60 minutes after inhalation of nebulized epinephrine. However, the authors were unable to show that these responses improved the overall course. A small, non-controlled trial investigated the use of nebulized l-epinephrine in intubated infants with bronchiolitis, showing a significant reduction in airway resistance after treatment with nebulized epinephrine ([Numa et al 2001](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b46-tcrm-4-895)). Despite this, there was no reduction in oxygen requirement.

More recently, a large RCT compared nebulized epinephrine with placebo in 194 infants hospitalized with bronchiolitis ([Wainwright et al 2003](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b66-tcrm-4-895)). Patients were randomized to receive 3 doses of nebulized epinephrine or placebo, 4 hours apart. The authors evaluated length of stay, respiratory and heart rates, work of breathing, and length of oxygen therapy, and, again, found no significant reduction in the measured outcomes.

Several studies have compared the efficacy of nebulized albuterol against epinephrine. In one such study, [Menon et al (1995)](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b43-tcrm-4-895) compared nebulized epinephrine to albuterol in an emergency department setting. Of those patients who received nebulized epinephrine, 33% required hospital admission compared with 81% of the albuterol group. In this study, the authors conclude that nebulized epinephrine is more effective than albuterol in preventing hospitalization of infants with bronchiolitis. In another evaluation of the efficacy of nebulized epinephrine versus albuterol, [Hartling et al (2003)](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b30-tcrm-4-895) conducted a meta-analysis of 14 available studies. Among outpatients, epinephrine was more effective than albuterol or placebo in the reduction of clinical score, improvement in oxygenation and respiratory rates, and overall improvement. The measured outcomes also indicated that epinephrine was more effective in the inpatient setting, with improvements in clinical score and respiratory rate. However, in 2004 a Cochrane report of the available data found a lack of evidence to support the use of epinephrine in the inpatient setting ([Hartling et al 2004](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b31-tcrm-4-895)). The report also determined that among outpatients, epinephrine may be more favorable than albuterol.

While no strong evidence exists to support the routine use of albuterol or epinephrine, the use of bronchodilators in select patients seems reasonable. When a bronchodilator trial is given, the available data supports the use of epinephrine over albuterol. If clinical improvement can be documented, then continued use is indicated. However, treatments should be discontinued if no improvement can be demonstrated. As epinephrine is typically not prescribed for use at home, albuterol may be a more appropriate choice for outpatient use.

**Anticholinergic agents**

Anticholinergic agents such as ipratropium bromide have not been demonstrated to be effective in the treatment of bronchiolitis. Several studies have evaluated ipratropium alone and with albuterol. While minor improvements in oxygenation have been reported, there is no consistent, significant benefit to the overall clinical course or outcome ([Wang et al 1992](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b67-tcrm-4-895); [Chowdhury et al 1995](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b12-tcrm-4-895); [Schuh et al 2002](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b53-tcrm-4-895)).

**Corticosteroids**

Corticosteroids are commonly used in the treatment of bronchiolitis as anti-inflammatory agents; their use may be as high as 60% of inpatient therapy ([Bronchiolitis 2006](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b8-tcrm-4-895)). Their appeal may be due to the similarities of bronchiolitis to asthma and to the role that corticosteroids play at many intracellular levels to reduce inflammation. In theory, corticosteroids should be of benefit in reducing the inflammatory response of the lower airways against viral infections, and for this reason they have been widely prescribed by physicians. But in reality, several studies and meta-analyses with corti-costeroids have failed to show any significant benefit in acute or long-term clinical outcomes of virus-induced wheezing, whether administered systemically or inhaled.

**Systemic corticosteroids**

Bulow et al investigated the short and long term effects of systemic corticosteroids in infants admitted with RSV bronchiolitis ([Bulow et al 1999](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b9-tcrm-4-895)). One hundred and forty-seven hospitalized infants were randomized to receive 2 mg/kg/day prednisolone or placebo for 5 days. Outcomes measured included length of stay and use of adjunctive medications and supportive therapies while hospitalized, as well as at 1 month and 1 year follow up. This study found no evidence that prednisolone effected any of the outcome measures. Schuh et al evaluated 70 children under the age of 2 years presenting to the emergency department with moderate or severe acute bronchiolitis ([Schuh et al 2002](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b53-tcrm-4-895)). The patients were randomized to receive 1 mg/kg of oral dexamethasone vs placebo, and were evaluated hourly for 4 hours. Each group also received nebulized albuterol at 0, 30, 60, and 120 minutes. The authors demonstrated a greater rate of clinical improvement among the dexamethasone group, to such extent that there was a decrease in the admission rate (19% vs 44%) compared with the placebo group.

In a more recent study conducted in Thailand, [Teeratakulpisarn et al (2007)](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b63-tcrm-4-895) evaluated 174 children hospitalized with acute bronchiolitis. The children were randomized to received 0.6 mg/kg of intramuscular dexamethasone or placebo. The authors evaluated the length of time to resolution of respiratory distress as the primary outcome. The duration of respiratory distress was decreased from 39 hours for the placebo group to 27.2 hours for the dexamethasone group, a difference of about 12 hours. The duration of oxygen was also reduced by 14.9 hours, and the hospital LOS was decreased by 13.4 hours.

Two meta-analyses are also available. [Garrison et al (2000)](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b23-tcrm-4-895) evaluated 6 studies with a combined total of 347 subjects. The outcomes measured included LOS and impact on severity of symptoms. The authors reported statistically significant reductions in clinical symptom scores and a reduction in LOS of 0.43 hospital days/patient. These numbers are similar to those reported by Teeratakulpisarn et al. Although the reduction of hospitalization by half a day would not be clinically significant for the individual patient, the authors argue that approximately 51,000 hospital days could be saved annually by the routine use of corticosteroids.

Patel et al conducted a larger systematic review of 13 trials of glucocorticoid therapy in 1198 children with viral wheezing aged 0–30 months ([Patel et al 2004](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b47-tcrm-4-895)). They found a similar decrease in LOS of 0.38 hospital days/patient, which however was not statistically significant. There was no difference in clinical scores, respiratory rate or oxygen saturation. For patients treated in the emergency department or clinic, there was no difference in admission rates. The authors do caution that significant heterogeneity of the included studies and results make the final analysis difficult to interpret with confidence, but concluded that this therapy lacks any significant clinical benefit compared to placebo and is not of benefit for this patient group.

In a more recent double blind, randomized trial, [Corneli et al (2007)](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b13-tcrm-4-895) compared oral dexamethasone with placebo to study whether a single dose of oral dexamethasone (1 mg/kg) could reduce the need for hospitalization. Over a 3-year period, the authors enrolled 600 infants between the ages of 2 and 12 months presenting to the emergency department with first-time wheezing and a diagnosis of moderate-severe bronchiolitis. The primary outcome was hospital admission after 4 hours of emergency department observation. Secondary and later outcomes measured included: change in a respiratory assessment score, length of hospital admission, later medical visits or hospital admissions and adverse events. The authors found that a single dose of dexamethasone did not change the rate of hospital admission or the severity score of bronchiolitis after 4 hours. They also found no change in later outcomes.

**Inhaled corticosteroids**

Several studies have evaluated inhaled corticosteroids in patients with bronchiolitis, but no consistent benefit has been demonstrated ([de Blic 2001](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b16-tcrm-4-895); [Chao et al 2003](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b11-tcrm-4-895)). A recent RCT compared 61 infants randomized to receive nebulized dexamethasone or saline; both groups also received nebulized epinephrine ([Bentur et al 2005](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b5-tcrm-4-895)). In this study, no statistically significant difference was noted in clinical score or oxygen saturation. There was, however, a significant reduction in LOS in the dexamethasone group, especially among the subgroup of prematurely born infants (6.5 ± 1.7 days vs 9.1 ± 1.9 days).

In a Cochrane review of 5 studies with a total of 374 infants, [Blom et al (2007)](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b6-tcrm-4-895) evaluated the use of inhaled corticosteroids to prevent post-bronchiolitic wheezing. This analysis demonstrated no reduction of wheezing, readmission rate, use of systemic corticosteroids or use of bronchodilators.

In general, young children without an atopic phenotype that wheeze in response to viral infections show a poor response to corticosteroids, and even children that will ultimately develop asthma are usually unresponsive to this therapy when they develop virus-induced wheezing during their first years of life. Another area of concern derives from safety considerations. In fact, severe RSV bronchiolitis typically occurs during the first year of life and coincides with a critical phase of rapid lung development. The safety of the therapeutic use of corticosteroids during this window, particularly at high doses and for prolonged periods, is virtually unknown and consequently no steroid has ever been approved by the US FDA for use in the first year of life.

We conclude that whether administered systemically or inhaled, corticosteroids should not be routinely used in the treatment of bronchiolitis. However, some specific patient populations may benefit from a trial of steroid therapy, particularly patients with family history (parental atopy or asthma) or medical history (atopic eczema) suggestive of atopic predisposition.

**Ribavirin**

Ribavirin is a synthetic nucleoside analog that demonstrates good in vitro activity against RSV. Several factors make its routine use controversial: it is expensive, difficult to administer, and possibly a teratogen. Furthermore, the available studies are all small, have inconsistent quality, and have produced conflicting results.

Early studies were encouraging. In 1983, [Hall et al (1983)](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b28-tcrm-4-895) randomized 33 infants hospitalized with RSV to continuous aerosolized ribavirin for 3–6 days versus placebo. The riba-virin group demonstrated a greater improvement in severity score, lower respiratory tract signs, oxygen saturations and viral shedding compared to the placebo group. [Rodriguez et al (1987)](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b50-tcrm-4-895) also demonstrated improved oxygenation and a greater rate of clinical improvement in patients receiving a short course of ribavirin, without evidence of adverse effects. [Smith et al (1991)](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b59-tcrm-4-895) conducted a double-blind, placebo-controlled trial of continuously aerosolized ribavirin in 28 mechanically ventilated infants with RSV infection, using nebulized sterile water as a control. This study reported a significant reduction in oxygen use and in the length of mechanical ventilation and hospitalization, especially among infants with no underlying illness, but these findings were criticized because bronchospasm associated with sterile water nebulization may artificially make ribavirin seem more effective ([Moler et al 1991](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b44-tcrm-4-895)).

A subsequent, well-designed study evaluated ribavirin against nebulized saline in 42 mechanically ventilated patients with RSV bronchiolitis and respiratory failure ([Guerguerian et al 1999](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b26-tcrm-4-895)). The authors found no significant improvement in the length of oxygen therapy, aerosol therapy, mechanical ventilation, PICU stay, or hospital stay. These findings were supported by a similar study performed by [Meert et al (1994)](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b42-tcrm-4-895). [Taber et al (1983)](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b62-tcrm-4-895) evaluated 26 infants randomized to receive ribavirin or placebo and found no difference in the rate of viral clearance between the two groups. In a longer outcome study, [Everard et al (2001)](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b18-tcrm-4-895) followed patients treated with ribavirin for RSV bronchiolitis over 1 year and was unable to demonstrate any short-term improvement in the clinical course or long-term reduction in the use of inhaled bronchodilators or steroids.

In the early 1990s, the AAP endorsed ribavirin use for RSV bronchiolitis. This stance has since changed and the current recommendation is that ribavirin should not be used routinely to treat children with bronchiolitis. It should, however, be considered to treat RSV infection in immuno-compromised hosts ([Bronchiolitis 2006](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b8-tcrm-4-895)).

**Antibiotics**

It is not uncommon for infants with bronchiolitis to receive antibiotic therapy. It is estimated that antibiotics are used in 34%–99% of uncomplicated bronchiolitis ([Kabir et al 2003](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b34-tcrm-4-895); [Vogel et al 2003](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b65-tcrm-4-895)). This therapy is frequently started because the patient is febrile, but fever per se cannot reliably differentiate viral from bacterial infections ([Putto et al 1986](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b49-tcrm-4-895)). In fact, the risk of bacterial superinfection in infants with bronchiolitis and fever is quite low (0.2%), even when the temperature is >39 °C ([Willwerth et al 2006](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b68-tcrm-4-895)). For intubated infants with severe bronchiolitis, the rate of secondary bacterial infection is much higher, and may be as high as 26% ([Spurling et al 2007](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b60-tcrm-4-895)).

When a secondary bacterial infection (SBI) is diagnosed, the most common sites are the urinary tract and the middle ear ([Andrade et al 1998](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b1-tcrm-4-895); [Purcell and Fergie 2004](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b48-tcrm-4-895)). In particular, infants with SBI are more likely to have a urinary tract infection than bacteremia or meningitis (12% vs 0.43%) ([Purcell and Fergie 2004](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b48-tcrm-4-895)). Acute otitis media (AOM) is also seen as a complication of RSV infection (57%–67%), but its presence does not seem to influence the severity of fever, respiratory distress, or the overall clinical course of the disease ([Shazberg et al 2000](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b57-tcrm-4-895)). In one series, evaluation of middle ear aspirates in children with bronchiolitis revealed RSV in 17 (71%) of 24 patients ([Andrade et al 1998](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b1-tcrm-4-895)). In addition, all patients with acute otitis media had bacterial pathogens isolated, the most common being Streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis. If present, AOM should be managed according to current AAP recommendations ([AOM 2004](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b2-tcrm-4-895); [Bronchiolitis 2006](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b8-tcrm-4-895)).

Several prospective RCTs have evaluated the clinical outcomes of infants who received antibiotics for the management of bronchiolitis. As early as 1966, a double blind RCT failed to demonstrate a benefit to treating bronchiolitis with antibiotics ([Field et al 1966](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b19-tcrm-4-895)). [Friis et al (1984)](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b21-tcrm-4-895) evaluated 136 children between the ages of 1 month and 6 years and found no difference in the course of the acute illness, fever relapse, or pulmonary complications in those patients with bronchiolitis who received antibiotics compared with those who did not ([Friis et al 1984](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b21-tcrm-4-895)).

We conclude that antibiotics should be used in patients with bronchiolitis only when specific evidence of coexistent bacterial infection is present and confirmed bacterial infections should be managed no differently than in the absence of bronchiolitis.

**Surfactant**

Beyond its role of decreasing surface tension in alveoli and bronchioles, thereby improving alveolar and small airway patency, surfactant has protein components (A and D) that bind viral and bacterial surface markers and facilitate their immune-mediated elimination ([Ventre et al 2006](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b64-tcrm-4-895)). In addition, surfactant protein D has been demonstrated to promote alveolar macrophage production of free radicals ([LeVine et al 2004](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b38-tcrm-4-895)). In acute bronchiolitis, there is decreased production of these surfactant proteins, which return to normal levels with the resolution of the illness ([Dargaville et al 1996](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b14-tcrm-4-895)).

Administration of exogenous surfactant to infants with severe respiratory failure due to bronchiolitis seems promising. Several small RCTs have been conducted to evaluate this therapy, with encouraging results. A recent meta-analysis by [Ventre et al (2006)](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b64-tcrm-4-895) included 3 studies with a total of 79 patients. The authors identify decreases in duration of mechanical ventilation and PICU stay. There also seem to be improvements in pulmonary mechanics and gas exchange. It is important to note that the available studies are small and underpowered, and that additional studies are required. However, exogenous surfactant therapy does appear to hold promise for use in patients with severe respiratory failure due to bronchiolitis.

**Heliox**

Medical helium for the treatment of upper airway obstruction and asthma was first described by Barach in the 1930s ([Barach and Eckman 1936](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b4-tcrm-4-895)). Heliox is a mixture of helium and oxygen in a 70:30 or 80:20 ratio that maintains greater laminar flow and less turbulence through constricted airways than does nitrogen-oxygen mixtures. This reduces work of breathing and improves ventilation in patients with lower respiratory tract disease. Heliox has been studied in the treatment of bronchiolitis by several investigators, although most of these studies are quite small. Some of the authors have shown small improvements in clinical scores and decreased tachypnea and work of breathing ([Hollman et al 1998](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b33-tcrm-4-895); [Martinon-Torres et al 2002](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b41-tcrm-4-895); [Cambonie et al 2006](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b10-tcrm-4-895)).

[Liet et al (2005)](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b39-tcrm-4-895) evaluated rates of positive pressure ventilation in patients receiving heliox therapy vs standard nitrogen-oxygen air and found no difference between the two groups. When heliox therapy was evaluated in intubated children with bronchiolitis, Gross et al found no improvement in ventilation or oxygenation, regardless of the ratio of helium to oxygen employed (50:50, 60:40, or 70:30) ([Gross et al 2000](https://pmc.ncbi.nlm.nih.gov/articles/PMC2621418/" \l "b25-tcrm-4-895)).

Heliox equipment is bulky and cumbersome and it can be problematic to administer. Furthermore, given that it is most effective at high helium to oxygen ratios, it is minimally effective in patients with higher oxygen requirements. In summary, the current evidence supporting heliox use for bronchiolitis is sparse, underpowered and conflicting, and therefore larger RCTs are required before it can be recommended for routine use.

**Summary**

Bronchiolitis is a common lower respiratory tract infection in infants caused by viral agents, the most common of which is RSV. Despite numerous attempts to identify pharmacological therapies to improve the clinical course and outcomes of this disease, the most effective therapy remains supportive care. Careful attention should be focused on maintaining patency of the infant’s airway with gentle nasal and pulmonary toilet. Supplemental humidified oxygen is frequently required to maintain oxygen saturations above 92%. Patients should be monitored to ensure adequate fluid and nutrition intake, which may require supplementation with naso-gastric feeds or intravenous fluids. Bronchodilators are not consistently effective, but may have some benefit in selected patients. If given to patients with bronchiolitis, their use should only be continued if objective measures demonstrate improvement in the patients oxygenation or work of breathing. Corticosteroids have not been shown to be effective and are not recommended for routine use. Ribavirin is not recommended for routine use in patients with bronchiolitis, although it may be of benefit in immunocompromised patients. Antibiotics should only be used in the presence of a confirmed bacterial infection. Surfactant and heliox therapies may be tried for the treatment of severe respiratory failure, although additional studies are needed before they can be recommended for routine use.

PROCEDURE EXPLANATIONS AND CLINICAL GUIDELINES

Oxygenation, hospitalization, airway clearance, and nutritional support as needed are often necessary in the hospitalized infant. The benefits of routine chest radiograms and antibiotics are unsupported. In addition, strong evidence of benefit from the routine use of bronchodilators, corticosteroids, and hypertonic saline remain inconclusive. With implementation of a guideline, we hope to reduce use of bronchodilators, corticosteroids, and nebulized hypertonic saline without adversely affecting outcomes or increasing length of stay (LOS).

PREDEFINED Q&A SETS (EXPERT-VALIDATED RESPONSES TO COMMON PATIENT QUERIES)

**What happens if a baby has bronchiolitis?**

Bronchiolitis causes the small breathing tubes of the lungs (bronchioles) to swell. This blocks airflow through the lungs, making it hard to breathe. It occurs most often in infants because their airways are smaller and more easily blocked than in older children.

**What is the difference between bronchiolitis and bronchitis?**

Bronchiolitis is not the same as bronchitis, which is an infection of the larger, more central airways that typically causes problems in adults.

**What causes bronchiolitis?**

Bronchiolitis is caused by one of several respiratory viruses such as influenza, respiratory syncytial virus (RSV), parainfluenza and human metapneumovirus. Other viruses can also cause bronchiolitis.

Infants with RSV infection are more likely to get bronchiolitis with wheezing and difficulty breathing. Most adults and many older children with RSV infection only get a cold.

RSV is spread by contact with an infected person's mucus or saliva (respiratory droplets produced during coughing or wheezing). It often spreads through families and child care centers.

What are the signs and ­symptoms of bronchiolitis?

Bronchiolitis often starts with signs of a [cold](https://www.healthychildren.org/English/health-issues/conditions/ear-nose-throat/Pages/Children-and-Colds.aspx), such as a runny nose, mild cough and [fever](https://www.healthychildren.org/english/health-issues/conditions/fever/Pages/default.aspx). After 1 or 2 days, the cough may get worse and an infant will begin to breathe faster. Your child may become dehydrated if they cannot comfortably drink fluids.

If your child shows any signs of troubled breathing or dehydration (see below), don't hesitate to call their pediatrician.

**The following signs may mean that your baby is having trouble breathing:**

* They may widen their nostrils and squeeze the ­muscles under their rib cage to try to get more air into and out of his lungs.
* When they breathe, they may grunt and tighten their stomach muscles.
* They will make a high-pitched whistling sound, called a wheeze, when they breathes out.
* They may have trouble drinking because they may have trouble sucking and swallowing.
* If it gets very hard for your baby to breathe, you may notice a bluish tint around their lips and fingertips. This tells you the airways are so blocked that there is not enough oxygen getting into their blood.

**Your child may become**[dehydrated](https://www.healthychildren.org/English/health-issues/injuries-emergencies/Pages/Avoiding-Dehydration.aspx)**if they cannot comfortably drink fluids. Call your child's doctor if your baby develops any of the following signs of dehydration:**

* Drinking less than normal
* Dry mouth
* Crying without tears
* Urinating less often than normal

Can bronchiolitis be treated at home?

There is no specific treatment for RSV or other viruses that cause bronchiolitis. Antibiotics are not helpful because they treat illnesses caused by bacteria, not viruses. However, you can try to ease your child's symptoms.

To relieve a stuffy nose

* Thin the mucus using saline nose drops recommended by your child's doctor. Never use nonprescription nose drops that contain medicine.
* Clear your baby's nose with a suction bulb. Squeeze the bulb first. Gently put the rubber tip into one nostril, and slowly release the bulb. This suction will draw the clogged mucus out of the nose. This works best when your baby is younger than 6 months.

To relieve fever

* Give your baby acetaminophen. (Follow the recommended dosage for your baby's age.) Do not give your baby aspirin because it has been associated with Reye syndrome, a disease that affects the liver and brain. Check with your child's doctor first before giving any other cold medicines.

**To prevent dehydration**

* Make sure your baby drinks lots of fluid. They may want clear liquids rather than milk or formula. Your baby may feed more slowly or not feel like eating because they are having trouble breathing.

Bronchiolitis and ­severe chronic illness

Bronchiolitis may cause more severe illness in ­children who have a chronic illness.

**If you think your child has bronchiolitis and they have any of the following conditions, be sure to call their doctor:**

* [Cystic fibrosis](https://www.healthychildren.org/English/health-issues/conditions/chronic/Pages/Cystic-Fibrosis.aspx)
* [Congenital heart disease](https://www.healthychildren.org/English/health-issues/conditions/heart/Pages/Congenital-Heart-Defects-Resources-to-Help-Your-Child-Thrive-From-Birth-to-Adulthood-.aspx)
* Chronic lung disease (seen in some infants who were on breathing machines or respirators as newborns)
* [Immune deficiency disease](https://www.healthychildren.org/English/health-issues/conditions/sexually-transmitted/Pages/HIV-Human-Immunodeficiency-Virus.aspx) such as acquired ­immunodeficiency syndrome (AIDS)
* Organ or bone marrow transplant
* A cancer for which she is receiving ­[chemotherapy](https://www.healthychildren.org/English/health-issues/conditions/cancer/Pages/Cancer-Therapies.aspx)

How will your child's doctor treat bronchiolitis?

Your child's doctor will evaluate your child and advise you on nasal suctioning, fever control and observation, as well as when to call back.

Some children with bronchiolitis need to be treated in a hospital for breathing problems or dehydration. Breathing problems may need to be treated with oxygen and medicine. Dehydration is treated with a special liquid diet or intravenous (IV) fluids.

In very rare cases when these treatments aren't working, an infant might have to be put on a respirator. This is usually only temporary until the infection is gone.

How can you prevent your baby from getting bronchiolitis?

The best steps you can follow to reduce the risk that your baby becomes infected with RSV or other viruses that cause bronchiolitis include

* Make sure everyone washes their hands before touching your baby.
* Keep your baby away from anyone who has a cold, fever, or runny nose.
* Avoid sharing eating utensils and drinking cups with anyone who has a cold, fever, or runny nose.
* [RSV immunization​](https://www.healthychildren.org/English/tips-tools/ask-the-pediatrician/Pages/is-the-rsv-immunization-available-for-infants.aspx) during pregnancy or for your baby right before or during RSV season.

**Medical Codes**

* **Includes: acute bronchiolitis with bronchospasm**
* **Excludes: respiratory bronchiolitis interstitial lung disease ([J84.115](https://www.aapc.com/codes/icd-10-codes/code_listing/J84.115" \t "_blank))**

|  |  |
| --- | --- |
| **J21** | **Acute bronchiolitis** |
| **[J21.0](https://www.aapc.com/codes/icd-10-codes/J21.0)** | **[Acute bronchiolitis due to respiratory syncytial virus](https://www.aapc.com/codes/icd-10-codes/J21.0)** |
| **[J21.1](https://www.aapc.com/codes/icd-10-codes/J21.1)** | **[Acute bronchiolitis due to human metapneumovirus](https://www.aapc.com/codes/icd-10-codes/J21.1)** |
| **[J21.8](https://www.aapc.com/codes/icd-10-codes/J21.8)** | **[Acute bronchiolitis due to other specified organisms](https://www.aapc.com/codes/icd-10-codes/J21.8)** |
| **[J21.9](https://www.aapc.com/codes/icd-10-codes/J21.9)** | **[Acute bronchiolitis, unspecified](https://www.aapc.com/codes/icd-10-codes/J21.9)** |

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**TUBERCULOSIS (TB)**

Definition

Tuberculosis, also called TB, is a serious illness that mainly affects the lungs. The germs that cause tuberculosis are a type of bacteria.

Tuberculosis can spread when a person with the illness coughs, sneezes or sings. This can put tiny droplets with the germs into the air. Another person can then breathe in the droplets, and the germs enter the lungs.

Tuberculosis spreads easily where people gather in crowds or where people live in crowded conditions. People with HIV/AIDS and other people with weakened immune systems have a higher risk of catching tuberculosis than people with typical immune systems.

TB is an infectious disease caused by a bacterium called *Mycobacterium tuberculosis*. It primarily affects the lungs but can also affect other parts of your body, such as the brain, lymph nodes, kidneys, bones, and joints.

While curable, TB remains a significant public health concern globally. In Singapore, TB is endemic and latent TB infection (LTBI) is not uncommon in our population. Refer to the Ministry of Health for the latest updates about the local TB situation.

What Are The Types Of Tb Conditions? /Other Names

Active TB disease occurs when the body is unable to kill or contain the bacteria, and the bacteria continues to grow. These individuals are infectious and may have symptoms. They should visit a doctor immediately to seek treatment.

However, not all individuals who are exposed to an infectious person will get active TB disease.

Some develop LTBI, (Latent Tuberculosis Infection) where the body is able to stop the bacteria from growing, rendering them inactive. These people do not have any symptoms (e.g. cough) and cannot spread TB to others.

In 90% of healthy persons with LTBI, the TB bacteria remain inactive throughout their life. However, the disease can be activated months or years later due to a weakened immune system, certain medical conditions, or other factors.

The most common type of TB is pulmonary (lung) tuberculosis. But the bacterium can also affect other parts of your body (extrapulmonary tuberculosis). You might also hear about miliary tuberculosis, which can spread throughout your body and cause:

* Meningitis, an inflammation of the lining of your brain
* Pott’s disease, also called spinal tuberculosis or tuberculosis spondylitis
* Addison’s disease, an adrenal gland condition
* Hepatitis, liver inflammation
* Scrofula, swollen lymph nodes in your neck

Causes

Tuberculosis is caused by a bacterium called Mycobacterium tuberculosis.

People with active TB disease in the lungs or voice box can spread the disease. They release tiny droplets that carry the bacteria through the air. This can happen when they're speaking, singing, laughing, coughing or sneezing. A person can get an infection after inhaling the droplets.

The disease is more likely to spread when people spend a lot of time together in an indoor space. So the disease spreads easily in places where people live or work together for long periods. Also, the disease spreads more easily in crowded gatherings.

A person with a latent TB infection cannot pass the disease to other people. A person taking medicine to treat active TB disease usually can't pass the disease after 2 to 3 weeks of treatment.

Risk Factors

Anyone can get tuberculosis, but certain factors increase the risk of getting an infection. Other factors increase the risk of an infection becoming active TB disease.

The Centers for Disease Control and Prevention recommends a TB test for people who have an increased risk of TB infection or active TB disease. Talk to your healthcare professional if you have one or more of the following risk factors.

**Risk of TB infection**

Certain living or working conditions make it easier for the disease to pass from one person to another. These conditions increase the risk of getting a TB infection:

* Living with someone with active TB disease.
* Living or traveling in a country where TB is common, including several countries in Latin America, Africa, Asia and the Pacific Islands.
* Living or working in places where people live close together, such as prisons, nursing homes and shelters for homeless people.
* Living in a community identified as being at high risk of tuberculosis.
* Working in healthcare and treating people with a high risk of TB.

**Risk of active TB disease**

A weakened immune system increases the risk of a TB infection becoming active TB disease. Conditions or treatments that weaken the immune system include:

* HIV/AIDS.
* Diabetes.
* Severe kidney disease.
* Cancers of the head, neck and blood.
* Malnutrition or low body weight.
* Cancer treatment, such as chemotherapy.
* Medicine to prevent rejection of transplanted organs.
* Long-term use of prescription steroids.
* Use of unlawful injected drugs.
* Misuse of alcohol.
* Smoking and using other tobacco products.

You might be at a higher risk for TB exposure if you:

* Are a resident or employee in group settings where TB can spread, such as jails, hospices, skilled nursing facilities, shelters and other healthcare facilities
* Work in a mycobacteriology laboratory
* Have lived in a region where TB is common, like Latin America, the Caribbean, Africa, Asia, Eastern Europe and Russia
* Have been in contact with someone who’s known or suspected to have TB disease

You might be at a higher risk for getting active TB if you:

* Inject intravenous drugs
* Have an immature, impaired or weakened immune system (including babies and children)
* Have kidney disease, diabetes or other chronic (long-term) illness
* Have received an organ transplant
* Are on chemotherapy treatment for cancer

**Age and active TB disease**

The risk of a TB infection becoming active TB disease changes with age.

* **Under 5 years of age.** Until children reach age 5, they have high risk of a TB infection becoming active TB disease. The risk is greater for children under age 2. Tuberculosis in this age group often leads to serious disease in the fluid surrounding the brain and spinal column, called meningitis.
* **Age 15 to 25.** People in this age group have an increased risk of developing more-severe active TB disease in the lungs.
* **Age 65 and older.** The immune system weakens during older age. Older adults have a greater risk of active TB disease. Also, the disease may be more difficult to treat.

Signs & Symptoms

When TB germs survive and multiply in the lungs, it is called a TB infection. A TB infection may be in one of three stages. Symptoms are different in each stage.

**Primary TB infection.** The first stage is called the primary infection. Immune system cells find and capture the germs. The immune system may completely destroy the germs. But some captured germs may still survive and multiply.

Most people don't have symptoms during a primary infection. Some people may get flu-like symptoms, such as:

* Low fever.
* Tiredness.
* Cough.

**Latent TB infection.** Primary infection is usually followed by the stage called latent TB infection. Immune system cells build a wall around lung tissue with TB germs. The germs can't do any more harm if the immune system keeps them under control. But the germs survive. There are no symptoms during latent TB infection.

**Active TB disease.** Active TB disease happens when the immune system can't control an infection. Germs cause disease throughout the lungs or other parts of the body. Active TB disease may happen right after primary infection. But it usually happens after months or years of latent TB infection.

Symptoms of active TB disease in the lungs usually begin gradually and worsen over a few weeks. They may include:

* Cough.
* Coughing up blood or sputum (mucus).
* Chest pain.
* Pain with breathing or coughing.
* Fever.
* Chills.
* Night sweats.
* Weight loss.
* Not wanting to eat.
* Tiredness.
* Not feeling well in general.

**Active TB disease outside the lungs.** TB infection can spread from the lungs to other parts of the body. This is called extrapulmonary tuberculosis. Symptoms vary depending on what part of the body is infected. Common symptoms may include:

* Fever.
* Chills.
* Night sweats.
* Weight loss.
* Not wanting to eat.
* Tiredness.
* Not feeling well in general.
* Pain near the site of infection.

Active TB disease in the voice box is outside the lungs, but it has symptoms more like disease in the lungs.

Common sites of active TB disease outside the lungs include:

* Kidneys.
* Liver.
* Fluid surrounding the brain and spinal cord.
* Heart muscles.
* Genitals.
* Lymph nodes.
* Bones and joints.
* Skin.
* Walls of blood vessels.
* Voice box, also called larynx.

**Active TB disease in children.** Symptoms of active TB disease in children vary. Typically, symptoms by age may include the following:

* **Teenagers.** Symptoms are similar to adult symptoms.
* **1- to 12-year-olds.** Younger children may have a fever that won't go away and weight loss.
* **Infants.**The baby doesn't grow or gain weight as expected. Also, a baby may have symptoms from swelling in the fluid around the brain or spinal cord, including:
  + Being sluggish or not active.
  + Unusually fussy.
  + Vomiting.
  + Poor feeding.
  + Bulging soft spot on the head.
  + Poor reflexes.

**Diagnosis and Testing**

WHO recommends the use of rapid molecular diagnostic tests as the initial diagnostic test in all persons with signs and symptoms of TB.

Rapid diagnostic tests recommended by WHO include the Xpert MTB/RIF Ultra and Truenat assays. These tests have high diagnostic accuracy and will lead to major improvements in the early detection of TB and drug-resistant TB.

A tuberculin skin test (TST), interferon gamma release assay (IGRA) or newer antigen-based skin tests (TBST) can be used to identity people with infection.

Diagnosing multidrug-resistant and other resistant forms of TB (see multidrug-resistant TB section below) as well as HIV-associated TB can be complex and expensive.

Tuberculosis is particularly difficult to diagnose in children.

Healthcare providers use a skin or blood test to diagnose TB. You might also need:

* Lab tests on sputum and lung fluid
* Chest X-ray
* Computed tomography (CT) scans

**Treatment**

Tuberculosis disease is treated with special antibiotics. Treatment is recommended for both TB infection and disease.

Healthcare providers treat both active and inactive tuberculosis with specific kinds of antibiotics. You’ll likely need to take a combination of medications to get rid of the infection.

You’ll have to take these medications for a long time — several months. You must take them exactly as your provider prescribes to get rid of all the bacteria. It’s very important to finish your entire prescription.

To be effective, medications need to be taken daily for 4–6 months. It is dangerous to stop the medications early or without medical advice as it can prompt TB bacteria in the body to become resistant to the drugs.

TB that doesn’t respond to standard drugs is called drug-resistant TB and requires treatment with different medicines.

If you have a latent TB infection, your healthcare professional may begin treatments. This is especially true for people with HIV/AIDS or other factors that increase the risk of active TB disease. Most latent TB infections are treated for three or four months.

Active TB disease may be treated for four, six or nine months. Specialists in TB treatment will determine which medicines are best for you.

You will have regular appointments to see if you're improving and to watch for side effects.

**Take all of the medicines**

It is important to take every dose as instructed. And you must complete the full course of treatment. This is important for killing the bacteria in your body and preventing new drug-resistant bacteria.

Your public health department may use a program called directly observed therapy (DOT). With DOT, a healthcare worker visits you at home to watch you take your dose of medicines.

Some healthcare departments have programs that let you take your medicines on your own. The Centers for Disease Control and Prevention has printable forms you can use to keep track of your daily doses.

**Most common TB medicines**

If you have a latent TB infection, you might need to take only one or two types of medicines. Active TB disease requires taking several medicines. Common ones used to treat tuberculosis include:

* Isoniazid (Hyzyd®).
* Rifampin (Rifadin®)
* Rifabutin (Mycobutin).
* Rifapentine (Priftin®).
* Pyrazinamide (Zinamide®).
* Ethambutol (Myambutol®).

You may be prescribed other medicines if you have drug-resistant tuberculosis or other complications from your illness.

Inactive TB

Treatment for inactive TB can take three, four, six, or nine months depending on the treatment plan.

The treatment plans for inactive TB use different combinations of medicines that may include:

* Isoniazid
* Rifampin
* Rifapentine

Keep Reading:Treating Inactive Tuberculosis

Active TB disease

Treatment for active TB disease can take four, six, or nine months depending on the treatment plan.

The treatment plans for active TB disease use different combinations of medicines that may include:

* Ethambutol
* Isoniazid
* Moxifloxacin
* Rifampin
* Rifapentine
* Pyrazinamide

For adolescents and adults with drug-susceptible pulmonary TB, the joint panel conditionally recommended the use of a 4-month regimen consisting of isoniazid, rifapentine, pyrazinamide, and moxifloxacin for 2 months, followed by isoniazid, rifapentine, and moxifloxacin for 2 months.

Dosing details are as follows:

* **Isoniazid**: 300 mg daily for 17 weeks
* **Rifapentine**: 1200 mg daily for 17 weeks
* **Pyrazinamide**: Weight-based dosing daily for 8 weeks
* **Moxifloxacin**: 400 mg daily for 17 weeks

The panel noted that this regimen avoids the potential ocular toxicity of the standard 6-month ethambutol-containing regimen. Baseline monitoring via electrocardiography (ECG) was not recommended for patients who initiate the shorter 4-month regimen unless certain clinical indications are present, such as older age, cardiac conditions, history of prolonged QT interval, or reported use of additional QT prolonging medications.

Prevention Tips

If you test positive for latent TB infection, you may need to take medicines to prevent active TB disease.

**Preventing the spread of disease**

If you have active TB disease, you'll need to take steps to prevent other people from getting an infection. You will take medicines for four, six or nine months. Take all of the medicines as directed during the entire time.

During the first 2 to 3 weeks, you will be able to pass TB bacteria to others. Protect others with these steps:

* **Stay home.** Don't go to work or school.
* **Isolate at home.** Spend as little time as possible among members of your household. Sleep in a separate room.
* **Ventilate the room.** Tuberculosis germs spread more easily in small, closed spaces. If it's not too cold outdoors, open the windows. Use a fan to blow air out. If you have more than one window, use one fan to blow air out and another to blow air in.
* **Wear face masks.** Wear a mask when you have to be around other people. Ask other members of the household to wear masks to protect themselves.
* **Cover your mouth.** Use a tissue to cover your mouth anytime you sneeze or cough. Put the dirty tissue in a bag, seal it and throw it away.
* [Washing your hands](https://my.clevelandclinic.org/health/articles/17474-hand-washing" \t "_blank) thoroughly and often
* Coughing into your elbow or covering your mouth when you cough
* Avoiding close contact with other people
* Making sure you take all your medications as prescribed
* Not returning to work or school until you’ve been cleared by your healthcare provider

Active TB

Active TB disease is treated with a combination of TB medications, administered for at least six to nine months. It is important for people with active TB disease to complete the course of the treatment, even if they feel better after the infectious period (first two weeks), as TB disease may recur or become resistant to medication, which becomes extremely difficult to treat.

For maximum efficacy, these individuals take their medication under the direct observation of a healthcare worker. This is called the Directly Observed Therapy (DOT). This ensures that they take the correct dosage and combination of medication, and are monitored to avoid treatment failure, drug resistance, and further spread of TB. Should their condition worsen, they may require hospitalisation or isolation.

Latent TB infection (LTBI)

Persons with LTBI may be offered preventive treatment, if suitable. It is important for these individuals to complete the course of their treatment (about four to six months) to reduce the risk of developing active TB disease in the future.

While the Bacillus Calmette-Guerin (BCG) Vaccine is available, it is only effective in protecting babies from TB meningitis and widespread TB. It offers limited protection against pulmonary (lung) TB, which is the most common form among adults.

**Vaccinations**

In countries where tuberculosis is common, infants often are vaccinated with the bacille Calmette-Guerin (BCG) vaccine. This protects infants and toddlers who are more likely to have active TB disease in the fluid surrounding the brain and spinal cord.

The vaccine may not protect against disease in the lungs, which is more likely in the United States. Dozens of new TB vaccines are in various stages of development and testing.

In children and adolescents aged 3 months to 16 years with nonsevere drug-susceptible pulmonary TB, the panel strongly recommended the use of a 4-month regimen consisting of a 2-month course of standard-dose isoniazid, rifampin, pyrazinamide, and ethambutol, followed by 2 months of isoniazid and rifampin. The 4-month regimen was recommended over the standard 6-month regimen of isoniazid, rifampin, pyrazinamide, and ethambutol for 2 months, followed by isoniazid and rifampin for 4 months.

Dosing details are as follows:

* Isoniazid: 10-15 mg/kg for 16 weeks
* **Rifampin**: 10-20 mg/kg for 16 weeks
* Pyrazinamide: 35 (range, 30-40) mg/kg for 8 weeks
* **Ethambutol**: 20 (range, 15-25) mg/kg for 8 weeks if indicated based on local guidelines

According to the panel, the shorter treatment regimen would be cost-saving but the extent of the savings is uncertain. They added that children and adolescents who do not meet criteria for nonsevere TB infection should receive the standard 6-month treatment regimen.

**Drug-Resistant TB**

In adults and adolescents aged 14 years and older infected with rifampin-resistant pulmonary TB, the panel recommended the use of a 6-month treatment regimen consisting of bedaquiline, pretomanid, and linezolid instead of previously endorsed 15-month regimens. They advised use of the 6-month regimen in patients with documented resistance or intolerance to fluoroquinolones who have either no history or less than 1 month of exposure to bedaquiline and linezolid.

Dosing details are as follows:

* **Bedaquiline**: 400 mg daily for 2 weeks, then 200 mg 3-times weekly for 24 weeks
* **Pretomanid**: 200 mg daily for 26 weeks
* **Linezolid**: 600 mg daily for 26 weeks

Patients with rifampin intolerance may also be eligible for the 6-month regimen of bedaquiline, pretomanid, and linezolid regardless of HIV status and CD4+ count. The panel recommended individualized regimens based on their 2019 guidelines for patients who are ineligible for the 6-month regimen due to multidrug- or rifampin-resistant TB.

Clinical monitoring should be performed at baseline, then in monthly intervals, and as needed. Moreover, baseline and follow-up ECG with QTc measurement should be performed during bedaquiline administration.

In adults and adolescents aged 14 years and older with rifampin-resistant, fluoroquinolone-susceptible pulmonary TB, the panel recommended a 6-month regimen consisting of bedaquiline, pretomanid, linezolid, and moxifloxacin instead of regimens lasting 15 months or longer.

Dosing details are as follows:

* Bedaquiline: 400 mg daily for 2 weeks, then 200 mg daily 3-times weekly for 24 weeks
* Pretomanid: 200 mg daily for 26 weeks
* Linezolid: 600 mg daily for 26 weeks
* Moxifloxacin: 400 mg daily for 26 weeks

The panel advised therapeutic drug monitoring to potentially help guide appropriate linezolid dosing, indicating a goal trough level above 2 µg/mL to minimize adverse reactions. They also stated that the 6-month regimen with moxifloxacin and the 6-month regimen without moxifloxacin require similar clinical considerations, including monitoring, as described above.

Limitations of this updated guidance include recommendations based on single or small studies that may not be representative of all TB populations in the US and Europe.

For TB management in adolescents and adults, “Studies assessing the cost-effectiveness, impact on health equity, acceptability, and feasibility of these newest regimens are needed,” study authors concluded.

Prognosis

**According to the Centers for Disease Control and Prevention (CDC)Trusted Source, TB is one of the world’s deadliest diseases, with approximately 1.3 million related deaths occurring worldwide in 2017. TB is also a leading cause of death among people who have HIV.**

**However, the CDC report Trusted Source that the incidence of TB in the U.S. has been steadily declining since 1993. The incidence of TB in 2018 was 2.8 cases per 100,000 persons, which is the lowest ever to be reported in the country.**

**In 2016, doctors attributed 528 deaths Trusted Source to TB in the U.S., an increase from the 470 deaths Trusted Source reported in 2015.**

**The CDC estimate Trusted Source that up to 13 million people in the U.S. may have latent TB and that around 1 in 10 of these individuals will develop active TB.**

**The risk of latent TB progressing to active TB is greater among people with weakened immune systems, including those who have HIV or who are receiving immunosuppressive therapy, such as for cancer or an organ transplant.**

**It is crucial that people seek medical attention if they experience symptoms of TB or have had contact with anyone who has active TB. The disease is highly treatable, especially when a person receives an early diagnosis.**

**Drug-Sensitive TB (Standard TB)**

* **Cure Rate:** ~**85-95%** with proper **6-month antibiotic treatment** (isoniazid, rifampin, ethambutol, pyrazinamide).
* **Relapse Rate:** **2-5%** after successful treatment, mostly if therapy was incomplete.
* **Mortality Rate:** **<5%** in healthy individuals, but higher in delayed treatment cases.

**. Multidrug-Resistant TB (MDR-TB)**

* **Cure Rate:** **60-70%** with **18-24 months of second-line drugs** (e.g., bedaquiline, linezolid).
* **Mortality Rate:** **Up to 30%** if untreated or poorly managed.
* **Higher relapse risk** compared to drug-sensitive TB.

**Extensively Drug-Resistant TB (XDR-TB)**

* **Cure Rate:** **30-50%**, depending on new treatments (e.g., pretomanid, delamanid).
* **Mortality Rate:** **40-60%** without effective therapy.

**TB in HIV-Positive Patients**

* **Higher mortality** (up to **20-30%**) if **CD4 count is very low**.
* **Antiretroviral therapy (ART) improves prognosis** (reduces mortality to **<10%**).

Possible Complications

Without treatment, TB can be fatal.

If it spreads throughout a person’s body, the infection can cause problems with the cardiovascular system and metabolic function, among other issues.

TB can also lead to sepsis, a potentially life threatening form of infection.

When To See A Doctor

If you’ve been exposed to TB, you should talk to your healthcare provider right away. They can talk to you about options for getting tested. It’s important to get tested if you’ve developed any symptoms — you could pass TB on to others.

If you’re taking medications to treat TB, talk to your provider about any side effects. Some side effects can be serious.

The symptoms of tuberculosis are similar to symptoms of many different illnesses. See your healthcare professional if you have symptoms that don't improve with a few days of rest.

Get emergency care if you have:

* Chest pain.
* Sudden, severe headache.
* Confusion.
* Seizures.
* Difficulty breathing.

Red Flags

Get immediate or urgent care if you

* Cough up blood.
* Have blood in your urine or stool.

Differential Diagnosis

To diagnosis a tuberculosis (TB) infection, your healthcare professional will do an exam that includes:

* Listening to you breathe with a stethoscope.
* Checking for swollen lymph nodes.
* Asking you questions about your symptoms.

**TB tests**

Your healthcare professional will order tests if:

* Tuberculosis is suspected.
* You were likely exposed to a person with active TB disease.
* You have health risks for active TB disease.

Your healthcare team will determine whether a skin test or blood test is the best option.

**Skin test**

A tiny amount of a substance called tuberculin is injected just below the skin on the inside of one forearm. Within 48 to 72 hours, a healthcare worker will check your arm for swelling at the injection site. The size of the raised skin is used to determine a positive or negative test.

This test is seeing if your immune system reacts, or has made an antibody, to tuberculosis. A positive test indicates you likely have either a latent TB infection or active TB disease. People who had a TB vaccination might get a positive test even if they have no infection.

A negative test means that your body didn't react to the test. It doesn't necessarily mean you don't have an infection.

**Blood tests**

A sample of blood is sent to a lab. One lab test finds out whether certain immune system cells can "recognize" tuberculosis. A positive test shows that you have either a latent TB infection or active TB disease. Other tests of the blood sample can help determine if you have active disease.

A negative result means you likely do not have a TB infection.

**X-ray**

A chest X-ray can show irregular patches in the lungs that are typical of active TB disease.

**Sputum tests**

Your healthcare professional may take a sample of the mucus that comes up when you cough, also called sputum. If you have active TB disease in your lungs or voice box, lab tests can detect the bacteria.

A relatively quick laboratory test can tell if the sputum likely has the TB bacteria. But it may be showing bacteria with similar features.

Another lab test can confirm the presence of TB bacteria. The results often take several weeks. A lab test also can tell if it's a drug-resistant form of the bacteria. This information helps your healthcare professional choose the best treatment.

**Other lab tests**

Other lab tests that may be ordered include:

* Breath test.
* Procedure to remove sputum from your lungs with a special tube.
* Urine test.
* Test of the fluid around the spine and brain, called cerebrospinal fluid.

Recent Guidelines

**EXECUTIVE SUMMARY**

Individuals infected with *Mycobacterium tuberculosis* (*Mtb*) may develop symptoms and signs of disease (TB disease) or may have no clinical evidence of disease (latent tuberculosis infection [LTBI]). TB disease is a leading cause of infectious disease morbidity and mortality worldwide, with many diagnostic uncertainties. A task force supported by the supported by the American Thoracic Society, Centers for Disease Control and Prevention, and Infectious Diseases Society of America appraised the evidence and derived the following recommendations using the Grading, Recommendations, Assessment, Development, and Evaluation (GRADE) approach (Table 1):

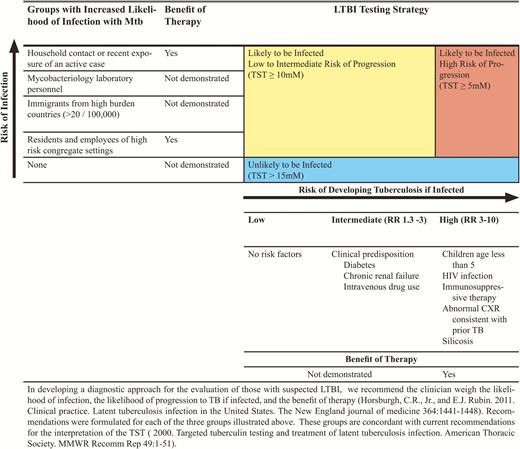
**Table 1.**

Interpretation of Strong and Weak (Conditional) Recommendations

|  | **Strong Recommendation** | **Weak (Conditional) Recommendation** |
| --- | --- | --- |
| Patients | Most individuals in this situation would want the recommended course of action, and only a small proportion would not. | The majority of individuals in this situation would want the suggested course of action, but many would not. |
| Clinicians | Most individuals should receive the intervention. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences. | Recognize that different choices will be appropriate for individual patients and that you must help each patient arrive at a management decision consistent with his or her values and preferences. Decision aids may be useful in helping individuals to make decisions consistent with their values and preferences. |
| Policy makers | The recommendation can be adopted as policy in most situations. | Policymaking will require substantial debate and involvement of various stakeholders. |

**Testing for LTBI**

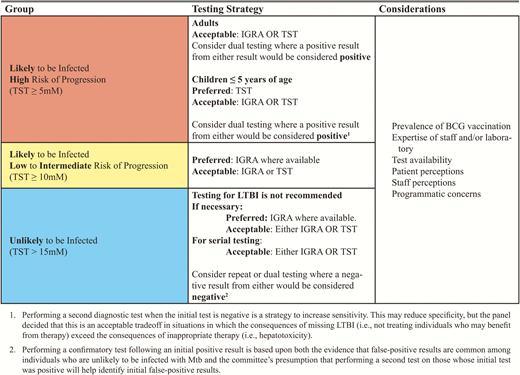
Our recommendations for diagnostic testing for LTBI are based upon the likelihood of infection with *Mtb* and the likelihood of progression to TB disease if infected, as illustrated in [Figure 1](javascript:;).



**Figure 1.**

Paradigm for evaluation of those with latent tuberculosis infection (LTBI) based on risk of infection, risk of progression to tuberculosis, and benefit of therapy. In developing a diagnostic approach for the evaluation of those with suspected LTBI, we recommend the clinician weigh the likelihood of infection, the likelihood of progression to tuberculosis if infected, and the benefit of therapy (Horsburgh and Rubin, Clinical practice: latent tuberculosis infection in the United States. N Engl J Med 2011; 364:1441–8). Recommendations were formulated for each of the 3 groups illustrated above. These groups are concordant with current recommendations for the interpretation of the tuberculin skin test (American Thoracic Society, Targeted tuberculin testing and treatment of latent tuberculosis infection. MMWR Recomm Rep 2000; 49:1–51). Abbreviations: CXR, chest radiograph; HIV, human immunodeficiency virus; LTBI, latent tuberculosis infection; *Mtb*, *Mycobacterium tuberculosis*; RR, ; TB, tuberculosis; TST, tuberculin skin test.

* We recommend performing an interferon-γ release assay (IGRA) rather than a tuberculin skin test (TST) in individuals 5 years or older who meet the following criteria: (1) are likely to be infected with *Mtb*, (2) have a low or intermediate risk of disease progression, (3) it has been decided that testing for LTBI is warranted, and (4) either have a history of BCG vaccination or are unlikely to return to have their TST read (*strong recommendation, moderate-quality evidence*). Remarks: A TST is an acceptable alternative, especially in situations where an IGRA is not available, too costly, or too burdensome.
* We suggest performing an IGRA rather than a TST in all other individuals 5 years or older who are likely to be infected with *Mtb*, who have a low or intermediate risk of disease progression, and in whom it has been decided that testing for LTBI is warranted (*conditional recommendation, moderate-quality evidence*). Remarks: A TST is an acceptable alternative, especially in situations where an IGRA is not available, too costly, or too burdensome.
* There are insufficient data to recommend a preference for either a TST or an IGRA as the first-line diagnostic test in individuals 5 years or older who are likely to be infected with *Mtb*, who have a high risk of progression to disease, and in whom it has been determined that diagnostic testing for LTBI is warranted.
* Guidelines recommend that persons at low risk for *Mtb* infection and disease progression NOT be tested for *Mtb* infection. We concur with this recommendation. However, we also recognize that such testing may be obliged by law or credentialing bodies. If diagnostic testing for LTBI is performed in individuals who are unlikely to be infected with *Mtb* despite guidelines to the contrary:
  + We suggest performing an IGRA instead of a TST in indivduals 5 years or older (*conditional recommendation, low-quality evidence*). Remarks: A TST is an acceptable alternative in settings where an IGRA is unavailable, too costly, or too burdensome.
  + We suggest a second diagnostic test if the initial test is positive in individuals 5 years or older (*conditional recommendation, very low-quality evidence*). Remarks: The confirmatory test may be either an IGRA or a TST. When such testing is performed, the person is considered infected only if both tests are positive.
* We suggest performing a TST rather than an IGRA in healthy children <5 years of age for whom it has been decided that diagnostic testing for LTBI is warranted (*conditional recommendation, very low-quality evidence*). Remarks: In situations in which an IGRA is deemed the preferred diagnostic test, some experts are willing to use IGRAs in children over 3 years of age.
* The preceding recommendations are summarized in [Figure 2](javascript:;). While both IGRA and TST testing provide evidence for infection with Mtb, they cannot distinguish active from latent TB. Therefore, the diagnosis of active TB must be excluded prior to embarking on treatment for LTBI. This is typically done by determining whether or not symptoms suggestive of TB disease are present, performing a chest radiograph and, if radiographic signs of active TB (eg, airspace opacities, pleural effusions, cavities, or changes on serial radiographs) are seen, then sampling is performed and the patient managed accordingly.



**Figure 2.**

Summary of recommendations for testing for latent tuberculosis infection (LTBI). 1Performing a second diagnostic test when the initial test is negative is a strategy to increase sensitivity. This may reduce specificity, but the panel decided that this is an acceptable trade-off in situations in which the consequences of missing LTBI (ie, not treating individuals who may benefit from therapy) exceed the consequences of inappropriate therapy (ie, hepatotoxicity). 2Performing a confirmatory test following an initial positive result is based upon both the evidence that false-positive results are common among individuals who are unlikely to be infected with *Mycobacterium tuberculosis* and the committee’s presumption that performing a second test on those patients whose initial test was positive will help identify initial false-positive results. Abbreviations: IGRA, interferon-γ release assay; LTBI, latent tuberculosis infection; TST, tuberculin skin test.

**Testing for TB Disease**

* We recommend that acid-fast bacilli (AFB) smear microscopy be performed, rather than no AFB smear microscopy, in all patients suspected of having pulmonary TB (*strong recommendation, moderate-quality evidence*). Remarks: False-negative results are sufficiently common that a negative AFB smear result does not exclude pulmonary TB. Similarly, false-positive results are sufficiently common that a positive AFB smear result does not confirm pulmonary TB. Testing of 3 specimens is considered the normative practice in the United States and is strongly recommended by the Centers for Disease Control and Prevention and the National Tuberculosis Controllers Association in order to improve sensitivity given the pervasive issue of poor sample quality. Providers should request a sputum volume of at least 3 mL, but the optimal volume is 5–10 mL. Concentrated respiratory specimens and fluorescence microscopy are preferred.
* We suggest that both liquid and solid mycobacterial cultures be performed, rather than either culture method alone, for every specimen obtained from an individual with suspected TB disease (*conditional recommendation, low-quality evidence*). Remarks: The conditional qualifier applies to performance of both liquid and solid culture methods on all specimens. At least liquid culture should be done on all specimens as culture is the gold standard microbiologic test for the diagnosis of TB disease. The isolate recovered should be identified according to the Clinical and Laboratory Standards Institute guidelines and the American Society for Microbiology Manual of Clinical Microbiology.
* We suggest performing a diagnostic nucleic acid amplification test (NAAT), rather than not performing a NAAT, on the initial respiratory specimen from patients suspected of having pulmonary TB (*conditional recommendation, low-quality evidence*). Remarks: In AFB smear-positive patients, a negative NAAT makes TB disease unlikely. In AFB smear-negative patients with an intermediate to high level of suspicion for disease, a positive NAAT can be used as presumptive evidence of TB disease, but a negative NAAT cannot be used to exclude pulmonary TB. Appropriate NAAT include the Hologic Amplified *Mycobacteria Tuberculosis* Direct (MTD) test (San Diego, California) and the Cepheid Xpert MTB/Rif test (Sunnyvale, California).
* We recommend performing rapid molecular drug susceptibility testing for rifampin with or without isoniazid using the respiratory specimens of persons who are either AFB smear positive or Hologic Amplified MTD positive and who meet one of the following criteria: (1) have been treated for tuberculosis in the past, (2) were born in or have lived for at least 1 year in a foreign country with at least a moderate tuberculosis incidence (≥20 per 100 000) or a high primary multidrug-resistant tuberculosis prevalence (≥2%), (3) are contacts of patients with multidrug-resistant tuberculosis, or (4) are HIV infected (*strong recommendation, moderate-quality evidence*). Remarks: This recommendation specifically addresses patients who are Hologic Amplified MTD positive because the Hologic Amplified MTD NAAT only detects TB and not drug resistance; it is not applicable to patients who are positive for types of NAAT that detect drug resistance, including many line probe assays and Cepheid Xpert MTB/RIF.
* We suggest mycobacterial culture of respiratory specimens for all children suspected of having pulmonary TB (*conditional recommendation, moderate-quality evidence*). Remarks: In a low incidence setting like the United States, it is unlikely that a child identified during a recent contract investigation of a close adult/adolescent contact with contagious TB was, in fact, infected by a different individual with a strain with a different susceptibility pattern. Therefore, under some circumstances, microbiological confirmation may not be necessary for children with uncomplicated pulmonary TB identified through a recent contact investigation if the source case has drug- susceptible TB.
* We suggest sputum induction rather than flexible bronchoscopic sampling as the initial respiratory sampling method for adults with suspected pulmonary TB who are either unable to expectorate sputum or whose expectorated sputum is AFB smear microscopy negative (*conditional recommendation, low-quality evidence*).
* We suggest flexible bronchoscopic sampling, rather than no bronchoscopic sampling, in adults with suspected pulmonary TB from whom a respiratory sample cannot be obtained via induced sputum (*conditional recommendation, very low-quality evidence*). Remarks: In the committee members’ clinical practices, bronchoalveolar lavage (BAL) plus brushings alone are performed for most patients; however, for patients in whom a rapid diagnosis is essential, transbronchial biopsy is also performed.
* We suggest that postbronchoscopy sputum specimens be collected from all adults with suspected pulmonary TB who undergo bronchoscopy (*conditional recommendation, low-quality evidence*). Remarks: Postbronchoscopy sputum specimens are used to perform AFB smear microscopy and mycobacterial cultures.
* We suggest flexible bronchoscopic sampling, rather than no bronchoscopic sampling, in adults with suspected miliary TB and no alternative lesions that are accessible for sampling whose induced sputum is AFB smear microscopy negative or from whom a respiratory sample cannot be obtained via induced sputum (*conditional recommendation, very low-quality evidence*). Remarks: Bronchoscopic sampling in patients with suspected miliary TB should include bronchial brushings and/or transbronchial biopsy, as the yield from washings is substantially less and the yield from BAL unknown. For patients in whom it is important to provide a rapid presumptive diagnosis of tuberculosis (ie, those who are too sick to wait for culture results), transbronchial biopsies are both necessary and appropriate.
* We suggest that cell counts and chemistries be performed on amenable fluid specimens collected from sites of suspected extrapulmonary TB (*conditional recommendation, very low-quality evidence*). Remarks: Specimens that are amenable to cell counts and chemistries include pleural, cerebrospinal, ascitic, and joint fluids.
* We suggest that adenosine deaminase levels be measured, rather than not measured, on fluid collected from patients with suspected pleural TB, TB meningitis, peritoneal TB, or pericardial TB (*conditional recommendation, low- quality evidence*).
* We suggest that free IFN-γ levels be measured, rather than not measured, on fluid collected from patients with suspected pleural TB or peritoneal TB (*conditional recommendation, low-quality evidence*).
* We suggest that AFB smear microscopy be performed, rather than not performed, on specimens collected from sites of suspected extrapulmonary TB (*conditional recommendation, very low-quality evidence*). Remarks: A positive result can be used as evidence of extrapulmonary TB and guide decision making because false-positive results are unlikely. However, a negative result may not be used to exclude TB because false-negative results are exceedingly common.
* We recommend that mycobacterial cultures be performed, rather than not performed, on specimens collected from sites of suspected extrapulmonary TB (*strong recommendation, low-quality evidence*). Remarks: A positive result can be used as evidence of extrapulmonary TB and guide decision making because false-positive results are unlikely. However, a negative result may not be used to exclude TB because false-negative results are exceedingly common.
* We suggest that NAAT be performed, rather than not performed, on specimens collected from sites of suspected extrapulmonary TB (*conditional recommendation, very low-quality evidence*). Remarks: A positive NAAT result can be used as evidence of extrapulmonary TB and guide decision making because false-positive results are unlikely. However, a negative NAAT result may not be used to exclude TB because false-negative results are exceedingly common. At present, NAAT testing on specimens other than sputum is an off-label use of the test.
* We suggest that histological examination be performed, rather than not performed, on specimens collected from sites of suspected extrapulmonary TB (*conditional recommendation, very low-quality evidence*). Remarks: Both positive and negative results should be interpreted in the context of the clinical scenario because neither false- positive nor false-negative results are rare.
* We recommend one culture isolate from each mycobacterial culture-positive patient be submitted to a regional genotyping laboratory for genotyping (*strong recommendation, very low-quality evidence*).

Persons infected with *Mycobacterium tuberculosis (Mtb*) have a broad array of presentations, ranging from those with clinical, radiographic, and microbiological evidence of tuberculosis (TB disease) to those who are infected with *Mtb* but have no clinical evidence of TB disease (latent tuberculosis infection [LTBI]). Individuals with LTBI who have been recently exposed have an increased risk of developing TB, whereas those with remote exposure have less risk over time unless they develop a condition that impairs immunity. Operationally, recent exposure can be defined either epidemiologically (ie, as might occur in the setting of the household of an infectious case or occupational exposure) or immunologically (ie, conversion of a tuberculin skin test or interferon-γ release assay [IGRA] from negative to positive).

These clinical practice guidelines on the diagnosis and classification of tuberculosis in adults and children were prepared by a task force supported by the American Thoracic Society (ATS), the Centers for Disease Control and Prevention (CDC), and the Infectious Diseases Society of America (IDSA). Additionally, Fellows of the American Academy of Pediatrics participated in the development of these guidelines. The specific objectives of these guidelines are as follows:

* To define high- and low-risk patient populations based upon the results of epidemiological studies.
* To provide diagnostic recommendations that lead to beneficial treatments and favorable clinical outcomes.
* To describe a classification scheme for tuberculosis that is based on pathogenesis.

These guidelines target clinicians in high-resource countries with a low incidence of TB disease and LTBI, such as the United States. The recommendations may be less applicable to medium- and high-tuberculosis incidence countries. For such countries, guidance documents published by the World Health Organization (WHO) may be more suitable.

**HOW TO USE THESE GUIDELINES**

These guidelines are not intended to impose a standard of care. They provide the basis for rational decisions in the diagnostic evaluation of patients with possible LTBI or TB. Clinicians, patients, third-party payers, stakeholders, or the courts should never view the recommendations contained in these guidelines as dictates. Guidelines cannot take into account all of the often compelling unique individual clinical circumstances. Therefore, no one charged with evaluating clinicians’ actions should attempt to apply the recommendations from these guidelines by rote or in a blanket fashion. Qualifying remarks accompanying each recommendation are its integral parts and serve to facilitate more accurate interpretation. They should never be omitted when quoting or translating recommendations from these guidelines.

Medication Side Effects

**Key TB Drugs & Side Effects**

| **Drug** | **Common Side Effects** | **Serious Risks** |
| --- | --- | --- |
| **Isoniazid** | Peripheral neuropathy, rash | Hepatotoxicity |
| **Rifampin** | Orange bodily fluids, GI upset | Liver injury, drug interactions |
| **Ethambutol** | Vision changes (color blindness) | Optic neuritis |
| **Pyrazinamide** | Joint pain, hyperuricemia | Hepatotoxicity |
| **Bedaquiline** | Nausea, headache | QT prolongation, cardiac arrhythmias |
| **Linezolid** | Anemia, neuropathy | Bone marrow suppression |

Most people can take TB medicines without serious side effects. If you have serious side effects, your healthcare professional may ask you to stop taking a medicine. You may have to change the dose of a medicine.

Talk to your healthcare professional if you experience any of the following:

* Upset stomach.
* Vomiting.
* Loss of appetite.
* Severe diarrhea.
* Light-colored stool.
* Dark urine.
* Yellowish skin or eye color.
* Changes in vision.
* Dizziness or trouble with balance.
* Tingling in hands or feet.
* Easy bruising or bleeding.
* Unexplained weight loss.
* Unexplained tiredness.
* Sadness or depression.
* Rash.
* Joint pain.

It is important for you to list all medicines, dietary supplements or herbal remedies you take. You may need to stop taking some of these during your treatment.

Side effects

Most people can take their TB medicines without any problems. However, like all medicines, the medicines you take for inactive TB or active TB disease can have side effects.

People react differently to medicines. Tell your health care provider about anything you think is wrong.

Some side effects are minor.

For example, any TB medicine can cause a skin rash. Other TB medicines may cause an upset stomach or nausea. Taking your TB medicine with food can help your body absorb the medicine better.

The rifampin or rifapentine medicines may cause some body fluids to turn an orange color, such as:

* Urine (pee),
* Saliva,
* Tears,
* Sweat, and
* Breast milk.

This is normal and harmless. The color may fade over time. Also, your health care provider may tell you not to wear soft contact lenses because they may get permanently stained.

If you have any of these side effects, you can continue taking your medicine.

Other side effects are more serious.

If you have a serious side effect, call your health care provider immediately. Your health care provider may tell you to stop taking your medicines or to return to the clinic for tests. Serious side effects include:

* Liver injury
  + Abdominal pain
  + Nausea and vomiting
  + Skin and eyes turning yellow (also called jaundice)
* Dizziness or lightheadedness
* Loss of appetite
* Flu-like symptoms
* Tingling or numbness in your hands or feet

If you are taking isoniazid, you may have tingling or numbness in your hands and feet. Your health care provider may add vitamin B6 to your treatment plan to prevent this.

Special considerations

Children

There are several treatments available for children with inactive TB or active TB disease. Health care providers will consider a child's age, weight, and other factors when prescribing treatment.

People with HIV

There are several treatment options for people with HIV who have inactive TB or TB disease. Your health care provider will choose TB medicines that are recommended for people with HIV.

Staying on a treatment plan can be hard. You may already be taking medicines for HIV infection, and now you may need to take more pills. Talk with your health care provider to make a plan that works for you.

Pregnant women

If you are pregnant, your health care provider will choose TB medicines that are recommended for use during pregnancy. Your health care provider will monitor you and your baby during treatment for inactive TB or active TB disease. Tell your health care provider if you have any problems taking your medicine.

Epidemiology

A full discussion of these topics can be found in the Supplementary Materials. TB disease remains one of the major causes of morbidity and mortality in the world. The WHO estimates that 8.6 million new cases of tuberculosis occurred in 2014 and approximately 1.5 million persons died from the disease [4]. The emergence of drug-resistant tuberculosis has become apparent over the past 2 decades, and in particular, multidrug-resistant tuberculosis (MDR-TB; resistant to isoniazid and rifampin) and extensively drug-resistant tuberculosis (XDR-TB; resistant to isoniazid and rifampin, plus any fluoroquinolone and at least 1 of 3 injectable second-line drugs [ie, amikacin, kanamycin, or capreomycin]), which are more difficult to treat than drug-susceptible disease [[5](javascript:;), [6](javascript:;)]. The approximate number of cases of MDR-TB in the world is roughly 500 000 reported from at least 127 countries, and XDR-TB has been reported from 105 countries [4].

In the United States, 9412 cases of TB disease were reported in 2014, with a rate of 3.0 cases per 100 000 persons. Sixty-six percent of cases were in foreign-born persons; the rate of disease was 13.4 times higher in foreign-born persons than in US- born individuals (15.3 vs 1.1 per 100 000, respectively) [[7](javascript:;)]. An estimated 11 million persons are infected with Mtb [8]. Thus, although the case rate of TB in the United States has declined during the past several years, there remains a large reservoir of individuals who are infected with Mtb. Without the application of improved diagnosis and effective treatment for LTBI, new cases of TB will develop from within this group, which is therefore a major focus for the control and elimination of tuberculosis [9].

Mtb is transmitted from person to person via the airborne route [10]. Several factors determine the probability of Mtb transmission: (1) infectiousness of the source patient—a positive sputum smear for acid-fast bacilli (AFB) or a cavity on chest radiograph being strongly associated with infectiousness; (2) host susceptibility of the contact; (3) duration of exposure of the contact to the source patient; (4) the environment in which the exposure takes place (a small, poorly ventilated space providing the highest risk); and (5) infectiousness of the Mtb strain. In the United States, among contacts of patients with TB disease evaluated during a contact investigation, about 1% have TB disease themselves and 23% have a positive tuberculin skin test (TST) without evidence of tuberculosis disease and are considered to have LTBI [[11](javascript:;)]. Those who are household contacts and are exposed to patients who are smear positive have higher rates of both infection and disease [[12](javascript:;)]. Medical procedures that generate aerosols of respiratory secretions, such as sputum induction and bronchoscopy, entail significant risk for Mtb transmission unless proper precautions are taken [[13](javascript:;)].

**Medical Codes**

|  |  |  |
| --- | --- | --- |
| **Code** | **Description** | **Source** |
| **A15.0** | **Tuberculosis of lung, confirmed by sputum microscopy with/without culture** | **CDC ICD-10-CM 2024** |
| **A15.4** | **Tuberculosis of intrathoracic lymph nodes, confirmed** | **CMS 2024 ICD-10-CM** |
| **A15.5** | **Tuberculosis of larynx, trachea, and bronchus, confirmed** | **CDC ICD-10-CM 2024** |
| **A15.6** | **Tuberculous pleurisy, confirmed** | **CMS 2024 ICD-10-CM** |
| **A15.7** | **Primary respiratory tuberculosis, confirmed** | **CDC ICD-10-CM 2024** |
| **A16.0** | **Tuberculosis of lung without confirmation** | **CMS 2024 ICD-10-CM** |
| **A16.2** | **Tuberculosis of lung without mention of confirmation** | **CDC ICD-10-CM 2024** |
| **A16.3** | **Tuberculosis of lymph nodes without confirmation** | **CMS 2024 ICD-10-CM** |
| **A17.0** | **Tuberculous meningitis** | **CDC ICD-10-CM 2024** |
| **A17.81** | **Tuberculoma of brain and spinal cord** | **CMS 2024 ICD-10-CM** |
| **A18.01** | **Tuberculosis of spine** | **CDC ICD-10-CM 2024** |
| **A18.02** | **Tuberculosis of other bones** | **CMS 2024 ICD-10-CM** |
| **A18.11** | **Tuberculosis of kidney and ureter** | **CDC ICD-10-CM 2024** |
| **A18.2** | **Tuberculous peripheral lymphadenopathy** | **CMS 2024 ICD-10-CM** |
| **A18.31** | **Tuberculous peritonitis** | **CDC ICD-10-CM 2024** |
| **A18.39** | **Tuberculosis of intestines and mesenteric glands** | **CMS 2024 ICD-10-CM** |
| **A18.4** | **Tuberculosis of skin and subcutaneous tissue** | **CDC ICD-10-CM 2024** |
| **A18.51** | **Tuberculous keratitis** | **CMS 2024 ICD-10-CM** |
| **A18.6** | **Tuberculosis of ear** | **CDC ICD-10-CM 2024** |
| **A18.7** | **Tuberculosis of adrenal glands** | **CMS 2024 ICD-10-CM** |
| **A18.81** | **Tuberculosis of thyroid gland** | **CDC ICD-10-CM 2024** |
| **A18.82** | **Tuberculosis of spleen** | **CMS 2024 ICD-10-CM** |
| **A18.83** | **Tuberculosis of pancreas** | **CDC ICD-10-CM 2024** |
| **A18.84** | **Tuberculosis of other endocrine glands** | **CMS 2024 ICD-10-CM** |
| **A18.89** | **Tuberculosis of other specified sites** | **CDC ICD-10-CM 2024** |
| **A19.0** | **Acute miliary tuberculosis of a single site** | **CMS 2024 ICD-10-CM** |
| **A19.1** | **Acute miliary tuberculosis of multiple sites** | **CDC ICD-10-CM 2024** |
| **A19.2** | **Acute miliary tuberculosis, unspecified** | **CMS 2024 ICD-10-CM** |
| **B90.0** | **Sequelae of central nervous system tuberculosis** | **CDC ICD-10-CM 2024** |
| **B90.1** | **Sequelae of genitourinary tuberculosis** | **CMS 2024 ICD-10-CM** |
| **Z11.1** | **Encounter for screening for respiratory tuberculosis** | **CDC ICD-10-CM 2024** |

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**WHOOPING COUGH**

Definition

Whooping cough is an illness that can spread easily. It's also called pertussis. An infection with bacteria causes it. Many people with the illness get a serious hacking cough. Breathing in after coughing often causes a high-pitched noise that sounds like a "whoop."

Before the vaccine for pertussis came out, whooping cough was thought of as a childhood disease. Today, whooping cough mainly affects children too young to have gotten all their shots of the vaccine. The illness also tends to affect teenagers and adults whose protection from the vaccine has faded.

Deaths linked with whooping cough are rare. Most often, they occur in infants. But pregnant people can help protect their babies by getting a booster shot of the vaccine during pregnancy. Vaccination also is recommended for other people who will have close contact with an infant.

* Pertussis, also known as whooping cough, is an acute infectious disease caused by the bacterium *Bordetella pertussis*.
* Pertussis is a human disease and no animal or insect source, or vector is known to exist.
* CDC recommends vaccination and postexposure antimicrobial prophylaxis to prevent pertussis.

Causes

A type of bacteria called Bordetella pertussis causes whooping cough. When an infected person coughs or sneezes, tiny germ-filled droplets spray into the air. Anyone who happens to be nearby can breathe in the droplets. The bacteria that cause whooping cough also can spread when people are together for a long time. Or these germs can spread when people share breathing space, such as while holding a newborn on your chest.

Risk Factors

The whooping cough vaccine you receive as a child wears off over time. This leaves many teenagers and adults prone to the infection during an outbreak. And regular outbreaks still happen.

Certain infants are most at risk for serious health problems and death from whooping cough. These include babies younger than 12 months old who are not vaccinated or haven't received all their vaccine doses.

Signs & Symptoms

Once you become infected with whooping cough, it takes about 5 to 10 days for symptoms to start. Sometimes it takes up to three weeks. The symptoms often are mild at first. They may seem like those of a common cold. They can include:

* Runny or stuffy nose.
* Red, watery eyes.
* Fever.
* Cough.

After a week or two, the symptoms become worse. Thick mucus builds up inside the airways. This causes rapid coughing that can't be controlled. The cough can last for weeks or months, and it may be worse at night. Intense coughing attacks may cause:

* Vomiting.
* A red or blue face.
* Extreme tiredness.
* A high-pitched "whoop" sound during the next breath of air.

People with mild illnesses often don't make the whooping sound. Sometimes, an ongoing hacking cough is the only symptom of whooping cough in teens and adults.

Many babies with the illness don't cough at all. Some babies and young children might.

* Gag or struggle to breathe.
* Have skin, lips or nails that turn blue or purple.
* Have life-threatening pauses in breathing called apnea.

Diagnosis and Testing

It may take time to find out if you have whooping cough. The symptoms can seem like those of other common illnesses, such as a common cold or the flu.

Sometimes, healthcare professionals can determine that you have whooping cough by asking about your symptoms and doing a physical exam.

But you may need medical tests such as:

* **A nose or throat culture and test.** Your healthcare professional takes a mucus sample from the back of the throat, where the nose and throat meet. The sample is checked for signs of whooping cough bacteria.
* **Blood tests.** A blood sample may be taken and sent to a lab. The lab checks for certain proteins called antibodies that the body makes to fight infections. This is a general test and not specific for whooping cough.
* **A chest X-ray.** This test may be recommended to check for signs of pneumonia due to whooping cough.

**How doctors diagnose whooping cough**

Healthcare providers diagnose whooping cough by:

* Doing a physical exam
* Asking about your symptoms
* Collecting a mucus sample (nasopharyngeal swab) to send to a lab for testing

Prevention Tips

The best way to prevent whooping cough is with the pertussis vaccine. It's often given together with vaccines against two other serious diseases: diphtheria and tetanus. Healthcare professionals recommend starting vaccination during infancy.

The vaccine is a series of five shots. You might hear it called DTaP. It's most often given to children at these ages:

* 2 months.
* 4 months.
* 6 months.
* 15 to 18 months.
* 4 to 6 years.

**Vaccine side effects**

Most often, side effects of the vaccine are mild. They may include a fever, crankiness, headache, fatigue or soreness at the site of the shot.

**Booster shots**

Booster shots strengthen the body's defenses against whooping cough. They help protect against whooping cough, diphtheria and tetanus. You might hear your healthcare professional call your booster shot Tdap. It's recommended for the following people.

* **Pre-teens.** Protection from the pertussis vaccine tends to fade by age 11. So, healthcare professionals recommend a shot of Tdap at 11 or 12 years old.
* **Pregnant women.** Health experts now recommend getting a shot of Tdap between 27 and 36 weeks of each pregnancy. This also may give some protection to an infant during the first few months of life.
* **Adults.** Sometimes, Tdap is given instead of a booster shot for tetanus and diphtheria. The tetanus and diphtheria booster shot is recommended for adults every 10 years. If you're due for that shot and you've never received Tdap before, your healthcare professional likely will give you Tdap instead. That's because Tdap protects against all three diseases. In general, adults who never received the Tdap booster shot can get one at any time. It's key to make sure you're up to date on your shots at least two weeks before you get close to a baby. The vaccine lowers your risk of spreading whooping cough to infants.

**Preventive medications**

If you or your infant has been exposed to someone with whooping cough, talk with your healthcare professional. Medicines called antibiotics may be recommended to protect against infection if you:

* Are a healthcare professional.
* Are pregnant.
* Are younger than 12 months old.
* Have a health condition that could put you at risk of serious illness or complications. This includes conditions such as a weakened immune system or asthma.
* Live with someone who has whooping cough.
* Live with someone who is at high risk of serious illness or complications from a whooping cough infection. This includes babies and pregnant women.

Outlook / Prognosis

**What can I expect if I have pertussis?**

Whooping cough can make you feel miserable for weeks or months. And it’s possible to develop severe complications.

The good news is that your body will likely build up some immunity against *Bordetella pertussis* bacteria. So, you won’t get whooping cough again for a while — anywhere from four to 20 years, according to some experts. But you can get whooping cough again in the future once immunity wanes.

Your child might need to stay in the hospital, especially if they’re very young.

**When is it safe to return to daycare, school or work?**

It depends. If you or your child is taking antibiotics, it’s generally safe to return after five full days of treatment. Otherwise, you’re still contagious for three weeks after the start of the coughing fits.

Possible Complication

Teens and adults often recover from whooping cough with no problems. When other health conditions happen, they tend to be side effects of intense coughing, such as:

* Bruised or cracked ribs.
* Tissue that bulges through a weak spot in the muscles of the stomach area, called an abdominal hernia.
* Broken blood vessels in the skin or the whites of the eyes.

Teens and adults also can have:

* Loss of bladder control.
* Weight loss.
* Fainting.

**Infants**

Health conditions that can happen with whooping cough are more serious in infants, especially those under 6 months of age. They can include:

* The lung infection pneumonia.
* Ear infection.
* Slowed or stopped breathing.
* Dehydration or weight loss due to trouble feeding.
* Seizures.
* Brain damage.

Infants and toddlers have the highest risk of other health conditions due to whooping cough. So, they're more likely to need treatment for these in a hospital. Health conditions due to whooping cough can be life-threatening for infants younger than 6 months old.

Possible complications of whooping cough in infants and children include:

* Ear infections
* Nosebleeds
* Nutritional deficiencies (malnutrition)
* Pneumonia
* Problems with brain function (encephalopathy), which can lead to permanent brain damage or death
* Pulmonary hypertension
* Respiratory failure

Complications are usually the most severe in babies under 12 months of age. Infants are most likely to be hospitalized due to pertussis. And those who face the greatest risk of severe complications or death include infants who:

* Aren’t vaccinated (or whose birth mother didn’t receive the vaccine during pregnancy)
* Are immunocompromised
* Have severe asthma

Possible complications in adolescents and adults include:

* Broken rib
* Ear infections
* Fainting
* Migraines
* Pee leaking out (urinary incontinence)
* Pneumonia
* Unintended weight loss

**When to see a doctor**

Call your healthcare professional if ongoing coughing spells cause you or your child to:

* Vomit.
* Turn red, purple or blue.
* Breathe in with a whooping sound.
* Not drink enough fluid.

Call 911 or your local emergency number right away if you or your child seems to struggle to breathe. Also call for emergency care if you notice pauses in breathing.

Self Care

The following tips can help you deal with coughing spells while you recover from whooping cough at home:

* **Get plenty of rest.** A cool, quiet and dark bedroom may help you relax and rest better.
* **Drink plenty of fluids.** Water, juice and soups are good choices. Be aware of dehydration symptoms, especially if your child is sick. The symptoms include dry lips, crying without tears and urinating much less often.
* **Eat smaller meals.** To help prevent vomiting after coughing, eat smaller, more-frequent meals rather than large ones.
* **Clean the air.** Keep your home free of irritants that can trigger coughing spells. These include dust, tobacco smoke and fumes from fireplaces.
* **Prevent the spread of whooping cough.** Cover your cough or sneeze with a tissue or the inside of your elbow. Throw away used tissues right away. Wash your hands often and for at least 20 seconds. If you must be around others, wear a mask.

Stay home from work or school until you've completed at least five days of treatment. If a young child is sick, keep the child home from daycare until finishing five days of treatment. If you don't get treatment, it's safest to stay away from others for three weeks after your symptoms start. Your body gets rid of the bacteria by then, even though you may still have symptoms.

Most people with whooping cough can manage their symptoms at home.

* Take antibiotics exactly as prescribed by your healthcare provider.
* Keep your home free from things that cause coughing like
  + Smoke
  + Dust
  + Chemical fumes
* Use a clean, cool mist humidifier to loosen mucus and soothe the cough.
* Eat small meals every few hours to help prevent vomiting.
* Get plenty of fluids, including water, juices, and fruits.

**Don't take** **cough medicine** unless your healthcare provider recommends it. Giving cough medicine probably won't help and isn't usually recommended for children younger than 4 years old.

Things you can do to feel a little better — and possibly ease coughing at night — include:

* **Take some honey**. This may help calm your cough. But it’s only safe for adults and kids over age 1. Never give honey to an infant (because of the risk of botulism).
* **Rest**. Getting lots of rest helps your body heal.
* **Keep up the fluids**. Drinking plenty of fluids can help thin the mucus that’s making you cough.
* **Use a cool-mist humidifier**. This helps break up mucus.
* **Eat small meals**. Eating just a small amount of food at a time may keep you from vomiting.
* **Avoid irritants**. Things like dust, smoke and chemical fumes (for example, from some cleaning supplies) might make you cough.

Epidemiology

Due to a low acceptance of active immunization against Bordetella pertussis, whooping cough continues to be a frequent childhood disease in parts of Germany. The age distribution in the lower Rhine area showed a peak incidence at 4.3 years of age, whereas 11% of all cases were observed in infants, and 6% were observed in adults. A significant sex difference was not found in children suffering from pertussis; in adult patients, however, women were more often affected. Whooping cough occurred during the whole year, its peak incidence was found during early winter. In children, paroxysmal coughing fits, vomiting and whooping were the primary symptoms of disease; adults and infants, however, developed these symptoms only in reduced frequency. About 25% of all cases showed an atypical course, and could only be diagnosed by laboratory tests. While leukocyte count and ESR did not have diagnostic significance, a combination of microbiological and serological tests showed a high diagnostic sensitivity and specificity. In contrast to the former GDR and to most European neighbours, the former Federal Republic overrated the side effects of active vaccination as compared to the various risks of natural infection. This resulted in a decline of vaccine acceptance to less than 10% in several areas of the former FRG. It is anticipated that the altered recommendation in favour of vaccination, and especially the future application of acellular vaccines with less side effects, will result in the elimination of whooping cough in all areas of Germany.

Medical Codes

|  |  |  |
| --- | --- | --- |
| Code | Description | Source |
| A37.0 | Whooping cough due to Bordetella pertussis | CDC ICD-10-CM 2024 |
| A37.1 | Whooping cough due to Bordetella parapertussis | CMS 2024 ICD-10-CM |
| A37.8 | Whooping cough due to other Bordetella species | CDC ICD-10-CM 2024 |
| A37.9 | Whooping cough, unspecified | CMS 2024 ICD-10-CM |
| A37.90 | Whooping cough, unspecified, without pneumonia | CDC ICD-10-CM 2024 |
| A37.91 | Whooping cough, unspecified, with pneumonia | CMS 2024 ICD-10-CM |

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PLEURISY

Definition

Pleurisy is an inflammation of the lining of your lungs (pleura) that causes sharp chest pains. The pain is usually worse when you breathe or cough. Viral or bacterial infections, autoimmune diseases and lung conditions are common causes of pleurisy. Some causes of chest pain are life-threatening. If you’re having chest pains, go to the nearest ER. Pleurisy (“PLUR-uh-see”) happens when the lining (tissue layer) around your lungs or the lining on the inside wall of your chest swells up. This makes the two layers rub against each other, causing sharp pains. Pleurisy is also called pleuritis. Your lungs and the inside of your chest are each lined with a thin layer called pleura. The space between them (pleural space) is filled with fluid that allows them to slide smoothly along each other when you breathe, like oil in a machine. When one or both layers become swollen (inflamed), they rub painfully against each other instead.

Causes

If you’re otherwise healthy, you’re most likely to get pleurisy from a virus (like the flu), bacteria or other infection in your lungs. Infections can cause inflammation in your pleurae, which gives you chest pain.

You can also get pleurisy from:

* Autoimmune diseases such as lupus, rheumatoid arthritis or familial Mediterranean fever (FMF).
* Lung or pleural disease such as lung cancer, mesothelioma, tuberculosis or asbestosis.
* Chest surgery or trauma.
* A blood clot in your lung (pulmonary embolism).
* Inflammatory bowel disease.
* Sickle cell disease.
* Certain medications, including hydralazine, isoniazid and procainamide.

Pleurisy can be triggered by various infectious agents, including:

* **Bacterial Infections:** Conditions like pneumonia can lead to pleurisy when bacteria infect the pleura.
* **Viral Infections:** Viruses such as influenza or the common cold can also cause pleurisy.
* **Fungal Infections:** In rare cases, fungal infections can lead to pleuritis, particularly in immunocompromised individuals.
* **Environmental Factors:** Exposure to certain environmental toxins or pollutants may increase the risk of pleurisy.

**Genetic/Autoimmune Causes**

Some individuals may have a genetic predisposition to autoimmune diseases that can lead to pleurisy. Conditions such as lupus or rheumatoid arthritis can cause inflammation in the pleura as part of a broader systemic issue.

**Lifestyle and Dietary Factors**

While lifestyle factors are not direct causes of pleurisy, they can influence overall lung health. Smoking, for instance, can damage lung tissue and increase susceptibility to infections that may lead to pleurisy. A diet low in antioxidants and high in processed foods may also negatively impact immune function.

**Key Risk Factors**

Several factors can increase the likelihood of developing pleurisy:

* **Age:** Older adults are at a higher risk due to a decline in immune function.
* **Gender:** Some studies suggest that women may be more prone to autoimmune-related pleurisy.
* **Geographic Location:** Certain regions may have higher incidences of infections that can lead to pleurisy.
* **Underlying Conditions:** Individuals with chronic lung diseases, autoimmune disorders, or a history of infections are at greater risk.

Signs & Symptoms

The main symptom of pleurisy is chest pain (pleuritic pain) that feels sharp, stabbing or knife-like, coming from one specific place. It’s worse when you breathe deeply or cough and sometimes spreads to your shoulder or back. You’ll probably find yourself breathing carefully to avoid the pain.

You might also have:

* **Shortness of Breath:** Difficulty breathing may occur, especially if fluid accumulates in the pleural space.
* **Cough:** A dry cough may accompany pleurisy.
* **Fever:** If an infection is present, fever may be a symptom.
* **Chills:** Accompanying fever, chills may also occur.

Diagnosis and Testing

**How is pleurisy diagnosed?**

To diagnose pleurisy, your healthcare provider will listen to your lungs and ask you about your health history. They’ll ask you questions about your pain, like where it hurts, what it feels like and if anything makes it worse. They may want you to get imaging or other tests done.

**What tests will be done to diagnose pleurisy?**

Your healthcare provider uses tests to diagnose pleurisy and figure out the underlying cause. Possible tests include:

* **Blood tests.** Your provider looks at a sample of your blood for signs of infection or autoimmune disorders.
* **Electrocardiogram (EKG or ECG).** Your provider may use small electrodes on your body to see how well your heart is working. This is to make sure a heart problem isn’t causing your chest pain.
* **Imaging tests.** Your provider takes pictures of your lungs using X-rays, CT scans and ultrasounds to help them figure out what’s causing your pain.
* **Fluid testing (thoracentesis).** Your provider inserts a small needle into the area around your lungs and removes fluid. They examine the fluid for signs of infection or clues to other causes of pleurisy.
* **Thoracoscopy**. Your provider uses a small, lighted tube with a camera to look inside your lungs and find any problems.

**Will a chest X-ray show pleurisy?**

Chest X-rays can’t show pleurisy directly, but they can give your provider clues about what might be causing your symptoms, like fluid around the lungs (pleural effusion) or an infection (pneumonia).

Treatment Options

**Medical Treatments**

**The treatment of pleurisy primarily focuses on addressing the underlying cause and managing symptoms. Common medical treatments include:**

* **Nonsteroidal Anti-Inflammatory Drugs (NSAIDs): Medications like ibuprofen or naproxen can help reduce pain and inflammation.**
* **Corticosteroids: In cases of autoimmune-related pleurisy, corticosteroids may be prescribed to reduce inflammation.**
* **Antibiotics: If a bacterial infection is the cause, antibiotics will be necessary.**
* **Surgical Options: In severe cases, procedures such as pleurodesis (to adhere the pleura together) or drainage of pleural effusion may be required.**

**Non-Pharmacological Treatments**

**In addition to medications, several non-pharmacological treatments can aid in recovery:**

* **Rest: Adequate rest is crucial for recovery.**
* **Hydration: Staying well-hydrated can help thin mucus and ease breathing.**
* **Breathing Exercises: Gentle breathing exercises can help improve lung function and reduce discomfort.**

**Special Considerations**

* **Pediatric Patients: Treatment in children may differ, focusing on gentle approaches and careful monitoring.**
* **Geriatric Patients: Older adults may require adjusted dosages of medications and closer monitoring for side effects.**

**How is pleurisy treated?**

Treatment for pleurisy depends on what’s causing it. Your healthcare provider will work with you to treat the underlying cause. They can also help you manage your pain in the meantime.

Your treatment options might include:

* **Medication for infection.** If your pleurisy is caused by an infection, your healthcare provider may prescribe antibiotics or antifungal medications.
* **Medication for symptom relief.** You provider may suggest nonsteroidal anti-inflammatory drugs (NSAIDs) or corticosteroids for your pain.
* **Fluid draining.** Your provider may remove fluid from your lungs (thoracentesis) to help ease your pain.

Prevention Tips

**Strategies for Prevention**

Preventing pleurisy involves addressing risk factors and maintaining overall lung health:

* **Vaccinations:** Staying up-to-date with vaccinations, such as the flu and pneumonia vaccines, can reduce the risk of infections that may lead to pleurisy.
* **Hygiene Practices:** Regular handwashing and avoiding close contact with sick individuals can help prevent respiratory infections.
* **Dietary Modifications:** A diet rich in fruits, vegetables, and whole grains can support immune function.
* **Lifestyle Changes:** Quitting smoking and avoiding exposure to pollutants can significantly improve lung health.

It's difficult to prevent pleurisy completely. But there are some things that can reduce the chances of developing one of the causes of pleurisy, such as:

* Getting vaccinations when recommended (eg the flu vaccine).
* Hygiene, such as washing your hands after using the toilet, before preparing or eating food, before touching your face, and before and after caring for other people. This can reduce the chances of getting viral or bacterial infections.
* Avoiding or stopping smoking. Smoking increases the risk of lung infections and other serious causes of pleurisy, like lung cancer.
* Maintaining a healthy weight. Having overweight or obesity increases the risk of blood clots.

Outlook / Prognosis

**What can I expect if I have pleurisy?**

Your outlook for pleurisy depends on what’s causing it. If your pleurisy is caused by infection, it should go away as you get better. If it’s caused by an ongoing illness like cancer or an autoimmune disease, you may always have some risk of pleurisy coming back.

Very rarely, pleurisy has life-threatening complications.

**Can pleurisy go away on its own?**

If pleurisy is caused by a virus, it can go away on its own as you get over being sick. More serious underlying causes (such as cancer or other illnesses) need to be treated before pleurisy will get better.

**Are there any complications of pleurisy?**

You may have other conditions along with pleurisy, including:

* Partial lung collapse (atelectasis).
* Excess fluid around your lungs (pleural effusion).
* Pus collecting around your lungs (empyema).

**Typical Course of the Disease**

The prognosis for pleurisy largely depends on the underlying cause and the timeliness of treatment. Many individuals recover fully with appropriate medical care, while others may experience chronic symptoms.

**Factors Influencing Prognosis**

Key factors influencing the overall prognosis include:

* **Early Diagnosis:** Prompt identification and treatment of the underlying cause can lead to better outcomes.
* **Adherence to Treatment:** Following medical advice and treatment plans is crucial for recovery.

Possible Complications

**Potential Complications**

If pleurisy is left untreated or poorly managed, several complications may arise:

* **Pleural Effusion:** Accumulation of fluid in the pleural space can lead to further breathing difficulties.
* **Empyema:** This is a collection of pus in the pleural space, often requiring drainage.
* **Chronic Pain:** Some individuals may experience ongoing chest pain even after treatment.

**Short-Term and Long-Term Complications**

Short-term complications may include acute respiratory distress, while long-term complications can involve chronic lung conditions or persistent pleuritic pain.

When to see a Doctor

It is crucial to seek medical attention if you experience any of the following serious symptoms:

* **Severe chest pain** that does not improve with rest.
* **Difficulty breathing** or rapid breathing.
* **Coughing up blood** or experiencing a persistent cough.
* **High fever** or chills that do not subside.

Red Flags

Certain symptoms warrant immediate medical attention, including:

* **Severe chest pain** that radiates to the shoulder or back.
* **Difficulty breathing** or rapid breathing.
* **Persistent cough** with blood.
* **High fever** or chills.

Clinical Guidelines

The following is a summary of the British Thoracic Society (BTS) Guideline for pleural disease and includes a summary of the guideline recommendations and good practice points (GPPs). The full guideline is published as a separate Thorax Supplement1 and is available from the BTS website.2 Please refer to the full guideline for full information about each section.1 All online supplemental appendices are also available via the BTS website.2 Background The aim of the guideline was to provide evidence-based guidance on the investigation and management of pleural disease. Pleural disease is common and represents a major and rapidly developing subspecialty that presents to many different hospital services. Since the last BTS Guideline for pleural disease published in 2010,3–9 many high quality and practice changing studies, using patient centred outcomes, have been published. The paradigms for the investigation and management of pleural disease have therefore shifted, so this guideline aimed to capture this evidence and use it to answer the most important questions relevant to today’s practice. Target audience for the guideline The guideline will be of interest to UK based clinicians caring for adults with pleural disease, including chest physicians, respiratory trainees, specialist respiratory nurses, specialist lung cancer nurses, specialist pleural disease nurses, pathologists, thoracic surgeons, thoracic surgeon trainees, acute physicians, oncologists, emergency physicians, hospital practitioners, intensive care physicians, palliative care physicians, radiologists, other allied health professional and patients and carers. Areas covered by the guideline The guideline focuses on the investigation and management of pleural disease in adults and covers four broad areas of pleural disease: a. Spontaneous pneumothorax b. Undiagnosed unilateral pleural effusion c. Pleural infection d. Pleural malignancy Adult patients in both inpatient and ambulatory settings are considered. The guideline does not cover mesothelioma (as alternative guidance is available10), benign (noninfectious, non-pneumothorax) pleural disease or rare pleural diseases. Guidance on pleural interventions is also covered in the BTS Clinical Statement on Pleural Procedures.11 Methodology BTS guidelines use the GRADE (Grading of Recommendations, Assessment, Development and Evaluations) methodology for guideline development.12 GRADE is a systematic and transparent process for assessing the quality of the evidence and the full GRADE process involves: i. Systematic review, ii. Critical appraisal; and iii. GRADE analysis. Full details of the BTS process are available in the BTS Guideline production manual (https:// www.brit-thoracic.org.uk/quality-improvement/ guidelines/). Clinical questions, patient-centred outcomes and literature search Clinical questions were defined from the scope of the guideline formulated into PICO (population, intervention, comparator, and outcome) style framework diagnostic accuracy, intervention or prognostic review formats. Patient-centred outcomes were agreed by the group for each question. The PICO framework formed the basis of the literature search. The initial searches were completed by the University of York, and the latter stages by BTS Head Office. Systematic electronic database searches were conducted to identify all papers that may be relevant to the guideline. For each question, the following databases were searched: Cochrane Database of Systematic Reviews (CDSR), Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE and EMBASE. The search strategy is available for review in Online Appendix 1 (accessible via the full guideline). Critical appraisal and GRADE analysis of the evidence After an initial screening to determine relevance to the clinical questions, each paper was assessed to determine if it addressed: Roberts ME, et al. Thorax 2023;0:1–10. doi:10.1136/thorax-2023-220304 1 Guideline summary Table 1 GRADE score definitions Grade Definition High High confidence that the true effect is close to the estimated effect Moderate Moderate confidence that the true effect is close to the estimated effect Low Low confidence that the true effect is close to the estimated effect Very Low Very low confidence that the true effect is close to the estimated effect Ungraded GRADE analysis not possible, but evidence deemed important Table 2 Explanation of the terminology used in BTS recommendations Strength Benefits and risks Implications Strong Recommended, so “offer” Benefits appear to outweigh the risks (or vice versa) for the majority of the target group Most service users would want to, or should receive this intervention Conditional Suggested, so “consider” Risks and benefits are more closely balanced, or there is more uncertainty in likely service users’ values and preferences Service users should be supported to arrive at a decision based on their values and preferences i. The clinical question population. ii. The index test and reference standard (for diagnostic accuracy questions), the intervention and comparator (for intervention questions), or the exposure and referent (for prognostic questions). iii. The study type(s) defined in the clinical question protocol; and iv. The clinical question outcome(s). Each full paper fulfilling the above criteria was ‘accepted’ for inclusion. In circumstances where there was little, or no supporting evidence that fulfilled the above criteria, the full paper inclusion strategy was widened to include evidence that partially addressed the clinical question. Following data extraction from the ‘accepted’ papers, evidence profiles were generated for each of the clinical questions and the quality of the evidence was assessed using the GRADE principles.12 Where GRADE analysis was not possible, but the evidence was deemed important enough to be included in the guideline, the evidence has been listed as (Ungraded), denoting that inclusion was reached by consensus of the guideline development group. A definition of the GRADE scores is shown in table 1. The direction and strength of the recommendations are then based on the quality of the evidence, the balance of desirable and undesirable outcomes and the values and preferences of patients/ carers. GRADE specifies two categories of strength for a recommendation as shown in table 2. From the outset, it was acknowledged that there would be little high-quality evidence for some of the clinical questions identified. In this instance, low grade evidence was considered, along with the expert opinion of the GDG via consensus at the meetings. Good practice points (GPPs) were also developed by informal consensus in areas where there was no quality evidence, but the GDG felt that some guidance, based on the clinical experience of the GDG, might be helpful to the reader. These are indicated as shown below: ✓ Advised best practice based on the clinical experience of the GDG. In some instances where evidence was limited, but GDG members felt that it was important to include a recommendation rather than a GPP, recommendations were agreed by informal consensus and categorised as (Conditional – by consensus), based on the same criteria detailed in table 1. Stakeholders Stakeholders were identified at the start of the process. All stakeholder organisations were notified when the guideline was available for public consultation and a list of all stakeholders is listed in Appendix 4 to the full guideline. Summary of recommendations and Good Practice Points Spontaneous pneumothorax Acute management for spontaneous pneumothorax Recommendations ► Conservative management can be considered for the treatment of minimally symptomatic (ie, no significant pain or breathlessness and no physiological compromise) or asymptomatic primary spontaneous pneumothorax in adults regardless of size. (Conditional – by consensus) ► Ambulatory management should be considered for the initial treatment of primary spontaneous pneumothorax in adults with good support and in centres with available expertise and follow-up facilities. (Conditional) ► In patients not deemed suitable for conservative or ambulatory management, needle aspiration or tube drainage should be considered for the initial treatment of primary spontaneous pneumothorax in adults. (Conditional) ► Chemical pleurodesis can be considered for the prevention of recurrence of secondary spontaneous pneumothorax in adults (eg, patients with severe COPD who significantly decompensated in the presence of a pneumothorax, even during / after the first episode). (Conditional) ► Thoracic surgery can be considered for the treatment of pneumothorax in adults at initial presentation if recurrence prevention is deemed important (eg, patients presenting with tension pneumothorax, or those in high risk occupations). (Conditional) Good practice points ✓ When establishing local ambulatory treatment pathways, planning and coordination between with the emergency department, general medicine and respiratory medicine is vital. ✓ When performing chemical pleurodesis for the treatment of pneumothorax in adults, adequate analgesia should be provided before and after treatment. ✓ All treatment options should be discussed with the patient to determine their main priority, with consideration for the least invasive option. 2 Roberts ME, et al. Thorax 2023;0:1–10. doi:10.1136/thorax-2023-220304 Guideline summary Optimal management after the resolution of a first episode of pneumothorax Good practice points ✓ Elective surgery may be considered for patients in whom recurrence prevention is deemed important (eg, at risk professionals (divers, airline pilots, military personnel), or those who developed a tension pneumothorax at first episode). ✓ Elective surgery should be considered for patients with a second ipsilateral or first contralateral pneumothorax. ✓ Discharge and activity advice should be given to all patients post pneumothorax. Optimal management for spontaneous pneumothorax and ongoing air leak Good practice point ✓ If a patient is not considered fit for surgery, autologous blood pleurodesis or endobronchial therapies should be considered for the treatment of pneumothorax with persistent air leak in adults. Optimal surgical approach and surgical operation for pneumothorax management Recommendations ► Video-assisted thoracoscopy access can be considered for surgical pleurodesis in the general management of pneumothorax in adults. (Conditional) ► Thoracotomy access and surgical pleurodesis should be considered for the lowest level of recurrence risk required for specific (eg, high risk) occupations. (Conditional) ► Surgical pleurodesis and/or bullectomy should be considered for the treatment of spontaneous pneumothorax in adults. (Conditional) Investigation of the undiagnosed unilateral pleural effusion Radiology for diagnosing unilateral pleural effusions of benign aetiology Good practice points ✓ Imaging findings of a unilateral pleural effusion should be interpreted in the context of clinical history and knowledge of pleural fluid characteristics. ✓ CT follow-up should be considered for patients presenting with pleural infection to exclude occult malignancy if there are ongoing symptoms, or other clinically concerning features. ✓ PET-CT should not be used in the assessment of pleural infection. Image guided versus non-image guided intervention for suspected unilateral pleural effusion Recommendation ► Image-guided thoracentesis should always be used to reduce the risk of complications. (Strong – by consensus) Optimal volume and container for pleural aspiration samples Recommendations ► 25–50mL of pleural fluid should be submitted for cytological analysis in patients with suspected malignant pleural effusion (MPE). (Strong – by consensus) ► Pleural fluid should be sent in both plain and blood culture bottle tubes in patients with suspected pleural infection. (Strong – by consensus) Good practice points ✓ At least 25mL, and where possible 50mL, of pleural fluid should be sent for initial cytological examination. ✓ If volumes of ≥25mL cannot be achieved, smaller volumes should also be sent, but clinicians should be aware of the reduced sensitivity. ✓ If small volume aspirate (7.2and 900IU/L intercostal drainage should be considered, especially if other clinical parameters support CPPE (specifically ongoing temperature, high pleural fluid volume, low pleural fluid glucose (72mg/dL ≤4.0 mmol/L), pleural contrast enhancement on CT or septation on ultrasound. (Strong – by consensus) – If pleural fluid pH ≥7.4this implies a low risk of CPPE or pleural infection and there is no indication for immediate drain. (Strong – by consensus) ► In the absence of readily available immediate pleural fluid pH measurement, an initial pleural fluid glucose 25%) nonexpandable lung requiring intervention for a symptomatic MPE, current evidence suggests the use of an indwelling pleural catheter rather than talc pleurodesis. ✓ In MPE patients with less than 25% non-expandable lung, talc slurry pleurodesis may improve quality of life, chest pain, breathlessness and pleurodesis rates. ✓ Decortication surgery may improve pleurodesis success in selected MPE patients with non-expanded lung, but the risks and benefits of IPC and surgical treatment should be discussed with patients, and treatment individualised according to circumstances (for example, fitness to undergo thoracic surgery). Managing malignant pleural effusion and septated effusion (on radiology) Intrapleural enzymes versus surgery, or no treatment Good practice points ✓ Intrapleural fibrinolytics can be considered in highly selected symptomatic patients with MPE to try to improve breathlessness. ✓ Intrapleural fibrinolytics may be used in patients with MPE and septated effusion and an indwelling pleural catheter (IPC) to improve drainage if flushing the IPC with normal saline or heparinised saline does not improve drainage. ✓ Surgery can be considered for palliation of symptoms in a minority of patients with significantly septated MPE and associated symptoms and otherwise good prognosis and performance status. Managing malignant pleural effusion treated with an indwelling pleural catheter (IPC) Symptom-based/conservative drainage versus daily drainage Recommendations ► Where IPC removal is a priority, daily IPC drainages are recommended to offer increased rates of pleurodesis when compared with less frequent drainages of symptom-guided or alternate drainage regimes. (Conditional) ► Patients should be advised that they do not require daily drainage to control symptoms of breathlessness and chest pain if they wish to opt for a less intensive regime. (Strong – by consensus) Good practice points ✓ Decisions on the optimal drainage should be based on patient choice. ✓ Informed decision making should include the explanation of the effect of drainage regimes on the patient-centre outcomes such as breathlessness and the possibility of auto-pleurodesis during the disease course. ✓ Although daily drainage may result in earlier removal of IPC, there may be an associated cost associated with the increased number of drainage events (both to the healthcare system, and to the patient). This has been addressed in a modelling study13 and should be considered. Intrapleural agents (talc or other pleurodesis agents) Recommendation ► Instillation of talc via an indwelling pleural catheter (IPC) should be offered to patients with expandable lung where the clinician or patient deems achieving pleurodesis and IPC removal to be important. (Conditional – by consensus) Intrapleural chemotherapy versus systemic treatment for treating pleural malignancy Recommendation ► Intrapleural chemotherapy should not be routinely used for the treatment of MPE. (Conditional – by consensus) Good practice point ✓ All patients of good performance status with metastatic malignancy should be considered for systemic anti-cancer therapy (SACT) as standard of care as per national guidelines. Using prognostic or predictive scores to provide prognostic information for patients with malignant pleural effusion Good practice points ✓ Clinicians may consider using a validated risk score for malignant pleural effusion if the information is of use in planning treatments or in discussion with patients. ✓ Patients with pleural malignancy should be managed in a multi-disciplinary way, including referral to specialist palliative care services where appropriate. Healthcare providers need to use clinical judgement, knowledge and expertise when deciding whether it is appropriate to apply recommendations for the management of patients. The recommendations cited here are a guide and may not be appropriate for use in all situations. The guidance provided does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer. Author affiliations 1 Respiratory Medicine, Sherwood Forest Hospitals NHS Foundation Trust, Nottinghamshire, UK 2 University of Oxford, Oxford Respiratory Trials Unit, Oxford, UK 3 Oxford NIHR Biomedical Research Centre, Oxford, UK 4 Oxford Pleural Unit, Churchill Hospital, Oxford, UK 5 Academic Respiratory Unit, University of Brisol and North Bristol NHS Trust, UK 6 Glasgow Pleural Disease Unit, Queen Elizabeth University Hospital, Glasgow, UK 6 Roberts ME, et al. Thorax 2023;0:1–10. doi:10.1136/thorax-2023-220304 Guideline summary 7 School of Cancer Sciences, University of Glasgow/Cancer Research UK Beatson Institute, Glasgow, UK 8 Interventional Pulmonology Service, University Hospitals Plymouth NHS Trust, Plymouth, UK 9 North Bristol NHS Trust, Westbury on Trym, UK 10North West Lung Centre, Manchester University NHS Foundation Trust, Manchester, UK 11Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK 12Oxford Centre for Respiratory Medicine, Oxford University Hospitals NHS Foundation Trust, Oxford, UK 13Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia 14Manchester University NHS Foundation Trust, Manchester, UK 15Academic Division of Thoracic Surgery, The Royal Brompton Hospital and Imperial College London, London, UK 16Regional Respiratory Centre, Belfast Health and Social Care Trust, Belfast, UK 17Portsmouth Hospitals University NHS Trust, Portsmouth, UK 18Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, UK 19Department of Histopathology, Royal Brompton and Harefield Hospitals, Guy’s and St Thomas’ NHS Foundation Trust and National Heart and Lung Institute, London, UK 20St George’s University Hospitals NHS Foundation Trust, London, UK 21British Thoracic Society, London, UK 22North Cumbria Integrated Care NHS Foundation Trust, Cumbria, UK 23Freeman Hospital, Newcastle Upon Tyne Hospitals NHS Foundation Trust, Newcastle Upon Tyne, UK Twitter Nick A Maskell @BristolARU, Anna C Bibby @BristolARU, Kevin G Blyth @ kevingblyth, Matthew Evison @matthewevison1, Duneesha de Fonseka @defonseka, Eleanor K Mishra @EleanorKMishra, Maria Parsonage @Parsonage and Andrew E Stanton @andrewestanton Contributors MER, NMR and NAM were the lead authors responsible for the final document. 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Predefined Q&A sets

1. **What are the main symptoms of pleurisy?**

Pleurisy typically presents with sharp chest pain that worsens with breathing, coughing, or sneezing. Other symptoms may include shortness of breath, cough, fever, and chills.

1. **How is pleurisy diagnosed?**

Diagnosis involves a clinical evaluation, including patient history and physical examination, along with imaging studies and laboratory tests to identify the underlying cause.

1. **What are the common causes of pleurisy?**

Common causes include infections (bacterial, viral, or fungal), autoimmune diseases, and environmental factors.

1. **Can pleurisy be treated at home?**

While some mild cases may be managed at home with rest and over-the-counter pain relievers, it is essential to consult a healthcare provider for proper diagnosis and treatment.

1. **What complications can arise from untreated pleurisy?**

Untreated pleurisy can lead to complications such as pleural effusion, empyema, and chronic pain.

1. **Is pleurisy contagious?**

Pleurisy itself is not contagious, but the infections that can cause it, such as pneumonia, may be.

1. **How long does it take to recover from pleurisy?**

Recovery time varies depending on the underlying cause and treatment, but many individuals see improvement within a few days to weeks.

1. **Are there any lifestyle changes that can help prevent pleurisy?**

Yes, maintaining a healthy lifestyle, including a balanced diet, regular exercise, and avoiding smoking, can help reduce the risk of pleurisy.

1. **When should I see a doctor for pleurisy symptoms?**

Seek immediate medical attention if you experience severe chest pain, difficulty breathing, or persistent cough with blood.

1. **Can pleurisy lead to chronic lung problems?**

In some cases, untreated or severe pleurisy can lead to chronic lung issues, emphasizing the importance of early diagnosis and treatment.

Medical Codes

|  |  |  |  |
| --- | --- | --- | --- |
| Code | Description | Type | Source |
| R09.1 | Pleurisy (unspecified cause) | Symptom Code | CDC ICD-10-CM 2024 |
| A15.6 | Tuberculous pleurisy, confirmed | Infectious | CMS 2024 ICD-10-CM |
| A16.6 | Tuberculous pleurisy without bacteriological/histological confirmation | Infectious | CDC ICD-10-CM 2024 |
| J86.9 | Pyothorax (empyema) without fistula | Bacterial Complication | CMS 2024 ICD-10-CM |
| M32.13 | Pleurisy in systemic lupus erythematosus (SLE) | Autoimmune | CDC ICD-10-CM 2024 |
| I30.1 | Infective pleurisy/pericarditis | Infectious | CMS 2024 ICD-10-CM |
| J94.8 | Other specified pleural conditions (includes pleurisy with effusion) | Pleural Disorder | CDC ICD-10-CM 2024 |
| M05.10 | Rheumatoid pleurisy without rheumatoid arthritis of specified site | Autoimmune | CMS 2024 ICD-10-CM |
| A40.8 | Other streptococcal infections (pleurisy as complication) | Infectious | CDC ICD-10-CM 2024 |
| B25.2 | Cytomegaloviral pneumonitis (with pleurisy) | Viral | CMS 2024 ICD-10-CM |

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>>> <https://www.apollohospitals.com/diseases-and-conditions/pleurisy>

>>> <https://www.mayoclinic.org/diseases-conditions/pleurisy/symptoms-causes/syc-20351863>

>>> <https://patient.info/signs-symptoms/chest-pain-leaflet/pleurisy>

>>> <https://www.brit-thoracic.org.uk/quality-improvement/guidelines/pleural-disease/>

>>><https://www.icd10data.com/ICD10CM/Codes/J00-J99/J90-J94/J90-/J90>

CONGENITAL AIRWAY ABNORMALITIES:

TRACHEOBRONCHOMALACIA

Definition

Tracheobronchomalacia (TBM) is a condition of the airways that causes them to become weak and floppy and collapse with breathing. Normally the central airways (the trachea and bronchi) remain open when you breathe.

Tracheobronchomalacia is a rare condition, and often misdiagnosed. In most cases, it is not clear what causes TBM. Sometimes it can be seen at the same time as another lung disorder, such as COPD, asthma, or cystic fibrosis. Our researchers are working to understand the underlying processes that lead to tracheobronchomalacia.

Tracheomalacia (TRAY-kee-oh-muh-LAY-shia) is when you have weak or floppy [cartilage](https://my.clevelandclinic.org/health/body/23173-cartilage" \t "_blank) in your [trachea](https://my.clevelandclinic.org/health/body/21828-trachea" \t "_blank) (windpipe). The walls of your windpipe can collapse or fall in, causing symptoms like high-pitched breathing. It can also trap mucus in your lungs, making it difficult to clear them out. In severe cases, tracheomalacia may be life-threatening, but it’s [curable](https://my.clevelandclinic.org/health/articles/24434-cure" \t "_blank) with treatment.

Tracheomalacia usually affects newborns, but anyone can develop it. Babies born with the condition often develop symptoms when they’re 1 to 2 months old. Then, symptoms improve over the first three years of life. That’s because cartilage strengthens as your baby’s windpipe grows. But severe cases may need surgery.

Causes

The cause of tracheobronchomalacia (TBM) depends on whether it is primary or acquired. Primary TBM is associated with prematurity or certain genetic conditions.

Acquired TBM can be *idiopathic* (have no known cause) or be related to other conditions, including:

* Prolonged *intubation* (breathing tube used during hospitalization)
* *Tracheostomy* (a hole surgically made in the neck for breathing)
* Long-term irritation and coughing from chronic obstructive pulmonary disease (COPD)
* Tumors or cysts that compress the trachea or bronchi

Congenital tracheomalacia happens when the cartilage in your baby’s windpipe doesn’t develop the way it should. The walls of their windpipe are floppy instead of rigid.

Acquired tracheomalacia causes include:

* Chronic acid reflux (GERD).
* Damage from surgery or other medical procedures.
* Emphysema.
* Polychondritis (inflammation of the cartilage) in your windpipe.
* Tracheoesophageal fistula repair (fixing an abnormal connection between your esophagus and trachea).
* Tracheostomy, or long-term use of a breathing tube.
* Upper respiratory infections, like bronchitis.

Tracheomalacia may be associated with other conditions like:

* Developmental delays.
* Ehlers-Danlos syndrome.
* Heart defects.

Signs & Symptoms

Symptoms of TBM include:

* Shortness of breath
* Labored breathing
* A persistent cough that sounds like a bark or very rumbling
* Difficulty clearing phlegm or mucus from your throat
* Build-up of secretions in your lungs
* Frequent respiratory infections

What does the TBM cough sound like?

Other lung conditions, such as asthma, COPD, or emphysema, can cause symptoms that are similar to TBM. To ensure an accurate diagnosis, we offer patients one-stop access to a multidisciplinary team of experts.

Our specialists will first ask about your symptoms and past health problems, and do a thorough physical exam. They may also ask you to undergo two specialized medical tests — a dynamic flexible bronchoscopy and a dynamic expiratory CT scan — to determine whether you have TBM – and if so, how severe it is.

The most common tracheomalacia symptom is high-pitched or noisy breathing ([stridor](https://my.clevelandclinic.org/health/diseases/23303-stridor" \t "_blank)). Other symptoms include:

Breathing issues that get worse when feeding, crying or coughing.

Choking.

* Chronic coughing.
* Cyanosis (a condition where your skin, lips or nails turn blue from a lack of oxygen).
* Difficulty swallowing.
* Hoarseness.
* Recurring (returning) airway infections like pneumonia or bronchitis.
* Shortness of breath.
* Wheezing or rattling sounds.

Diagnosis

**A diagnosis of TBM begins with a physical exam and discussion of your symptoms. Additional tests may include:**

* **Pulmonary function testing (PFT): Tests to determine the severity of your respiratory impairment, often using a spirometer, measure the volume of air inhaled and exhaled by your lungs.**
* **Computed tomography (CT) scan: This test combines X-ray and computer technology to produce detailed cross-sectional images of your chest cavity.**
* **Bronchoscopy: An *endoscope* (a thin, flexible tube with a light and camera on the end) is inserted into your airway to check for blockages.**

**Dynamic Expiratory CT Scan**

During a computed tomography (CT) scan, you lie very still on a table while multiple x-rays are taken of your throat and upper chest. A computer assembles these images to provide a detailed view of your airways.

To confirm or rule out a diagnosis of TBM, we conduct a dynamic expiratory CT scan. This means the CT scan will capture images of your airways as you breathe.

**Dynamic Flexible Bronchoscopy**

A bronchoscope is a long, thin, flexible tube that enables a doctor to look into your airways. This is the gold standard for diagnosing TBM because it permits real-time examination of the airways while you breathe. It also provides information on the extent and location of airway collapse.

A healthcare provider will do a physical examination. If they’re treating your child, they’ll ask you about their symptoms, their overall health and any medical conditions that may be the reason why your child is coughing, wheezing or has trouble breathing.

If you’re having symptoms, your provider will do a physical examination and ask the same sorts of questions. They may ask if you have frequent respiratory infections or other conditions that affect how you breathe.

They may do the following tests:

* **Pulmonary function tests**: These are tests to see how well air moves in and out of your lungs.
* **Bronchoscopy**: In this test, your provider checks how narrow your trachea becomes when you take a deep breath or cough.
* **Computed tomography (CT) scan**: Your provider may order this test to make sure other conditions aren’t causing your symptoms.

Treatment

Treatments vary depending on how tracheobronchomalacia affects your or your baby’s ability to breathe. For example:

* Your baby’s healthcare provider may prescribe antibiotics to treat any underlying infections. They may show you ways to breastfeed or bottle feed your baby that don’t affect their ability to breathe.
* They may prescribe medications to help manage your baby’s symptoms.
* They may prescribe pulmonary rehabilitation programs that teach you or your child ways to manage symptoms.
* You may use supportive devices that help you breathe.
* You or your child may need surgery to support weakened tracheas.

**Supportive devices for TBM treatment**

Several kinds of supportive devices or durable medical equipment treat TBM symptoms. These devices can help you or your child manage symptoms and limit how much tracheobronchomalacia affects your quality of life. Treatments include:

* **CPAP or BiPAP® machines**: These machines help to keep your trachea open.
* **External percussion vests**: TBM can make it hard to cough up mucus. External percussion vests connect to a machine that vibrates very fast, shaking up mucus in your bronchi so you can cough up mucus more easily.
* **Nebulizer**: Nebulizers change liquid medication into fine droplets that you or your child inhale through a mask or mouthpiece.

**Surgery for tracheobronchomalacia**

There are several surgical treatments for TBM. They include:

* **Bronchoscopy**: This is the same procedure that healthcare providers use to diagnose issues with your lungs or airway. In treatment, healthcare providers use a rigid bronchoscope to place a temporary stent in your airway. A stent is a small plastic, rubber or metal tube that holds your airway open. Stents help healthcare providers decide if you need additional surgery.
* **Tracheobronchoplasty:** This procedure involves sewing mesh to the outside of your trachea. The mesh gives your trachea more structure so it’s less likely to collapse.
* **Tracheopexy**: This is surgery that attaches the back of your trachea to ligaments in your spine to keep your trachea from collapsing.

BIDMC is a world leader in diagnosing and treating tracheobronchomalacia (TBM). When you make an appointment with our TBM Program, you will benefit from the expertise of a multidisciplinary team of interventional pulmonologists, thoracic surgeons, ear/nose/throat specialists, speech pathologists, endocrinologists, general pulmonologists, behavioral health providers, anesthesiologists, and radiologists.

We evaluate and treat more patients with TBM than anywhere else in the United States. Through our TBM Program, we offer you an extraordinary level of expertise and care.

**Treatment of Mild or Moderate TBM**

We determine whether you have TBM, and how severe it is, by assessing your symptoms and how much your airway narrows when you breathe. If your TBM is diagnosed as mild or moderate, treatment is symptomatic and options include:

Airway oscillatory devices (flutter valve)

* These are hand-held devices to help clear your airways. You inhale, and then exhale forcefully. This helps clear phlegm and mucus.

External percussion vests

* These inflatable vests are connected to a compressor and help clear the lungs of mucus and phlegm. These are usually used 2 or 3 times a day.

Expectorant

* This is a medication that makes it easier to cough up mucus and phlegm, clearing the airways.

Pulmonary rehabilitation

* This involves education and training to improve your quality of life. You will learn more about TBM, and how to breathe more productively, conserve energy, and keep active.

Pursed lip breathing

* This is a breathing technique in which you inhale through your nose, while keeping your lips closed, and then exhale through tightly pursed lips. It is a simple yet effective way to slow your breathing and alleviate shortness of breath.

CPAP (continuous positive airway pressure) or BiPap (Bilevel positive airway pressure)

* A CPAP or BiPap device is used while you sleep. Both devices increase the air pressure in your throat, so that your airway doesn't collapse when you breathe.

**Treatment of Severe TBM**

If your TBM is severe, we conduct further tests to determine if you might benefit from a surgical procedure called tracheobronchoplasty. This procedure offers effective and permanent treatment for TBM.

To ensure that you will benefit from surgery, our multidisciplinary team will first determine whether you have other conditions that commonly occur in addition to TBM and need to be treated. For this reason, we will assess:

* Your vocal cord health
* Whether you have GERD (gastroesophageal reflux disease)
* Whether you have other lung disorders (asthma, COPD, emphysema)
* We also determine whether you are healthy enough to undergo surgery.

Stent trial

The final step in determining whether you will benefit from surgery is a 1-2 week "stent trial." The stent will keep your airways open, much as a cardiac stent keeps blood vessels open. This mimics what happens to your airways after surgery, so it will give you some idea of how much your symptoms will improve after surgery.

During the stent trial, using validated questionnaires (to assess shortness of breath, quality of life, and cough) we will monitor how you are doing and ask that you return to the TBM clinic for follow-up. In addition, you will undergo physiological evaluation using tests to assess lung function and 6-minute walking capacity. When the trial is over, we remove the stent. (We prefer not to implant stents permanently, as they can cause irritation or become infected. Surgery offers a better long-term solution for most patients.)

Tracheobronchoplasty

If your symptoms improve during the stent trial, and your overall health suggests you may benefit from surgery, we will schedule you for tracheobronchoplasty. This is an open surgical procedure, which means that you will have a long incision in your chest. During the procedure, the surgeon opens the chest wall to reach the airways. The surgeon sutures sections of mesh at multiple points on the outside of the floppy airway, to stabilize it (much like a splint will keep a broken bone steady). As you heal, scar tissue forms around the mesh, making it stable.

You will spend several days in the Intensive Care Unit, followed by a longer stay in the hospital. After you are discharged, we will monitor your recovery closely. Patients from out of state may need to find temporary housing in the area for the first month after discharge.

Monitoring after surgery

We want to ensure that you recover as well as possible. For that reason, we ask that you return three months after surgery for evaluation. From then on, we will ask you to return to the TBM clinic once a year, so that we can continue to monitor your recovery.

Prevention Tips

**Can tracheobronchomalacia be prevented?**

**There’s no way to prevent congenital tracheobronchomalacia in children. Adults can develop TBM over time if they have certain medical conditions or have exposure to secondhand smoke or toxic gases.**

**Tracheobronchomalacia gets worse over time, so talk to a healthcare provider if you know you have exposure to secondhand smoke, toxic gases or conditions that may increase your risk. You may not be able to keep TBM from happening, but there may be ways to keep it from getting worse.**

Prognosis / Outlook

**What can I expect if my child has tracheobronchomalacia?**

Your child’s trachea cartilage will become stiffer as they grow up. That means there’s less chance that their trachea and bronchi will collapse and affect their breathing. But often, children with TBM need ongoing medical treatment and support to help them breathe.

**What can I expect if I have TBM?**

Sometimes, losing weight or treatment may help with TBM symptoms. But TBM in adults is often a chronic (continuing) condition. If you have tracheobronchomalacia, you’ll probably work with a healthcare provider who specializes in airway treatment for the rest of your life.

Studies suggest that surgery helps ease tracheobronchomalacia symptoms right away and for several years after surgery. If you’re like many people with tracheobronchomalacia, you have other medical conditions that affect your overall health. Those conditions can make it more difficult for you to respond to treatment or recover from surgery.

**What is the life expectancy for people with tracheobronchomalacia?**

People who develop TBM often have other serious medical conditions that may affect their life expectancy. Your healthcare provider is your best source if you want to know if having tracheobronchomalacia could affect how long you’ll live.

**Does tracheobronchomalacia go away?**

TBM in adults can be life-threatening because it doesn’t go away and gets worse over time. TBM in babies may cause less serious symptoms as they grow up.

Possible Complication

**Complications of TBM surgery**

Tracheobronchoplasty and tracheopexy are major surgeries. Like most surgeries, there may be complications, including:

* Excessive bleeding.
* Blood clots.
* Infection of the surgical site.

If your healthcare provider recommends surgery to treat TBM, they’ll explain the risk of complications.

When to see a Doctor

If you have TBM, you’ll have ongoing medical care and regular medical checkups. Contact your provider if you notice your symptoms like coughing or wheezing get worse.

Medication

Healthcare providers use several different medications to treat tracheomalacia, including:

* **Antibiotics** to treat bacterial infections.
* **Bronchodilators** to relax the muscles that help you breathe.
* **Corticosteroids** to reduce inflammation.
* **Mucolytics** to thin out mucus.

**What conditions might be confused for tracheomalacia?**

The following conditions may be confused for tracheomalacia:

* **Laryngomalacia**: This condition refers to floppy tissue above your voice box. Your voice box sits above your windpipe.
* **Tracheobronchomalacia**: This describes weak bronchi (the tubes that run from your windpipe to your lungs). Some people with tracheomalacia also have tracheobronchomalacia.

Medical Codes

|  |  |  |  |
| --- | --- | --- | --- |
| Code | Description | Type | Source |
| J39.8 | Other specified diseases of upper respiratory tract |  |  |
| (Includes acquired tracheobronchomalacia) | Acquired | CDC ICD-10-CM 2024 |  |
| Q32.0 | Congenital tracheomalacia | Congenital | CMS 2024 ICD-10-CM |
| Q32.2 | Congenital bronchomalacia | Congenital | CDC ICD-10-CM 2024 |
| Q32.4 | Other congenital malformations of bronchus |  |  |
| (May apply to complex cases) | Congenital | CMS 2024 ICD-10-CM |  |

Reference

>>><https://www.bidmc.org/conditions-and-treatments/airway-breathing-and-lung/tbm>

>>><https://www.nm.org/conditions-and-care-areas/pulmonary/tracheobronchomalacia-tbm/symptoms>

>>><https://my.clevelandclinic.org/health/diseases/24504-tracheomalacia>

**PULMONARY HYPERTENSION**

**Definition:**

Pulmonary hypertension is a type of high blood pressure that affects the arteries in the lungs and the right side of the heart.

In one form of pulmonary hypertension, called pulmonary arterial hypertension (PAH), blood vessels in the lungs are narrowed, blocked or destroyed. The damage makes it hard for blood to move through the lungs. Blood pressure in the lung arteries goes up. The heart must work harder to pump blood through the lungs. The extra effort eventually causes the heart muscle to become weak and fail.

In some people, pulmonary hypertension slowly gets worse. It can be life-threatening. There's no cure for pulmonary hypertension. But treatments are available to help you feel better, live longer and improve your quality of life.

Pulmonary hypertension (PH) is a general diagnosis that means you have high blood pressure in your pulmonary arteries. These are the blood vessels that carry oxygen-poor blood from your heart to your lungs.

Pulmonary hypertension has many different causes. It’s usually a complication of heart disease or lung disease. But many other diseases and environmental factors can raise your risk for PH.

Pulmonary hypertension is dangerous because it disrupts the flow of blood through your heart and lungs. High blood pressure in your pulmonary arteries causes these arteries to become narrow. As a result, your heart must work harder to pump oxygen-poor blood to your lungs.

Over time, PH damages your heart and causes problems throughout your body. It can be fatal without treatment.

**Symptoms**

The symptoms of pulmonary hypertension develop slowly. You may not notice them for months or even years. Symptoms get worse as the disease continues.

Pulmonary hypertension symptoms include:

* Shortness of breath. It may first start during exercise and eventually happen at rest.
* Blue or gray skin. Depending on skin color, these changes may be harder or easier to see.
* Chest pressure or pain.
* Dizziness or fainting.
* Fast pulse or pounding heartbeat.
* Fatigue.
* Swelling in the ankles, legs and belly area.

These symptoms may be caused by many other health conditions. See a healthcare professional for an accurate diagnosis.

**Causes**

Pulmonary hypertension is caused by changes in the cells that line the lung arteries. The changes can make the artery walls narrow, stiff, swollen and thick. It gets harder for blood to flow through the lungs.

Pulmonary hypertension is sorted into five groups, depending on the cause.

**Group 1: Pulmonary arterial hypertension (PAH)**

Causes include:

* Unknown cause, called idiopathic pulmonary arterial hypertension.
* Changes in a gene passed down through families, called heritable pulmonary arterial hypertension.
* Use of some medicines or illicit drugs, including methamphetamine.
* Heart condition present at birth, called a congenital heart defect.
* Other health conditions, including scleroderma, lupus and cirrhosis.

**Group 2: Pulmonary hypertension caused by left-sided heart disease**

This is the most common form of pulmonary hypertension. Causes include:

* Left heart failure.
* Left-sided heart valve disease, including mitral valve or aortic valve disease.

**Group 3: Pulmonary hypertension caused by lung disease**

Causes include:

* Scarring of the lungs, called pulmonary fibrosis.
* Chronic obstructive pulmonary disease, also called COPD.
* A sleep disorder in which breathing repeatedly stops and starts, called sleep apnea.
* Being at high altitudes for extended periods of time, if you are at high risk of pulmonary hypertension.

**Group 4: Pulmonary hypertension caused by blockages in the pulmonary artery**

Causes include:

* Blood clots in the lungs that don't go away.
* Tumors that block the pulmonary artery.

**Group 5: Pulmonary hypertension triggered by other health conditions**

Causes include:

* Blood disorders, including polycythemia vera and essential thrombocythemia.
* Inflammatory disorders such as sarcoidosis.
* Conditions that affect the body's ability to break down certain sugars, including glycogen storage disease.
* Kidney disease.

**Eisenmenger syndrome and pulmonary hypertension**

Eisenmenger syndrome can lead to pulmonary hypertension.

Eisenmenger syndrome is a long-term complication of an unrepaired heart condition present at birth. An example is a large hole in the heart between the two lower heart chambers called a ventricular septal defect.

The unrepaired hole in the heart causes oxygen-rich blood to mix with oxygen-poor blood. The blood then goes to the lungs instead of going to the rest of the body. This increases pressure in the pulmonary arteries.

**What are the different types of pulmonary hypertension?**

The World Health Organization (WHO) divides pulmonary hypertension into five groups based on its cause.

* **Group 1 PH due to pulmonary arterial hypertension (PAH)**. PAH has many different causes, ranging from underlying diseases to certain drugs. PAH makes your pulmonary arteries become narrow, thick or stiff. Less blood can flow through, which raises the pressure in your pulmonary arteries.
* **Group 2 PH due to left-sided heart disease**. The left side of your heart pumps out blood to your entire body. If there’s a problem on this side of your heart, it affects the right side of your heart and your entire pulmonary circuit. Blood backs up in your heart, raising the pressure in your pulmonary arteries.
* **Group 3 PH due to lung disease or hypoxia**. Certain lung problems cause the arteries in your lungs to tighten. Less blood can flow through your lungs, raising the pressure in your pulmonary arteries.
* **Group 4 PH due to blockages in your lungs**. Blood clots or scars from blood clots prevent your blood from flowing normally through your lungs. This puts more stress on the right side of your heart and raises pulmonary blood pressure.
* **Group 5 PH due to other disorders.**PH occurs along with other conditions like blood disorders and metabolic disorders. The exact mechanisms for how the condition triggers PH aren’t always clear.

**Who does pulmonary hypertension affect?**

Pulmonary hypertension can affect adults at any age. It commonly affects people who have heart or lung conditions. It’s also more common among people with other medical conditions. PH affects:

* Nearly 100% of people with severe [mitral valve disease](https://my.clevelandclinic.org/health/treatments/17239-mitral-valve-disease-percutaneous-interventions" \t "_blank).
* About 65% of people with [aortic valve](https://my.clevelandclinic.org/health/body/22458-aortic-valve" \t "_blank) disease.
* Up to 30% of people with scleroderma.
* About 20% to 40% of people with sickle cell disease.
* About 1 in 200 people with [HIV](https://my.clevelandclinic.org/health/diseases/4251-aids--hiv" \t "_blank).

PH usually affects adults. But rarely, it can affect newborns. This is called [persistent pulmonary hypertension of the newborn (PPHN)](https://my.clevelandclinic.org/health/diseases/16020-persistent-pulmonary-hypertension-in-the-neonate-pphn" \t "_blank). Infants with this condition may need treatment in the intensive care unit.

**How common is pulmonary hypertension?**

Some types of PH are rare, such as pulmonary arterial hypertension (PAH) and PH caused by blood clots. But other types are much more common, especially PH caused by heart or lung problems.

We don’t know exactly how many people around the world have pulmonary hypertension. But some estimates show PH may affect 1 in 100 people. This means 50 million to 70 million people are living with PH.

PH is even more common among older adults. Around the world, about 1 in 10 adults over age 65 have PH.

Researchers believe the number of people diagnosed with PH will rise in the next few decades.

**Risk factors**

Pulmonary hypertension is usually seen in people ages 30 to 60. Growing older can increase the risk of developing Group 1 pulmonary hypertension, called pulmonary arterial hypertension (PAH). PAH from an unknown cause is more common in younger adults.

Other things that can raise the risk of pulmonary hypertension are:

* A family history of the condition.
* Being overweight.
* Smoking.
* Blood-clotting disorders or a family history of blood clots in the lungs.
* A history of being around asbestos.
* A heart condition present at birth, called a congenital heart defect.
* Living at an altitude of 8,000 feet (2,438 meters) or higher.
* Use of some medicines, including those used for weight loss.
* Illicit drugs such as cocaine or methamphetamine.

**Complications**

Potential complications of pulmonary hypertension are:

* **Right-sided heart enlargement and heart failure.** Also called cor pulmonale, this condition causes the heart's right lower chamber to get larger. The chamber has to pump harder than usual to move blood through narrowed or blocked lung arteries.

As a result, the heart walls get thick. The right lower heart chamber stretches to increase the amount of blood it can hold. These changes create more strain on the heart. Eventually the right lower heart chamber fails.

* **Blood clots.** Pulmonary hypertension increases the risk of blood clots in the small arteries in the lungs.
* **Irregular heartbeats, also called arrhythmias.** Pulmonary hypertension can cause changes in the heartbeat, which can be life-threatening.
* **Bleeding in the lungs.** Pulmonary hypertension can lead to life-threatening bleeding in the lungs and coughing up blood.
* **Pregnancy complications.** Pulmonary hypertension can be life-threatening for the mother and the developing baby.

**Diagnosis**

Pulmonary hypertension is hard to diagnose early. It's not often found during a routine physical exam. Even when pulmonary hypertension is more advanced, its symptoms are similar to those of other heart and lung conditions.

To diagnose pulmonary hypertension, a healthcare professional examines you and asks about your symptoms. You are usually asked questions about your medical and family history.

**Tests**

Tests to diagnose pulmonary hypertension may include:

* **Blood tests.** Blood tests can help find the cause of pulmonary hypertension. The test also may help find complications of the disease.
* **Chest X-ray.** A chest X-ray is a picture of the heart, lungs and chest. It may be used to check for other lung conditions that can cause pulmonary hypertension.
* **Electrocardiogram (ECG or EKG).** This simple test records the electrical activity of the heart. It shows how the heart is beating.
* **Echocardiogram.** Sound waves create pictures of the beating heart. An echocardiogram shows how blood flows through the heart and heart valves. This test may be done to help diagnose pulmonary hypertension or to learn how treatments are working.

Sometimes, an echocardiogram is done while exercising on a stationary bike or treadmill to learn how activity affects the heart. If you have this test, you may be asked to wear a mask that checks how well the heart and lungs use oxygen and carbon dioxide.

* **Right heart catheterization.** If an echocardiogram shows pulmonary hypertension, this test may be done to confirm the diagnosis.

During this procedure, a doctor places a thin, flexible tube called a catheter into a blood vessel, usually in the neck. The tube is gently guided into the lower right heart chamber and the pulmonary artery. The doctor can then measure blood pressure in the main pulmonary arteries and the right ventricle.

Other tests may be done to check the condition of the lungs and pulmonary arteries. The following tests may give more information about the cause of pulmonary hypertension:

* **Exercise stress tests.** These tests often involve walking on a treadmill or riding a stationary bike while the heartbeat is watched. They can show how the heart reacts to exercise.
* **Computerized tomography (CT) scan.** This test uses X-rays to make pictures of specific parts of the body. Dye called contrast may be given into a vein to help the blood vessels show up more clearly on the images.

A heart CT scan, called a cardiac CT scan, can show the size of the heart and any blockages in the pulmonary arteries. It can help diagnose lung diseases that might lead to pulmonary hypertension. Examples are COPD or pulmonary fibrosis.

* **Magnetic resonance imaging (MRI).** This test uses magnetic fields and radio waves to make detailed pictures of the heart. It can show blood flow in the pulmonary arteries. The test may be done to learn how well the right lower heart chamber is working.
* **Lung function test.** For this test, you blow into a special device. The device measures how much air the lungs can hold. It shows how air flows in and out of the lungs.
* **Sleep study.** A sleep study measures brain activity, heart rate, blood pressure, oxygen levels and other things as you sleep. The test can help diagnose sleep apnea, which can cause pulmonary hypertension.
* **Ventilation/perfusion (V/Q) scan.** In this test, a radioactive tracer is given through a vein (IV). The tracer shows how blood flows. You also may breathe in a tracer that shows airflow to the lungs. A V/Q scan can tell whether blood clots are causing symptoms of pulmonary hypertension.
* **Lung biopsy.** Rarely, a sample of tissue may be taken from the lung to check for a possible cause of pulmonary hypertension.

**Genetic testing**

Screening for gene changes that cause pulmonary hypertension may be recommended. If you have these gene changes, other family members may need to be screened too.

Because symptoms are similar to other common lung diseases, it can often be hard to diagnose PAH. Diagnosis is a process of eliminating other diseases. With the help of lung and heart specialists (pulmonologist and cardiologist) you will need to complete several tests, such as:

* **Blood tests**: Your healthcare provider may check for a variety of other diseases when ordering blood tests to rule out any other reason for your symptoms, including HIV, thyroid tests, autoimmune disease panels (test for systemic lupus erythematosus, scleroderma, and rheumatoid arthritis), liver tests and blood chemistry tests.
* **BNP Test**, also called B-type natriuretic peptide test, is a simple blood test that helps to determine if your heart is working harder than it should which could indicate PAH. Your doctor may order a similar test called NT-proBNP which also checks how your heart is working.
* **Lung function tests (breathing tests)**: Checks for diseases like asthma or COPD.
* **6-Minute Walk Test**: Objectively measures how far you can walk and to see if your oxygen levels drop when you are physically active.
* **Right Heart Catheterization**:  This test is invasive, so it is not usually performed until your provider reviews other tests and determines if you would benefit from this procedure. It involves inserting a catheter (small tube) into a large vein in either the neck, arm, or groin, and threading it through the right side of the heart and into the pulmonary artery. This allows measurement of the blood pressure in the lungs.

**Pulmonary hypertension functional classification**

Once a diagnosis of pulmonary hypertension is confirmed, the condition is classified according to how the symptoms affect you and your ability to do everyday tasks.

Pulmonary hypertension may fall into one of the following groups:

* **Class I.** Pulmonary hypertension is diagnosed, but there are no symptoms during rest or exercise.
* **Class II.** There are no symptoms at rest. Everyday chores or activities such as going to work or the grocery store may cause some shortness of breath or mild chest pain. There's a slight limitation of physical activity.
* **Class III.** It's comfortable at rest, but doing simple tasks such as bathing, dressing or preparing meals causes fatigue, shortness of breath and chest pain. The ability to do physical activity becomes very limited.
* **Class IV.** Symptoms occur at rest and during physical activity. Any type of activity causes increasing discomfort.

Your healthcare team may use a risk calculator that looks at symptoms and test results to understand what type of treatment is needed. This is called pulmonary hypertension risk stratification.

**What are the stages of pulmonary hypertension?**

There are four main stages of pulmonary hypertension. The World Health Organization (WHO) calls these “functional classes.” They’re based on the symptoms you feel and refer to how well you can carry out your daily activities. As PH gets worse, the symptoms become more noticeable and more disruptive to your daily life.

* **Class 1**: You don’t have any symptoms.
* **Class 2**: You don’t have symptoms when you’re resting. But you feel some discomfort or shortness of breath during some routine activities. These include household chores and climbing stairs.
* **Class 3**: You may still feel fine when you’re resting. But it’s now much harder to do normal tasks because you feel tired or short of breath.
* **Class 4**: You have symptoms even when you’re resting. The symptoms get worse when you try to do any normal task.

**Treatment**

There's no cure for pulmonary hypertension. But treatments can improve symptoms and help you live longer. Treatment also can help keep the disease from getting worse.

It often takes some time to find the best pulmonary hypertension treatment. The treatments are often complex. You usually need a lot of health checkups.

Pulmonary hypertension treatment depends on the type of PH you have and your other medical conditions. Your healthcare team will tailor treatment to your individual needs.

Right now, only two types of PH can be treated directly:

* Pulmonary artery hypertension (PAH).
* Chronic thromboembolic pulmonary hypertension (CTEPH).

Treatment for other types of PH involves managing the underlying medical conditions.

Treatment for pulmonary arterial hypertension (PAH) includes:

* **Calcium channel blockers**. These medications can help lower the blood pressure in your pulmonary arteries and throughout your body.
* **Diuretics**. These “water pills” help your body clear out extra fluid.
* **Oxygen therapy**. You may need this treatment if you don’t have enough oxygen in your blood.
* **Pulmonary vasodilators**. These medications help your pulmonary arteries relax and open up better. This improves blood flow and lowers the strain on your heart.

Treatment for CTEPH includes:

* **Anticoagulants**. These medicines help prevent blood clots.
* **Balloon atrial septostomy (BAS)**. This procedure is typically used for babies with critical heart defects. However, it’s also used for adults with pulmonary hypertension. It’s a bridge that helps keep you stable as you wait for a lung transplant.
* **Balloon pulmonary angioplasty (BPA)**. This catheter-based procedure uses a balloon to widen your pulmonary artery. It’s usually done if you can’t have open surgery.
* **Medication**. A soluble guanylate cyclase stimulator (SGCS) may help slow down the disease progression.
* **Pulmonary endarterectomy (PEA)**. This surgery removes blood clots from your lungs. It’s currently the only possible cure for pulmonary hypertension, and it’s only for people with CTEPH.

Treatment for PH caused by heart or lung problems focuses on managing the underlying conditions. Because so many different heart and lung conditions cause PH, treatment plans can be vastly different from person to person. Talk with your provider about what’s best for you. In general, your provider may recommend:

* Dietary changes.
* Lifestyle changes.
* Medication to manage problems like hypertension or heart failure.
* Oxygen therapy.
* Surgery, such as heart valve repair.

Treatments for PH caused by other medical conditions (WHO Group 5) are still evolving. Your provider will work with you to determine the best care plan.

A last resort option for some people with severe pulmonary hypertension is a lung transplant.

**Medications**

If you have pulmonary hypertension, you may get medicines to treat your symptoms and help you feel better. Medicines also may be used to treat or prevent complications. Treatment may include:

* **Medicines to relax blood vessels, called vasodilators.** These medicines open narrowed blood vessels and improve blood flow. The medicine may be breathed in, taken by mouth or given through a vein. Sometimes, it's given continuously through a small pump attached to the body.

Examples of vasodilators to treat pulmonary hypertension include epoprostenol (Flolan, Veletri), treprostinil (Remodulin, Tyvaso, others), iloprost and selexipag (Uptravi).

* **Soluble guanylate cyclase (sGC) stimulators.** This type of medicine relaxes the pulmonary arteries and lowers pressure in the lungs. An example is riociguat (Adempas). Do not take these medicines if you're pregnant.
* **Medicines to widen blood vessels.** Medicines called endothelin receptor antagonists reverse the effect of a substance in the walls of blood vessels that causes them to narrow. Such medicines include bosentan (Tracleer), macitentan (Opsumit) and ambrisentan (Letairis). They may improve energy level and symptoms. Do not take these medicines if you're pregnant.
* **Medicines to increase blood flow.** Medicines called phosphodiesterase 5 (PDE5) inhibitors may be used to increase blood flow through the lungs. These medicines also are used to treat erectile dysfunction. They include sildenafil (Revatio, Viagra) and tadalafil (Adcirca, Alyq, Cialis).
* **High-dose calcium channel blockers.** These medicines help relax the muscles in the walls of blood vessels. They include amlodipine (Norvasc), diltiazem (Cardizem, Tiazac, others) and nifedipine (Procardia). Although calcium channel blockers can be effective, only a small number of people with pulmonary hypertension improve while taking them.
* **Blood thinners.** Also called anticoagulants, these medicines help prevent blood clots. One example is warfarin (Jantoven). The medicines can increase the risk of bleeding. This is especially true if you're having surgery or a treatment that enters the body or creates an opening in the skin. Talk to your healthcare team about your risk.
* **Digoxin (Lanoxin).** This medicine helps the heart beat stronger and pump more blood. It can help control irregular heartbeats.
* **Water pills, also called diuretics.** These medicines help the kidneys remove excess fluid from the body. This reduces the amount of work the heart has to do. Diuretics also may be used to reduce fluid buildup in the lungs, legs and belly area.
* **Oxygen therapy.** Breathing pure oxygen may be suggested if you live at a high altitude or have sleep apnea. Some people with pulmonary hypertension need oxygen therapy all the time.

**Surgery or other procedures**

If medicines do not help control the symptoms of pulmonary hypertension, surgery may be recommended. Surgeries and procedures to treat pulmonary hypertension may include:

* **Atrial septostomy.** This treatment may be done if medicines don't control pulmonary hypertension symptoms. In an atrial septostomy, a doctor creates an opening between the upper left and right chambers of the heart. The opening reduces the pressure on the right side of the heart. Potential complications include irregular heartbeats called arrhythmias.
* **Lung or heart-lung transplant.** Sometimes, a lung or heart-lung transplant may be needed, especially for younger people who have idiopathic pulmonary arterial hypertension. After a transplant, medicine must be taken for life to prevent the body from rejecting the new organ.

**Lifestyle and home remedies**

Lifestyle changes may help improve pulmonary hypertension symptoms. Try these tips:

* **Eat healthy.** Eat a healthy diet rich in whole grains, fruits and vegetables, lean meats, and low-fat dairy products. Try to stay away from saturated fat, trans fat and cholesterol. Use less salt.
* **Stay as active as possible and manage weight.** Even mild forms of activity might be too exhausting for some people who have pulmonary hypertension. For others, moderate exercise, such as walking, might be helpful — especially when done during oxygen therapy. Your healthcare team can help you plan an appropriate exercise program.
* **Don't smoke.** If you smoke, quit. If you need help, ask your healthcare team for treatment that can help. Avoid secondhand smoke too, if possible.
* **Get plenty of rest.** Resting can reduce tiredness related to pulmonary hypertension.
* **Avoid high altitudes.** High altitudes can make pulmonary hypertension worse. If you live at an altitude of 8,000 feet (2,438 meters) or higher, you might be told to consider moving to a lower altitude.
* **Avoid activities that can lower blood pressure a lot.** These include sitting in a hot tub or sauna or taking long hot baths or showers. Such activities lower blood pressure and can cause fainting. Also, do not do activities that cause a lot of straining, such as lifting heavy objects or weights.
* **Tell your healthcare team about the medicines you take.** Some medicines can make pulmonary hypertension worse or affect its treatment.
* **Get regular health checkups.** Tell your healthcare team about any new or worsening symptoms or medicine side effects. If pulmonary hypertension affects your quality of life, ask about treatments that could help.
* **Get recommended vaccines.** Respiratory infections can cause serious health concerns for people with pulmonary hypertension. Ask your healthcare team which vaccines you need to prevent common viral infections.
* **Talk to a healthcare professional before becoming pregnant.** Pulmonary hypertension can cause serious complications for the pregnant person and unborn baby, also called a fetus. Birth control pills can increase the risk of blood clots. Talk to your healthcare team about other birth control options.

**Outlook / Prognosis**

**What is the outlook for people with pulmonary hypertension?**

The outlook for people with pulmonary hypertension depends on:

* The cause of PH.
* How early it’s diagnosed.
* The severity of symptoms.
* Associated medical conditions.

The outlook for each person is different. Talk with your provider to learn more about your prognosis and how to manage your condition.

**Preparing for your appointment**

If you think that you are at risk of or that you might have pulmonary hypertension, make an appointment for a health checkup.

There's often a lot to discuss at your appointment, so it's a good idea to be prepared. Here's some information to help you get ready for your appointment.

**What you can do**

* **Be aware of any pre-appointment restrictions.** When you make your appointment, ask if there is anything you need to do before your checkup. For example, you might be told not to eat or drink before some medical tests.
* **Write down any symptoms you're having,** including any that might not seem related to pulmonary hypertension. Try to remember when they began. Be specific, such as days, weeks and months.
* **Make a list of important personal information.** Include any family history of pulmonary hypertension, lung disease, heart disease, stroke, high blood pressure or diabetes. Also list any major stresses or recent life changes.
* **Make a list of all medicines that you take.** Also include vitamins, herbal products, supplements and any medicines bought without a prescription.
* **Take someone with you,** if possible. Someone who goes with you can help you remember information you're given.
* **Be prepared to discuss** your diet and exercise habits. If you don't already follow a diet or exercise routine, talk to your healthcare team about any challenges you might face in getting started.
* **Make a list of questions to ask** your healthcare team. List your questions from most important to least important in case time runs out.

**For pulmonary hypertension, some questions to ask your healthcare team are:**

* What is the likely cause of my symptoms or condition?
* What are other possible causes?
* What tests do I need?
* What treatment do you recommend?
* What are the other treatment options?
* Is there a generic form of the medicine you're prescribing?
* What's an appropriate level of physical activity?
* Are there any restrictions that I need to follow?
* How often do I need health checkups?
* I have other health conditions. How can I best manage them together?
* Should I see a specialist?
* Is there any information that I can take home? What websites do you suggest?

**What to expect from your doctor**

Your healthcare team may ask you many questions. Being ready to answer them might give you more time to discuss any concerns. You may be asked:

* When did you first begin having symptoms?
* Do you always have symptoms, or do they come and go?
* On a scale of 1 to 10, with 10 being the worst, how bad are your symptoms?
* What, if anything, seems to make your symptoms better?
* What, if anything, seems to make your symptoms worse?

**When should I call my healthcare provider?**

Call your provider if you’re having problems with:

* A fast heart rate (120 beats per minute).
* A respiratory infection or cough that’s getting worse.
* Constantly feeling dizzy or lightheaded.
* Episodes of chest pain or discomfort with physical activity.
* Extreme fatigue or decreased ability to do your normal activities.
* Nausea or lack of appetite.
* Restlessness or confusion.
* Shortness of breath that’s gotten worse, especially if you wake up feeling short of breath.
* Swelling in your ankles, legs or tummy that’s gotten worse.
* Trouble breathing with regular activities or at rest.
* Weight gain (2 pounds in one day or 5 pounds in one week).

**Can pulmonary hypertension be cured?**

Most cases of pulmonary hypertension can’t be cured. Your provider may prescribe medications to:

* Ease your symptoms.
* Improve your quality of life.
* Slow down the progression of the disease.

Your provider may also recommend lifestyle changes.

However, surgery can cure some people with chronic thromboembolic pulmonary hypertension (CTEPH).

**What is the life expectancy for people with pulmonary hypertension?**

The life expectancy varies from person to person. It depends how quickly you’re diagnosed and what other medical conditions you have. Talk with your provider about what you can expect in your individual situation.

Pulmonary hypertension is a progressive disease. That means it gets worse over time. It progresses more quickly in some people than in others. Treatment can improve your chances of surviving pulmonary hypertension for many years.

**How can I prevent pulmonary hypertension?**

It’s not always possible to prevent pulmonary hypertension. Some risk factors are out of your control. If you have risk factors, your provider may recommend preventive screenings to check your heart and lung function.

Doing whatever you can to prevent or manage other medical conditions can help lower your risk of pulmonary hypertension. Steps you can take include:

* **Create an exercise plan**. Ask your provider what exercises are safe for you.
* **Follow a heart-healthy diet**. Avoid processed foods, fast food and other foods high in salt and saturated fat.
* **Quit smoking and stop using tobacco**. Smoking and tobacco use are top risk factors for heart and lung problems. Quitting isn’t easy, especially if you’ve been smoking or using tobacco for a long time. But your provider can help provide resources. Support groups may also help.
* **Take medications** for blood pressure and other conditions as prescribed.

**What dietary changes should I make?**

Your provider will give you specific recommendations. One key step involves reducing your sodium intake. This means:

* Avoid adding salt at the table or using “seasoning salt.”
* Avoid smoked, cured, salted and canned meat products.
* Buy foods that are “low sodium” or “low salt.”
* Limit fast foods and prepared foods.

Other dietary changes include:

* Eat foods high in fiber (like whole grains, bran, fruits and vegetables).
* Eat foods high in potassium (like dried fruits, bananas and oranges).
* Eat foods high in magnesium (like peanuts, tofu and broccoli).
* Limit foods that contain refined sugar, saturated fat and cholesterol.

**Medical Codes**

|  |  |  |  |
| --- | --- | --- | --- |
| **Code** | **Description** | **WHO Group** | **Source** |
| **I27.0** | **Primary pulmonary hypertension (Idiopathic PAH)** | **Group 1** | **CDC ICD-10-CM 2024** |
| **I27.2** | **Secondary pulmonary hypertension** | **NOS** | **CMS 2024 ICD-10-CM** |
| **I27.21** | **Secondary pulmonary arterial hypertension** | **Group 1** | **CDC ICD-10-CM 2024** |
| **I27.22** | **Pulmonary hypertension due to left heart disease** | **Group 2** | **CMS 2024 ICD-10-CM** |
| **I27.23** | **Pulmonary hypertension due to lung diseases and hypoxia** | **Group 3** | **CDC ICD-10-CM 2024** |
| **I27.24** | **Chronic thromboembolic pulmonary hypertension (CTEPH)** | **Group 4** | **CMS 2024 ICD-10-CM** |
| **I27.29** | **Other secondary pulmonary hypertension** | **Group 5** | **CDC ICD-10-CM 2024** |
| **I27.81** | **Cor pulmonale (chronic)** | **Complication** | **CMS 2024 ICD-10-CM** |
| **I27.82** | **Chronic pulmonary embolism with pulmonary hypertension** | **Group 4** | **CDC ICD-10-CM 2024** |
| **I27.83** | **Eisenmenger's syndrome** | **Group 1** | **CMS 2024 ICD-10-CM** |
| **I27.89** | **Other specified pulmonary heart diseases** | **Varied** | **CDC ICD-10-CM 2024** |
| **P29.3** | **Persistent pulmonary hypertension of newborn (PPHN)** | **Neonatal** | **CMS 2024 ICD-10-CM** |

**References**

<https://www.mayoclinic.org/diseases-conditions/pulmonary-hypertension/multimedia/vid-20078204>

<https://www.mayoclinic.org/diseases-conditions/pulmonary-hypertension/symptoms-causes/syc-20350697>

<https://my.clevelandclinic.org/health/diseases/6530-pulmonary-hypertension-ph>

<https://www.lung.org/lung-health-diseases/lung-disease-lookup/pulmonary-arterial-hypertension/symptoms-diagnosis>

**CONGENITAL LUNG MALFORMATIONS AND RESTRICTIVE LUNG DISEASE**

**Definition**

Congenital lung malformations are rare disorders that emerge during a fetus’ development in the womb and are present at birth. Although usually one area of the lung is affected, the malformations can cause difficulty with breathing, recurrent lung infection and, in very rare instances, lung cancer.

Congenital lung malformations occur in 4 of 10,000 live births. Though they are rare, congenital lung malformations are the most common birth defect affecting the lungs.

**Types of Congenital Lung Malformations**

There are two primary types of malformations:

**Congenital Pulmonary Airway Malformation (CPAM)**

Sometimes called congenital cystic adenomatoid malformation (CCAM), a CPAM is a benign mass that forms in the lower respiratory tract when lung tissue in the fetus grows larger than normal. This lesion may cause large fluid-filled cysts (macrocysts), small cysts (microcysts) or a mix of both. The fetus can have one or more CPAMs, and most occur in only one section (known as the lobe) of the lung.

The lesions usually stop growing at approximately 26 weeks gestation, at which time many begin to slowly shrink until term.

Large CPAMs can lead to a dangerous condition in the womb known as hydrops, the accumulation of fluid in two or more compartments of the body of the fetus. Hydrops develops when too much blood flows into the area of the lesion. This causes the fetus’ heart to work harder to support the extra blood flow in the body, which can lead to congenital heart failure. Hydrops can be life-threatening to the fetus, especially those under 30 weeks gestation.

**Bronchopulmonary Sequestration (BPS)**

Bronchopulmonary sequestrations are solid masses of lung tissue that do not connect to the rest of the lung airways. BPS lesions have an abnormal blood supply through a vessel connected to the aorta. These lesions can be inside the lungs (known as intralobar) or outside the lungs (known as extralobar).

**Other Types of Congenital Lung Malformations**

* **Hybrid lesion:** a combination of CPAM and BPS
* **Bronchogenic cysts**: A growth of tissue that usually develops on the esophagus or trachea. They can cause blocked airways when large or infected.
* **Bronchial atresia:**A rare condition that causes partial blockage of the bronchus, the part of the airway that lets air into the lungs.
* **Congenital lobar emphysema:** A rare, yet serious, condition in which a blockage of the airway traps the airflow during breathing and leads to overinflation of the newborn’s lungs.

**Causes of Congenital Lung Malformations**

The causes of congenital lung malformations are not yet known.

**Congenital Lung Malformation Diagnosis**

**Before Birth**

Congenital lung malformations are typically found on a [prenatal ultrasound](https://www.hopkinsmedicine.org/health/treatment-tests-and-therapies/fetal-ultrasound).

Additional imaging may sometimes be helpful. These include:

* Fetal MRI (magnetic resonance imaging). Imaging used to see the lesion in more detail and measure the air moving in and out of the lungs.
* [Fetal echocardiogram](https://www.hopkinsmedicine.org/health/treatment-tests-and-therapies/echocardiogram/fetal-echocardiography). An ultrasound of the fetus’ heart that can view the function of the heart.

A measurement called CVR (CPAM-volume-ratio) is usually performed during each ultrasound evaluation. CVR helps to determine the risk of hydrops, and it may help predict the risk of breathing problems at birth.

More than 90% of babies diagnosed with congenital lung malformations during pregnancy do not have any fetal problems. More than 80% of babies diagnosed with a congenital lung malformation during pregnancy do not have any breathing problems at birth.

**After Birth**

All babies with a suspected congenital lung malformation are recommended to undergo a CT scan to best characterize the anatomy of the lesion. In those who have no symptoms, the study may be delayed until a child is at least 2 months old. X-rays alone are not helpful in determining the best treatment plan.

**Congenital Lung Malformation Symptoms**

A child with a congenital lung malformation may show symptoms after birth, such as:

* Rapid breathing
* Shortness of breath or wheezing
* Recurring [pneumonia](https://www.hopkinsmedicine.org/health/conditions-and-diseases/pneumonia) (lung infections)
* Collapsed lung (pneumothorax)

**Congenital Lung Malformation Treatment**

**Treatment Before Birth**

* When a congenital lung malformation is found, the care team will monitor the lesion’s size through regular prenatal ultrasounds. If hydrops occurs, several fetal treatments may be suggested:
* **Steroid Therapy**
* For microcystic lesions, two doses of a steroid called betamethasone may be given to the mother to prevent hydrops in the fetus when large lesions are present, or reverse hydrops that is already present.
* **Thoracoamniotic shunts**
* A thin tube is placed into a large macrocyst to drain the extra fluid from around the fetus’ lung and into the womb. This decreases the mass, which removes pressure on the fetus’ lungs, heart and blood vessels in an effort to remove hydrops.
* **Fetal Surgery**
* **Lobectomy** – Surgical removal of the entire mass while still in the womb may be recommended if the baby has severe hydrops and evidence of heart failure. Fortunately, the need to do fetal surgery to remove congenital lung malformations is very rare.
* **EXIT (ex utero intrapartum treatment) delivery**: Another option is a special type of cesarean section in which the lung mass is removed by pediatric surgeons while the fetus is still attached to the placenta. The umbilical cord is then cut, and the baby is supported by a breathing machine. This allows the surgeon to remove the tumor before delivery so that the remaining lungs can expand and function better.

**Treatment After Birth**

**Postnatal Surgery**

Most babies born with a congenital lung malformation will usually require surgery soon after birth to remove the lesions. Many lesions that remain in the lungs will eventually become infected and cause pneumonia. There is also a small risk that some will become cancerous. Babies with breathing problems at birth due to congenital lung malformations need to have surgery soon after birth to remove the mass. Babies who do not have breathing problems are observed for 48 hours and discharged home with outpatient surgical follow-up care arranged.

The typical age recommendation of surgery for babies with a congenital lung malformation and no breathing problems is between 3 and 6 months of age. Delaying the procedure until an infant is a little older is ideal because they can better handle anesthesia and have grown enough to undergo minimally invasive (keyhole) surgery to remove the lesion. Keyhole surgery results in less pain and smaller scars. Most babies do not need to recover in an intensive care unit, and they can be discharged within two to three days of the surgery.

There are situations in which it may be better to observe small congenital lung malformations rather than to remove them. This recommendation is determined by the surgeon. In those cases, follow up CT scans or other imaging is recommended.

**Outlook**

The prognosis is excellent in the vast majority of children with congenital lung malformations. After treatment, most children go on to lead normal, healthy lives.

**Mesdical Codes**

|  |  |  |  |
| --- | --- | --- | --- |
| **Code** | **Category** | **Description** | **Source** |
| **Q30-Q34** | **CONGENITAL LUNG MALFORMATIONS** | **Congenital malformations of respiratory system** | **CDC ICD-10-CM 2024** |
| **Q33.0** | **Congenital** | **Congenital cystic lung** | **CMS 2024 ICD-10-CM** |
| **Q33.1** | **Congenital** | **Accessory lobe of lung** | **CDC ICD-10-CM 2024** |
| **Q33.3** | **Congenital** | **Congenital hypoplasia and dysplasia of lung** | **CMS 2024 ICD-10-CM** |
| **Q33.4** | **Congenital** | **Congenital bronchiectasis** | **CDC ICD-10-CM 2024** |
| **Q33.6** | **Congenital** | **Congenital pulmonary sequestration** | **CMS 2024 ICD-10-CM** |
| **Q33.8** | **Congenital** | **Other congenital malformations of lung** | **CDC ICD-10-CM 2024** |
| **Q32.2** | **Congenital** | **Congenital bronchomalacia** | **CMS 2024 ICD-10-CM** |
| **Q79.0** | **Congenital** | **Congenital diaphragmatic hernia** | **CDC ICD-10-CM 2024** |
| **J60-J70** | **RESTRICTIVE LUNG DISEASES** | **Pulmonary diseases due to external agents** | **CDC ICD-10-CM 2024** |
| **J84.10** | **Restrictive** | **Pulmonary fibrosis, unspecified** | **CMS 2024 ICD-10-CM** |
| **J84.112** | **Restrictive** | **Idiopathic pulmonary fibrosis** | **CDC ICD-10-CM 2024** |
| **J84.2** | **Restrictive** | **Lymphoid interstitial pneumonia** | **CMS 2024 ICD-10-CM** |
| **J84.89** | **Restrictive** | **Other specified interstitial pulmonary diseases** | **CDC ICD-10-CM 2024** |
| **J98.4** | **Restrictive** | **Other disorders of lung (includes alveolar proteinosis)** | **CMS 2024 ICD-10-CM** |
| **M33.0** | **Restrictive** | **Dermatopolymyositis with respiratory involvement** | **CDC ICD-10-CM 2024** |
| **M33.2** | **Restrictive** | **Polymyositis with respiratory involvement** | **CMS 2024 ICD-10-CM** |
| **G70.0** | **Restrictive** | **Myasthenia gravis with respiratory involvement** | **CDC ICD-10-CM 2024** |
| **M41.00** | **Restrictive** | **Adolescent idiopathic scoliosis, site unspecified (if causing restriction)** | **CMS 2024 ICD-10-CM** |
| **J63.6** | **Restrictive** | **Pneumoconiosis due to asbestos (asbestosis)** | **CDC ICD-10-CM 2024** |
| **J64** | **Restrictive** | **Unspecified pneumoconiosis** | **CMS 2024 ICD-10-CM** |
| **E84.0** | **Restrictive** | **Cystic fibrosis with pulmonary manifestations** | **CDC ICD-10-CM 2024** |
| **D86.0** | **Restrictive** | **Sarcoidosis of lung** | **CMS 2024 ICD-10-CM** |

**References**

**<https://www.hopkinsmedicine.org/health/conditions-and-diseases/congenital-lung-malformations>**

<https://www.childrensnational.org/get-care/health-library/congenital-pulmonary-airway-malformations>

**AERODIGESTIVE DISORDER AFFECTING BOTH BREATHING AND SWALLOWING**

**Definition**

The term "aerodigestive" refers to the organs and tissues of the respiratory tract and the upper part of the digestive tract. This includes the mouth and throat (oropharynx), voice box (larynx), windpipe (trachea), lungs, food pipe (esophagus), and stomach.

Conditions of the aerodigestive system often are complex because each of the systems is linked and interconnected, and a problem in one system can cause issues in another. This requires a team of experts from each of the relevant medical specialties to properly diagnose and treat your child's symptoms.

**Symptoms**

The typical child evaluated by the Aerodigestive Program is a child who experiences one or more of the following:

* Difficulty with eating or drinking
* Failure to gain weight
* Frequent coughing or choking episodes while eating or drinking
* A wet cough or voice
* Frequent diagnoses of pneumonia
* Multiple hospitalizations for illnesses that look like a cold
* An early diagnosis of asthma (younger than 6 months old)

Sometimes, these children have been born premature, had a stay in the Neonatal Intensive Care Unit (NICU), or had a diagnosis of cerebral palsy, global developmental delays, or a genetic syndrome.

**Types of Pediatric Aerodigestive Disorders**

Aerodigestive disorders can affect multiple parts of your child’s aerodigestive tract, which includes their airways, lungs and upper digestive tract. It’s possible for a child to have more than one type of aerodigestive disorder.

Aerodigestive disorders we treat include:

* Achalasia
* Airway malacias, including laryngomalacia and tracheomalacia
* Airway obstructions, including laryngeal cysts and tumors
* Aspiration
* Bronchiectasis and bronchomalacia
* Chronic aspiration and recurrent aspiration pneumonia
* Chronic cough
* Dysphagia
* Eosinophilic gastrointestinal diseases (EGIDs), such as eosinophilic esophagitis (EoE)
* Esophageal atresia, strictures and webs
* Feeding disorders, including sensory or texture issues (oral aversions) and intestinal failure
* Feeding tube dependency
* **[Infant chronic lung disease](https://www.chla.org/infant-chronic-lung-disease-program)** (bronchopulmonary dysplasia)-related swallowing and airway disorders
* Laryngeal and tracheal stenosis
* Laryngeal clefts and webs
* Noisy or high-pitched breathing (stridor)
* Gastroesophageal reflux disease (GERD) with persistent symptoms
* Recurrent croup, recurrent pneumonia, recurrent respiratory infections
* Respiratory papillomatosis
* Tracheoesophageal fistula (TEF) with or without esophageal atresia
* Tracheostomy dependency
* Vocal cord dysfunction or paralysis

**Diagnosis**

. These might include:

* Blood tests
* Breathing tests
* Impedance/pH probe to measure acid in the esophagus
* Swallow (video fluoroscopic) study
* Imaging of the chest or esophagus (X-rays or computed tomography)
* Flexible laryngoscopy to view throat and voice box

For many children, an evaluation of the entire upper aerodigestive tract might be recommended.

This involves three evaluation studies, when taken together are called triple endoscopy or "triple scope." This evaluation provides direct observation of all structures in the aerodigestive tract by each specialist. Coordinating these procedures decreases your child's exposure to anesthesia and allows for a more comprehensive evaluation. The triple scope procedures include:

* Direct rigid laryngobronchoscopy (DLB) by a pediatric otolaryngologist
* Flexible bronchoscopy with bronchoalveolar lavage (BAL) by a pediatric pulmonologist
* Esophagogastroduodenoscopy (EGD) with biopsies by a pediatric gastroenterologist

**Common conditions diagnosed by the Aerodigestive Program**

The Aerodigestive Program focuses on providing comprehensive diagnosis services for children suffering from complex problems. Once we have identified the condition, your treatment might be with one or more experts from our pediatric specialties listed above.

**Breathing conditions**

There are a variety of airway conditions that stem from issues affecting the voice box (larynx) or breathing tube (trachea).

* **Stertor, stridor and wheezing.**These can be signs of airway problems such as **subglottic stenosis, tracheal stenosis**, or **vocal cord dysfunction/paralysis.**
* **Laryngomalacia, tracheomalacia or bronchomalacia.** These conditions refer to abnormalities with the voice box (laryngomalacia), trachea (tracheomalacia) and lungs (bronchomalacia) that can cause noisy breathing.
* **External esophageal or airway compression from a vascular ring or sling:** rare conditions in which blood vessels are wrapped around the esophagus or airway, causing obstruction and difficulty with breathing and swallowing.
* **Laryngeal cleft, laryngotracheal cleft, laryngotrachealesophageal cleft.** These are a group of rare inherited disorders in which there is an abnormal opening between the airway and the esophagus. This can cause children to inhale food into their airway. These conditions require surgery to repair, and this can significantly improve a child's swallowing function

**Digestive conditions**

* **Eosinophilic Esophagitis:** an autoimmune disease that increase inflammation in the esophagus
* **Gastroesophageal reflux (GERD)**
* Feeding disorders such as **dysphagia**, or swallowing difficulties, **chronic aspiration**, **G-tube dependency**

**Lung conditions**

* **Aspiration pneumonia/pneumonitis, or reoccurring pneumonia**
* **Chronic cough**

**Treatment and follow-up care**

Once we have met your child and reviewed his or her evaluation tests, our team meets as a group to discuss and develop a tailored treatment plan. The plan likely will include dietary modifications, medications, and could involve surgery. No matter your child's treatment, our team will be by your side throughout the process, providing follow-up visits to ensure your child is doing well. The Aerodigestive Program is part of Children's Hospital, which means you have access to a wide array of other medical experts who specialize in the care of children.

The C.S. Mott Children’s Hospital team is committed to supporting both the short and long-term medical needs of our patients.

Your child’s care team will first review available medical therapies to determine if alternative medical treatment or modifications of the current treatment would be appropriate.

For those children whose conditions aren’t well managed through medication alone, we offer expertise in a full range of procedural and surgical techniques to give patients the most up-to-date and effective options for resolving their aerodigestive conditions.

Surgical techniques that may be recommended include laser surgery, minimally invasive techniques using endoscopic balloon dilation, and cartilage and mucosal grafting .

Other procedures that we offer include:

* **Laryngoscopy** to visualize the throat and voice box.
* **Bronchoscopy** to examine the airway within the lungs.
* **Esophagogastroduodenoscopy with biopsies and/or dilation** used to examine the esophagus, stomach, and duodenum for signs of infection, inflammation, or narrowing.
* **Endoscopic laryngotracheal cleft repair,**a procedure used to fix a cleft between the esophagus and trachea.
* **Treatment of laryngeal webs and stenosis**using microscopic instruments as well as the laser to restore normal anatomy and function.
* **Vocal cord medialization**, a procedure in which the paralyzed vocal cord is advanced to the middle so that the functioning vocal cords can close as necessary for normal voice and swallowing.
* **Vocal cord reinnervation,** an innovative procedure for vocal cord paralysis in which the surgeon takes a branch of the ansa cervicalis, a motor nerve in the neck, and sews it to the recurrent laryngeal nerve.   The nerve graft gives the vocal cord tone and can improve vocal quality and swallowing in children with a paralyzed vocal cord.
* **Nissen fundoplication,**a procedure used to treat severe gastroesophageal reflux to stop the acid going up the esophagus as easily.
* **Gastrostomy tube placement**enables nutrition to be delivered directly to the stomach.

**Rehabilitation and support:**  Your child will have access to our specialized pediatric social work team and child life therapists to understand and cope with anxiety related to his or her condition and treatment.  We also coordinate with our audiology and speech-language pathology team to provide integrated support for children with speech, language and swallowing/feeding disorders.

**Medical Codes**

|  |  |  |  |
| --- | --- | --- | --- |
| **Code** | **Description** | **Key Components** | **Source** |
| **J39.2** | **Other diseases of pharynx (includes neuromuscular dysfunction)** | **Swallowing + Breathing impairment** | **CDC ICD-10-CM 2024** |
| **G12.2** | **Motor neuron disease with bulbar palsy** | **Neuromuscular swallowing/breathing failure** | **CMS 2024 ICD-10-CM** |
| **Q31.8** | **Other congenital malformations of larynx (e.g., laryngomalacia with dysphagia)** | **Congenital airway + Swallowing defect** | **CDC ICD-10-CM 2024** |
| **Q39.4** | **Congenital tracheoesophageal fistula** | **Airway-swallowing connection anomaly** | **CMS 2024 ICD-10-CM** |
| **J47.0** | **Bronchiectasis with acute exacerbation and dysphagia** | **Airway obstruction + Swallowing issue** | **CDC ICD-10-CM 2024** |
| **G70.00** | **Myasthenia gravis without acute crisis with dysphagia** | **Neuromuscular respiratory/swallow failure** | **CMS 2024 ICD-10-CM** |
| **R13.1** | **Dysphagia, oropharyngeal phase** | **Swallowing impairment affecting airway** | **CDC ICD-10-CM 2024** |
| **J38.3** | **Other diseases of vocal cords (e.g., paradoxical movement)** | **Airway protection compromise** | **CMS 2024 ICD-10-CM** |
| **P28.89** | **Other respiratory conditions of newborn (e.g., laryngeal incoordination)** | **Neonatal aerodigestive dysfunction** | **CDC ICD-10-CM 2024** |
| **M35.8** | **Other specified systemic connective tissue disorders with respiratory involvement** | **Autoimmune-related dysfunction** | **CMS 2024 ICD-10-CM** |
| **J98.09** | **Other diseases of trachea (e.g., tracheobronchomalacia with aspiration)** | **Airway collapse + Aspiration risk** | **CDC ICD-10-CM 2024** |

|  |  |
| --- | --- |
| **Code Pair** | **Use Case** |
| **R13.1 + J98.09** | **Oropharyngeal dysphagia with tracheomalacia-induced aspiration** |
| **Q39.4 + J22** | **Tracheoesophageal fistula with recurrent acute lower respiratory infection** |
| **G12.2 + J96.90** | **Bulbar palsy with respiratory failure** |
| **Q31.8 + P92.8** | **Congenital laryngeal anomaly with feeding difficulties** |

**References**

<https://www.muhealth.org/conditions-treatments/pediatrics/pediatric-ent/aerodigestive-program>

<https://www.chla.org/aerodigestive-program/disorders>

<https://www.childrenshospital.org/programs/aerodigestive-center/conditions-and-treatments>

**NEUROMUSCULAR DISEASE-CAUSING RESPIRATORY COMPROMISE**

**Definition**

Pulmonologists from the Respiratory Institute operate a neuromuscular disease clinic with a singular focus on managing pulmonary complications from restrictive thoracic disorders, hypoventilation and obesity hypoventilation, neurologic and neuromuscular diseases including conditions such as multiple sclerosis, Parkinson, paraplegia, post-polio syndrome, amyotrophic lateral sclerosis, spinal muscular atrophy, diaphragm paralysis, Charcot-Marie-Tooth, myasthenia gravis, muscular dystrophies, mitochondrial diseases, inclusion body myositis, lysosomal storage diseases, mucopolysaccharidoses, polymyositis, and other neuromuscular disorders.

Our team works in partnership with neurologists, the mitochondrial medicine group, Genomics institute, sleep physicians, physical therapists, respiratory therapists, and thoracic surgeons, to provide the most comprehensive medical care for our patients. Our team monitors patients’ symptoms and provides therapeutic interventions, when needed, including cough assistance methods, ventilatory assistance and tracheostomy.

Neuromuscular diseases affect the function of muscles due to problems with the nerves and muscles in your body. The most common sign of these diseases is muscle weakness. Mayo Clinic neurologists provide comprehensive evaluation of these diseases, including electrodiagnostic studies and other tests.

**Conditions and symptoms**

* [Amyotrophic lateral sclerosis (ALS)](https://www.mayoclinic.org/diseases-conditions/amyotrophic-lateral-sclerosis/care-at-mayo-clinic/mac-20354030)
* [Botulism](https://www.mayoclinic.org/diseases-conditions/botulism/symptoms-causes/syc-20370262)
* [Congenital myasthenic syndromes](https://www.mayoclinic.org/diseases-conditions/congenital-myasthenic-syndrome/symptoms-causes/syc-20354754)
* Congenital myopathies
* Cramp-fasciculation syndrome
* Elevated creatine kinase
* Inclusion-body myositis
* Lambert-Eaton syndrome
* Mitochondrial myopathy
* Motor neuron disease
* [Muscular dystrophy](https://www.mayoclinic.org/diseases-conditions/muscular-dystrophy/symptoms-causes/syc-20375388)
* [Myasthenia gravis](https://www.mayoclinic.org/diseases-conditions/myasthenia-gravis/symptoms-causes/syc-20352036)
* Myotonic dystrophy
* Neuromyotonia
* [Peripheral neuropathy](https://www.mayoclinic.org/diseases-conditions/peripheral-neuropathy/symptoms-causes/syc-20352061)
* [Polymyositis](https://www.mayoclinic.org/diseases-conditions/polymyositis/symptoms-causes/syc-20353208)

**Diagnosis**

Patients presenting with respiratory muscle weakness will typically have nocturnal symptoms including orthopnea, sleep disruption, and headache upon awakening. These symptoms are very similar to the presentation of obstructive sleep apnea. Daytime symptoms include hypersomnolence, dyspnea (positional or nonspecific), tachypnea, and dysarthria. Symptoms may have insidious onset, and are often difficult to recognize.[1](https://pmc.ncbi.nlm.nih.gov/articles/PMC6053085/" \l "b1-dnnd-6-111)

At initial presentation, the patient should be investigated for any coexistent pathology that may explain the symptoms (pulmonary infection, pneumothorax, or other pulmonary or cardiac pathology). Neuromuscular conditions with the possibility of rapid deterioration should be considered first, such as MG or acute inflammatory demyelinating poly-neuropathy. If respiratory failure is impending, supportive management should be instituted. When acute conditions have been excluded and the patient is stable with regard to his/her respiratory condition, they should be investigated for the underlying cause. Subsequent investigations should depend upon the clinical scenario.

Approach to diagnostic investigations

| **Clinical presentation** | **Differential diagnosis** | **Initial testing** |
| --- | --- | --- |
| Bulbar weakness | Amyotrophic lateral sclerosis Myasthenia gravis | Electromyography Single-fiber EMG Electromyography Single-fiber EMG AchR-antibody serology |
| Ophthalmoplegia/ptosis | Myasthenia gravis Mitochondrial myopathy Oculopharyngodistal myopathy | Single-fiber EMG AchR-antibody serology Muscle biopsy Genetic testing Muscle biopsy |
| Proximal myopathy | Pompe disease Inflammatory myopathy • polymyositis • dermatomyositis • sarcoidosis Limb-girdle muscular dystrophy (2C, D, I) | GAA dried blood-spot assay Muscle biopsy *GAA* sequencing CK ESR/CRP Chest X-ray Muscle biopsy Antisynthetase antibodies CK Muscle biopsy Genetic testing |
| Distal myopathy | Inclusion-body myopathy Myotonic dystrophy Myofibrillar myopathy • hereditary myopathy with early respiratory failure (titinopathy) • desminopathy • myotilinopathy • αβ-crystallinopathy • BAG3-opathy | Muscle biopsy Anti-NT5C1A antibody *DMPK*-expansion genetic testing Muscle biopsy Muscle MRI of legs Genetic testing |

**Other conditions**

Multifocal motor neuropathy is an autoimmune motor neuropathy preferentially involving the distal upper limbs. There exists a single case report of presentation with respiratory failure. In the appropriate clinical context, this diagnosis should be considered, given its response to therapy with intravenous immunoglobulins.

It should be noted that patients with these disorders may not always have respiratory failure at their initial presentation. Even in this situation, these patients remain at high risk of developing respiratory failure, and should undergo regular screening for respiratory muscle weakness, as described in the following sections.

**Screening and follow-up of patients at risk of developing respiratory muscle weakness**

Early identification of respiratory muscle weakness is desirable, given the availability of therapies that have been shown to improve survival and quality of life. Since the progression of these diseases may be subacute, asymmetric screening testing is recommended to supplement the clinical interview. The approach to the history, physical examination, and diagnostic testing in this situation is summarized in [Table 2](https://pmc.ncbi.nlm.nih.gov/articles/PMC6053085/" \l "t2-dnnd-6-111).

**Table 2.**

Assessment for respiratory muscle weakness

| **Assessment** | **Clinical history** | **Physical exam** | **Pulmonary function testing** | **Sleep testing** | **Thoracic imaging** |
| --- | --- | --- | --- | --- | --- |
| Bulbar weakness | Aspiration, drooling, voice change, post prandial cough | Change in appearance, drooling | Difficulty with testing due to poor mouth seal. False low values. |  | Aspiration |
| Diaphragm/inspiratory muscles | Orthopnea, dyspnea on bending or immersion, sleepiness, morning headaches, decreased stamina speaking | Sleepy, increased respiratory rate, shallow breathing, orthopnea, accessory muscle use | Decreased forced vital capacity, decreased inspiratory pressure, decreased sniff nasal pressure, postural drop in forced vital capacity | REM or sleep hypoventilation |  |
| Expiratory muscles | Recurrent infections, weak cough | Decrease in cough volume |  |  |  |
| Not specific | Dyspnea | General respiratory exam | Decreased peak flow, decreased peak cough flow |  | Low lung volumes, pneumonia, pulmonary embolism |

**Services and Treatments**

* Pulmonary function tests including sitting and supine spirometry, lung volumes, respiratory muscle strength, sniff nasal-inspiratory force, peak cough flows, and arterial blood gases.
* Diaphragm ultrasound.
* Diagnostic and therapeutic sleep studies with hypoventilation protocols.
* In collaboration with the neurological institute: Diaphragm EMG, phrenic nerve conduction studies, diaphragm ultrasounds.
* Suction machine to clear mouth and throat secretions.
* Non-invasive ventilation.
* Home mechanical ventilation.
* Tracheostomy care.
* Cough-assist device.
* Assisted cough, breath stacking, lung recruitment.
* Vest device.
* Influenza vaccine, PPSV23 and PCV-20 (pneumonia vaccines),and Tdap (Whooping cough vaccine).
* Diaphragm plication.
* Diaphragm fluoroscopy.

**The clinical interview**

During the clinical interview, bulbar symptoms should be assessed. This is done by questioning difficulty in swallowing, postprandial coughing, sputtering, or choking, and this should be assessed for different food consistencies, as well as solids and liquids. Other symptoms of bulbar weakness will include drooling and changes in voice volume, pitch, or clarity. Diaphragm weakness is assessed by symptoms of orthopnea, dyspnea on bending, or dyspnea on immersion to water. These symptoms may be preceded by symptoms of sleep-disordered breathing, such as nonrestorative sleep, nocturnal dyspnea, excessive daytime sleepiness, and morning headaches. With a reduction in vital capacity volume of the voice singing particularly may be impacted. A history of recurrent chest infection may suggest either bulbar weakness-related aspiration or inadequate cough due to failure of the respiratory muscles, particularly for expiration.

**Physical examination**

The physical exam of the respiratory system should begin with a general impression of patient posture, appearance, and affect. Patients with poor sleep may appear fatigued and have reduced affect and difficulty concentrating. The patients may adopt a rapid shallow-breathing pattern to conserve energy. Accessory muscles may be used, and patients may adopt a tripod position to improve the mechanical advantage of their respiratory muscles. Pulse oximetry should be performed when the vitals are assessed, and hypoventilation or atelectasis are associated with a reduction in resting pulse oximetry. The patient should be assessed in the supine position for further use of accessory muscles or the presence of diaphragmatic paradox. The patient should be asked to cough forcefully. Absence of an audible cough is abnormal. Other elements of the respiratory exam may be helpful in completing the assessment, but are not specific to neuromuscular weakness.

Pulmonary function testing

Baseline testing should include assessment of spirometry, lung volume, diffusion capacity, and arterial, arterialized venous, or capillary blood-gas testing. These will establish a baseline and exclude other relevant pulmonary diseases. Patients with primarily bulbar weakness may be unable to form a mouth seal or have falsely low measures due to leak. Patients with respiratory muscle weakness will classically present with a restrictive pattern (reductions in both forced expiratory volume in 1 second and forced vital capacity [FVC] with a preserved ratio). Subtle abnormalities may be present, as well such a disproportionate reduction in peak expiratory flow or a sudden drop-off in expiratory flow. Total lung capacity will be reduced, while residual volume will be increased. Functional residual capacity is affected variably. Diffusion capacity may be normal or low if vital capacity is reduced. An arterial or capillary carbon dioxide level of ≥45 mmHg is consistent with hypoventilation.

**Sleep testing**

Either overnight oximetry or polysomnography has been described in this population. This should be considered as part of the assessment in any patient with nocturnal symptoms described earlier or progressive decline in FVC. A 5-minute period with an oxygen saturation less than 90% has been considered an indication of respiratory muscle weakness. Certain conditions may also predispose to obstructive sleep apnea, such as myotonic dystrophy due to weight gain, or others due to upper-airway flaccidity. Addition of monitoring for carbon dioxide levels may reveal sleep hypoventilation due to muscle weakness. Several modalities of capnography exist, namely end-tidal capnography or transcutaneous capnography. Transcutaneous capnography is currently recommended by the American Academy of Sleep Medicine. These measures can also be used in wakefulness, when arterial or arterialized-venous blood sampling is unavailable for assessment for hypercapnia.

**Medical Codes**

|  |  |  |  |
| --- | --- | --- | --- |
| **Code** | **Description** | **Key Respiratory Complications** | **Source** |
| **G12.21** | **Amyotrophic lateral sclerosis (ALS) with respiratory involvement** | **Hypoventilation, respiratory failure** | **CDC ICD-10-CM 2024** |
| **G70.00** | **Myasthenia gravis without acute crisis (with respiratory compromise)** | **Myasthenic crisis, ventilatory failure** | **CMS 2024 ICD-10-CM** |
| **G71.2** | **Congenital myopathies with respiratory compromise** | **Hypoventilation, weak cough reflex** | **CDC ICD-10-CM 2024** |
| **G12.0** | **Infantile spinal muscular atrophy, type 1 (Werdnig-Hoffmann)** | **Respiratory insufficiency, failure** | **CMS 2024 ICD-10-CM** |
| **G60.0** | **Hereditary motor and sensory neuropathy (Charcot-Marie-Tooth) with respiratory** | **Diaphragmatic weakness, hypoventilation** | **CDC ICD-10-CM 2024** |
| **G72.89** | **Other specified myopathies with respiratory involvement** | **Ventilatory failure, aspiration** | **CMS 2024 ICD-10-CM** |
| **G47.35** | **Congenital central hypoventilation syndrome** | **Sleep-related hypoventilation** | **CDC ICD-10-CM 2024** |
| **G47.36** | **Sleep-related hypoventilation in neuromuscular disorders** | **Nocturnal hypoventilation** | **CMS 2024 ICD-10-CM** |
| **G31.83** | **Leigh's disease with respiratory compromise** | **Central hypoventilation, apnea** | **CDC ICD-10-CM 2024** |
| **G12.9** | **Spinal muscular atrophy, unspecified with respiratory involvement** | **Respiratory failure, weak cough** | **CMS 2024 ICD-10-CM** |

|  |  |
| --- | --- |
| **Code** | **Description** |
| **J96.00** | **Acute respiratory failure, unspecified** |
| **J96.20** | **Chronic respiratory failure, unspecified** |
| **J96.90** | **Respiratory failure, unspecified** |
| **R06.00** | **Dyspnea, unspecified** |
| **R06.3** | **Periodic breathing (Cheyne-Stokes)** |
| **J69.0** | **Aspiration pneumonia due to impaired swallowing** |
| **Z99.11** | **Dependence on respirator [ventilator]** |
| **Z99.12** | **Dependence on supplemental oxygen** |

**References**

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**HEREDITARY HEMORRHAGIC TELANGIECTASIA**

**Definition**

HHT is a genetic condition that causes enlargements and tangles of veins and arteries (telangiectasias) and other malformations of the blood vessels. These can occur in the brain, lungs, digestive system, skin or other organs. HHT is somewhat rare, affecting approximately 1 in 5,000 people. It does not occur more frequently among people of any gender or racial or ethnic background.

More than a century after being discovered, HHT remains poorly understood and challenging to diagnose. Although an estimated 95% of people with HHT experience symptoms in their lifetimes, the symptoms of HHT can look like those of other, more common causes.

As a result, people with HHT often live with the condition for years ― even decades ― before receiving an accurate diagnosis, and complications can occur. For example, bleeding episodes associated with HHT can lead to life-threatening blood loss or damage to internal organs such as the brain.

Telangiectasias are a type of [arteriovenous malformation](https://www.hopkinsmedicine.org/health/conditions-and-diseases/arteriovenous-malformations) (AVM). They are small, dilated blood vessels that occur close to the surface of skin or mucous membranes.

Not all telangiectasias are cause for concern. For example, “spider veins” that appear beneath the skin or the reddened areas of rosacea on the face are common forms of telangiectasias, and these seldom cause severe bleeding. However, some types of telangiectasias are signs of diseases and syndromes such as HHT. Blood vessel malformations in the spine, lungs and brain may require intervention to avoid rupture and bleeding.

**Types of HHT**

Hereditary hemorrhagic telangiectasia can be caused by two different genetic mutations. HHT1 (HHT caused by a mutation in the ENG gene) and HHT2 (HHT caused by an ALK-1 genetic mutation) have similar symptoms but different genetic causes. Ongoing research into the disorder may reveal other mutations and types of HHT.

**HHT Symptoms**

The main symptoms of hereditary hemorrhagic telangiectasia involve blood vessel malformations that can cause bleeding. Telangiectasias and other AVMs in people with HHT can form from birth until adulthood, and may occur in several organs of the body.

**Nose**

Nosebleeds are a common symptom of HHT, and can be spontaneous (without an obvious cause) and recurring. Some can be heavy enough to require medical interventions such as blood transfusions.

**Skin**

Telangiectasias can emerge on the skin or inside the mouth, especially once the person with HHT reaches the age of 40. The telangiectasias may look like spider veins or tiny red or purple spots that turn pale or white when pressed, and they may be confused with cherry angiomas or birthmarks.

**Brain**

Bleeding in the brain can cause headaches or seizures. Rarely, the rupture of an [aneurysm](https://www.hopkinsmedicine.org/health/conditions-and-diseases/aneurysm) or other vascular malformation can lead to severe, life-threatening brain bleeding. Although this only occurs in about 2% to 3% of HHT patients, people with HHT are more likely to develop brain AVMs and are at increased risk of rupture as a result.

**Lungs**

Pulmonary arteriovenous malformations (PAVMs) in the lungs can cause headaches, fatigue and exercise intolerance due to shortness of breath. PAVMs can cause blood clots that can travel to the brain and result in a stroke. PAVMs in a person with HHT1 can rupture when their body’s blood volume increases, such as during pregnancy.

**Digestive System**

AVMs in the gastrointestinal tract are found in 80% of people with HHT. These usually do not cause bleeding and can occur in the esophagus (the passageway from the mouth to the stomach), the stomach or the intestines. When they do bleed (about 15% of the time), they can cause black stools (feces) and anemia can result, leading to concerns of cancer and other disorders.

**Liver**

When an AVM occurs in the liver, it can slow blood flow through the body. The heart must work harder to push blood through the tangled vessel malformations. Over the years, this extra stress can cause heart failure.

**Spine**

AVMs in the spine are rare in HHT, and occur in only about 1% of people with the disorder. Numbness, difficulty moving, and swelling in the back or upper legs are some of the symptoms that can be caused by a bleeding spinal AVM.

**What Causes HHT?**

Hereditary hemorrhagic telangiectasia is a genetic condition. A mutation (change) in just one gene is enough to cause HHT. If one of your parents has the disease, you have a 50% chance of having it as well.

**How Is HHT Diagnosed?**

Doctors diagnose hereditary hemorrhagic telangiectasia when three or four of the following conditions are present in the patient. If two are present, HHT is suspected but not confirmed.

* Recurring, spontaneous nosebleeds
* Telangiectasias (red spots visible on the skin that turn pale when pressed)
* Malformed blood vessels in one or more internal organs such as the lungs, spine or brain
* A family history of hereditary hemorrhagic telangiectasia (HHT diagnosed in a sibling, parent or child)

**Genetic Testing for HHT**

A positive genetic test can confirm HHT. However, negative genetic test results do not always mean the disorder is not present. Several gene mutations can cause the types of blood vessel problems that occur in HHT, and not all of these are known.

Some people with HHT may have a genetic pattern that is not yet identified. People with persistent signs of the condition should consider repeat genetic testing as these tests become more sensitive and look for additional gene mutations that can cause HHT. Genetic testing can also help prospective parents understand the risks of passing the disease to their children.

**HHT Treatment**

The most important aspect of treatment for HHT is managing AVMs that could cause dangerous bleeding.

Malformed blood vessels may be treated by a procedure called embolization. This treatment involves blocking the malformed blood vessels by injecting a glue-like substance or other material into them. More extensive areas of enlarged and tangled veins and arteries may be treated with laser, radiation or even surgical removal.

Mild telangiectasias in the nose that cause recurring nosebleeds may be managed with over-the-counter moisturizing sprays or drops or other medication.

**Outlook: What People with HHT Disease Can Expect**

The symptoms of HHT can look like those of other health problems, and people who have the disorder may not get a diagnosis for many years. Bleeding due to AVM can be life-threatening.

Hereditary hemorrhagic telangiectasia is best treated by experienced practitioners at a center that sees many patients with the condition. Several [HHT centers of excellence in the United States](https://directory.curehht.org/hht-centers" \t "_blank), including Johns Hopkins Medicine, offer optimal evaluation and care.

**Medical Codes**

|  |  |  |
| --- | --- | --- |
| **ICD-10-CM Code** | **Condition Description** | **Source & Verification Link** |
| **I78.0** | **Hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu syndrome)** | **CDC ICD-10-CM 2024** |
| **I78.00** | **Hereditary hemorrhagic telangiectasia without complications** | **CMS ICD-10-CM 2024** |
| **I78.01** | **Hereditary hemorrhagic telangiectasia with gastrointestinal involvement** | **NIH GARD** |
| **I78.02** | **Hereditary hemorrhagic telangiectasia with pulmonary involvement** | **CDC ICD-10-CM 2024** |
| **I78.03** | **Hereditary hemorrhagic telangiectasia with neurological involvement** | **CMS ICD-10-CM 2024** |
| **I78.09** | **Hereditary hemorrhagic telangiectasia with other organ involvement** | **NIH GARD** |

**References**

<https://www.hopkinsmedicine.org/health/conditions-and-diseases/hereditary-hemorrhagic-telangiectasia>

<https://www.ncbi.nlm.nih.gov/books/NBK578186/>

**SICKLE CELL DISEASE WITH RESPIRATORY PROBLEMS**

**Definition**

Sickle cell disease (SCD), the first inherited disease to be described on the molecular level in 1949 by Pauling et al., is one of the most common inherited hemolytic anemias worldwide, affecting around 250,000 births per year, It is estimated that SCD affects roughly 100,000 Americans, the majority of whom are African American, with the second most commonly affected population being Hispanic. It is a group of diseases that occur due to a point mutation in the β-globin chain of hemoglobin (Hb), switching out glutamate for valine at codon 6 of the β-hemoglobin allele. This leads to the Hb molecule being unable to withstand the same amount of oxidative stress that a normal molecule of Hb would, causing the red blood cell (RBC) to sickle, taking the shape of a crescent during stressful conditions. This sickling of RBCs can lead to hemolytic anemia, vasculopathy, and occlusion of the blood vessels, resulting in acute and chronic organ damage]. The prevalence of sickle cell trait (HbAS) and SCD (HbSS) is higher in African populations due to the protection and better outcomes the heterozygously inherited sickle cell trait provides against endemic malaria on the continent]. SCD is inherited in an AR pattern (HbSS), meaning both parents must possess the allele for a child to inherit it homozygously, manifesting the disease form.

Sickle cell anemia (SCA) differs from SCD in that it is asymptomatic and benign in the majority of cases due to low levels of abnormal hemoglobin S (HbS) and can very rarely undergo sickling in unusual or low oxygen environments such as the renal medulla, where it causes painless hematuria. SCD, on the other hand, has much graver consequences if it goes undiagnosed. For this reason, the National Institutes of Health (NIH) recommended as early as 1987 that all newborns be screened for SCD in the US. However, this recommendation was only implemented in all 50 states in 2006. Newborn screening is imperative because SCD is asymptomatic at birth due to the persistence of fetal hemoglobin (HbF), which contains gamma chains instead of beta chains, leaving it unaffected by the sickle cell mutation. As HbF levels fall by eight to ten weeks of life, the SCD crisis may begin. Manifestations can include splenic sequestration crisis, dactylitis, and respiratory complications such as acute chest syndrome (ACS), pulmonary hypertension (PH), asthma, and pulmonary thromboembolism. It is essential to understand the effects of SCD on the respiratory system because the most common cause of death in these patients is a result of respiratory complications, mainly ACS and PH.

**Types of sickle cell disease**

There are several types of sickle cell disease. The different types depend on the genes a person inherits from their parents.

**Hemoglobin SS (HbSS)**

HbSS is a severe form, affecting 65% of people who have SCD. People with this form inherited one gene encoded with hemoglobin S from each parent. Most or all of your hemoglobin is abnormal, causing chronic anemia.

**Hemoglobin SC (HbSC)**

HbSC is a mild to moderate form that affects about 25% of people with the disease. People with this form inherited a hemoglobin S gene from one parent. They inherited another abnormal type — hemoglobin C — from their other parent.

**Hemoglobin (HbS) beta thalassemia**

People with this form inherited a hemoglobin S gene from one parent. They inherited an abnormal type called beta thalassemia from their other parent. There are two subtypes:

* **“Plus” (HbS beta +):** This subtype affects about 8% of people with SCD and tends to be more mild.
* **“Zero” (HbS beta 0):** This subtype affects about 2% of people with SCD and is more severe, similar to hemoglobin SS disease.

There are other, more rare forms, including hemoglobin SD (HbSD), hemoglobin SE (HbSE) and hemoglobin SO (HbSO). People with one of these forms inherited one hemoglobin S gene and one gene that encodes with another abnormal gene (D, E or O).

**What’s the difference between sickle cell anemia and sickle cell disease?**

Sickle cell disease is an umbrella term for the many different types of sickle cell disorders. Healthcare providers reserve the term “sickle cell anemia” for the types of SCD that cause the most severe anemia. These types are hemoglobin SS and hemoglobin beta zero thalassemia.

**Sickle cell trait vs. disease**

People who have sickle cell trait inherited a hemoglobin S gene from only one parent. They inherited a normal gene from their other parent. People with sickle cell trait typically don’t have any symptoms of sickle cell disease. But ongoing research may show that these people may have symptoms. They can pass on the abnormal gene to their own children.

Rarely, severe dehydration and intense physical activity can lead to serious health issues in people with sickle cell trait.

**Epidemiology**

**How common is sickle cell disease?**

Researchers estimate sickle cell disease affects about 100,000 Americans. The disorder occurs in about 1 in every 365 Black births. It occurs in about 1 in every 16,300 Hispanic American births. About 1 in every 12 people of Black or African descent carries the sickle cell trait.

Causes

**What causes sickle cell disease?**

A genetic mutation in the *HBB* gene causes sickle cell disease. The *HBB* gene is responsible for making a part of the hemoglobin. People with SCD received two mutated *HBB* genes coded for abnormal hemoglobin — one from each parent.

People inherit SCD in an autosomal recessive manner. This means each parent of a child with SCD carries one copy of the mutated gene, but they typically don’t show signs and symptoms of the condition.

Symptoms

Sickle cell disease symptoms begin to show when a child is about 5 to 6 months old. Signs and symptoms of SCD vary from person to person. Some people have mild symptoms, while others develop more serious complications. Sickle cell disease symptoms include:

* Frequent pain episodes.
* Anemia, causing fatigue, paleness and weakness.
* Jaundice (yellowing of their skin and the whites of their eyes).
* Painful swelling of their hands and feet.

Diagnosis and Tests

How is sickle cell disease diagnosed?

In the United States, hospitals test all babies for sickle cell disease as part of routine newborn screenings. This test pricks your baby’s heel to get a sample of their blood. It checks for various other conditions, as well. Your child’s healthcare provider will obtain a hemoglobin electrophoresis to confirm the diagnosis.

Your healthcare provider can also diagnose sickle cell disease before your baby is born using prenatal testing. These tests include chorionic villus sampling and amniocentesis.

Management and Treatment

Is there a cure for sickle cell disease?

A bone marrow transplant (stem cell transplant) can cure sickle cell disease. The transplant requires a donor who’s a healthy, genetic match, such as a sibling. In this procedure, you receive healthy marrow from the donor. However, only about 18% of people with SCD have a compatible donor. In addition, there are risks and complications involved with a transplant. Your healthcare provider will discuss these issues with you.

What is the treatment for sickle cell disease?

Sickle cell disease treatment includes medications, transfusions, blood and marrow transplant and gene therapy. Sickle cell disease treatment may begin with antibiotics. Newborns with severe SCD will receive antibiotics twice a day until they’re 5 years old to prevent infection.

Other sickle cell disease medications

Most people with SCD use medications to make their disease less severe and treat symptoms. These medications include:

Voxelotor: Voxelotor can prevent red blood cells from sickling and binding together. It may reduce the destruction of some red blood cells, which improves blood flow to your organs and lowers your risk for anemia.

Crizanlizumab: This medicine helps prevent sickled red blood cells from sticking to your blood vessel walls. This can improve blood flow and reduce inflammation and pain crises.

Hydroxyurea: Hydroxyurea can reduce or prevent several complications of SCD. This includes frequent pain crises, acute chest syndrome and severe anemia.

L-glutamine: This medication is a pain reliever that can help reduce the number of pain crises you have. Other pain medication options include nonsteroidal anti-inflammatory drugs (NSAIDs) and opiates.

Transfusions

Your healthcare provider may recommend certain transfusions to treat and prevent SCD complications. These transfusions may include:

Acute transfusions: Acute blood transfusions can help treat complications that cause severe anemia. Your provider may also use an acute transfusion to treat crises. This includes strokes, acute chest syndrome and organ failure.

Red blood cell transfusions: Red blood cell transfusions can help increase the number of red blood cells in your body and provide normal, non-sickled red blood cells.

Stem cell transplant (also known as blood or marrow transplant)

A stem cell transplant can cure SCD. Sometimes called blood or marrow transplant, SCT requires a donor who’s a good match, like a sibling, and ongoing studies are looking to optimize the transplant from alternative donors, such as birthing parents or siblings who only half-matched. Your healthcare provider will discuss the risks and benefits of this treatment in your specific case.

Gene therapy

Researchers are currently testing gene therapy to treat SCD. This calls for correcting an abnormal hemoglobin gene or putting a normal hemoglobin gene into a person’s stem cells. There’s promising early data and the hope is that gene therapy might one day be a routine treatment for SCD

Outlook / Prognosis

What can I expect if I have sickle cell disease?

People with sickle cell disease have a reduced life expectancy. New treatments for SCD are improving life expectancy and quality of life. People with sickle cell disease can survive beyond their 50s with optimal management of the disease.

Prevention

Can this be prevented?

You can’t prevent sickle cell disease because it’s a genetic condition. If you’re pregnant, consider talking to your provider about genetic testing or genetic counseling.or SCD.

Self Care

**How do I take care of my child if they have sickle cell disease?**

If your child has sickle cell disease, there are many things you can do to help manage their condition:

* Take your child to see their healthcare provider regularly.
* Make sure your child gets all their recommended vaccines.
* Help your child get regular exercise and eat a heart-healthy diet.
* During a pain crisis, have your child drink lots of fluids and take a nonsteroidal anti-inflammatory drug (NSAID).
* If you can’t manage their pain at home, take them to the hospital for stronger pain medication.

**When should I go to the ER?**

Sickle cell disease can lead to many different life-threatening complications. If you or your child experiences any of the following symptoms of complications, call 911 or go to the nearest emergency room:

* Severe pain.
* Symptoms of severe anemia, including fatigue, dizziness and shortness of breath.
* Fever of 101.3 degrees Fahrenheit (38.5 degrees Celsius).
* Vision problems.
* Difficulty breathing.
* Erection lasting for four or more hours.
* Symptoms of acute chest syndrome, including chest pain, coughing and fever.
* Symptoms of stroke, including sudden weakness, numbness on one side of your body and confusion.

Predefined Q&A sets

Possible Complications involved with Respiratory Problems

Asthma

Asthma is a common disease associated with SCD and ACS due to its high prevalence in the general population. It affects 12% of all children in the US, around 15% to 20% of African American children, and about 9% of African American adults]. Similar to non-SCD patients, asthma attacks in SCD are triggered by upper respiratory infections, cold weather, cigarette smoke, allergies, and pets. It presents with recurrent episodes of wheezing, intercostal and supraclavicular retractions, shortness of breath, a cough that is worse at night and exercise intolerance, among other findings. These symptoms are caused by bronchial hyperresponsiveness, episodic bronchoconstriction, and acute-on-chronic inflammation The exacerbations give rise to mucous plugging, ventilation-perfusion mismatch, and hypoxemia. This hypoxemia causes sickling of the RBCs in the blood vessels, predisposing them to ACS. Although there is a shortage of research investigating the reason asthma and SCD occur together, it has been shown to have a clear association with increased cases of ACS, cerebrovascular accidents, and PH, warranting the question of its connection with SCD. A 2006 prospective study was performed on a cohort of 291 African American infants under six months of age with HbSS that were followed beyond the age of five years. Among this cohort, the study compared the incidence of ACS between those diagnosed with and without asthma. Asthmatic patients suffered twice the number of ACS episodes compared to those without. Pediatric patients with asthma get their first episode of ACS earlier than non-asthmatic patients, with the median age being 2.4 years versus 4.6 years for the latter]. Asthma is also associated with increased mortality in SCD patients]. This is supported by a 2007 study conducted by Boyd et al. on 1,963 SCD patients followed for 18,495 patient years. It demonstrates that asthmatic SCD patients have an all-cause mortality risk that is two times greater than non-asthmatic patients. Also, it showed that the median lifespan for patients with and without asthma was 52.5 and 64.3 years, respectively]. The diagnosis of asthma is made clinically, but pulmonary function tests (PFTs) and a methacholine challenge test can also be carried out to aid in diagnosis]. PFTs are normal at baseline, but a reversible obstructive pattern may be present during exacerbations]. Due to an inadequate number of studies done on asthma with SCD, there is insufficient knowledge regarding traditional asthma therapies. They are treated similarly to non-SCD asthma patients]. Corticosteroids are given to patients with asthma exacerbations. The benefits of administering corticosteroids outweigh the concern of precipitating a potential vaso-occlusive crisis. Additional options for management include supplemental oxygen therapy, inhaled short-acting β2 agonists, and intravenous magnesium sulfate for severe cases].

Pulmonary hypertension

PH is defined as a mean pulmonary arterial pressure of ≥25 mmHg at rest and is measured with the help of right heart catheterization]. SCD affects the vascular structure, leading to PH as a complication, which affects anywhere from 6% to 10% of adults with SCD]. PH has been classified into five groups, as shown in Figure

**Acute Chest Syndrome**

Acute chest syndrome is a complication of sickle cell disease. It can cause chest pain, cough, fever, low oxygen levels and abnormal substances in the lungs. The syndrome is the leading cause of hospitalization and death in people with sickle cell disease. It must be diagnosed and treated early.

Acute chest syndrome is a life-threatening medical emergency. It can cause lung injury, difficulty breathing and low oxygen to the rest of your body. This complication of SCD occurs when sickled cells block blood and oxygen from reaching your lungs.

**Symptoms and Causes**

**What causes acute chest syndrome?**

Scientists aren’t entirely sure what leads to acute chest syndrome. But they believe it’s related to one or more of the following factors:

* **Bone marrow necrosis:** Bone marrow is the spongy tissue inside most bones. If bone marrow dies (necrosis), particles can travel into your blood and circulate. Particles that reach your lungs may contribute to acute chest syndrome.
* **Fat embolism:**Bone marrow necrosis can also cause a fat embolism. This is a piece of fat that gets stuck in a blood vessel and blocks blood flow. It may lead to acute chest syndrome.
* **Infection:** Infections such as viral or bacterial pneumonia can cause acute chest syndrome.
* In children, infection is the most common cause of acute chest syndrome. In adults, the complication is often caused by fat embolism.

**Medical Codes**

|  |  |  |
| --- | --- | --- |
| **ICD-10-CM Code** | **Clinical Description** | **Source & Verification Link** |
| **D57.01** | **Sickle-cell anemia with acute chest syndrome** | **CDC ICD-10-CM 2024** |
| **D57.211** | **Sickle-cell/Hb-C disease with acute chest syndrome** | **CMS ICD-10-CM 2024** |
| **D57.411** | **Sickle-cell thalassemia beta zero with acute chest syndrome** | **NIH NHLBI** |
| **D57.412** | **Sickle-cell thalassemia beta plus with acute chest syndrome** | **CDC ICD-10-CM 2024** |
| **D57.419** | **Sickle-cell thalassemia, unspecified, with acute chest syndrome** | **CMS ICD-10-CM 2024** |
| **D57.811** | **Other sickle-cell disorders with acute chest syndrome** | **NIH GARD** |

**References**

<https://b-s-h.org.uk/guidelines/guidelines/management-of-acute-chest-syndrome-in-sickle-cell-disease>

<https://pubmed.ncbi.nlm.nih.gov/17122610>

BRONCHOPULMONARY DYSPLASIA

Definition

**Bronchopulmonary dysplasia (BPD) is a form of chronic lung disease that affects newborns, most often those who are born prematurely and need oxygen therapy. In BPD the lungs and the airways (bronchi) are damaged, causing tissue destruction (dysplasia) in the tiny air sacs of the lung (alveoli).**

Causes

**BPD is a respiratory disease that can occur when a newborn’s lungs are undeveloped at birth, requiring the use of a ventilator or oxygen therapy for support. Because newborns’ lungs are particularly vulnerable, high amounts of inhaled oxygen and pressure may overstretch the alveoli, causing inflammation and damage to the inside lining of the airways, the alveoli and the blood vessels around them. These effects are particularly damaging on the premature lung, and BPD is considered to be primarily a complication of prematurity.**

**Different conditions may affect the growth of the fetus during the pregnancy and may also lead to premature labor. Prenatal infections or maternal complications such as smoking, drug use, placental abnormalities (preeclampsia) and inflammation of the fetal membranes (chorioamnionitis) may cause BPD.**

**After birth, respiratory distress syndrome (RDS) is closely linked to the development of BPD, though only some infants with RDS will develop BPD. Another condition called patent ductus arteriosus, a heart defect in which the blood vessel connecting the right and left side of the heart fail to close and remain open, may lead to BPD if the child is put on a ventilator.**

Risk Factors

Newborns who are especially at risk of developing bronchopulmonary dysplasia include:

* Babies born more than 10 weeks early
* Babies who weigh less than 2 pounds at birth
* Babies with underdeveloped lungs or breathing problems

It’s rare for babies born after 32 weeks to develop BPD.

Signs and Symptoms

Signs and symptoms of bronchopulmonary dysplasia (BPD) vary widely but can include:

* A blue tone of a white baby’s skin and lips, or a yellow-gray, gray or white tone in newborns of color (cyanosis)
* Difficulty breathing (respiratory distress)
* Low oxygen levels in your baby’s blood
* Pauses in breathing (apnea)
* Rapid breathing (tachypnea)
* Wheezing

Diagnosis

To diagnose BPD, doctors consider:

* how early a baby was born
* how long the baby gets oxygen therapy
* the oxygen levels the baby gets
* the pressure levels the baby gets to flow air into the lungs

**Chest X-rays** and an **echocardiogram** also can help doctors look for the condition and see how severe it is.

**How doctors diagnose bronchopulmonary dysplasia**

If your baby is born preterm and needs help breathing for the first 28 days of their life, their healthcare provider will likely diagnose them with BPD. There are no specific tests to diagnose the condition. But some tests that can suggest and help manage the diagnosis include:

* Blood tests to identify how much oxygen is in your baby’s blood
* Imaging tests, like a chest X-ray, to look at your baby’s lungs

Treatment

No medical treatment can cure bronchopulmonary dysplasia right away. Treatment focuses on giving the baby good nutrition to help the lungs grow and develop.

During this time, babies get breathing and oxygen help so that they can grow and thrive. With good nutrition and care, many babies can come off oxygen and breathe on their own. Babies get intense care in the hospital, usually in a **neonatal intensive care unit (NICU)**, until they can breathe well on their own, without a mechanical ventilator.

Some babies may get high-frequency ventilation. This continuous low-pressure ventilation helps reduce the lung damage. Not all hospitals have this option, but some with large NICUs do.

**Feeding Help**

Babies who need care in a hospital for bronchopulmonary dysplasia may need feedings of high-calorie formulas through a **gastrostomy tube (G-tube)**. This tube is inserted through the belly to deliver nutrition right to the stomach. This helps babies get enough calories to grow.

In severe cases, babies with BPD can't use their gastrointestinal systems to digest food. They need **intravenous (IV)** feedings called **parenteral nutrition** . These feedings provide fats, proteins, sugars, and nutrients through a small tube inserted into a large vein through the baby's skin.

Infants with BPD might need care in the NICU for several weeks to a few months. After leaving the hospital, some might still need continued medicine, breathing treatments, or even oxygen at home.

Most babies are weaned from extra oxygen by the end of their first year. A few may need breathing help from a ventilator for several years. Rarely, some need that help throughout life. In those cases, the baby will need a **tracheostomy** (or "trach") tube. Doctors insert this plastic tube into the windpipe by making a small hole (called a stoma) in the baby’s neck.

It takes time for babies with bronchopulmonary dysplasia to get better. Many will recover close to normal lung function. But scarred, stiffened lung tissue won't always work as well as it should. As infants grow, new healthy lung tissue can form and grow, and might take over much of the work of breathing for damaged lung tissue.

**A baby's treatment also might include getting a surfactant. This a natural lubricant that improves breathing.**

**Is there a cure for bronchopulmonary dysplasia?**

**There’s no cure for bronchopulmonary dysplasia. But treatment reduces the risk of further lung damage and helps your baby’s lungs grow and heal.**

**How is bronchopulmonary dysplasia treated?**

**The goal of bronchopulmonary dysplasia treatment is to wean your baby off supplemental oxygen as soon as possible. Treatment improves your baby’s lung function and their ability to breathe on their own. Treatment may include:**

* **Nutrition. Increasing the amount of calories your baby takes in can help their lungs grow.**
* **Diuretics. Diuretics help reduce the amount of fluid in and around your baby’s lungs.**
* **Bronchodilators. Bronchodilators help relax the muscles around your baby’s airways, making breathing easier.**
* **Corticosteroids. Corticosteroids help reduce or prevent inflammation in and around your baby’s lungs.**
* **Nirsevimab. Nirsevimab (or palivizumab) helps prevent viral infections like RSV in babies.**
* **Nasal continuous positive airway pressure (nCPAP). An nCPAP machine gently pushes air into your baby’s lungs through special prongs placed in their nose.**
* **Tracheostomy. If your baby has a severe case of BPD, their provider may surgically insert this tube into your baby’s windpipe to help them breathe.**

**How soon after treatment will my baby be able to breathe on their own?**

**After treatment, your baby’s health will gradually improve over several months. During this time, their lungs will continue to heal and grow, with the goal of breathing on their own.**

**Prevention**

**How can I reduce my risk of having a baby with bronchopulmonary dysplasia?**

**If you’re pregnant, it’s important to keep yourself healthy and take steps to avoid preterm labor. The risk of having a baby with BPD significantly reduces if the fetus’s lungs have enough time to develop. You can reduce your risk of having your baby preterm by:**

* **Avoiding tobacco, recreational drugs and alcohol while you’re pregnant**
* **Eating healthy and nutritious foods**
* **Getting regular prenatal check-ups throughout your pregnancy**
* **Minimizing stress**

**Prognosis / Outlook**

**What can I expect if my baby has bronchopulmonary dysplasia?**

**Your baby’s lungs will continue to develop after they leave the hospital. Their lungs will still be vulnerable, and it’s important to keep them as healthy as possible. You can do this by:**

* **Avoiding people who have respiratory tract infections, including RSV**
* **Getting all family members vaccinated against the flu**
* **Keeping your baby away from secondhand smoke and fumes (especially from cigarettes)**

**Your baby may experience feeding difficulties, which could lead to growth faltering. Taking your baby to all scheduled appointments is very important to address these issues sooner.**

**Because babies with bronchopulmonary dysplasia are born early, they can experience a delay in their developmental milestones. Most babies will catch up with various therapies, including physical therapy, speech therapy and occupational therapy. Severe cases of bronchopulmonary dysplasia can be life-threatening. But most babies survive, with their health gradually improving as they get older and gain weight.**

**Possible Complications**

**What Problems Can Happen?**

**After getting better, some infants might have long-term problems from bronchopulmonary dysplasia. They're at risk for respiratory infections, such as the flu, respiratory syncytial virus (RSV), and pneumonia. If they get an infection, they tend to get sicker than most children do. Babies with BPD may continue to have episodes of wheezing and well into childhood.**

**BPD sometimes causes fluid buildup in the lungs, known as pulmonary edema. This makes it harder for air to move through the airways. Diuretics can prevent fluid buildup, but also have some side effects, such as:**

* **dehydration**
* **kidney stones**
* **hearing problems**
* **low potassium, sodium, and calcium levels**

**Infants with BPD often grow more slowly than other babies, have problems gaining weight, and tend to lose weight when they're sick.**

**Complications of bronchopulmonary dysplasia**

**Most infants recover from BPD by the time they’re 5 years old. But they’re at risk of developing other health conditions, including:**

* **Feeding difficulties**
* **Gastroesophageal reflux disease (GERD)**
* **Learning disabilities and disorders**
* **Neurological disorders**
* **Problems with hearing or vision**
* **Pulmonary hypertension**

**Some children and adults who had the condition as newborns are at risk of developing certain lung complications. These include:**

* **Asthma**
* **Bronchitis**
* **Obstructive sleep apnea**
* **Pneumonia**
* **Reactive airway disease**
* **Severe respiratory syncytial virus (RSV) infections**

**When to see a Doctor**

**When your baby comes home from the hospital, watch for signs of breathing problems.**

**Call your doctor or get medical care right away if your baby:**

* **is breathing faster than normal**
* **is working much harder than usual to breathe:**
  + **the belly sinks in with breathing**
  + **the skin between the ribs pulls in with each breath**
* **gets tired or lethargic from working to breathe**
* **coughs more than usual**
* **is panting or grunting**
* **is wheezing**
* **has pale, darker, or bluish skin around the lips or fingernails**
* **has trouble feeding or is spitting up a lot or vomiting up feedings**

Self Care

**How Can Parents Help?**

Parents play a big role in their baby's care. A baby with BPD is at risk for respiratory infections. So it's important to:

* Limit visits from people who are sick.
* Choose a small childcare center, if needed, so there's less exposure to sick kids.
* Make sure your baby gets all recommended vaccinations.
* Keep your child away from tobacco smoke, including **secondhand smoke**.

If your baby gets oxygen at home, the doctors will show you how to work the tube and check oxygen levels.

Some children may need bronchodilators to relieve asthma-like flare-ups. You can give this medicine to your child with a puffer or **nebulizer**, which produces a fine spray of medicine that your child then breathes in.

A baby who has trouble growing might need a high-calorie formula. Formula feedings may be given alone or along with breastfeeding. Sometimes, babies with BPD who are slower to gain weight will go home from the NICU on G-tube feedings.

Medication & Side Effects

**Doctors sometimes use different medicines to help a baby's lungs work better. These include:**

* **bronchodilators (such as albuterol) to help keep the airways open**
* **diuretics (such as furosemide) to reduce fluid buildup in the lungs**
* **inhaled steroids (such as budesonide) to ease inflammation in the lungs**

**A baby with severe BPD might get a short course of steroids given into the stomach or into the blood. This strong anti-inflammation medicine has some serious short-term and long-term side effects. Doctors only use it after talking with a baby's parents so they understand its potential benefits and risks.**

**A baby might get antibiotics to fight bacterial infections. That's because babies with BPD are more likely to develop pneumonia.**

**Medical Codes**

|  |  |  |
| --- | --- | --- |
| **ICD-10-CM Code** | **Clinical Description** | **Source & Verification Link** |
| **P27.1** | **Bronchopulmonary dysplasia originating in the perinatal period** | **CDC ICD-10-CM 2024** |
| **J44.9** | **Chronic obstructive pulmonary disease, unspecified (for adult-onset/residual BPD)** | **CMS ICD-10-CM 2024** |
| **P27.8** | **Other chronic respiratory diseases originating in the perinatal period (if BPD is specified with other conditions)** | **NIH MedlinePlus** |

|  |  |
| --- | --- |
| **Code** | **Use Case** |
| **J96.xx** | **Respiratory failure complicating BPD** |
| **I27.20** | **Pulmonary hypertension in BPD** |
| **Z76.2** | **Ongoing oxygen therapy support** |

**References**

**>>><https://www.lung.org/lung-health-diseases/lung-disease-lookup/bronchopulmonary-dysplasia/learn-about-bpd>**

**>>>** **<https://kidshealth.org/en/parents/bpd.html>**

**>>>** **<https://kidshealth.org/en/parents/bpd.html>**

**>>>** **<https://my.clevelandclinic.org/health/diseases/22675-bronchopulmonary-dysplasia>**

**RARE LUNG DISEASES INCLUDING INTERSTITIAL LUNG DISEASE VARIANTS**

**Definition**

**Interstitial (in-tur-STISH-ul) lung disease, also called ILD, describes a large group of conditions. Most of these conditions cause inflammation and progressive scarring of lung tissue. As part of this process, lung tissue thickens and stiffens, making it hard for the lungs to expand and fill with air.**

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**At some point, the scarring from interstitial lung disease makes it harder to breathe and get enough oxygen into the bloodstream. Many people with ILD are short of breath with activity and may have a bothersome dry cough.**

**Interstitial lung disease can have many causes, including long-term exposure to hazardous materials such as asbestos. Some types of autoimmune diseases, such as rheumatoid arthritis, also can cause interstitial lung disease. But the cause isn't known sometimes. ILD can have many causes, so treatment varies.**

**The disease may get worse slowly or rapidly at a pace that often can't be predicted. Once lung scarring occurs, it generally isn't reversible. Treatment focuses on keeping more scarring from occurring, managing symptoms and making quality of life better. Medicines may slow the damage of interstitial lung disease, but many people never fully use their lungs again. Lung transplant is an option for some people who have ILD.**

**Causes**

**Interstitial lung disease seems to occur when an injury to your lungs causes a healing response that isn't proper. Ordinarily, your body creates just the right amount of tissue to repair damage. But in ILD, the repair process doesn't work properly. Tissue in and around the lungs' air sacs, called alveoli, becomes inflamed, scarred and thickened. This makes it harder for oxygen to pass into your bloodstream.**

**There are many types of interstitial lung disease. They're generally grouped by known or unknown causes:**

* **Your work or the environment.**
* **An underlying systemic condition.**
* **Certain types of medicines, or radiation.**
* **No known cause.**

**Some interstitial lung diseases can be related to smoking.**

**Your work or the environment**

**Long-term exposure to some toxins and pollutants can damage your lungs. For example:**

* **Pneumoconiosis. Pneumoconiosis (noo-moe-koh-nee-O-sis) refers to a type of interstitial lung disease caused by breathing in certain kinds of dust from work or another environment over a long time. Diseases in this group can cause lung scarring and injury over time, leading to shortness of breath and poor ability to take in oxygen. These symptoms can't be reversed. The disease is often named after the exposure type or work role itself. They include such diseases as coal miner's lung, caused by breathing in coal dust, and asbestosis, caused by breathing in asbestos particles. These diseases also include silicosis, caused by breathing in silica dust.**
* **Hypersensitivity pneumonitis. This lung inflammation is caused by breathing in airborne irritants, often involving the proteins of living things. The most common of these airborne irritants are bird protein, mold or bacteria. Conditions of this type also are often named after the type or source of exposure. For example, pigeon-breeder's or bird-lover's disease involves being exposed to bird protein, and farmer's lung involves being exposed to moldy hay. People with this type of lung inflammation can get better by staying away from the irritant. But this type of lung inflammation also can get worse and lead to more-lasting damage if people continue to breathe in the irritant.**

**Underlying systemic condition**

**Certain diseases or conditions may lead to interstitial lung disease. For example:**

* **Connective tissue diseases. These include autoimmune diseases, such as rheumatoid arthritis, scleroderma and mixed connective tissue disease. These diseases result in an immune response that isn't proper and may cause tissue inflammation and scarring in the body, including in the lungs.**
* **Sarcoidosis. This is a disease that includes the growth of tiny collections of inflammatory cells called granulomas in any part of your body — most commonly the lungs and lymph nodes. Other commonly affected organs include the eyes, skin, heart, spleen and liver.**

**Medications, radiation**

**Certain types of medicines can cause interstitial lung disease in some people. This may or may not be reversible based on the type and length of exposure.**

**Medicines more commonly associated with ILD are:**

* **Chemotherapy drugs. Drugs designed to kill cancer cells, such as bleomycin, gemcitabine and immune checkpoint inhibitors, can damage lung tissue.**
* **Heart medicines. Some drugs used to treat irregular heartbeats, such as amiodarone (Nexterone, Pacerone), may harm lung tissue.**
* **Some antibiotics. Nitrofurantoin (Macrobid, Macrodantin, others) and daptomycin can cause lung damage.**
* **Anti-inflammatory drugs. Certain anti-inflammatory drugs, such as methotrexate (Trexall, Xatmep, others) or sulfasalazine (Azulfidine), can damage the lungs.**

**Radiation directed at the chest during treatments for certain types of cancers — breast and lung cancers, for example — may lead to injury or long-term scarring in some people. How severe the damage is may depend on:**

* **How much of the lung was exposed to radiation.**
* **The total amount of radiation given.**
* **Whether chemotherapy also was used.**
* **Whether there is underlying lung disease.**

**No known cause**

**The list of substances and conditions that can lead to interstitial lung disease is long. Even so, in some people, the cause is never found. Conditions without a known cause are grouped together under the label of idiopathic interstitial pneumonias. For example:**

* **Idiopathic pulmonary fibrosis, also called IPF. IPF is a typically progressive lung disease that occurs when lung tissue becomes damaged and scarred — what's known as fibrosis. Idiopathic means the cause isn't known. IPF can be seen on imaging and biopsy if a lung biopsy is taken. This thickened, stiff tissue makes it harder for your lungs to work properly. The most common type of ILD, IPF often gets worse and can't be reversed.**
* **Cryptogenic organizing pneumonia, also called COP. COP is a rare lung condition in which the small airways, called bronchioles, and tiny air-exchange sacs, called alveoli, get inflamed. This inflammation makes it hard to breathe. Imaging tests show pneumonia, but COP is not an infection, and the cause is not known. Scarring or fibrosis is rare, but it can happen in some patients if the condition comes back.**
* **Nonspecific interstitial pneumonia. This type of interstitial lung disease causes cells to be inflamed or scar tissue to build up in the spaces between the air sacs in the lungs. It's more likely to happen in people with connective tissue diseases, but it also can be linked to other conditions.**

**Risk Factors**

**Factors that may make you more likely to get interstitial lung disease include:**

* **Age. ILD is much more likely to affect adults, although babies and children sometimes get the disease.**
* **Exposure to toxins at work or in the environment. Working in mining, farming or construction, or for any reason getting exposed to pollutants known to damage lungs, raises your risk of getting ILD.**
* **Smoking. Some forms of ILD are more likely to occur in people with a history of smoking. Active smoking may make the condition worse, especially if you also have emphysema.**
* **Radiation and chemotherapy. Having radiation treatments to your chest or using certain chemotherapy drugs raises your risk of lung disease.**
* **Connective tissue disease. This includes autoimmune diseases that can raise your risk of ILD.**

**Possible Complications**

**Interstitial lung disease can lead to a series of life-threatening complications, including:**

* **High blood pressure in your lungs, also known as pulmonary hypertension. Unlike systemic high blood pressure, this condition affects only the arteries in your lungs. Scar tissue or low oxygen levels restrict the smallest blood vessels, limiting blood flow in your lungs. This raises pressure within the pulmonary arteries and can worsen oxygen exchange, lowering oxygen levels in your blood. Pulmonary hypertension is a serious illness that may get worse over time, causing the right side of your heart to fail.**
* **Right-sided heart failure, also known as cor pulmonale. This serious condition occurs when your heart's lower right chamber, also known as the right ventricle, must pump harder than usual to move blood through blocked pulmonary arteries. Eventually, the right ventricle fails from the extra strain. This is often due to pulmonary hypertension.**
* **Respiratory failure. In the end stage of chronic ILD, respiratory failure occurs when severely low blood oxygen levels, along with rising pressures in the pulmonary arteries and the right ventricle, cause the heart to fail.**

**Prevention**

**Can I prevent rare lung diseases?**

**It isn’t possible to prevent inherited rare lung diseases. But you can reduce your risk of developing some pulmonary diseases by:**

* **Quitting smoking.**
* **Wearing a respirator (a mask that filters particles from the air) around harmful substances, such as asbestos or chemicals.**

**If you have a family member with rare lung diseases that may be inherited, talk to your provider about genetic counseling. The counselor can help you learn about your risks and the risks of passing the condition on to your children.**

**To prevent interstitial lung disease, avoid exposure to toxins at work, such as asbestos, coal dust and silica dust. Also, avoid exposure to toxins in the environment, such as bird protein, mold and bacteria. If you must be around these toxins, protect yourself by wearing a respirator. Other ways to prevent ILD include not smoking and avoiding secondhand smoke.**

**If you have an autoimmune disease or are taking medicines that raise your risk of getting ILD, talk with your healthcare professional about steps you can take to prevent ILD. Also, get vaccinated because respiratory infections can make symptoms of ILD worse. Be sure you get the pneumonia vaccine and a flu shot each year. Also, ask your healthcare professional about getting vaccinated for pertussis, COVID-19 and respiratory syncytial virus, also called RSV.**

**Prognosis / Outlook**

**What is the prognosis (outlook) for people with rare lung diseases?**

**The prognosis for people with rare lung diseases varies depending on the specific disease and severity of the disease. Many rare pulmonary diseases become more serious over time.**

**A lung transplant may stop the disease. Not everyone qualifies for a lung transplant or matches with a donor. Unfortunately, there are more people in need than there are donors.**

**Researchers are conducting many clinical trials on rare lung diseases in the U.S. and Europe. They continue to make advances that may lead to promising new therapies for these conditions.**

**Getting the right treatment and support for your disease can lead to a longer, healthier life. Treatment can also help you manage your symptoms and improve your quality of life.**

**Sign & Symptoms**

**Symptoms**

**The main symptoms of interstitial lung disease are:**

* **Shortness of breath at rest or shortness of breath that worsens with physical activity.**
* **Dry cough.**

**Diagnosis**

**Finding the cause of interstitial lung disease can be challenging, and sometimes the cause can't be found. Many conditions fall into the category of ILD. In addition, the symptoms of a wide range of medical conditions can appear to be ILD. Healthcare professionals must rule out these conditions before making a diagnosis.**

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**Some of the following tests may be necessary.**

**Lab tests**

* **Blood tests. Certain bloodwork can detect proteins, antibodies and other markers of autoimmune diseases or inflammatory responses to environmental exposures, such as those caused by molds or bird protein.**

**Imaging tests**

* **Computerized tomography, also called a CT scan. This imaging test is key to the diagnosis of interstitial lung disease. It's sometimes the first test in the diagnosis. CT scanners produce 3D images of internal structures. A high-resolution CT scan can be especially helpful in figuring out how much lung damage there is. It can show details of the fibrosis, which can help narrow the diagnosis and guide treatment decisions.**
* **Echocardiogram. An echocardiogram uses sound waves to visualize the heart. It can create still images of your heart's structures and videos that show how your heart is working. This test can measure the amount of pressure in the right side of your heart.**

**Pulmonary function tests**

* **Spirometry and diffusion capacity. This test requires you to breathe out quickly and forcefully through a tube connected to a machine. The machine measures how much air your lungs can hold and how quickly you can move air out of your lungs. It also measures how easily oxygen can move from your lungs into your bloodstream.**
* **Oximetry. A small device is placed on one of your fingers to measure the oxygen level in your blood. This test may be done at rest or with activity to monitor the course of the lung disease and figure out how serious it is.**

**Lung tissue analysis**

**Sometimes interstitial lung diseases can be diagnosed only by looking at a small amount of lung tissue in a lab — what's known as a biopsy.**

**Your doctor or other healthcare professional may take a tissue sample using one of these methods:**

* **Bronchoscopy. In this procedure, your healthcare professional removes very small tissue samples — generally no larger than the head of a pin. This is done by using a small, flexible tube, also known as a bronchoscope, that's passed through your mouth or nose into your lungs. The risks of bronchoscopy are generally minor, namely a sore throat for a limited time and hoarseness from the bronchoscope. But the tissue samples are sometimes too small to make a diagnosis.**
* **Bronchoalveolar lavage. In this procedure, your doctor injects about a tablespoon of sterile salt water through a bronchoscope into a section of your lung and then suctions it out right away. The solution that's removed contains cells from your air sacs. Although bronchoalveolar lavage samples a larger area of the lung than other procedures do, it may not give enough information to find out what's causing pulmonary fibrosis.**
* **Surgical biopsy. Although this is a more invasive procedure with potential complications, it's often the only way to get a large enough tissue sample to make the correct diagnosis. General anesthesia is used for this test. Surgical instruments and a small camera are inserted through one or more small incisions between the ribs. The camera allows a surgeon to view the lungs on a video monitor while removing tissue samples from the lungs.**

**Treatment**

**Lung scarring that already has occurred in interstitial lung disease can't be reversed, and treatment won't always stop the disease from getting worse. Some treatments may make symptoms better for a short time or slow the disease. Others help maintain quality of life.**

**Because many of the different types of scarring diseases have no approved or proven therapies, clinical trials may be an option to get an experimental treatment.**

**Medications**

**Intense research to find treatment options for specific types of interstitial lung disease is ongoing. Treatment may vary depending on the cause of ILD and what damage has happened in the lungs. Using on the latest scientific evidence, your healthcare professional may recommend:**

* **Corticosteroid medicines. At first, many people diagnosed with ILD are treated with a corticosteroid, namely prednisone (Prednisone Intensol, Rayos). Sometimes people are treated with other drugs that suppress the immune system. Depending on the cause of ILD, these medicines may slow or even keep the disease from getting worse.**
* **Medicines that slow the worsening of idiopathic pulmonary fibrosis. Pirfenidone (Esbriet) and nintedanib (Ofev) are medicines that may slow the rate at which IPF worsens. Ofev also has been approved for people with lung fibrosis that's getting worse due to other types of interstitial lung disease. Side effects for both drugs are common. Talk with your healthcare professional about the pros and cons of these medicines.**
* **Medicines that reduce stomach acid. Gastroesophageal reflux disease, also known as GERD, affects most people with idiopathic pulmonary fibrosis. GERD is linked to worse lung damage. If you have symptoms of acid reflux, your healthcare professional may prescribe ways to treat GERD that reduce stomach acid.**

**Oxygen therapy**

**Using oxygen can't stop lung damage, but it can:**

* **Make it easier to breathe and exercise.**
* **Prevent or lessen complications from low blood oxygen levels.**
* **Lower blood pressure in the right side of your heart.**
* **Make your sleep and sense of well-being better.**

**You're most likely to get oxygen when you sleep or exercise, although some people may use it around the clock.**

**Pulmonary rehabilitation**

**The aim of pulmonary rehabilitation is to make you better able to function and live a full, satisfying life. That's why pulmonary rehabilitation programs focus on:**

* **Learning more about your lung disease.**
* **Exercise, so you can become more physically active for longer periods of time.**
* **Breathing techniques that make your lungs more efficient.**
* **Emotional support.**
* **Nutritional counseling.**

**Surgery**

**A lung transplant may be an option of last resort for some people with severe interstitial lung disease when other treatment options haven't helped.**

**Providers often treat rare lung diseases with medications used to treat other conditions. Treatments usually help slow the progression of the disease rather than cure it. Depending on the pulmonary disease, treatments may include:**

* **Airway clearance therapy to treat cystic fibrosis by loosening mucus from your airways.**
* **Bronchodilators, inhalers that clear mucus from your lungs to make breathing easier.**
* **Medications, such as corticosteroids, immune-suppressing drugs, antibiotics and enzymes. These drugs can make it easier for you to breathe.**
* **Oxygen therapy, providing extra oxygen through a mask or tube in your nostrils to make breathing easier and improve your sleep.**
* **Whole-lung lavage, where a provider inserts a tube with saline into your lungs to clean them. Whole-lung lavage treats pulmonary alveolar proteinosis (PAP).**

**People with severe lung disease may need lung transplant surgery. A transplant is an option if other treatments don’t help. This surgery may prolong your life.**

**When To See A Doctor**

**By the time symptoms appear in certain types of interstitial lung disease, lasting lung damage has already occurred. That's why it's important to see your healthcare professional at the first sign of breathing problems. Many conditions other than ILD can affect your lungs. Getting an early and correct diagnosis is important for proper treatment.**

**See your healthcare provider right away if you experience signs of lung disease. Always contact your provider if you develop new or worrisome symptoms.**

**If a rare lung disease runs in your family, you may choose to talk to your provider about genetic counseling before you have children. A genetic counselor can assess your risk and the risk of passing on a gene for an inherited lung disease.**

**Self Care**

**Lifestyle and home remedies**

**You must be actively involved in your own treatment and stay as healthy as possible when you're living with interstitial lung disease. For that reason, it's important to:**

* **Learn about your disease. Understanding your condition and how it can be treated can help you decide about your care. Including family members and friends can help them learn your needs.**
* **Stop smoking. If you have lung disease, the best thing you can do for yourself is to stop smoking. Talk with your healthcare professional about options for quitting, including programs to help you stop smoking. These programs use various proven techniques to help people quit. And because secondhand smoke also can harm your lungs, don't allow people to smoke around you.**
* **Avoid exposure at work or during hobbies. When possible, stay away from substances that can irritate your lungs. Ask your healthcare professional for more information and advice.**
* **Eat well. If you have lung disease, you may lose weight because it isn't comfortable to eat and because of the extra energy it takes to breathe. Aim to eat a nutritionally rich diet that contains enough calories. A dietitian can give you more guidelines for healthy eating.**
* **Get vaccinated. Respiratory infections can make symptoms of ILD worse. Make sure you get the pneumonia vaccine and a flu shot each year.**

**Coping and support**

**Living with a chronic lung disease is emotionally and physically challenging. You may need to change your daily routines and activities — sometimes a lot — as breathing problems worsen or health care needs become more important. Feelings of fear, anger and sadness are typical as you grieve for the loss of your old lifestyle and worry about what's next for you and your family.**

**Share your feelings with your loved ones and your healthcare professional. Talking openly may help you and your loved ones cope with the emotional challenges of your disease. Also, clear communication can help you and your family plan for your needs if your disease gets worse.**

**Think about joining a support group, where you can talk with people who are facing challenges like yours. Group members may share coping strategies, exchange information about new treatments or simply listen as you express your feelings. If a group isn't for you, you may want to talk with a counselor in a one-on-one setting.**

**How can I manage my lung disease symptoms?**

**Researchers are developing new treatments for rare lung diseases. In the meantime, healthcare providers focus on treating the disorder's symptoms. Your team of providers may recommend:**

* **A targeted nutrition plan can help you maintain your weight and overall health.**
* **Pulmonary rehabilitation, including exercises and behavior changes that can improve your day-to-day life.**

**Medical Codes**

|  |  |  |  |
| --- | --- | --- | --- |
| **ICD-10-CM Code** | **Disease Name** | **Clinical Context** | **Verification Source** |
| **J84.111** | **Idiopathic Pulmonary Fibrosis (IPF)** | **Usual Interstitial Pneumonia (UIP) pattern** | **CDC ICD-10-CM 2024** |
| **J84.112** | **Idiopathic Nonspecific Interstitial Pneumonia (NSIP)** | **Fibrotic/cellular subtypes** | **ATS Clinical Guidelines** |
| **J84.113** | **Respiratory Bronchiolitis-ILD (RB-ILD)** | **Smoking-related ILD** | **NIH GARD** |
| **J84.114** | **Desquamative Interstitial Pneumonia (DIP)** | **Smoking-related, diffuse alveolar damage** | **ERS White Book** |
| **J84.2** | **Lymphangioleiomyomatosis (LAM)** | **Cystic lung disease, mTOR pathway disorder** | **CDC ICD-10-CM 2024** |
| **J84.81** | **Bronchiolitis Obliterans (Constrictive Bronchiolitis)** | **Post-transplant/non-transplant; includes popcorn lung** | **CMS ICD-10-CM 2024** |
| **J84.83** | **Cryptogenic Organizing Pneumonia (COP)** | **Formerly BOOP; steroid-responsive** | **ATS/ERS Joint Statement** |
| **J84.84** | **Acute Interstitial Pneumonia (AIP)** | **Hamman-Rich syndrome, rapidly progressive** | **NIH MedlinePlus** |
| **J84.89** | **Other Interstitial Lung Diseases (e.g., Pleuroparenchymal Fibroelastosis)** | **Rare upper-lobe predominant fibrosis** | **Orphanet** |
| **D86.0** | **Pulmonary Sarcoidosis** | **Granulomatous ILD, Löfgren's syndrome** | **CDC ICD-10-CM 2024** |
| **J84.010** | **Pulmonary Alveolar Proteinosis (PAP)** | **Autoimmune, congenital, or secondary forms** | **Rare Lung Diseases Consortium** |
| **J98.4** | **Pulmonary Alveolar Microlithiasis** | **Calcium deposits in alveoli** | **NIH GARD** |
| **J82** | **Pulmonary Eosinophilia (incl. Eosinophilic Granulomatosis with Polyangiitis)** | **Churg-Strauss syndrome** | **ACR/Vasculitis Foundation Guidelines** |
| **J84.17** | **Neuroendocrine Hyperplasia of Infancy (NEHI)** | **Childhood diffuse lung disease** | **CHEST Journal** |
| **Q85.8** | **Tuberous Sclerosis Complex with Lung Involvement (LAM/TSC)** | **Multisystem genetic disorder** | **NIH NINDS** |

**References**

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1. **Bronchitis**

**Definition:**

Bronchitis is an inflammation of the lining of your bronchial tubes. These tubes carry air to and from your lungs. People who have bronchitis often cough up thickened mucus, which can be discolored. Bronchitis may start suddenly and be short term (acute) or start gradually and become long term (chronic).

Acute bronchitis, which often develops from a cold or other respiratory infection, is very common. Also called a chest cold, acute bronchitis usually improves within a week to 10 days without lasting effects, although the cough may linger for weeks.

Chronic bronchitis, a more serious condition, is a constant irritation or inflammation of the lining of the bronchial tubes, often due to smoking. If you have repeated bouts of bronchitis, you may have chronic bronchitis, which requires medical attention. Chronic bronchitis is one of the conditions included in chronic obstructive pulmonary disease (COPD).

**Causes:**

Acute bronchitis is usually caused by infectious agents such as bacteria or viruses. It may also be caused by physical or chemical agents minus; dusts, allergens, strong fumes, and those from chemical cleaning compounds, or tobacco smoke. (Acute asthmatic bronchitis may happen as the result of an asthma attack, or it may be the cause of an asthma attack.)

In children, the most common cause of bronchitis is a virus, although in children over 6 years of age, it can be caused by bacteria. Acute bronchitis is usually a mild condition. Acute bronchitis may follow the common cold or other viral infections in the upper respiratory tract. It may also occur in children with chronic sinusitis, allergies, or those with enlarged tonsils and adenoids. Pneumonia is a complication that can follow bronchitis.

You almost always get bronchitis from a virus. However, nearly anything that irritates your airways can cause it. Infectious and noninfectious causes of bronchitis include:

* **Viruses**. Viruses that cause bronchitis include influenza (the flu), respiratory syncytial virus (RSV), adenovirus, rhinovirus (the common cold) and coronavirus.
* **Bacteria**. Bacteria that cause bronchitis include *Bordetella pertussis, Mycoplasma pneumonia* and *Chlamydia pneumonia.*
* **Toxins in the air.**
* **Smoking cigarettes or marijuana (cannabis).**

**How do you get bronchitis?**

You get bronchitis when your airways swell up and fill with mucus. You can get the viruses and bacteria that cause bronchitis from close contact (shaking hands, hugging, touching the same surfaces) with someone who has them. You don’t have to have bronchitis yourself to pass on a virus to someone else who ends up with bronchitis.

Other irritants are in the air you breathe.

**Is bronchitis contagious?**

Bronchitis itself — inflammation of your airways — isn’t contagious, but the viruses and bacteria that can cause it are. For instance, if you’re sick with the flu, you might get bronchitis too. But when your friend gets the flu from you, their airways don’t get inflamed like yours did.

**Is bronchitis a side effect of COVID-19?**

You can get bronchitis with almost any virus, including SARS-CoV2, the virus that causes COVID-19. The symptoms of bronchitis can be similar to COVID-19, so make sure you get tested to know which one you have. There haven’t been any studies that show that COVID-19 is any more likely to cause bronchitis than other viral illnesses.

**Risk Factors:**

* Age < 2 yrs, especially < 3 months for bronchiolitis
* Prematurity, chronic lung/heart disease, immunodeficiency
* Day-care attendance, household crowding, homelessness[64 in 6]
* Passive or active exposure to tobacco or e-cigarette smoke
* Under-vaccination (influenza, pertussis, measles, COVID-19, RSV antibody nirsevimab)

Anyone can get bronchitis, but you’re at higher risk if you:

Smoke or are around someone who does.

Have asthma, COPD or other breathing conditions.

Have GERD (chronic acid reflux).

Have an autoimmune disorder or other illness that causes inflammation.

Are around smoke, chemicals or toxins in the air.

**Signs & Symptoms:**

Each child may experience symptoms differently. Symptoms may include:

* Runny nose, usually before a cough starts
* Malaise (an overall body discomfort or not feeling well )
* Chills
* Slight fever
* Back and muscle pain
* Sore throat

In the earlier stages of the condition, children may have a dry, non-productive cough which progresses later to a mucus-filled cough. Younger children may have some vomiting or gagging with the cough. The symptoms of bronchitis usually last seven to 14 days, but may also persist for three to four weeks.

The symptoms of acute bronchitis may resemble other conditions or medical problems. Typical findings appear after an upper-respiratory prodrome:

* **Cough** – initially dry, then productive or wet; may persist 3–4 weeks.
* Chest congestion or mild substernal pain.
* Low-grade fever, malaise, myalgia, chills.
* Wheeze or coarse crackles (“rhonchi”) that clear with coughing.

**Medical Codes:**

ICD-10 coding for bronchitis requires selecting the most specific code based on the type, underlying cause, and duration of the condition.

**Acute bronchitis**

J20 Acute bronchitis  
J20.0 Acute bronchitis due to Mycoplasma pneumoniae  
J20.1 Acute bronchitis due to Hemophilus influenzae  
J20.2 Acute bronchitis due to streptococcus  
J20.3 Acute bronchitis due to coxsackievirus  
J20.4 Acute bronchitis due to parainfluenza virus  
J20.5 Acute bronchitis due to respiratory syncytial virus  
J20.6 Acute bronchitis due to rhinovirus  
J20.7 Acute bronchitis due to echovirus  
J20.8 Acute bronchitis due to other specified organisms  
J20.9 Acute bronchitis, unspecified

Codes in the J20.0 – J20.9 range specify acute bronchitis caused by different organisms (e.g., Mycoplasma pneumoniae, rhinovirus, or unspecified acute bronchitis). J20.9 is used for unspecified acute bronchitis when the cause is unknown or not documented.

**Chronic bronchitis**

J40- Bronchitis that is not specified as acute or chronic  
J41 Simple and mucopurulent chronic bronchitis  
J41.0 Simple chronic bronchitis  
J41.1 Mucopurulent chronic bronchitis  
J41.8 Mixed simple and mucopurulent chronic bronchitis  
J42 Unspecified chronic bronchitis

**Related codes:**  
J44.89: Other specified chronic obstructive pulmonary disease  
J44.9: Chronic obstructive pulmonary disease, unspecified

**Diagnosis Mapping:**

Your child’s healthcare provider can tell if you have bronchitis based on your health history and symptoms (clinical diagnosis). They’ll listen to your lungs for signs of congestion and to make sure you’re breathing well. They might test you for viral infections, like the flu or COVID-19.

What tests will be done to diagnose this condition?

There aren’t any specific tests to diagnose bronchitis, but you might be tested for other conditions. Possible tests include:

Nasal swab. Your healthcare provider may use a soft-tipped stick (swab) in your nose to test for viruses, like COVID-19 or the flu.

Chest X-ray. If your cough lasts for a long time, you may get a chest X-ray to rule out more serious conditions. Your healthcare provider will use a machine to get pictures of your heart and lungs. They’ll look for signs of other diseases that could cause your symptoms.

Blood tests. Your provider may do blood tests, using a needle in your arm, to look for infections or check your overall health.

Sputum test. Your provider may have you cough and then spit into a tube. Your sample will be tested for signs of a virus or bacteria.

Pulmonary function tests. If your provider thinks you have chronic bronchitis, they may use a machine to test how well your lungs work.

**Treatment Options:**

Your child's doctor will decide the treatment for acute bronchitis based on:

* Your child's age, overall health, and medical history
* Extent of the condition
* Your child's tolerance for specific medications, procedures, or therapies
* Expectations for the course of the condition
* Your opinion or preference

Acute bronchitis is usually not treated with medications. If you have the flu and your symptoms started within the past two days, your provider may prescribe antivirals to help it go away faster. Since bronchitis is almost never caused by bacteria, antibiotics won’t help you get better and might even make you feel worse.

What medications are used to treat bronchitis?

Your healthcare provider probably won’t prescribe medications to treat bronchitis. In some cases, you can use medications to help you with symptoms or to treat the underlying cause, including:

Antiviral medications. If your bronchitis is caused by the flu, your healthcare provider might prescribe an antiviral medication, like Tamiflu®, Relenza® and Rapivab®. If you start taking antivirals quickly after your symptoms start, you might feel better sooner.

Bronchodilators. Your provider might prescribe a bronchodilator (a drug that helps open your airways) if you’re having trouble breathing.

Anti-inflammatory medications. Your doctor might prescribe corticosteroids and other medications to reduce inflammation.

Cough suppressants. Over-the-counter or prescription cough suppressants (antitussives) may help with a nagging cough. This includes dextromethorphan (Robitussin®, DayQuil™, PediaCare®) and benzonatate (Tessalon Perles®, Zonatuss™).

Antibiotics. It’s very unlikely that you’ll be treated with antibiotics for bronchitis, unless your healthcare provider thinks you have a bacterial infection.

COPD/asthma treatment. If you have COPD or asthma, your provider may use additional medications or breathing treatments for chronic bronchitis.

**Prevention Tips:**

The best way to reduce the risk of bronchitis is to avoid getting sick from viruses and other causes of lung irritation. Specific ways to reduce your risk include:

* Try to avoid being around other people if you or they may be sick. This is especially true in the winter months when people gather indoors.
* Avoid smoke and other irritants.
* If your child has asthma or allergies, avoid any triggers (including pets, dust and pollen).
* Run a humidifier. Moist air is less likely to irritate your lungs.
* Ensure plenty of rest.
* Ensure a healthy and nutritional diet.
* Wash your child’s hands and yours often with soap and water. If you’re not able to use soap and water, use a hand sanitizer that contains alcohol.
* Make sure you are up-to-date on flu, pneumonia and COVID-19 vaccines.

**Prognosis:**

Acute bronchitis is almost always a self-limited process in the otherwise healthy child. However, it frequently results in absenteeism from school and, in older patients, work. Chronic bronchitis is manageable with proper treatment and avoidance of known triggers (e.g, tobacco smoke). Proper management of any underlying disease process, such as asthma, cystic fibrosis, immunodeficiency, heart failure, bronchiectasis, or tuberculosis, is also key. These patients need careful periodic monitoring to minimize further lung damage and progression to chronic irreversible lung disease.

A long-term prospective study found that children who had bronchitis at least once before the age of 7 years were more likely to have been diagnosed with asthma and pneumonia by age 53 years. The association with asthma and pneumonia in adulthood was strongest for participants who had a history of recurrent-protracted childhood bronchitis.

An analysis of data from a nationwide British cohort study showed that children who had a lower respiratory tract infection (LRTI) such as bronchitis by the age of 2 years were 93% more likely to die of respiratory disease by age 73 years than children who had not had a LRTI by age 2 years. The rate of premature adult death caused by respiratory disease was a 2.1% among those who had a LRTI during early childhood, versus 1.1% among those who did not report a LRTI before age 2 years.

**Complications:**

Untreated or severe cases may lead to pneumonia, transient asthma-like reactive airway disease, PBB, bronchiectasis, recurrent otitis media, or (rarely) respiratory failure requiring ventilation. If you have an ongoing condition like asthma, diabetes, chronic obstructive pulmonary disease or heart failure, bronchitis might make it worse (exacerbation).

**When to see a Doctor/Red Flags:**

Seek same-day care if a child:

* Breathes > 60/min (< 2 mos) or shows retractions/nasal flaring.
* Has skin, lips or nail beds turning blue/gray.
* Cannot feed, is dehydrated or vomits all feeds.
* Has fever ≥ 38 °C in < 3 mos, or ≥ 39 °C in older infants.
* Coughs > 3 weeks, worsens after initial improvement, or produces blood-tinged sputum.

Call emergency services for apnea, severe distress, altered consciousness, or seizures

**Differential Diagnoses:**

* Acute Sinusitis
* Aspiration Syndromes
* Atypical Mycobacterial Infection
* Bacterial Tracheitis
* Bronchiolitis
* IgA and IgG Subclass Deficiencies
* Bronchopulmonary Dysplasia (BPD) Imaging
* Influenza
* Passive Smoking and Lung Disease
* Pediatric Aspergillosis
* Pediatric Asthma
* Pediatric Bronchiectasis
* Pediatric Bronchogenic Cyst
* Pediatric Common Variable Immunodeficiency
* Pediatric Gastroesophageal Reflux
* Pediatric Pneumonia
* Pediatric Tracheomalacia
* Pediatric Tuberculosis
* Respiratory Syncytial Virus Infection
* Rhinovirus (RV) Infection (Common Cold)
* Sinonasal Manifestations of Cystic Fibrosis
* Smoke Inhalation Injury

**Guidelines:**

Agency Key recommendation set

WHO IMCI 2014: Classify “pneumonia” vs “severe pneumonia”; treat first-line with oral amoxicillin; no antibiotics for simple cough/cold.

CDC 2024: Avoid antibiotics for chest colds; emphasize vaccination, hand hygiene, smoke avoidance.

NICE NG9 (UK): Hospital referral when SpO₂ < 92%, RR above age norms or feeding < 50%; no bronchodilators/antibiotics in routine bronchiolitis.

ATS 2021 PBB factsheet: Wet cough > 4 wks warrants 2–4 wk amoxicillin-clavulanate; investigate recurrent episodes

**Expert-Reviewed Q&A:**

**Q: Why won’t the doctor give my child an antibiotic?**  
A: Because over 9 of 10 children’s chest colds are viral. Antibiotics do not kill viruses and can cause diarrhea, rashes and antibiotic resistance.

**Q: How long will the cough last?**  
A: The intense phase usually subsides in 7–14 days, but a mild, dry “post-bronchitic” cough can linger up to 4 weeks and still be normal.

**Q: What can I do for the cough at night?**  
A: Offer warm fluids, ensure good hydration, use a cool-mist humidifier, and raise the head of the bed. Cough medicines are not advised for young children and rarely shorten recovery

**Q: Is wheezing during bronchitis the same as asthma?**  
A: Viral inflammation can temporarily narrow airways and mimic asthma. Most children outgrow this, but persistent or recurrent wheeze should be re-evaluated for asthma.

**Q: Could this turn into pneumonia?**  
A: The vast majority recover without pneumonia. Watch for high fever, fast breathing, or chest indrawing—these prompt a doctor visit.

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1. **Chronic Respiratory Failure:**

**Definition:**

Pediatric chronic respiratory failure is a serious condition where the respiratory system fails to maintain adequate gas exchange over an extended period, typically weeks to months, resulting in chronically insufficient oxygen delivery to tissues or inadequate carbon dioxide elimination from the blood. This condition is defined by the inability to maintain adequate oxygenation (oxygen saturation) or ventilation (carbon dioxide elimination) despite medical intervention.

**Causes:**

The most common reasons for respiratory failure in the pediatric population can be divided by anatomic compartments, as follows.

Acquired extrathoracic airway causes include the following:

* Infections (eg, bacterial tracheitis, laryngotracheobronchitis, retropharyngeal abscess, peritonsillar abscess, Ludwig angina)
* Trauma (eg, postextubation croup, thermal burns, foreign-body aspiration)
* Other (eg, hypertrophic tonsils and adenoid)

Congenital extrathoracic airway causes include the following:

* Subglottic stenosis
* Subglottic web or cyst
* Laryngomalacia
* Tracheomalacia
* Vascular ring
* Cystic hygroma
* Craniofacial anomalies

Intrathoracic airway and lung causes include the following:

* Acute respiratory distress syndrome (ARDS)
* Asthma
* Aspiration of a foreign body
* Bronchiolitis
* Bronchomalacia
* Left-sided valvular abnormalities
* Pulmonary contusion
* Near drowning
* Pneumonia
* Pulmonary edema
* Pulmonary embolus
* Sepsis

Respiratory pump causes include the following:

* Diaphragm eventration
* Diaphragmatic hernia
* Flail chest
* Kyphoscoliosis
* Duchenne muscular dystrophy
* Guillain-Barré syndrome
* Infant botulism
* Myasthenia gravis
* Spinal cord trauma
* Spinal muscular atrophy (SMA)

Central control causes include the following:

* CNS infection
* Drug overdose
* Sleep apnea
* Stroke
* Traumatic brain injury

**Risk Factors:**

**Prenatal and Perinatal Factors:**

* Prematurity (especially <29 weeks gestation)
* Low birth weight (<4 lbs, 6 oz)
* Maternal infections during pregnancy
* Patent ductus arteriosus

**Patient-Specific Factors:**

* Age <6 months (higher vulnerability)
* Male gender (higher risk for bronchopulmonary dysplasia)
* American Indian and Alaska Native ethnicity
* Immunocompromised status
* Severe malnutrition

**Medical History:**

* Previous mechanical ventilation or CPAP exposure
* Chronic underlying conditions (neuromuscular diseases, congenital heart disease)
* History of severe respiratory infections

**Signs & Symptoms:**

Very often, chronic respiratory failure symptoms will develop slowly over a period of time. These gradual symptoms can include:

* Shortness of breath or labored breathing, especially after physical activities
* Persistent coughing and wheezing
* Fatigue
* Noticeable bluish tint to the extremities, such as the fingertips and lips
* Confusion and drowsiness
* Headaches

These symptoms should always be taken seriously if they continue for days or weeks and should be checked out by a doctor. Watch out for any symptoms that may constitute a medical emergency, such as an inability to breathe, heart arrhythmias, or loss of consciousness.

**Early/Chronic Symptoms**

**Respiratory Signs:**

* Shortness of breath, especially with activity
* Persistent cough and wheezing
* Rapid or labored breathing (tachypnea)
* Use of accessory muscles for breathing
* Nasal flaring

**Systemic Symptoms:**

* Chronic fatigue and decreased activity tolerance
* Sleep disturbances and daytime somnolence
* Poor feeding and growth failure
* Morning headaches (due to CO2 retention)

**Physical Examination Findings:**

* Cyanosis (bluish discoloration of lips, fingernails)
* Pallor
* Chest retractions
* Grunting respirations
* Head bobbing in infants

**Progressive Warning Signs:**

Increasing somnolence and altered mental status

Worsening exercise tolerance

Polycythemia (increased red blood cell count)

Signs of cor pulmonale (right heart strain)

**Medical Codes:**

The primary ICD-10-CM code for pediatric chronic respiratory failure is J96.1. For more specific coding, J96.10 indicates chronic respiratory failure, unspecified whether with hypoxia or hypercapnia.

Key Points:

* **J96.1**: is the general code for chronic respiratory failure.
* **J96.10**: is a more specific code for chronic respiratory failure when the presence of hypoxia or hypercapnia is not specified.
* **J96.2**: can be used for acute and chronic respiratory failure, also unspecified.
* **J96.20**: is a more specific code for acute and chronic respiratory failure, unspecified whether with hypoxia or hypercapnia.
* Additional codes from the J96 range may be used depending on the specific circumstances of the case, such as whether it's with hypoxia or hypercapnia.

Important Considerations:

* Always consult with a qualified medical professional or coding specialist for accurate and specific coding in individual cases.
* The ICD-10-CM codes are used for medical billing and record-keeping purposes.
* The codes may vary slightly depending on the specific version of the ICD-10-CM manual being used.

**Diagnosis Mapping:**

A doctor will usually diagnose a patient with chronic respiratory failure after performing the following steps:

* Reviewing medical history
* Discussing symptoms and how they affect activities
* Conducting a thorough physical evaluation, particularly breathing and heart tests
* Ordering lab tests, such as pulse oximetry, arterial blood gas testing, and bronchoscopy to measure oxygen levels in the blood and test lung tissue
* Imaging tests for a closer look at the lungs and to identify possible breathing obstructions

Upon diagnosis, treatment may depend on the individual patient and his or her underlying conditions and state of health. Chronic respiratory failure can often be managed at home through certain medications, oxygen therapy, and physical and occupational therapy techniques.

In severe cases of respiratory failure, doctors may recommend more serious measures, including tracheostomy and mechanical ventilation. Although there is not currently a cure for chronic respiratory failure, it is often possible to manage this condition successfully on a long-term basis. Many patients with chronic respiratory failure can benefit from specialized assistance, including[home health care](https://careoptionsforkids.com/nursing/adult-home-health).

**Diagnostic Criteria for Acute Respiratory Failure in Pediatric Patients**

* Pediatric patients often present differently than adults and can also decompensate more quickly. Children may present with the following:
* Lethargy or irritability
* Appear anxious or demonstrate inability to concentrate
* May prefer positioning to aid in breathing (i.e sitting up, leaning chest/head forward)
* Mouth breathing, drooling
* Interrupted feeding and diet patterns
* Generally, oxygen saturation <88% on room air is supportive of acute hypoxemic respiratory failure. ABGs are rarely measured when assessing children’s respiratory function. However, diagnostic ABG levels include:
* PaO2 of < 60 mmHg on room air
* Acute increase in pCO2 of 10-15 mmHg
* pH decreasing to 7.32 or less
* PaO2 / FiO2 (PF) ratio of < 200 or < 300
* Intubation/mechanical ventilation is not required to support the presence of acute respiratory failure. An acute respiratory condition and any of the following treatments may support the presence of acute respiratory failure:
* Supplemental oxygen with FiO2 ≥ 0.30–0.35 to maintain SpO2 ≥ 90%
* Any level of high-flow nasal cannula
* Any level of nasal continuous positive airway pressure (nCPAP) or nasal bilevel positive airway pressure (BiPAP) (except for obstructive sleep apnea)
* Provider documentation often describes the patient’s symptoms and assessment without stating the words “acute respiratory failure.” If clinical indicators support the presence of acute respiratory failure, a query should be sent.
* For example, “acute respiratory distress”, “acute exacerbation”, “respiratory insufficiency”, “respiratory acidosis” are frequently used terms that may not capture the patient’s true complexity.
* Providers frequently use templated notes that are copied/pasted into subsequent notes. This is a great opportunity for CDI to provide education on customizing these templates.
* Templated notes often have statements such as “no acute distress”, and “normal appearance” which can suggest that the patient did not have respiratory failure.

**Additional Tips:**

• Chapter-specific coding guidelines (particularly with newborns) that provide sequencing direction take precedence when determining the principal diagnosis.

• A code from subcategory J96.0, Acute respiratory failure, or subcategory J96.2, Acute and chronic respiratory failure, may be assigned as a principal diagnosis when it is the condition established after study to be chiefly responsible for occasioning the admission to the hospital.

• Although acute respiratory failure always has an underlying cause, do not default to the etiology as the principal diagnosis. The circumstances of the admission must be considered. Respiratory failure may be listed as either the principal or a secondary diagnosis.

• For acute respiratory failure due to COVID-19, assign code U07.1, COVID-19, followed by code J96.0-, Acute respiratory failure.

• If the documentation is not clear as to whether acute respiratory failure and other conditions are equally responsible for occasioning the admission, query the provider for clarification.

• Common respiratory failure risk factors to look out for in pediatric patients include: young age, premature birth, immunodeficiency, chronic pulmonary/cardiac/neuromuscular diseases, anatomic abnormalities, cough/rhinorrhea/other URI symptoms, and lack of immunizations.

• Other conditions that are not pulmonary in nature which may lead to acute respiratory failure include: status epilepticus leading to encephalopathy and decreased respiratory drive, a traumatic head injury or anoxic brain injury that stops respiratory drive, and septic shock.

**Treatment Options:**

**Approach Considerations:**

Management of acute respiratory failure begins with a determination of the underlying etiology. While supporting the respiratory system and ensuring adequate oxygen delivery to the tissues, initiate an intervention specifically defined to correct the underlying condition. For example, a patient with status asthmaticus is given supplemental oxygen to treat hypoxemia, but corticosteroids and beta-agonist drugs are also given to treat the underlying pathology.

**Extrathoracic airway support**

For partial upper-airway obstruction (eg, from anesthesia or acute tonsillitis), place a nasopharyngeal airway to provide a passageway for air.[[10](javascript:void(0);)]An oropharyngeal airway can be used temporarily in the unconscious patient.

For extrathoracic airway obstruction, as in croup, the following measures may be helpful:

* Racemic epinephrine 2.25% (an aerosolized vasoconstrictor) or an equivalent dose of L-epinephrine
* Systemic corticosteroids: To decrease airway edema
* Heliox (helium and oxygen gas mixture): To decrease the work of breathing
* Inspired humidity: To liquefy secretions
* Nebulized hypertonic (3%) saline

Heliox has a helium concentration of 60-80% and thus has a density lower than that of air; it improves breathing by reducing turbulent airflow through a narrowed area.

**Tracheal Intubation**

Endotracheal intubation is occasionally needed to maintain airway patency in certain cases (eg, epiglottitis, thermal burns to the airway, severe croup). In general, uncuffed tubes are used in children younger than 8 years because the subglottic trachea surrounded by the cricoid cartilage is the narrowest part of the pediatric airway.

Cuffed endotracheal tubes are typically preferred over uncuffed endotracheal tubes in the pediatric population[[11](javascript:void(0);), [12](javascript:void(0);), [13](javascript:void(0);)](cuffs provide a seal against the tracheal wall), particularly those with a high volume and low pressure, as well as a standard internal-to-external diameter ratio and clear length markers.[[14](javascript:void(0);), [15](javascript:void(0);)]Several studies have concluded that the incidence of postextubation stridor and subglottic stenosis are not increased with high-volume, low-pressure cuffed endotracheal tubes.[[16](javascript:void(0);), [17](javascript:void(0);), [18](javascript:void(0);)]

The appropriate endotracheal tube size is generally based on the age of the child. In neonates and infants younger than 6 months, a cuffed endotracheal tube with an inner diameter (ID) of 3.5-4 mm is appropriate. In infants aged 6-12 months, a cuffed tube with a 4-4.5 mm ID is appropriate. A useful bedside or field guideline for appropriate endotracheal tube size is approximately the size of the patient’s fifth finger.

In children older than 1 year, the following formula can be used: Tube size (ID in millimeters) = (age in years + 16)/4

**Lung and Respiratory Pump Support**

Oxygen therapy

The initial treatment for hypoxemia is to provide supplemental oxygen. High-flow (>15 L/min) oxygen delivery systems include a Venturi-type device that places an adjustable aperture lateral to the stream of oxygen. Oxygen is mixed with entrained room air, and the amount of air is adjusted by varying the aperture size. The oxygen hoods and tents also supply high gas flows.

Low-flow (< 6 L/min) oxygen delivery systems include the nasal cannula and simple face mask.

Humidified high-flow nasal cannula therapy

In the last decade, HHFNC has been shown to be a safe, tolerable, available/portable, and easily manageable noninvasive ventilatory support in children with respiratory failure, as well as a viable alternative to nasal continuous positive airway pressure (nCPAP).[[8](javascript:void(0);), [20](javascript:void(0);)]

Indications for use of HHFNC in infants and children include the following[[20](javascript:void(0);)]:

* Acute bronchiolitis
* Asthma
* Congenital heart disease
* Obstructive sleep apnea
* Pneumonia

No single universally accepted definition is available for what constitutes humidified high-flow nasal cannula (HHFNC) therapy in neonates; however, a widely used and reasonable definition is optimally warmed (body temperature) and humidified respiratory gases delivered by nasal cannula at flow rates of 2-8 L/min.[[21](javascript:void(0);)]Temperature, gas flow, and fraction

**Adjunctive Therapies for Severe Hypoxemia**

Prone positioning

Prone positioning reduces compliance of the thoracoabdominal cage by impeding the compliant rib cage. Gases should distribute toward the sternal and anterior diaphragmatic regions that become dependent on prone positioning. Improved homogeneity of ventilation improves oxygenation. This measure may cause a redistribution of blood flow, improving the V/Q match.

Researchers in a multicenter randomized controlled clinical trial concluded that prone positioning did not significantly reduce ventilator-free days, mortality, or time to recovery in pediatric patients with acute lung injury.[[24](javascript:void(0);)]

Inhaled nitric oxide

Nitric oxide (NO) is an endogenous free radical that mediates smooth muscle relaxation throughout the body. When delivered by means of inhalation, the potential benefit of NO is to improve ventilation to perfusion matching by enhancing pulmonary blood flow to well-ventilated parts of the lung.

This therapy is relatively safe because hemoglobin inactivates it quickly and because does not cause systemic vasodilation leading to hypotension. However, methemoglobin and nitrogen dioxide (NO2) levels should be monitored.

Inhaled NO is being studied for use in type I respiratory failure; in 1999, the FDA approved its use in neonates with hypoxic respiratory failure and evidence of pulmonary hypertension. Research continues on the value of inhaled NO for other pulmonary conditions, such as bronchopulmonary dysplasia, as well as possible roles for other mediators of pulmonary vasodilation, such as sildenafil and bosentan.

**Prevention Tips:**

**Primary Prevention**

**Prenatal Care:**

* Maternal RSV vaccination during pregnancy (32-36 weeks)
* Optimal management of maternal diabetes and infections
* Appropriate timing of delivery when possible

**Early Childhood Interventions:**

* **RSV Immunoprophylaxis**: Nirsevimab (Beyfortus) for high-risk infants
* **Routine Immunizations**: COVID-19 and influenza vaccines as age-appropriate
* **Infection Control**: Hand hygiene, avoiding sick contacts

**Secondary Prevention**

**For High-Risk Children:**

* Regular monitoring of respiratory status
* Early intervention for respiratory infections
* Optimization of nutrition and growth
* Management of underlying conditions

**Environmental Modifications:**

* Smoke-Air quality improvement
* Allergen avoidance when indicated
* free environments

**Prognosis:**

**Survival Outcomes**

**Overall Mortality Rates:**

* Home mechanical ventilation programs report mortality rates of 19% over extended periods
* Chronic respiratory failure patients have relatively good prognosis compared to acute cases
* Long-term survival is possible with appropriate support, with some patients maintained on home ventilation for over 18 years (219 months maximum)

**Prognostic Factors:**

* **Favorable**: Stable underlying condition, good family support, access to specialized care
* **Unfavorable**: Progressive neuromuscular disease, severe comorbidities, inadequate social support

**Quality of Life Outcomes**

**Functional Status:**

* 20% of children experience decline in functional status from baseline to post-discharge
* Children with chronic respiratory failure may have normal cognitive development with appropriate support
* Home ventilation allows participation in family and community activities

**Long-term Complications:**

* Growth and developmental delays if inadequately managed
* Recurrent respiratory infections
* Social and educational challenges
* Family stress and caregiver burden

**Positive Outcomes:**

* 73% of children on home mechanical ventilation demonstrate therapeutic effectiveness
* Significant cost savings through reduced hospitalizations (347.59% reduction in ICU costs)
* Improved quality of life for patients and families

**Complications:**

**Acute Complications**

**Respiratory Emergencies:**

* Tracheostomy obstruction or accidental decannulation
* Pneumothorax (especially with positive pressure ventilation)
* Ventilator malfunction or power failure

**Infectious Complications:**

* Ventilator-associated pneumonia
* Tracheostomy site infections
* Increased risk of respiratory tract infections

**Chronic Complications**

**Cardiovascular:**

* Pulmonary hypertension and cor pulmonale
* Systemic hypertension

**Growth and Development:**

* Failure to thrive due to increased metabolic demands
* Delayed speech and language development (with tracheostomy)
* Psychosocial developmental challenges

**Equipment-Related:**

* Skin breakdown from masks or equipment
* Dental and facial deformities from long-term mask use
* Equipment dependency and loss of spontaneous breathing ability

**When to see a Doctor/Red Flags:**

**Immediate Life-Threatening Signs:**

* Severe respiratory distress with inability to speak or cry
* Cyanosis (blue coloration) of lips, face, or fingernails
* Altered level of consciousness or unresponsiveness
* Apnea (cessation of breathing) episodes

**Critical Warning Signs:**

* Oxygen saturation <88% despite usual interventions
* Severe chest retractions or accessory muscle use
* Inability to feed or maintain oral intake
* Persistent high fever (>100.4°F in infants <3 months)

**Urgent Medical Attention Required**

**Respiratory Status Changes:**

* Increased work of breathing or respiratory rate
* New or worsening wheezing or stridor
* Persistent cough with blood or significant secretions
* Decreased activity tolerance or increased fatigue

**Equipment-Related Emergencies:**

* Tracheostomy tube displacement or obstruction
* Ventilator alarms that cannot be resolved
* Unexpected oxygen requirement increases

**Routine Follow-up Indicators**

**Schedule Appointment Within 24-48 Hours:**

* Low-grade fever with increased respiratory symptoms
* Changes in appetite or sleep patterns
* Mild increase in secretions or cough
* Equipment concerns or caregiver questions

**Differential Diagnoses:**

**Diagnostic Considerations**

In addition to the conditions listed in Differentials (below), the following are also common causes of respiratory failure in children:

* Asthma or reactive airway disease
* Bacterial or viral infection
* Bronchiolitis or pneumonia
* Near drowning
* Toxic ingestion or inhalation
* Trauma (eg, chest injuries)

Other, less common, problems to be considered in the differential diagnosis of pediatric respiratory failure include the following:

* Guillain-Barré syndrome
* Ludwig angina
* Neuromuscular disorders (eg, Duchenne muscular dystrophy or spinal muscular atrophy [SMA] type 1)
* Pulmonary embolus
* Spinal cord injury
* Tracheal foreign bodies
* Transverse myelitis, cervical or high thoracic
* Vascular slings

**Differential Diagnoses**

* Asphyxiating Thoracic Dystrophy (Jeune Syndrome)
* Aspiration Syndromes
* Bronchopulmonary Dysplasia
* Congenital Central Hypoventilation Syndrome
* Congenital Diaphragmatic Hernia (CDH) Imaging
* Laryngomalacia
* Neonatal Sepsis
* Pediatric Subglottic Stenosis Surgery
* Physical Child Abuse
* Respiratory Syncytial Virus Infection

**Guidelines:**

**Evidence-Based Guidelines**

**Second Pediatric Acute Lung Injury Consensus Conference (PALICC-2) 2023 Recommendations:**

**Ventilation Parameters:**

* Tidal volume: 6-8 mL/kg (may reduce to 4-6 mL/kg if pressures exceed limits)
* Plateau pressure: ≤28 cmH2O (≤32 cmH2O if chest wall compliance reduced)
* Driving pressure: ≤15 cmH2O
* Permissive hypercapnia: pH ≥7.20 acceptable

**Oxygenation Targets:**

* Mild PARDS: SpO2 92-97%
* Severe PARDS: SpO2 88-92% (permissive hypoxemia)
* PEEP: Follow ARDS Network protocol tables
* Avoid routine bicarbonate supplementation

**Home Ventilation Guidelines**

**Patient Selection Criteria:**

* Age ≥3 months
* Clinical stability for ≥2 weeks
* Adequate family/caregiver support
* Safe home environment with reliable power
* Access to emergency medical services

**Equipment Requirements:**

* Primary ventilator with backup device
* Tracheostomy supplies and spare tubes
* Suction equipment (portable and stationary)
* Manual resuscitation bag
* Pulse oximeter
* Emergency oxygen supply

**Caregiver Training Components:**

* Ventilator operation and troubleshooting
* Tracheostomy care and tube changes
* Airway suctioning techniques
* Emergency procedures and CPR
* Equipment maintenance and cleaning
* Recognition of complications

**Regular Assessments:**

* Monthly home visits by healthcare team
* Quarterly pulmonology clinic visits
* Annual comprehensive evaluations
* Equipment function checks and maintenance

**Outcome Monitoring:**

* Growth and developmental assessments
* Quality of life measurements
* Hospitalization rates and complications
* Family satisfaction and burden assessment

**Expert-Reviewed Q&A**

**"How long will my child need ventilator support?"**

**Expert Response:** The duration of ventilator support varies significantly based on the underlying condition. Some children with reversible conditions may eventually be weaned off support, while others with progressive neuromuscular diseases may require lifelong assistance. Our data shows that 4 out of 46 children (8.7%) in home ventilation programs were able to discontinue support due to improvement in their condition. Regular assessments help determine weaning potential, and the goal is always to provide the minimum support necessary for your child's health and development.

**"What are the risks of home mechanical ventilation?"**

**Expert Response:** While home mechanical ventilation carries inherent risks, comprehensive training and proper support systems minimize these significantly. The most serious risks include equipment malfunction, power outages, and airway emergencies such as tracheostomy obstruction. However, our experience shows that with proper preparation, including backup equipment, emergency power supplies, and thorough caregiver training, families can safely manage these situations. The benefits of being home - including normal family life, better development, and reduced infection risk - typically outweigh the risks.

**"Will my child be able to attend school and participate in normal activities?"**

**Expert Response:** Many children on home mechanical ventilation successfully attend school and participate in age-appropriate activities. The key is working with your healthcare team, school personnel, and equipment suppliers to develop appropriate accommodations. Portable ventilators allow mobility, and many children participate in educational, social, and recreational activities. Some limitations may exist, particularly with contact sports or activities in environments where equipment support is challenging, but creative solutions often allow meaningful participation.

**"How does this affect my child's development and quality of life?"**

**Expert Response:** Research shows that children on home mechanical ventilation can achieve normal cognitive and social development with appropriate support. While there may be some delays, particularly in speech development for children with tracheostomies, early intervention services can address these challenges. Studies indicate that 73% of children show therapeutic effectiveness with home ventilation, and families report significant improvements in quality of life compared to hospital-based care. The key is maintaining developmental activities, social interactions, and educational opportunities.

**"What should I do if the ventilator alarms or stops working?"**

**Expert Response:** This is why we provide comprehensive emergency training and backup equipment. First, ensure your child is breathing by listening and watching for chest movement. If not breathing adequately, immediately begin manual ventilation with the backup bag while calling for emergency help. For alarms, check basic troubleshooting steps we've taught you: verify connections, check for obstructions, and ensure power supply. Always have emergency contact numbers readily available, including your equipment supplier's 24-hour service line and your medical team.

**"How often will my child need to be hospitalized?"**

**Expert Response:** Our data shows that children on home mechanical ventilation have relatively low hospitalization rates when properly managed. In our program, the annual hospitalization rate was 0.17 episodes per child, primarily for respiratory infections or scheduled procedures. The significant cost savings (347.59% reduction in ICU costs) demonstrate that home care is not only better for families but also reduces overall healthcare utilization. Regular follow-up care and prompt treatment of minor issues help prevent serious complications requiring hospitalization.

**"What happens as my child grows older - can they transition to adult care?"**

**Expert Response:** Transition to adult care is an important consideration that we begin planning for early in adolescence. Many adult pulmonologists and healthcare systems are experienced in caring for patients with chronic respiratory failure who transition from pediatric care. The process involves gradually introducing adult providers, ensuring continuity of care plans, and adapting equipment and support systems for adult needs. Some patients successfully transition to more independent management of their condition as they mature.

**"Are there any new treatments or technologies that might help my child?"**

**Expert Response:** The field of pediatric respiratory care continues to advance. New technologies include improved portable ventilators with better monitoring capabilities, advanced airway clearance devices, and telemedicine options for remote monitoring. Research into gene therapies for some genetic conditions causing respiratory failure shows promise. We stay current with developments and will discuss any applicable new treatments as they become available. Regular reassessment ensures your child benefits from the most current therapeutic approaches.

**Summary**

Pediatric chronic respiratory failure is a complex medical condition requiring comprehensive, multidisciplinary management. While challenging, advances in home mechanical ventilation technology, improved clinical protocols, and family-centered care approaches have significantly improved outcomes for affected children. The condition affects approximately 5% of children hospitalized with respiratory disorders, with survival rates of 81% in well-managed home ventilation programs.

Success depends on early recognition, appropriate diagnostic evaluation, evidence-based treatment approaches, and strong family support systems. The prognosis varies by underlying condition, but many children achieve good quality of life with proper management. Key factors for optimal outcomes include comprehensive caregiver training, reliable equipment and support systems, regular medical follow-up, and prompt intervention for complications.

The field continues to evolve with new technologies, improved understanding of pediatric-specific considerations, and enhanced support systems for families. While chronic respiratory failure presents significant challenges, many children successfully participate in normal childhood activities, attend school, and maintain meaningful family and social relationships with appropriate respiratory support and comprehensive care planning.

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1. **Respiratory Failure and Ventilator Dependency**

**Definition:**

**Respiratory failure:**a syndrome in which the respiratory system fails in one or both of the functions of gas exchange, which are oxygenation and carbon dioxide elimination. It can be classified as hypoxemic (type 1), hypercapnic (type 2), or a combination of both.

Respiratory failure can be acute or chronic. The etiology of acute respiratory failure is often determined to be pneumonia, bronchiolitis, croup, trauma, or exacerbation of a chronic condition such as asthma.

* Chronic respiratory failure: a condition in which the inability to effectively exchange carbon dioxide and oxygen results in chronically low oxygen levels or chronically high carbon dioxide levels. Usually the underlying etiology is chronic lung disease such as cystic fibrosis, neuromuscular disorders, or muscular dystrophy. Diagnosis requires the use of home oxygen or ventilator support, or having baseline SaO2 < 88% on room air or pCO2 > 50 with normal pH.
* Acute respiratory distress syndrome (ARDS): often considered the end stage of acute respiratory failure, occurring when fluid builds up in the alveoli which prevents the lungs from filling with enough air. This leads to less oxygen reaching the bloodstream and organs, reducing organ function. ARDS patients have a moderate to severe impairment of oxygenation as defined by the ratio of partial pressure arterial oxygen and fraction of inspired oxygen (PaO2/FiO2). Chest imaging exhibits bilateral opacities/pulmonary edema not explained by cardiac failure or fluid overload.

**Ventilator dependency** in children refers to the reliance on mechanical ventilation to support breathing, either continuously or intermittently. A child is considered ventilator-dependent when they require mechanical support for breathing that cannot be readily discontinued without compromising their survival or adequate gas exchange.

**Causes:**

**What causes respiratory failure?**

Conditions that affect your breathing can cause respiratory failure. These conditions may affect the muscles, nerves, bones, or tissues that support breathing. Or they may affect the lungs directly. These conditions include:

* Diseases that affect the lungs, such as COPD (chronic obstructive pulmonary disease), cystic fibrosis, pneumonia, pulmonary embolism, and COVID-19
* Conditions that affect the nerves and muscles that control breathing, such as amyotrophic lateral sclerosis (ALS), muscular dystrophy, spinal cord injuries, and stroke
* Problems with the spine, such as scoliosis (a curve in the spine). They can affect the bones and muscles used for breathing.
* Damage to the tissues and ribs around the lungs. An injury to the chest can cause this damage.
* Drug or alcohol overdose
* Inhalation injuries, such as from inhaling smoke (from fires) or harmful fumes

**Risk Factors:**

Some conditions associated with respiratory failure and found that NNMD (OR 6.0; 95% CI, 2.7–13.5), hemoglobinopathy (OR 4.8; 95% CI, 1.5–15.1), immunosuppressive therapy (OR 4.0; 95% CI, 1.6–10.2), and chronic kidney disease (OR 3.9; 95% CI, 0.7–20.7) were risk factors for mechanical ventilation. Of the 5 children who died, only 1 had no preexisting medical condition.

Pediatricians – both primary care and specialty providers – must focus on immunization for both healthy children 6 to 23 months of age and children with high-risk medical conditions. A recent publication regarding missed influenza vaccination opportunities among children with asthma reported that over 80% of asthma-related visits.

**Age-Related Vulnerabilities:**

* Infants under 6 months have hospitalization rates similar to adults aged 65-74 years for COVID-19
* Children under 5 years face higher risks of serious complications from respiratory viruses
* Premature birth significantly increases risk (24.4% vs 14.1% in prolonged mechanical ventilation)

**Medical Comorbidities:**

* Immunodeficiency states
* Congenital heart disease
* Chronic kidney disease
* Hemoglobinopathies
* Neurological and neuromuscular diseases (OR 6.0 for mechanical ventilation)

**Environmental and Social Factors:**

* Environmental smoke exposure
* Air pollution exposure (nitrogen dioxide, sulfur dioxide, particulate matter)
* Lower socioeconomic status

**Signs & Symptoms:**

Patients may be lethargic, irritable, anxious, or unable to concentrate. Children with respiratory distress commonly sit up and lean forward to improve leverage for the accessory muscles and to allow for easy diaphragmatic movement. Children with epiglottitis sit upright with their neck extended and head forward while drooling and breathing through their mouth.

The respiratory rate and work of breathing can provide diagnostic information, as exemplified by the following:

* Accessory muscle use and nasal flaring
* Paradoxical movement of the chest wall
* Bradypnea: Most often observed in central control abnormalities
* Tachypnea: Fast and shallow breathing is most efficient in intrathoracic airway obstruction; it decreases dynamic compliance of the lung

The patient should also be evaluated for the following:

* Stridor (an inspiratory sound)
* Wheezing (an expiratory sound)
* Crackles
* Decreased breath sounds (eg, alveolar consolidation, pleural effusion)

Cardiovascular signs in patients with respiratory failure can include the following:

* Tachycardia and hypertension: May occur

**Medical Codes:**

**Primary Respiratory Failure Codes:**

* **J96.90** - Respiratory failure, unspecified, unspecified whether with hypoxia or hypercapnia
* **J96.00** - Acute respiratory failure, unspecified whether with hypoxia or hypercapnia
* **J96.1** - Chronic respiratory failure
* **J96.2** - Acute and chronic respiratory failure

**Neonatal-Specific Codes:**

* **P28.5** - Respiratory failure of newborn

**Ventilator Dependency Codes:**

* **Z99.11** - Dependence on respirator [ventilator] status
* **Z99.12** - Encounter for respirator [ventilator] dependence during power failure

**Diagnosis Mapping:**

The diagnosis of acute or chronic respiratory failure begins with clinical suspicion of its presence. Confirmation of the diagnosis is based on arterial blood gas analysis (see Workup). Evaluation of an underlying cause must be initiated early, frequently in the presence of concurrent treatment for acute respiratory failure. The cause of respiratory failure is often evident after a careful history and physical examination.

A study by Canet et al, examining acute respiratory failure in kidney transplant recipients, determined that 200 of 6,819 kidney transplant recipients required admission to the intensive care unit (ICU) for acute respiratory failure, which was associated with high mortality and graft loss rates.Early ICU admission and increased bacterial and *Pneumocystis* prophylaxis may improve outcomes.

The diagnosis of respiratory failure is primarily based on the patient’s clinical presentation and medical history. Clinical signs of common causes of ARF are summarized in [Table 1](https://pmc.ncbi.nlm.nih.gov/articles/PMC11506303/" \l "children-11-01232-t001).

Table 1.

Clinical presentation of major causes of ARF.

|  |  |
| --- | --- |
| Asthma exacerbation | Wheezing, difficulty breathing, chest tightness, cough, and use of accessory muscles |
| Bronchiolitis | Rapid breathing, wheezing and crepitations, cough, nasal flaring, retractions, and use of accessory muscles |
| Pneumonia | Rapid breathing, fine crepitations, fever, increased respiratory rate, difficulty breathing, use of accessory muscles, and retractions |
| Foreign Body Aspiration | Sudden onset of coughing, choking, wheezing, unilateral breath sounds reduction or wheezing, and possibly cyanosis |
| Epiglottitis | Severe sore throat, fever, drooling, difficulty swallowing, muffled voice, and stridor |
| Pulmonary Edema | Tachypnea, respiratory distress, cyanosis, and rales or crackles on auscultation |
| Septic Shock | Rapid breathing, altered mental status, fever or hypothermia, signs of poor perfusion, warm extremities |
| Anaphylaxis | Sudden respiratory distress, wheezing, possible stridor, skin rash, facial swelling, and shock |

Laboratory tests and instrumental examinations may support the assessment of the etiological cause underlying ARF and its severity. Two distinct clinical forms that may sometimes be confused are respiratory distress and ARF.

ARF is the pulmonary inability to ensure sufficient gas exchange to meet the body’s metabolic needs. Respiratory distress is a clinical definition and a compensatory condition in which the patient compensates for inadequate gas exchange by increasing respiratory rate and efforts, requiring prompt intervention. PARDS is a peculiar form of ARF characterized by severe lung inflammation and injury, requiring specific diagnostic criteria. It is defined as affecting children without birth-related lung disease, with symptoms emerging within a week of a clinical event, characterized by lung edema not due to heart failure or fluid overload, chest imaging showing new lung opacities, and specific oxygenation levels for children on nasal respiratory support.

Thoracic inspection and auscultation are essential for clinical diagnosis. Notably, the sensitivity of lung auscultation is low compared with imaging tests.

4.1. Chest X-ray

Chest X-ray (CXR) is by far the most widely used imaging examination as a frontline tool in cases of ARF. It is also the first radiological technique widely available at the bedside. The diffusion in hospitals of any level and its simplicity of execution are key elements, yet it requires a radiological service. CXR often provides critical information that aids in the rapid diagnosis of various conditions, although its use can sometimes be inappropriate. In fact, despite guidelines advising against routine CXR for pediatric patients with mild and moderate asthma exacerbations and bronchiolitis, these radiographs are still frequently performed.

Pneumonia is a primary cause of ARF in the pediatric population. It is an infection of the lungs caused by bacteria, viruses, or fungi. Pneumonitis, on the other hand, is a more general term that refers to inflammation of lung tissue, which is not necessarily infectious. It is often caused by exposure to irritants such as chemicals, drugs, or radiation. Although the diagnosis of pneumonia is clinical, based on the presence of persistent fever, increased respiratory rate, retractions indicating respiratory effort, and characteristic auscultatory sounds such as crackles, CXR is often requested as a confirmatory diagnostic test. The Infectious Diseases Society of America and the Pediatric Infectious Diseases Society discourage the routine use of CXR in well-appearing children being evaluated for community-acquired pneumonia (CAP) in outpatient and emergency department (ED) settings.

In the current literature, few studies correlate the performance of CXR with the outcome of patients with pneumonia. Particularly, a retrospective cohort study involving 206,694 patients, demonstrated that the execution of a CXR reduces hospitalization by approximately 7 days for these patients. On the other hand, a meta-analysis from 2018 highlighted that lung ultrasound has better sensitivity than CXR in diagnosing pneumonia in the pediatric population. Considering these results, improving ultrasound technique would bring significant advantages in diagnosing pneumonia, both in terms of diagnostic accuracy and in reducing radiation exposure to the patient.

In the case of ARF following an acute asthma attack, CXR is reserved for patients with severe manifestations and features suggesting the presence of complications (such as pneumothorax and pneumomediastinum), with the most common radiological abnormalities being: hyperinflation, segmental and subsegmental atelectasis, and pneumomediastinum (<1% of cases). Although complications associated with acute asthma attacks are not common, CXR is performed in 33–43% of patients, and the factors that most frequently drive the performance of this examination include the presence of fever, younger age, and an initial SpO2 < 91%.

CXR remains the diagnostic standard for two clinical conditions that often lead to ARF in the pediatric population: pneumothorax and foreign body inhalation.

Foreign body aspiration is a condition that pediatricians often encounter in the emergency department, and CXR represents the initial step in diagnosis. It helps recognize the position of the inhaled object and estimate its size, facilitating planning for subsequent invasive removal intervention through tracheobronchoscopy. A challenge frequently faced is that these objects often appear radiolucent due to the material they are made of, necessitating the use of alternative investigative strategies.

Finally, in cases of suspected pneumothorax, CXR is the initial examination to request, allowing for visualization of small collections of air. The issue is that there is an absence of pediatric management guidelines, leading to controversial management strategies.

The primary challenge is assessing the risk of pneumothorax recurrence in the patient, which influences the decision regarding a more or less invasive approach. Many authors agree that pleural blebs are the main culprits of pneumothorax, and their presence is predictive of the recurrence of this clinical condition. Pleural blebs are better visualized through chest CT scans, so their current line of thought is consistent in recommending a chest CT scan for patients who experience multiple episodes of pneumothorax. Conversely, other studies in the literature do not demonstrate a strict correlation between the presence of pleural blebs and the recurrence of the phenomenon, so they recommend performing a chest CT scan only in case of persistent air leaks in selected cases.

**Treatment Options:**

Approach Considerations

The risks of oxygen therapy are oxygen toxicity and carbon dioxide narcosis. Pulmonary oxygen toxicity rarely occurs when a fractional concentration of oxygen in inspired gas (FiO2) lower than 0.6 is used; therefore, an attempt to lower the inspired oxygen concentration to this level should be made in critically ill patients.

Carbon dioxide narcosis occasionally occurs when some patients with hypercapnia are given oxygen to breathe. Arterial carbon dioxide tension (PaCO2) increases sharply and progressively with severe respiratory acidosis, somnolence, and coma. The mechanism is primarily the reversal of pulmonary vasoconstriction and the increase in dead space ventilation.

Hypoxemia is the major immediate threat to organ function. After the patient’s hypoxemia is corrected and the ventilatory and hemodynamic status have stabilized, every attempt should be made to identify and correct the underlying pathophysiologic process that led to respiratory failure in the first place. The specific treatment depends on the etiology of respiratory failure.

Patients generally are prescribed bed rest during early phases of respiratory failure management. However, ambulation as soon as possible helps ventilate atelectatic areas of the lung.

Consultation with a pulmonary specialist and an intensivist are often required. Patients with acute respiratory failure or exacerbations of chronic respiratory failure need to be admitted to the intensive care unit for ventilatory support.

* Paxlovid (nirmatrelvir-ritonavir) antiviral treatment for COVID-19 is not authorized for use in children younger than 12 years of age. Other treatment may be available, speak with a healthcare provider.
* There are flu antiviral drugs recommended by CDC for use in children. Oseltamivir (available as a generic version or under the trade name Tamiflu®) is approved for treatment of flu in children 14 days old and older.
  + Note: Although not part of the FDA-approved indications, use of oral oseltamivir for treatment of flu in infants less than 14 days old, and for chemoprophylaxis in infants 3 months to 1 year, is recommended by the CDC and the American Academy of Pediatrics. If a child is younger than 3 months old, use of oseltamivir for chemoprophylaxis is not recommended unless the situation is judged critical due to limited data in this age group.

**Non-Invasive Respiratory Support**

**High-Flow Nasal Cannula (HFNC):**

* Flow rates: ≥1.5 L/kg/min or ≥30 L/min
* Provides heated, humidified oxygen
* Reduces work of breathing

**Continuous Positive Airway Pressure (CPAP):**

* Minimum 5 cmH₂O for ARDS diagnosis criteria
* Prevents alveolar collapse
* First-line therapy for many conditions

**Bi-level Positive Airway Pressure (BiPAP):**

* Allows different inspiratory and expiratory pressures
* Useful for neuromuscular conditions

**Mechanical Ventilation Strategies**

**Lung-Protective Ventilation (PALICC-2 Guidelines):**

* **Tidal Volume:** 6-8 mL/kg (may reduce to 4-6 mL/kg if pressures excessive)
* **Inspiratory Pressures:** Plateau pressure ≤28 cmH₂O (≤32 cmH₂O if chest wall compliance reduced)
* **Driving Pressure:** Limited to 15 cmH₂O
* **PEEP:** Maintain at or above ARDS Network lower PEEP/higher FiO₂ table

**Oxygenation Targets:**

* **Mild-Moderate PARDS:** SpO₂ 92-97%
* **Severe PARDS:** SpO₂ <92% acceptable after PEEP optimization

**Advanced Ventilation Modes:**

* High-frequency oscillatory ventilation for refractory cases
* Airway pressure release ventilation
* Prone positioning for severe ARDS

**Pharmacological Management**

**Bronchodilator Therapy:**

* **Albuterol:** First-line short-acting β₂-agonist for acute bronchospasm
* **Ipratropium bromide:** Can be added for moderate-severe exacerbations
* Limited evidence for routine use in bronchiolitis under 12 months

**Corticosteroid Therapy:**  
**Indications and Dosing:**

* **Acute asthma:** Prednisolone 1-2 mg/kg/day (max 40 mg unless on regular steroids)
* **Croup:** Dexamethasone 0.15-0.6 mg/kg, single dose

**PARDS Considerations:**

* Routine use not recommended per PALICC guidelines
* May consider in specific patient populations
* Significant side effects include hyperglycemia, immunosuppression, and growth suppression

**Sedation and Analgesia for Mechanically Ventilated Children:**

**Analgesic Medications:**

* **Morphine:** 0.05-0.2 mg/kg/dose every 2-4 hours; infusion 10-30 μg/kg/h
* **Fentanyl:** 1-2 μg/kg/dose; infusion 1-3 μg/kg/h
* **Hydromorphone:** 0.01-0.015 mg/kg/dose every 3-6 hours

**Sedative Medications:**

* Midazolam: Load 0.05-0.2 mg/kg, then 0.06-0.12 mg/kg/h
* Lorazepam: 0.02-0.1 mg/kg/dose every 4-8 hours
* Dexmedetomidine: 0.2-1.5 μg/kg/h (reduces opioid/benzodiazepine exposure)

**Specialized Therapies**

**Surfactant Replacement Therapy:**

* Indications: Neonatal RDS, meconium aspiration syndrome
* Timing: Early administration preferred (within 2 hours for intubated infants)
* INSURE Strategy: Intubate, surfactant, extubate to CPAP
* **Dosing:** Per manufacturer guidelines, typically 2.5-4 mL/kg

**Extracorporeal Support:**

* ECMO for refractory respiratory failure
* Considered when conventional therapy fails
* Requires specialized centers and expertise

**Prevention Tips:**

Studies have shown that:

* Infants under 6 months of age have similar COVID-19–associated hospitalization rates to adults ages 65–74 years old.
* Each year in the United States, an estimated 58,000-80,000 children younger than 5 years are hospitalized due to RSV infection, with infants being among those at greatest risk.
* Children younger than 5 years old, but especially those younger than 6 months, are at higher risk of developing serious flu-related complications. CDC estimates that from 2010 to 2020, flu-related hospitalizations among children younger than 5 years ranged from between 6,000 to 27,000 per year in the United States. Many more have to go to a doctor, an urgent care center, or the emergency room because of flu.

Reducing risk

Immunizations

*COVID-19*

Parents of children ages 6 months to 17 years should discuss the benefits of an updated COVID-19 vaccine with a health care provider.

*Flu*

* Children ages 6 months and older are recommended to get an annual flu vaccine.
  + September and October are generally good times to be vaccinated.
  + Vaccination during July and August also can be considered for children who need only one dose.
* Some children need two doses of flu vaccine.
  + For those children, it is recommended to get the first dose as soon as vaccine is available—even if this is in July or August—because the second dose needs to be given at least four weeks after the first.
* Though they are not eligible for flu vaccines, infants under age 6 months can still receive some protection. Getting vaccinated while pregnant or breastfeeding can help protect your baby after birth because antibodies are passed to the baby during pregnancy or through the milk.

*RSV*

* To prevent severe RSV disease in infants, CDC recommends either maternal RSV vaccination while pregnant or infant immunization with RSV protective antibody. Most infants will not need both.
* Maternal RSV vaccination in pregnancy takes place during weeks 32 through 36 of pregnancy and is administered September through January in most parts of the United States. Pfizer's Abrysvo is the only RSV vaccine recommended during pregnancy.
* An RSV antibody (nirsevimab) is recommended for all babies younger than 8 months of age born to mothers who did not receive a maternal RSV vaccine (Pfizer's Abrysvo) during pregnancy. A nirsevimab dose should be given to babies shortly before the RSV season.
  + Nirsevimab is also recommended for a small number of young children 8 through 19 months of age who are at increased risk for severe RSV. This nirsevimab dose should be given shortly before the child's second RSV season.

Hygiene

* Handwashing can become a lifelong healthy habit if you start teaching it at an early age. Teach kids the five easy steps for handwashing—wet, lather, scrub, rinse, and dry—and the key times to wash hands, such as after using the bathroom or before eating..
* Supervise young children when they use hand sanitizer to prevent swallowing alcohol.

Masks

* Masks should not be worn by children younger than 2 years because of suffocation risk.

**Prognosis:**

Respiratory failure is a very serious condition. Many people survive it, depending on what’s causing it, the severity and how quickly they’re treated.

While many causes of acute respiratory failure are treatable, it can be fatal if not treated quickly. Up to 1 in 3 people who are hospitalized for acute respiratory failure don’t survive. Chronic respiratory failure is usually caused by an ongoing condition that gets worse over time.

**Mortality Rates**

**Pediatric ARDS:**

* + Overall mortality: approximately 24%
  + Mild ARDS: 10-12% mortality
  + Severe ARDS: 33% mortality
  + Mortality has decreased over time with improved management

**Causes of Death:**

* + Early deaths (<7 days): Predominantly neurological causes
  + Late deaths (≥7 days): Multi-system organ failure
  + Refractory hypoxemia accounts for only 20% of deaths

**Long-Term Outcomes**

**Survivors of Pediatric ARDS:**

* Potential for complete recovery in many cases
* Risk of chronic lung disease
* Possible neurocognitive effects from critical illness
* Quality of life generally good in survivors

**Home Mechanical Ventilation:**

* Many children can achieve good quality of life
* Educational needs can be met with appropriate support
* Family adaptation improves over time

**Complications:**

1**. Atelectasis**

Atelectasis describes a state of volume loss and non-aerated region of an otherwise normal region of the lung parenchyma. Atelectasis is the most frequent complication of mechanical ventilation in pediatric patients. The implementation of lung protective ventilation strategies with low tidal volume ventilation may contribute to the increased development of atelectasis secondary to underinflation of alveolar units. The management of atelectasis is increasing airway pressure to a level higher than the critical opening pressure. However, in most pediatric lung diseases the critical opening pressure is elevated in a heterogeneous manner, and using positive pressure to maintain open recruitment of injured lung segments can potentially result in overdistention of healthier lung segments. Positive end-expiratory pressure (PEEP) is used frequently to treat atelectasis by successfully overcoming the closing pressure of smaller airways. Recruitment maneuvers through sustained inflation or stepwise increases in PEEP have demonstrated improvements in lung reaeration, however, the optimum method of recruitment remains under discussion.

2. **Perioral tissue damage**

The most common cause of medical device-related pressure ulcer are the mucosal pressure ulcers caused by prolonged pressure from endotracheal tubes. When compared to adult ICUs, the duration of intubation and invasive mechanical ventilation is longer in pediatric ICUs and the threshold for tracheostomy is much higher. This is understandable given the greater regenerative and healing capacity of pediatric lung tissues, but unfortunately predisposes to higher incidence of oral pressure injuries. Frequent monitoring and proper repositioning of mechanical pressure on the oral mucosa is an effective preventive strategy for reducing the development and advancement of mucocutaneous complications. Pressure-induced injury to the oropharyngeal tissues secondary to laryngeal mask airway insertion, forceful suctioning of posterior teeth, spasm of the masseter muscle secondary to hypothermia induced shivering and biting forces against antagonist teeth are additional etiologies of perioral tissue damage.

3. **Ventilator associated pneumonia**

After blood stream infections, ventilator associated pneumonia is the second most frequently occurring nosocomial infection in the PICU. The origin of ventilator associated pneumonia is likely the result of micro-aspirations. The most accepted definition of ventilator associated pneumonia is pneumonia occurring after the patient has been intubated and received mechanical ventilation for at least 48 hours. The initial diagnosis is based on clinical suspicion and the presence of at least one of the following on two or more serial chest radiographs: new or progressive radiographic infiltrates, consolidation, cavitation, and pneumatoceles in an infant 1-year-old or above. Additionally, the standard diagnostic criteria include at least two of the following (or three in patients under the age of 12 years): hyperthermia or hypothermia; change in character or volume of sputum production, or increased requirement for secretion clearance; new onset cough or worsening of pre-existing cough, respiratory distress, tachypnea or apnea; rhonchi, wheezing, rales, or bronchial breath sounds.

4. **Mucus plugging**

Pediatric intensive care units patients with increased length of stays can develop critical illness myopathy and neuropathy which contributes to weakened cough and pooling of secretions. The utilization of sedatives and neuromuscular blockade exacerbates this problem by impairing muco-ciliary clearance and natural cough mechanisms. Smaller airways in the pediatric population are especially susceptible to obstruction by secretions, thereby leading to ventilation-perfusion mismatch and further worsening of respiratory failure. Acute decompensation can occur if the endotracheal tube becomes obstructed with mucus, whereby suctioning or exchange of the endotracheal tube may be necessary. Several strategies are employed to minimize and treat mucus plugging, include ventilator circuit humidification, utilization of mucolytic agents, and use of mechanical devices or techniques to mechanically disrupt mucus. Airway clearance can be accomplished through nebulization with hypertonic saline to thin out tenacious secretions that are otherwise difficult to suction. Several mechanical airway clearance techniques are commonly used in the PICU: chest physiotherapy, intermittent percussive ventilation, and cough assist.

**When to see a Doctor/Red Flags:**

Irregular breathing in newborns

Newborns will often begin breathing faster for a few seconds and then slow down their breathing, especially when sleeping. This type of irregular breathing is normal and does not require treatment. If irregular breathing persists past the age of six months, call your pediatrician to ensure your child’s breathing is healthy. If your infant displays any of the symptoms listed below, immediately seek emergency care.

If your child stops breathing

If your child has stopped breathing and is not responsive, immediately begin CPR and call for help.

If your child ceases breathing for 15 seconds or more, and then resumes breathing, visit the pediatric ER. Even if your child seems fine, it is important to make sure the underlying reason for the episode has been resolved.

Many children between the age of six months and six years will experience breath-holding spells, involuntary breath holding that usually occurs when the child is crying or upset. Children who experience these spells do not need to seek emergency care unless the incident results in unconsciousness or a seizure. In these cases, it is best to visit the pediatric ER to make sure there are no other reasons for the seizure or unconsciousness.

Changes in breathing

If your child seems to be having a hard time breathing, or you notice abnormal behaviors or actions, it may be time to seek emergency care. Visit the pediatric ER if you notice these symptoms:

* Breathing that is faster than normal
* Breathing harder than usual without exertion
* Chest and abdomen look like a seesaw (one goes up while the other goes down)
* Bluish hue to the lips or skin
* Persistent barking cough or wheezing
* High-pitched squeaky sound in the upper airway
* Placing weight on the hands in a tripod position while hyperextending the neck

If your child is recovering from a choking episode in which he or she turned blue but returned to normal, it is still a good idea to visit the pediatric ER to ensure there are no longer-term consequences.

**Differential Diagnosis:**

Diagnostic Considerations

In addition to the conditions listed in Differentials (below), the following are also common causes of respiratory failure in children:

* Asthma or reactive airway disease
* Bacterial or viral infection
* Bronchiolitis or pneumonia
* Near drowning
* Toxic ingestion or inhalation
* Trauma (eg, chest injuries)

Other, less common, problems to be considered in the differential diagnosis of pediatric respiratory failure include the following:

* Guillain-Barré syndrome
* Ludwig angina
* Neuromuscular disorders (eg, Duchenne muscular dystrophy or spinal muscular atrophy [SMA] type 1)
* Pulmonary embolus
* Spinal cord injury
* Tracheal foreign bodies
* Transverse myelitis, cervical or high thoracic
* Vascular slings

**Differential Diagnoses**

* Asphyxiating Thoracic Dystrophy (Jeune Syndrome)
* Aspiration Syndromes
* Bronchopulmonary Dysplasia
* Congenital Central Hypoventilation Syndrome
* Congenital Diaphragmatic Hernia (CDH) Imaging
* Laryngomalacia
* Neonatal Sepsis
* Pediatric Subglottic Stenosis Surgery
* Physical Child Abuse
* Respiratory Syncytial Virus Infection

**Guidelines:**

European Society of Intensive Care Medicine (ESICM)

The 2023 guidelines on acute respiratory distress syndrome published by the European Society of Intensive Care Medicine (ESICM) contain the following key recommendations regarding the management of acute hypoxemic respiratory failure (AHRF):

* Patients with AHRF not due to cardiogenic pulmonary edema or acute exacerbation of COPD should receive high-flow nasal cannula oxygen (HFNO) as compared to conventional oxygen therapy (COT) to reduce the risk of intubation
* Continuous positive airway pressure (CPAP)/noninvasive mechanical ventilation (NIV) can be considered instead of HFNO for the treatment of AHRF due to COVID-19 to reduce the risk of intubation

No recommendations could be made for or against the following treatments:

* Use of HFNO compared to CPAP/NIV to treat AHRF in unselected patients with acute hypoxemic respiratory failure not due to cardiogenic pulmonary edema or acute exacerbation of COPD
* Use of NIV compared to CPAP for the treatment of AHRF

European Respiratory Society (ERS)

In 2022, the European Respiratory Society (ERS) published guidelines on the use of HFNO in acute respiratory failure with the following conditional recommendations:

* Use HFNO over COT in adults with AHRF
* Use HFNO over NIV in patients with AHRF

**Expert-Reviewed Q&A:**

**Expert-Validated Responses to Common Patient Queries**

**"Why does my child need a ventilator?"**

A ventilator helps your child breathe when their lungs or breathing muscles are not working well enough on their own. The machine provides the right amount of oxygen and removes carbon dioxide from their body. This gives their lungs time to heal while ensuring their brain and other organs get the oxygen they need. Many children who need ventilators recover and no longer need this support.

**"How long will my child be on the ventilator?"**

The duration varies greatly depending on your child's condition. Some children need ventilator support for just a few days while recovering from an acute illness, while others with chronic conditions may need long-term support. Our team assesses your child daily to determine when it's safe to reduce support or remove the ventilator completely.

**"What are the risks of mechanical ventilation?"**

While ventilators are life-saving, they do carry some risks including lung injury, infections, and the need for sedating medications. Our team uses lung-protective strategies and infection prevention protocols to minimize these risks. The benefits of ventilator support typically far outweigh the risks when your child cannot breathe adequately on their own.

**"Can children on ventilators go to school?"**

Yes, many children who require ventilator support can attend school with proper planning and support. Schools are required to accommodate children with medical needs, including providing trained staff to monitor equipment. The transition requires collaboration between medical teams, families, and educational professionals.

**"How can I learn to care for my child at home with a ventilator?"**

Comprehensive training programs teach families all aspects of ventilator care, including equipment operation, emergency procedures, and when to seek help. Training typically takes several weeks and includes hands-on practice with healthcare professionals. Ongoing support is available after discharge to help families feel confident in providing care.

**"What should I do if the ventilator alarms go off?"**

Always check your child first - look at their color, breathing effort, and responsiveness. Many alarms are not emergencies, such as tubing disconnections that can be easily fixed. However, call for emergency help immediately if your child appears distressed, turns blue, or becomes unresponsive. Your training will cover specific alarm meanings and appropriate responses.

*This comprehensive guide provides evidence-based information for healthcare professionals caring for children with respiratory failure and ventilator dependency. All recommendations should be individualized based on patient-specific factors and institutional protocols. Regular updates to clinical guidelines should be consulted for the most current evidence-based practices.*

**Summary:**

Pediatric respiratory failure and ventilator dependency represent complex clinical conditions requiring multidisciplinary expertise and family-centered care. Early recognition of warning signs, appropriate diagnostic evaluation, and evidence-based treatment protocols are essential for optimal outcomes. The management approach must be individualized based on the child's age, underlying conditions, and severity of illness.

Key principles include lung-protective ventilation strategies, judicious use of medications with careful monitoring for side effects, prevention of complications, and comprehensive family education and support. While mortality rates have improved with advances in care, these conditions still carry significant risks and potential for long-term complications.

Success in managing these challenging cases depends on close collaboration between intensivists, pulmonologists, nurses, respiratory therapists, and families, with emphasis on communication, education, and preparation for transitions of care, whether to home or other care settings.

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1. **Neuroendocrine Cell Hyperplasia of Infancy (NEHI)**

**Definition:**

Neuroendocrine cell hyperplasia of infancy (NEHI) is a non-lethal pediatric form of interstitial lung disease (ILD) characterized by tachypnea without respiratory failure.  It is a rare childhood interstitial lung disease characterized by a gradual onset of tachypnea, hypoxemia, and failure to thrive in the first 2 years of life.

Originally termed "persistent tachypnea of infancy," NEHI was renamed in 2005 after the discovery of characteristic hyperplasia of pulmonary neuroendocrine cells (PNECs) on histological examination. This condition represents a distinct entity within the broader spectrum of childhood interstitial lung diseases (chILD).

**Causes:**

The precise cause of this rare disease (3 to 4 children in a million) is still unknown. To date, we do not know whether these neuroendocrine cells have:

= Persisted in excessive numbers since fetal life

= Or decreased at birth but increased again in the first months of life

**Pathophysiology**

The condition is characterized by an abnormal increase in neuroendocrine cells within the airways after birth. These cells, which are normally present in small numbers, become hyperplastic in NEHI patients, leading to an excessive number that likely contributes to chronic lung inflammation and bronchoconstriction.

Several proposed mechanisms for NEHI pathogenesis include:

* Abnormalities in acute or chronic oxygen sensor function of PNECs
* Dysregulation of neurogenic gene expression
* Effects of cytokines derived from low-grade airway inflammation
* Possible airway dysmaturation that may co-exist with other maturational lung defects

**Genetic Factors**

Evidence suggests a genetic component to NEHI development. Familial cases have been reported, with some studies identifying affected siblings. Research has identified mutations in the NKX2-1 gene in though this appears to be uncommon and not the predominant cause. The familial occurrence suggests an autosomal recessive inheritance pattern, though autosomal dominant mechanisms with incomplete penetrance are also possible.

The underlying cause of the elevated and overexpressed NECs in the lungs and NEHI development remains unclear. Several studies have revealed that neither pulmonary infections nor environmental toxins are implicated in the disease's development. Others reported that acute respiratory viral infections might be implicated in the pathogenesis of NEHI. This was supported by a study observing the presence of the Epstein–Barr virus in the peribronchial lymphocytes of children with NEHI.

In 2010, Popler et al. published a report on a case series of NEHI involving siblings from four distinct families, all of whom were diagnosed with NEHI, highlighting the crucial role of genetic factors in NEHI pathogenesis. Young et al. detected a heterozygous substitution in the NKX2.1 gene, which encodes TTF-1 (also referred to as Thyroid Transcription Factor 1), in families with a history of NEHI in childhood. However, later research indicated that NKX2.1 mutations were associated with the “brain-thyroid-pulmonary” syndrome and a variety of more severe pulmonary phenotypes. NKX2.1 mutations may contribute, but they are not the primary cause of NEHI. Aberrant expression of NKX2.1 target genes may be responsible for the pulmonary pathophysiology of NEHI. In 2016, Berteloot, Galmiche-Rolland, and Abou-Taam reported one case of a single mutation in the ABCA3 gene in a child clinically diagnosed with NEHI, identified through gene sequencing during follow-up. Nevertheless, none of the existing reports have been able to pinpoint the causative gene of NEHI.

**Risk Factors:**

**Demographic Factors:**

* Male predominance (approximately 66% of cases)
* Most commonly affects full-term infants
* Typical onset within the first year of life, with mean age of presentation at 3-4 months

**Clinical Risk Factors:**

* Family history of respiratory symptoms in infancy
* Rarely reported in premature infants

**Signs & Symptoms:**

Pulmonary Signs and Symptoms

NEHI typically develops within the first year of life. The median age of symptom onset is 3 months old, whereas a formal diagnosis is typically given at 6 months of age. The most prevalent pulmonary signs and symptoms of NEHI include tachypnea, shortness of breath, hypoxemia (> 90%), and pulmonary crackles (> 80%). More severely, NEHI can cause intercostal retractions, which can be aggravated by acute viral infections. In addition, acropachy, cough, and/or gasp are also seen in NEHI patients. Pediatric patients with NEHI are generally clinically stable, and the disease is often self‐limited, with respiratory failure rarely reported.

Extrapulmonary Manifestations and Complications

Failure to thrive and developmental delay over the long term are common extrapulmonary signs, primarily attributed to long‐standing systemic hypoxia, recurrent hospitalizations, and undertreatment resulting from misdiagnosis and a lack of experience in disease management. Other complications of NEHI have also been documented. According to a study of 199 children diagnosed with NEHI, more than half of the children had dysplasia, 101 of them had gastroesophageal reflux, 75 of them suffered from aspiration or were at risk of aspiration, and 34 of them demonstrated signs of abnormalities associated with the immune system. The gastroesophageal reflux may be attributed to increased elastic resistance in the lungs due to hyperinflation, which subsequently results in heightened negative intrapleural pressure. This higher negative intrathoracic pressure then leads to a diminished pressure gradient from the stomach to the intrathoracic esophagus, causing an increase in reflux. A significant proportion of patients with NEHI experience misaspiration because of difficult breathing and increased respiratory load, which hinders respiratory‐swallowing coordination. Besides these conditions, it was documented that a few NEHI patients also exhibited transient hypogammaglobulinemia, characterized by elevated IgA, IgE, IgG, and IgM and decreased IgA and Complement 3, although the underlying mechanism remains unclear.

**Medical Codes:**

**ICD-10 Classifications:**

* **Primary Code:** J84.841 - Neuroendocrine cell hyperplasia of infancy
* **Alternative Code:** J84.8 - Other specified interstitial pulmonary diseases
* **ICD-11:** CB04.7

**Other Coding Systems:**

* **ORPHA Code:** 217560
* **UMLS:** C3161105
* **MedDRA:** 10072968

**Diagnosis Mapping:**

When any form of chILD is suspected, there are several tests that are commonly done to help with the diagnosis. Lab work to rule out other causes of these symptoms, such as cystic fibrosis or immunodeficiency, is often performed. A bronchoscopy with bronchoalveolar lavage (BAL) is often performed which can look for infection, inflammation, and signs of aspiration into the lungs.

A high-resolution computed tomography (CT) scan of the lungs is often useful in the diagnosis of NEHI, showing a characteristic pattern called ground glass opacities. The lungs also show areas that are inflated to different extents, with some areas being overinflated and some underinflated, creating a mosaic pattern on CT.

An Infant Pulmonary Function Test (infant PFT) has become more important in diagnosing NEHI. This test is not always used, because it takes specialized equipment that is not always available to the clinician. These usually show trapping of air in the lungs in NEHI patients and characteristic results.

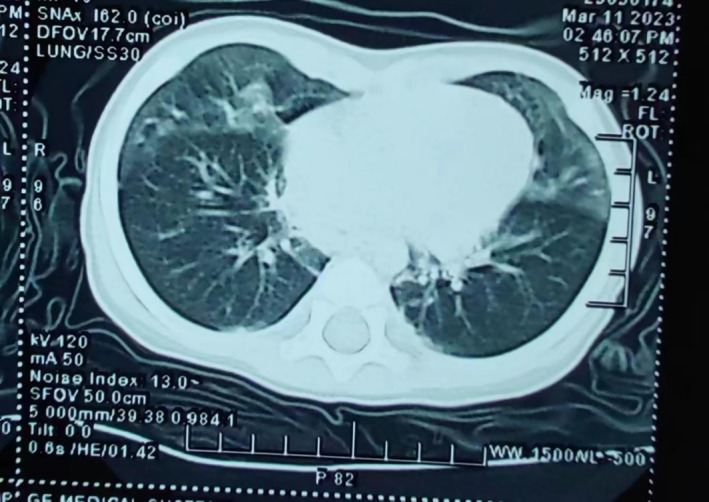
**The Gold Standard for Diagnosing NEHI**

If all of these tests are characteristic of NEHI, the child may receive a diagnosis of NEHI Syndrome without a biopsy. However, if any of the results or symptoms are not typical, the only way to conclusively confirm the NEHI diagnosis is through a lung biopsy. The biopsy tissue typically has little or no inflammation and when stained with a particular bombesin stain, demonstrates an abnormally increased number of pulmonary endocrine cells (PNECs) within the small airways. PNECs are cells that are usually present in the lining of the airways, alone or in clusters called neuroepithelial bodies (NEBs), and are thought to be involved in lung development. In NEHI, the number of PNECs and NEBs in the airways is always significantly increased.

Lung biopsies served as a gold standard for NEHI diagnosis. However, the invasive nature of lung biopsies and the associated procedural challenges contribute to their practical difficulty. In a 2011 study by Young et al., it was demonstrated that the increased presence of NECs in NEHI was not specific compared to other lung injuries or diseases, and diagnosis still requires a combination of clinical, radiological, and pathological assessments. With a deeper understanding of the disease, an increasing number of scholars contend that lung biopsy‐based NEHI diagnosis should be gradually replaced by a clinical and radiological diagnostic approach assessing clinical significance, sociological aspects, invasiveness, and acceptance by the child's family.

**Radiological Findings**

Imaging studies have shown that NEHI can be identified on high‐resolution computed tomography (HRCT) by characteristic air trapping presenting in a mosaic pattern and ground glass opacities (GGOs) primarily occurring in the right middle lobe, lingula, and/or perihilar regions (Figure [4](https://pmc.ncbi.nlm.nih.gov/articles/PMC11322232/" \l "crj13827-fig-0004)). The CT images of 23 children with biopsy‐confirmed NEHI were evaluated without any clinical information from a radiologist, and six CT images of children with other interstitial lung diseases (ILDs) were included for comparison. According to the study, CT imaging was capable of diagnosing NEHI with a sensitivity and specificity of at least 78% and 100%, respectively. Using a specific Hounsfield unit threshold, Spielberg quantified GGO in 21 children with NEHI and investigated their HRCTs. The study demonstrated that GGO was predominant in the right middle and lingual lobes in subjects with NEHI and that it was more prevalent in children who required continuous oxygen as opposed to those who only received oxygen at night, suggesting that the size of the GGO correlates with the severity of the child's hypoxic symptoms.

FIGURE 4. 

Typical ground glass opacities and air retention on chest CT of children with NEHI.

Mastej et al. studied the airway and lung shape in children with NEHI compared to children in the control group in a series of studies and revealed statistical differences between the two groups, with children diagnosed with NEHI exhibiting wider apices and significantly larger anteroposterior diameters of the lung apex. The use of logistic regression models to differentiate children with NEHI from children without NEHI showed an accuracy rate of up to 90%. Additionally, Barrera et al. utilized quantitative chest CT to diagnose NEHI and found that patients with this condition had a lower mean lung density, a higher ventilation heterogeneity, an increased lung mass, and a larger lung volume.

**Lung Function Test and Ultrasound Findings**

Over recent years, there has been an increased use of lung function testing and lung ultrasound to aid in diagnosing NEHI. A significant degree of air retention was found in children with NEHI that is not directly related to the degrees of obstructive lesions. The results of an infant pulmonary function test (iPFT) with an FRCpleth of 150% of the predicted value have also been shown to be highly specific for diagnosing NEHI and may aid in the detection of the disease at an early stage. Lung ultrasound was also found to be highly sensitive, albeit nonspecific, in diagnosing children with NEHI. Children with NEHI were found to have increased numbers and density of B‐lines, as well as pleural thickness and irregularity. Nonetheless, if GGO is centrally located, the ultrasound results may appear normal. It is worth noting that increased B‐lines can also be seen in other lung diseases such as pulmonary edema, respiratory tract infections, and atelectasis. Similarly, pleural thickness is commonly seen in pleural diseases such as pleuritis. In the future, lung ultrasound may become a useful initial evaluation for NEHI diagnosis in children suspected of NEHI due to its simplicity, noninvasive nature, and lack of radiation before performing HRCT, which is associated with the risk of radiation exposure and is costly.

**Polysomnography (PSG)**

Previous studies also found that PSG is useful for assisting clinicians in differentiating NEHI from other lung diseases in pediatric patients. Among 14 children diagnosed with NEHI, PSG found that patients with NEHI were likely to experience sleep‐related breathing disorders, such as obstructive or central sleep apnea, hypoxemia, adenoidal/tonsillar hypertrophy, low sleep efficiency, and increased periodic limbic dyskinesia. Despite not being routinely recommended, PSG may be useful for pediatric patients with NEHI who also present with sleep‐related disorders. PSG will also be helpful in determining the need for prolonged oxygen therapy during the night and monitoring sleep‐related breathing diseases in children with NEHI.

**Risk Scores for NEHI**

In 2020, Karpenko et al. conducted a multicenter study involving 83 patients with NEHI and proposed a 10‐point scale for the diagnosis of NEHI. The scale is comprised of scores for various symptoms such as chest wall depression, immune abnormality (low immunoglobulin G), hypoxemia, shortness of breath, dysplasia, chest burst sound, activity intolerance, irregular cough, and irregular wheeze, with each item being scored as 1 point. The proposed scale sets a score greater than 7 points as a diagnostic criterion for NEHI, with a sensitivity of 87%. The study's sample size is relatively large and provides a high reference value for the diagnosis of the disease using a scale‐based approach. The author recommends the inclusion of complications such as gastroesophageal reflux and dysphagia reported in recent years, along with clinical auxiliary examinations such as CT, lung function, lung ultrasound, and sleep monitoring, coupled with an adjustment of the scoring rules relative to the clinical manifestations and diagnostic significance of each auxiliary examination, potentially leading to a more effective diagnosis of NEHI. A more recent study found that, by using this scoring algorithm, only around two‐thirds of NEHI cases reached Score 7 or higher. They recommend removing less pertinent criteria to improve the discrimination ability of this scoring. More studies are needed to validate this scoring algorithm and identify the best scoring approach with both high sensitivity and specificity.

**NEHI Clinical Score**  
A validated clinical scoring system has been developed comprising 10 items:

1. Symptom onset before 12 months of age
2. Failure to thrive
3. Absence of clubbing
4. Absence of cough when well
5. Absence of wheeze when well
6. Abnormal chest wall (barrel chest or pectus excavatum)
7. Crackles on examination
8. Hypoxemia
9. Tachypnea
10. Retractions

A score of 7 or higher is considered consistent with NEHI, with sensitivity of 87-93%

**Differentiating NEHI From Other Child ILDs**

Given that NEHI is one form of childhood ILD and corticosteroids are not effective in treating NEHI, differentiating NEHI from other ILDs and common pediatric respiratory diseases is important for guiding appropriate treatments in clinical practice. Pulmonary interstitial glycogenosis (PIG), surfactant dysfunction disorders, and alveolar capillary dysplasia with misalignment of pulmonary veins are other ILDs commonly seen in pediatric populations. The first step in the NEHI investigation is to exclude non‐ILD diseases. To trigger the investigation of childhood ILD, at least three of the following four criteria have to be met. The first is the presence of any respiratory symptoms, including cough, tachypnoea, and/or not being able to tolerate exercise; the second is clinical signs, which include resting tachypnoea, adventitious sounds, retraction, finger clubbing, failure to thrive, and aggressive respiratory failure. The third is the presentation of hypoxemia, and the last is the diffuse abnormalities on chest X‐rays or CT scanning. For the specific types of ILD, symptoms of PIG and surfactant dysfunction disorder more commonly occur shortly after birth. Alveolar capillary dysplasia with misalignment of pulmonary veins is more commonly seen in those with congenital abnormalities. In addition to the common lung function, full blood testing, and ECG, an echocardiogram is recommended to preclude any structural cardiovascular disease and pulmonary hypertension, which account for approximately 9% of pediatric patients suspected of ILD.

A lung biopsy is useful for the diagnosis of most ILDs. For example, PIG can be diagnosed via the observation of histological changes, including the presence of a circle of glycogen‐laden mesenchymal cells that widen the interstitial walls. However, one must be vigilant when using a lung biopsy due to the potential risk of this invasive procedure. Therefore, noninvasive techniques in combination with age at presentation, clinical manifestations, and consistent pulmonary function presentation would be useful in diagnosing the disease. Chest X‐ray, ultrasound, and pulmonary function tests may serve as initial evaluations to exclude other common entities of ILD, such as cystic fibrosis and infection, before HRCT. In the suspected NEHI cases, an HRCT scan with the lowest radiation dose can provide accurate information. Two studies also reported that bronchoscopy with bronchoalveolar lavage (BAL) cellular analysis can differentiate NEHI from other types of ILD and lung diseases (e.g., cystic fibrosis and follicular bronchiolitis) in pediatric patients. In Deterding et al.'s study, children with NEHI had more aptamers in BAL fluid compared to those with other ILDs. Conversely, proteins associated with pulmonary fibrosis and inflammation were found in children with surfactant dysfunction mutations but not in NEHI patients. NHEI patients were also found to have lower total white blood cells, IL‐1β, MIP‐1β, and IL‐8 and higher alveolar macrophages in BAL fluid compared with patients with other airway diseases]. These findings need to be confirmed by more studies. In addition, BAL analysis can also be used to rule out infection, aspiration, pulmonary hemorrhage syndromes, and pulmonary alveolar proteinosis. Genetic tests can be performed if genetic mutations and family inheritance are suspected, which were assumed to be the reasons for NEHI. A lung biopsy with immunostaining for bombesin is only needed when other tests will not be able to give a precise diagnosis, and the diagnosis is necessarily needed for guiding disease management.

**Treatment Options:**

**Treatment for NEHI**

The progression of NEHI is slow and prolonged, and at this point, there have been no reports of fatalities. Despite extensive research, there is no specific treatment available for NEHI. Previous studies and empirical evidence showed that antibiotic and glucocorticoid treatments provide little benefit in treating NEHI. Therefore, the treatment principles involve supportive care and infection prevention. Oxygen supplement is the cornerstone of supportive therapy, which can alleviate hypoxemia and improve breath difficulty. Of note, it is important to monitor the patient regularly with nocturnal saturation recording to adapt to oxygen therapy. In clinical practice, the degree of hypoxia in children varies: most children with NEHI are asymptomatic at rest and require oxygen supplementation only after exercise or during respiratory infections, while a few children require long‐term oxygen therapy with a proactive approach taken to prevent complications such as gastroesophageal reflux and misaspiration.

Because of the rarity and heterogeneity of NEHI and other child ILDs, there is intrinsic difficulty in conducting randomized trials to test the efficacy of new treatments in this patient group. The current therapeutic strategies for NEHI are empirical and mainly based on case series. A recent Phase 2a, double‐blind randomized clinical trial comparing hydroxychloroquine versus placebo in 26 pediatric patients with ILD found no noticeable benefits of hydroxychloroquine in improving O2 saturation, pulmonary function, and quality of life. Gene transfer therapies have shown some promise in treating child ILD in vitro and in vivo. Clinical studies are needed to assess whether gene transfer confers any benefits to NEHI cases with specific gene mutations.

NEHI management is primarily supportive, as no specific curative treatment exists

**Nutritional Support**

* **Critical component** due to increased caloric demands from labored breathing
* May require concentrated formula or supplements
* Some children need feeding tubes for adequate nutrition
* Gastroesophageal reflux management often necessary (present in 51% of cases)

**Medication Considerations**

**Corticosteroids:**

* **Limited efficacy** in most NEHI patients
* Oral corticosteroids have not shown consistent benefit
* Debate exists regarding IV methylprednisolone pulses
* Clinical response to steroids is generally poor

**Bronchodilators:**

* **Typically ineffective** as primary treatment
* May provide some symptomatic relief in selected cases

**Azithromycin:**

* Emerging evidence for potential benefit
* Anti-inflammatory properties may be helpful
* Used as adjunctive therapy in some centers

**Prevention Tips:**

Oxygen supplementation may also be required. The amount of oxygen needed varies in NEHI patients. Some need oxygen 24 hours a day, while others will only wear it at night and during illness, while some do not require it at all. Most NEHI patients decrease their need for oxygen over time and most eventually grow out of the need for supplementation.

Common colds and flu can be more severe in NEHI patients, so limiting exposure to respiratory infections is also important. Seasonal flu shots and prevention of Respiratory Syncytial Virus (RSV) is recommended.

Oral corticosteroids, which are used to decrease inflammation in other lung disorders, have not been shown to be helpful with the symptoms in most NEHI patients. This is consistent with the limited inflammation seen on lung biopsy.

**Environmental Measures**

* Avoiding secondhand smoke exposure
* Minimizing exposure to respiratory irritants
* Good hand hygiene practices

**Prognosis:**

In terms of prognosis, it is recommended that gamma globulin levels be routinely assessed in patients with NEHI in order to monitor their risk of respiratory infections, and prophylactic antibiotic therapy and/or intravenous immunoglobulin should be administered if necessary. In addition, many patients with NEHI require nutritional supplementation when presenting difficulty feeding and poor weight gain. Pneumococcal and influenza vaccines are recommended for NEHI patients at 6 months of age to prevent pneumonia and other infections. Avoiding exposure to detrimental environments, for example, second‐hand smoke, and keeping good hygiene for children and their parents are also important. In the early years, NEHI was often misdiagnosed as a pulmonary infection or other ILDs, leading to the administration of unnecessary empiric medications such as antibiotics and corticosteroids. Such treatments hurt the child's immune system and adversely impact their physical and mental health. However, clinical treatment for NEHI is typically straightforward with a precise diagnosis.

In general, NEHI offers a favorable prognosis. The majority of children in multicenter case follow‐ups were no longer dependent on oxygen supplementation by the age of 2 years (20–60 months), and their clinical symptoms had disappeared by that time. However, some patients developed bronchial asthma during the follow‐up. A recent study showed that NEHI has a general positive, good, but not all consistent, improvement over time, and they emphasize the importance of needing future studies to better identify different prognosis trajectories in NEHI patients. In spite of the possibility that NEHI may have long‐term adverse effects on lung function and lifelong complications, it remains unclear whether NEHI is linked to the idiopathic proliferation of pulmonary NECs in adults.

**Psychosocial Impact of NEHI on Patients and Their Caregivers**

NEHI may cause anxiety and distress, even depression, in patients and their caregivers due to the persistence of symptoms, delay in diagnosis, unpredictable course of the disease, and lack of effective treatment. In addition, navigating the healthcare system can pose formidable challenges for families having kids affected by NEHI, particularly when confronted with the complexities of diagnosis and treatment. The journey often entails enduring a series of medical consultations and diagnostic tests, which can be distressing. Furthermore, any misdiagnosis along this journey can exacerbate the stress and anxiety of patients and their caregivers. In such circumstances, providing not only physical care but also robust emotional support becomes imperative. It is crucial to reassure patients and their families that while NEHI presents challenges, the majority of cases exhibit a self‐limited trajectory, and there is a lack of recorded fatalities directly attributable to NEHI. Fostering a supportive environment where patients and caregivers feel heard and understood can significantly mitigate the adverse psychosocial impact of NEHI.

**Complications:**

**Respiratory Complications**

* Recurrent respiratory infections
* Persistent hypoxemia
* Air trapping and hyperinflation
* Possible development of asthma-like symptoms

**Non-Respiratory Complications**

* **Failure to thrive** (74% of patients)
* **Developmental delays** (38% of patients)
* Feeding difficulties requiring intervention
* **Gastroesophageal reflux** (51% of patients)
* **Aspiration risk** (35% of patients at risk)

**Rare Complications**

* **Immune system abnormalities** (17% of patients)
* Prolonged hospitalization
* Family stress and quality of life impacts

**When to see a Doctor/Red Flags:**

**Immediate Medical Attention Required**

* **Severe respiratory distress**
* **Cyanosis** (blue coloring of lips or fingernails)
* **Inability to feed** due to breathing difficulties
* **Lethargy or unresponsiveness**
* **Persistent fever** with respiratory symptoms

**Urgent Evaluation Needed**

* **Worsening tachypnea** or increased work of breathing
* **New or increased oxygen requirements**
* **Poor weight gain** or failure to thrive
* **Recurrent hospitalizations** for respiratory symptoms
* **Feeding difficulties** or poor oral intake

**Regular Monitoring Indicators**

* Persistent rapid breathing beyond newborn period
* Chronic cough in an otherwise well infant
* Exercise intolerance as child grows
* Family history of unexplained infant respiratory symptoms

**Differential Diagnoses:**

NEHI must be differentiated from other causes of chronic tachypnea and respiratory symptoms in infancy:

* Afebrile Pneumonia Syndrome
* Anti-GBM Antibody Disease
* Aspiration Syndromes
* Bone Marrow Transplantation
* Bronchopulmonary Dysplasia
* Cystic Fibrosis
* Granulomatosis with Polyangiitis (GPA, formerly Wegener Granulomatosis)
* Hemosiderosis
* Histiocytosis
* Histoplasmosis
* Hypersensitivity Pneumonitis
* Inhalation Injury
* Juvenile Systemic Sclerosis
* Long-Term Effects of Bone Marrow Transplantation
* Lymphoproliferative Disorders
* Partial Anomalous Pulmonary Venous Connection
* Pediatric Anti-GBM Disease (Goodpasture Syndrome)
* Pediatric Sarcoidosis
* Pediatric Severe Combined Immunodeficiency
* Posttransplant Lymphoproliferative Disease (PTLD)
* Idiopathic Pulmonary Arterial Hypertension
* Systemic Lupus Erythematosus (SLE)
* Total Anomalous Pulmonary Venous Connection

**Guidelines:**

**Diagnostic Procedures**

**Bronchoscopy with Bronchoalveolar Lavage:**

* Performed to rule out infection and other causes
* Generally shows normal findings in NEHI
* May reveal mild inflammatory changes

**Lung Biopsy (when indicated):**

* Video-assisted thoracoscopic surgery (VATS) preferred
* Reserved for atypical cases or diagnostic uncertainty
* Complications include pneumothorax, bleeding, infection
* Requires general anesthesia and hospitalization

**Genetic Testing:**

* Consider in familial cases
* Testing for surfactant protein mutations
* *NKX2-1* mutation analysis in selected cases

**Follow-up Protocols**

* Regular pediatric pulmonology visits
* Growth and developmental monitoring
* Pulmonary function testing as age-appropriate
* Nutritional assessment
* Oxygen saturation monitoring

**Expert-Reviewed Q&A:**

**"Will my child outgrow NEHI?"**

Most children with NEHI do show gradual improvement over time, with many eventually discontinuing oxygen support and living normal, active lives. However, the timeline varies significantly between patients, with some requiring support for several years.

**"Is NEHI hereditary?"**

While most cases are sporadic, familial cases have been reported, suggesting a genetic component in some families. If you have a family history of similar symptoms, genetic counseling may be beneficial.

**"What is the long-term outlook?"**

The long-term prognosis is generally good, with no deaths directly attributed to NEHI reported in the literature. Most children develop normally, though some may have persistent mild respiratory symptoms or exercise limitations.

**"Will corticosteroids help my child?"**

Unlike many other lung diseases, NEHI typically shows limited response to corticosteroids. The mainstay of treatment remains supportive care with oxygen and nutritional support.

**"Can my child receive normal vaccinations?"**

Yes, children with NEHI should receive all routine childhood vaccinations on schedule, as they may be at higher risk for severe respiratory infections. This includes annual influenza vaccination and RSV prevention measures.

**"When can we expect to stop oxygen therapy?"**

The duration of oxygen therapy varies widely. Studies suggest that about half of children discontinue daytime oxygen around 32 months of age, while nighttime oxygen may be needed longer, with 50% stopping by about 87 months.

**"Is there a risk of complications during common illnesses?"**

Children with NEHI may experience more severe symptoms during common respiratory illnesses like colds or flu, potentially requiring hospitalization or increased oxygen support. Close monitoring during illness is important.

**Summary:**

Neuroendocrine Cell Hyperplasia of Infancy (NEHI) is a rare but increasingly recognized form of childhood interstitial lung disease that primarily affects infants in their first year of life. Characterized by persistent tachypnea, hypoxemia, and failure to thrive, NEHI has a distinctive pattern on high-resolution CT imaging and specific histopathological findings of increased neuroendocrine cells in the airways.

While the exact etiology remains unknown, evidence suggests both genetic and environmental factors may contribute to its development. Diagnosis relies heavily on clinical presentation, characteristic imaging findings, and exclusion of other conditions, with lung biopsy reserved for atypical cases.

Treatment is primarily supportive, focusing on oxygen supplementation and nutritional support, as corticosteroids and bronchodilators show limited efficacy. The prognosis is generally favorable, with most children showing gradual improvement over time, though the clinical course can be prolonged and variable.

Early recognition and appropriate management can significantly improve outcomes and quality of life for affected children and their families. Ongoing research continues to enhance our understanding of this condition and may lead to more targeted therapeutic approaches in the future.

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1. **Surfactant Metabolism Dysfunction Disorder**

**Definition:**

Surfactant dysfunction is a lung disorder that causes breathing problems. This condition results from abnormalities in the composition or function of surfactant, a mixture of certain fats (called phospholipids) and proteins that lines the lung tissue and makes breathing easy. Without normal surfactant, the tissue surrounding the air sacs in the lungs (the alveoli) sticks together (because of a force called surface tension) after exhalation, causing the alveoli to collapse. As a result, filling the lungs with air on each breath becomes very difficult, and the delivery of oxygen to the body is impaired.

**Causes:**

Surfactant dysfunction is caused by mutations in one of several genes, including *SFTPB*, *SFTPC*, and *ABCA3*. Each of these genes is involved in the production of surfactant. The production and release of surfactant is a complex process. The phospholipids and proteins that make up surfactant are packaged in cellular structures known as lamellar bodies. These structures are also important for some processing of surfactant proteins, which is necessary for the proteins to mature and become functional. Surfactant is released from the lung cells and spreads across the tissue that surrounds alveoli. This substance lowers surface tension, which keeps the alveoli from collapsing after exhalation and makes breathing easy.

The *SFTPB* and *SFTPC* genes provide instructions for making surfactant protein-B (SP-B) and surfactant protein-C (SP-C), respectively, two of the four proteins in surfactant. These two proteins help spread the surfactant across the surface of the lung tissue, aiding in the surface tension-lowering property of surfactant. In addition, SP-B plays a role in the formation of lamellar bodies.

Mutations in the *SFTPB* gene cause a type of surfactant dysfunction sometimes referred to as SP-B deficiency. These mutations lead to a reduction in or absence of mature SP-B. In addition, *SFTPB* gene mutations cause abnormal processing of SP-C, resulting in a lack of mature SP-C and a buildup of unprocessed forms of SP-C. These changes lead to abnormal surfactant composition and decreased surfactant function. The loss of functional surfactant raises surface tension in the alveoli, causing severe breathing problems. The combination of SP-B and SP-C dysfunction may explain why the signs and symptoms of SP-B deficiency are so severe.

Mutations in the *SFTPC* gene are involved in a type of surfactant dysfunction sometimes called SP-C dysfunction. These mutations result in a reduction or absence of mature SP-C and the buildup of abnormal forms of SP-C. It is unclear which of these outcomes causes the signs and symptoms of SP-C dysfunction. Lack of mature SP-C can lead to abnormal composition of surfactant and decreased surfactant function. Alternatively, research suggests that abnormally processed SP-C proteins form the wrong three-dimensional shape and accumulate inside the lung cells. These misfolded proteins may trigger a cellular response that results in cell damage and death. This damage may disrupt surfactant production and release.

The *ABCA3* gene provides instructions for making a protein that is found in the membrane that surrounds lamellar bodies. The ABCA3 protein transports phospholipids into lamellar bodies where they form surfactant. The ABCA3 protein also appears to be involved in the formation of lamellar bodies.

*ABCA3* gene mutations, which cause a type of surfactant dysfunction sometimes referred to as ABCA3 deficiency, lead to reduction or absence of the protein's function. Without ABCA3 protein function, the transport of surfactant phospholipids is decreased. In addition, lamellar body formation is impaired, which causes abnormal processing of SP-B and SP-C. *ABCA3* gene mutations result in abnormal surfactant composition and function. It has been suggested that mutations that eliminate ABCA3 protein function cause severe forms of surfactant dysfunction, and mutations that leave some residual ABCA3 activity cause milder forms of the condition.

**Risk Factors:**

Several factors increase the risk of developing surfactant metabolism dysfunction:

**Genetic Factors**

* **Family history**: Autosomal recessive disorders (SP-B and ABCA3 deficiency) require both parents to be carriers, conferring a 25% risk with each pregnancy
* **Autosomal dominant inheritance**: SP-C dysfunction and some NKX2.1 mutations show dominant inheritance with variable penetrance
* **Consanguinity**: Increases risk for autosomal recessive forms

**Clinical Risk Factors**

* **Full-term birth with unexplained respiratory distress**: Unlike typical respiratory distress syndrome that affects premature infants
* **Lack of response to conventional treatments**: Poor response to surfactant replacement therapy or corticosteroids
* **Multiple affected siblings**: Suggests genetic etiology

**Signs & Symptoms:**

The signs and symptoms of surfactant dysfunction can vary in severity. The most severe form of this condition causes respiratory distress syndrome in newborns. Affected babies have extreme difficulty breathing and are unable to get enough oxygen. The lack of oxygen can damage the baby's brain and other organs. This syndrome leads to respiratory failure, and most babies with this form of the condition do not survive more than a few months.

Less severe forms of surfactant dysfunction cause gradual onset of breathing problems in children or adults. Signs and symptoms of these milder forms are abnormally rapid breathing (tachypnea); low concentrations of oxygen in the blood (hypoxemia); and an inability to grow or gain weight at the expected rate (failure to thrive).

There are several types of surfactant dysfunction, which are identified by the genetic cause of the condition. One type, called SP-B deficiency, causes respiratory distress syndrome in newborns. Other types, known as SP-C dysfunction and ABCA3 deficiency, have signs and symptoms that range from mild to severe

The clinical presentation varies significantly depending on the specific genetic defect, age at onset, and disease severity:

**Neonatal Presentation**

* **Severe respiratory distress**: Occurs within hours to days of birth in previously healthy full-term infants
* **Tachypnea**: Abnormally rapid breathing (>60 breaths per minute)
* **Cyanosis**: Blue discoloration around lips, fingernails, or mucous membranes
* **Grunting**: Audible sounds with expiration as the body attempts to maintain lung volume
* **Nasal flaring**: Widening of nostrils during inspiration
* **Retractions**: Visible sinking of chest wall below neck, between ribs, or under breastbone
* **Hypoxemia**: Low blood oxygen levels despite supplemental oxygen

**Later Childhood/Adult Presentation**

* **Chronic cough**: Persistent, often non-productive cough
* **Exercise intolerance**: Shortness of breath with physical activity
* **Failure to thrive**: Poor weight gain and growth retardation
* **Recurrent respiratory infections**: Frequent pneumonia or bronchitis episodes
* **Digital clubbing**: Enlargement of fingertips and toes

**Associated Symptoms**

* **Thyroid dysfunction**: Hypothyroidism may occur with NKX2.1 mutations
* **Neurological symptoms**: Movement disorders, ataxia, or developmental delays with NKX2.1 mutations
* **Pulmonary hypertension**: Secondary to chronic hypoxemia

**Medical Codes:**

**ICD-10 Codes**

| **Code** | **Description** | **Clinical Context** |
| --- | --- | --- |
| J84.83 | Surfactant mutations of the lung | Primary genetic surfactant disorders |
| P22.0 | Respiratory distress syndrome of newborn | Neonatal respiratory distress |
| P28.89 | Other specified respiratory conditions of newborn | Additional neonatal respiratory conditions |
| Q33.6 | Congenital hypoplasia and dysplasia of lung | Congenital lung abnormalities |

**Additional Relevant Codes**

* **Z87.891**: Personal history of nicotine dependence (if applicable)
* **Z83.430**: Family history of other chronic disabling diseases
* **Z13.83**: Encounter for screening for respiratory disorder

**Diagnosis Mapping:**

The identification of specific genetic causes of lung diseases allows for the opportunity for non-invasive diagnosis based upon analysis of DNA prepared from peripheral blood or other samples (saliva, buccal swabs). Retrospective diagnosis is also feasible based upon molecular studies on archived tissue, or potentially through analysis of DNA from parents of children who died from lung disease of unknown cause. Currently there is no prospectively validated algorithm for genetic evaluation of patients suspected as having surfactant dysfunction as the basis for their lung disease, but an overall approach may be suggested based upon the typical clinical presentations of each disorder, family history, associated findings, and postulated relative frequencies of each disorder.

Testing for surfactant dysfunction should be considered in neonates who present with diffuse lung disease and hypoxaemic respiratory failure. As RDS develops in some near-term or full-term infants and is more common than surfactant dysfunction, it may be difficult to decide when and in which infants to pursue such testing. Gestational age < 38 weeks, operative delivery, and male gender have been associated with increased risk for RDS, and it is thus reasonable to defer testing if these risk factors are present and the child’s condition is stable or improving.[54](https://pmc.ncbi.nlm.nih.gov/articles/PMC3201772/" \l "R54) A family history of neonatal lung disease or ILD in older family members should prompt earlier consideration of testing. Disease that persists after the first week of life or is especially severe should also be considered for earlier testing. With neonatal onset of disease, *ABCA3* and *SFTPB* analyses should be considered first. If there is evidence for hypothyroidism, analysis for *NKX2.1* should be strongly considered. If testing for these genes is negative, and the lung disease does not resolve, or if there is a family history of lung disease inherited in a dominant pattern, then *SFTPC* mutational analysis should be pursued.

Children who present outside of the neonatal period with diffuse lung disease of unknown etiology should be considered for genetic testing for surfactant dysfunction, especially if there is a family history of similar lung disease. Findings such as digital clubbing, failure to thrive and pectus excavatum have been frequently observed in affected children and should prompt consideration for testing.As SP-B deficiency almost always presents in the neonatal period, analysis of *SFTPB* can be deferred in older children. A history of neonatal lung disease is more consistent with ABCA3 deficiency and onset later in childhood more consistent with *SFTPC* mutations, but there is sufficient overlap in clinical presentations such that both genes should be analyzed, either sequentially or concurrently. An *ABCA3* mutation on one allele might also modify the course of lung disease in patients with *SFTPC* mutations.[44](https://pmc.ncbi.nlm.nih.gov/articles/PMC3201772/" \l "R44) If testing for these genes is negative, analysis for *NKX2.1* deletions or mutations should be considered. While neurological findings or a history of hypothyroidism should prompt consideration for *NKX2.1* haploinsufficiency, the absence of these findings should not preclude testing for this gene if testing for other genes is negative and the clinical history and other findings are consistent with surfactant dysfunction. Younger infants with *NKX2.1* mutations may have non-specific findings such as hypotonia and may not develop chorea until later in life.

It is important to recognize the limitations of genetic testing. Current approaches involve sequencing the coding regions of the genes of interest, a process which may take several weeks before results are available. In a child whose condition is rapidly deteriorating this may be inadequate. The sensitivity of this mode of testing is not known, but is not 100%.Mutations outside of translated regions that affect gene expression will not be detected and complete or partial gene deletions, duplications or rearrangements will not be detected by current PCR based approaches unless specific methods to detect such variants are employed. Interpretation of results may also not be straightforward. There is no simple or definitive way of ascertaining whether some variants, particularly missense mutations, are likely disease-causing or benign sequence variants that have no functional consequence. In the case of recessive disorders such as ABCA3 and SP-B deficiency, if only one mutation is identified, it may not be feasible to determine whether the child is affected with an unidentified mutation on the other allele, or whether the child is simply a carrier and the true cause of lung disease is unrelated to the variant that has been found. Currently there is no simple biochemical or clinical test for these disorders analogous to the sweat test for cystic fibrosis. Elevated levels of serum KL-6, a protein of unknown function expressed by lung epithelial cells, have been observed in children with surfactant dysfunction, and may be useful in distinguishing them from those with other forms of diffuse childhood lung disease.Currently testing for KL-6 is not widely available as a clinical test, but these observations support the existence of specific biomarkers that could aid in diagnosis of surfactant dysfunction disorders. Such markers might also be useful for following disease severity and response to therapy. Finally, genetic testing can be quite costly, and the costs for such testing are often not covered by health insurance. In such cases, parents are asked to pay out of pocket, which may not be feasible, particularly in resource limited settings. Despite these limitations genetic testing allows for the possibility of establishing a diagnosis without the need for lung biopsy.

While specific, directed therapies do not exist for the genetic disorders of surfactant dysfunction, establishing this diagnosis is nonetheless important. It provides some information about prognosis, and obviates the need for further expensive and time-intensive diagnostic testing. Finally, identification of a causative gene allows families of affected children to be informed about risks to other family members and of disease with future pregnancies.

The diagnostic approach requires a systematic, stepwise evaluation to establish both the presence of surfactant dysfunction and identify the specific genetic cause:

**Initial Clinical Assessment**

* **Detailed history**: Focus on family history, consanguinity, previous affected siblings
* **Physical examination**: Document signs of respiratory distress, growth parameters, extrapulmonary features
* **Gestational age assessment**: Rule out prematurity-related surfactant deficiency

**Laboratory Investigations**

* **Complete blood count**: Assess for infection, anemia
* **Blood gas analysis**: Document degree of hypoxemia and acid-base status
* **C-reactive protein**: Evaluate for inflammatory processes
* **Thyroid function tests**: Screen for NKX2.1-related hypothyroidism

**Imaging Studies**

* **Chest X-ray**: Shows diffuse bilateral ground-glass opacities, similar to respiratory distress syndrome
* **High-resolution computed tomography (HRCT)**: Reveals ground-glass opacities with interlobular septal thickening ("crazy-paving" pattern)
* **Echocardiography**: Assess for pulmonary hypertension and cardiac abnormalities

**Pulmonary Function Testing**

* **Infant pulmonary function tests**: May show restrictive pattern with reduced diffusion capacity
* **Oxygen saturation monitoring**: Document hypoxemia severity

**Advanced Diagnostic Procedures**

* **Bronchoscopy with bronchoalveolar lavage (BAL)**: Exclude infection, analyze surfactant composition
* **Genetic testing**: Molecular analysis using next-generation sequencing panels
* **Lung biopsy**: Rarely needed but may show characteristic histopathology

**Genetic Testing Strategy**

Testing should be prioritized based on clinical presentation:

1. **Neonatal onset with severe disease**: Test SFTPB and ABCA3 first
2. **Family history of dominant inheritance**: Consider SFTPC testing
3. **Associated hypothyroidism**: Test NKX2.1
4. **Comprehensive panels**: Include all surfactant-related genes for broader screening

**Treatment Options:**

**Oxygen support**

Long-term oxygen therapy and, rarely, non-invasive or invasive ventilation may be required in chILDs with respiratory failure. As for other indications, a mean oxygen saturation of 92% with more than 5% of the time below 90% is essential. If chILD is complicated by pulmonary hypertension, the indication for long-term oxygen therapy is even broader (especially if oxygen reactivity of pulmonary hypertension has been confirmed).

**Nutrition**

Respiratory insufficiency occurs in chILDs in up to 80% of the cases and results in increased energy consumption, which has to be compensated by increased energy intake (around 120% of age-appropriate daily dose). However, patients with chILD also experience oral feeding difficulties and/or gastro-enteral reflux and vomiting that make this goal hard to achieve. Additionally, chILD treatments, especially glucocorticoids, require regimen adaptation and eventual increase in nutrition difficulties. Taking into consideration these aspects while optimizing nutrition in chILD is a major part of the management of these children. While most patients will be managed with enriched oral feeding, more invasive management may be needed for others with enteral nutrition *via* nasogastric tube or gastrostomy.

**Immunizations**

Immunizations schedule should be adapted in chILD patients with respect to possible immunosuppressive treatment and increased risk of respiratory infection. In patients with glucocorticoid pulses or long-term oral corticosteroids, live vaccines should be avoided (or given at least two weeks before starting these treatments). Chickenpox vaccine may be discussed before introducing selective immunosuppressive therapeutics. Additional immunizations include influenza, *Streptococcus pneumoniae* and respiratory syncytial virus.

**Adapted physical activity**

Respiratory insufficiency and eventual oxygen or ventilatory support impair exercise tolerance. However, maintaining physical activity is essential in chILD management and a personalised programme with an adapted physical activity instructor may be of benefit to the patient's physical and mental health.

**Patients’ groups and social support**

Patients’ groups are critical in improving patients care. General chILD groups as well as disease-specific groups are increasingly being formed and the information should be systematically delivered to the patients. In line with the needs highlighted by parents and teenagers, optimal information at each step of the disease is still insufficiently provided, despite the increase in specific booklets and websites in many languages.

Social support is also an important part of the management that may notably improve daily life. Depending on local social offers, patients may benefit from various helps (*e.g.*, financial, human, scholarly). A systematic consultation with a social worker may allow optimizing these needs, when available.

Main nonspecific and specific treatments in childhood interstitial lung diseases (chILDs)

| **Treatment** | **Indication** | **Specific/nonspecific** | **Currently used (Curr); clinical trial (CT); research protocol or compassionate use (R); Prospective (P)** |
| --- | --- | --- | --- |
| **Glucocorticoids: methylprednisolone *i.v.* pulses; oral prednisolone** | Almost all chILDs | Nonspecific | Curr |
| NEHI | Nonspecific | CT: [NCT06471556](https://clinicaltrials.gov/ct2/show/NCT06471556" \t "_blank) |
| **Long-term azithromycin** | Surfactant metabolism disorders | Nonspecific | Curr |
| **Hydroxychloroquine** | Surfactant metabolism disorders and other chILDs | Nonspecific | Curr/CT: [NCT02615938](https://clinicaltrials.gov/ct2/show/NCT02615938" \t "_blank) |
| **Immunosuppressive drugs: mycophenolate mofetil, ciclosporin, azathioprine, rituximab, cyclophosphamide, methotrexate** | Auto-immune and auto-inflammatory disorders; disorders related to systemic disease processes; sarcoidosis | Nonspecific | Curr |
| **Antifibrosing therapies: pirfenidone, nintedanib** | Fibrosing surfactant metabolism disorders; undefined fibrosing ILD | Nonspecific | CT: [NCT05285982](https://clinicaltrials.gov/ct2/show/NCT05285982" \t "_blank) (nintedanib); [NCT04093024](https://clinicaltrials.gov/ct2/show/NCT04093024" \t "_blank) (nintedanib) R (pirfenidone) |
| **Janus kinase inhibitors: ruxolitinib, baricitinib, tofacitinib** | Auto-inflammatory disorders (SAVI, COPA); | Specific | Curr/CT: [NCT04517253](https://clinicaltrials.gov/ct2/show/NCT04517253" \t "_blank) |
| Undefined chILD with elevated IFN signature, FARSA, STAT1 GOF, STAT3 GOF | Nonspecific | R |
| **CFTR modulators** | ABCA3 deficiency | Specific | R |
| **Cyclosporine A** | ABCA3 deficiency | Nonspecific | R |
| **Methionine** | MARS1-related PAP | Specific | Curr CT: [NCT03887169](https://clinicaltrials.gov/ct2/show/NCT03887169" \t "_blank) |
| **Amino acids: phenylalanine, isoleucine, tyrosine, leucine, alanine** | FARSA, FARSB, YARS1, LARS1, IARS1, AARS | Specific | R |
| **Inhaled sargramostim (recombinant human GM-CSF)** | Autoimmune PAP | Specific | CT: [NCT01511068](https://clinicaltrials.gov/ct2/show/NCT01511068" \t "_blank) R |
| **Inhaled sargramostim (recombinant human GM-CSF)** | CSF2RA and CSF2RB-related PAP | Specific | CT: [NCT01511068](https://clinicaltrials.gov/ct2/show/NCT01511068" \t "_blank) (interrupted, insufficient recruitment) CT: [NCT02835742](https://clinicaltrials.gov/ct2/show/NCT02835742" \t "_blank) |
| **Whole lung lavages** | PAP | Nonspecific | Curr |
| **Lung transplantation** | End-stage irreversible chILD | Nonspecific | Curr |
| **Gene transfer therapy** | SP-B deficiency CSF2RA-related PAP Potentially all monogenic chILDs | Specific | P |
| **Mesenchymal stromal cell therapy** | CSF2RA-related PAP |  | CT: [NCT01828957](https://clinicaltrials.gov/ct2/show/NCT01828957" \t "_blank) |

NEHI: neuroendocrine cell hyperplasia of infancy; SAVI: STING-associated vasculopathy of infancy; COPA: coatomer protein complex, subunit alpha; IFN: interferon; FARSA: phenylalanine-tRNA synthetase A; STAT: signal transducer and activator of transcription; GOF: gain of function; CFTR: cystic fibrosis transmembrane conductance regulator; ABCA3: ATP binding cassette subfamily A member 3; MARS: methionine-tRNA synthetase; PAP: pulmonary alveolar proteinosis; FARSB: phenylalanine-tRNA synthetase B; YARS1: tyrosyl tRNA synthetase 1; LARS1: leucyl tRNA synthetase 1; IARS1: isoleucyl-tRNA synthetase 1; AARS: alanyl tRNA synthetase; GM-CSF: granulocyte–macrophage colony stimulating factor; CSF2R: colony stimulating factor 2 receptor; SP-B: surfactant protein B.

**Prevention Tips:**

**Primary Prevention**

Currently, no primary prevention strategies exist for genetic surfactant dysfunction disorders. However, several approaches can help prevent disease occurrence:

**Genetic Counseling**

* **Preconception counseling**: For couples with family history or known carrier status
* **Risk assessment**: Calculation of recurrence risks based on inheritance patterns
* **Prenatal testing**: Available for known familial mutations through amniocentesis or chorionic villus sampling

**Reproductive Options**

* **Preimplantation genetic diagnosis (PGD)**: For couples at high risk
* **Donor gametes**: Consider when both partners are carriers of autosomal recessive disorders

**Secondary Prevention**

Focus on early detection and intervention:

**Newborn Screening**

* **Clinical vigilance**: High index of suspicion for full-term infants with unexplained respiratory distress
* **Family screening**: Genetic testing for siblings and parents of affected children
* **Early genetic testing**: Rapid genetic panels for suspected cases

**Tertiary Prevention**

Aims to prevent complications and optimize outcomes:

**Infection Prevention**

* **Respiratory isolation**: During acute exacerbations
* **Vaccination**: Complete immunization schedules including influenza and pneumococcal vaccines
* **RSV prophylaxis**: Consider palivizumab for high-risk infants

**Complications Prevention**

* **Pulmonary hypertension monitoring**: Regular echocardiography
* **Nutritional optimization**: Prevent growth failure and malnutrition
* **Bone health**: Monitor for steroid-induced osteoporosis

**Prognosis:**

Giving the baby's mother [glucocorticoids](https://en.wikipedia.org/wiki/Glucocorticoids" \o "Glucocorticoids) speeds the production of surfactant. For very premature deliveries, a glucocorticoid is given without testing the fetal lung maturity. The [American College of Obstetricians and Gynecologists](https://en.wikipedia.org/wiki/American_College_of_Obstetricians_and_Gynecologists" \o "American College of Obstetricians and Gynecologists) (ACOG), Royal College of Medicine and other major organizations have recommended antenatal glucocorticoid treatment for women at risk for preterm delivery prior to 34 [weeks of gestation](https://en.wikipedia.org/wiki/Gestational_age_(obstetrics)" \o "Gestational age (obstetrics)).Multiple courses of glucocorticoid administration, compared with a single course, do not seem to increase or decrease the risk of death or [neurodevelopmental disorders](https://en.wikipedia.org/wiki/Neurodevelopmental_disorder" \o "Neurodevelopmental disorder) of the child.

In pregnancies of longer than 30 weeks, the fetal lung maturity may be tested by sampling the amount of surfactant in the amniotic fluid by [amniocentesis](https://en.wikipedia.org/wiki/Amniocentesis" \o "Amniocentesis), wherein a needle is inserted through the mother's abdomen and uterus. Several tests are available that correlate with the production of surfactant. These include the [lecithin-sphingomyelin ratio](https://en.wikipedia.org/wiki/Lecithin-sphingomyelin_ratio" \o "Lecithin-sphingomyelin ratio) ("[L/S ratio](https://en.wikipedia.org/wiki/L/S_ratio" \o "L/S ratio)"), the presence of [phosphatidylglycerol](https://en.wikipedia.org/wiki/Phosphatidylglycerol" \o "Phosphatidylglycerol) (PG), and, more recently, the [surfactant/albumin (S/A) ratio](https://en.wikipedia.org/wiki/Surfactant-albumin_ratio" \o "Surfactant-albumin ratio). For the [L/S ratio](https://en.wikipedia.org/wiki/L/S_ratio" \o "L/S ratio), if the result is less than 2:1, the fetal lungs may be deficient in surfactant. The presence of PG usually indicates fetal lung maturity. For the S/A ratio, the result is given as milligrams of surfactant per gram of protein. A S/A ratio less than 35 indicates immature lungs, between 35 and 55 is indeterminate, and greater than 55 indicates mature surfactant production (correlating with an L/S ratio of 2.2 or greater).

The prognosis varies dramatically depending on the specific genetic defect, severity of mutations, and age at presentation:

**SP-B Deficiency (SMDP1)**

* **Prognosis**: Generally poor with high mortality
* **Survival**: Most infants die within 3-6 months without lung transplantation
* **Treatment response**: Poor response to conventional therapies including surfactant replacement
* **Transplant outcomes**: Lung transplantation offers potential for survival with 5-year survival rates around 50%

**ABCA3 Deficiency (SMDP3)**

* **Neonatal presentation**: Severe phenotype with high mortality (>90%) within first year
* **Later-onset forms**: Some patients with milder mutations may survive to adulthood
* **Treatment response**: Limited response to medical therapy
* **Natural history**: Disease progression varies with specific mutations

**SP-C Dysfunction (SMDP2)**

* **Variable prognosis**: Ranges from asymptomatic to severe progressive disease
* **Age at onset**: Can present from neonatal period to adulthood
* **Treatment response**: May respond to hydroxychloroquine and corticosteroids
* **Long-term outcomes**: Some patients may improve spontaneously over time

**Factors Affecting Prognosis**

* **Genetic mutation type**: Null mutations generally have worse prognosis than missense mutations
* **Age at onset**: Earlier presentation typically associated with more severe disease
* **Response to treatment**: Patients responding to medical therapy have better outcomes
* **Complications**: Development of pulmonary hypertension worsens prognosis

**Survival Data**

Recent registry data suggest improving outcomes

* **Early intervention**: Prompt diagnosis and treatment initiation improve survival
* **Multidisciplinary care**: Comprehensive management reduces morbidity
* **Long-term follow-up**: Some patients may experience disease stabilization or improvement

**Complications:**

Surfactant dysfunction disorders can lead to numerous serious complications affecting multiple organ systems:

**Respiratory Complications**

* **Respiratory failure**: Progressive deterioration requiring mechanical ventilation
* **Pneumothorax**: Spontaneous air leaks due to increased ventilatory pressures
* **Pulmonary hypertension**: Secondary to chronic hypoxemia and lung disease
* **Cor pulmonale**: Right heart failure from pulmonary hypertension
* **Chronic lung disease**: Progressive pulmonary fibrosis
* **Recurrent infections**: Increased susceptibility to respiratory pathogens

**Growth and Developmental Complications**

* **Failure to thrive**: Poor weight gain and linear growth
* **Developmental delays**: May occur secondary to chronic hypoxemia
* **Feeding difficulties**: Due to respiratory distress and increased metabolic demands

**Treatment-Related Complications**

* **Steroid-induced complications**: Growth retardation, osteoporosis, adrenal suppression
* **Mechanical ventilation complications**: Ventilator-associated pneumonia, barotrauma
* **Oxygen toxicity**: Bronchopulmonary dysplasia from prolonged high-concentration oxygen

**Systemic Complications**

* **Cardiac complications**: Right ventricular dysfunction, arrhythmias
* **Neurological complications**: Hypoxic brain injury, seizures
* **Metabolic complications**: Acidosis, electrolyte imbalances

**Long-term Complications**

* **Progressive pulmonary fibrosis**: Irreversible lung damage
* **Chronic respiratory failure**: Requiring long-term ventilatory support
* **Quality of life impairment**: Significant functional limitations

**When to see a Doctor/Red Flags:**

When children are having hard time breathing, they will show signs that they are not getting enough air. Learning these signs will help you decide if you should call your child’s doctor, or bring them to the Emergency Room.

**This is a list of signs children show when they are in respiratory distress (not getting enough air):**

* **Breathing Rate:** Your child breathes fast. You see an increase in the number of breaths they usually take in a minute. Besides breathing fast, the child appears to be working harder to breathe.
* **Color Changes:** A pale grey or bluish color is seen around your child's mouth, on the inside of the lips, or on the fingernails.
* **Grunting:** A grunting sound can be heard as your child breathes out with each breath.
* **Nasal Flaring:**The openings of your child's nose spread open when they breathe in.
* **Retractions:** The chest appears to sink in with each breath. You may be able to see it sink in just below the neck and/or under the breastbone. You may also see it sink between your child's ribs.
* **Sweating:**You may notice sweat on your child’s head, but their skin feels cool or clammy, rather than hot. This may happen when your child's breathing rate is very fast.
* **Wheezing:**A tight, whistling or musical sound is heard when your child breathes.

**Other signs of respiratory distress include:**

* Head bobbing – Your child’s head moves forward each time they take a breath.
* Your child insists on an upright, forward leaning position.
* Your child is restless, agitated or irritable.
* Your child is sleepy, limp, or not interested in what is going on around them.

**If you notice any of these signs, call your child's doctor, or bring them to the Emergency Room right away.**

Immediate medical attention is crucial when certain warning signs develop, as surfactant dysfunction can rapidly progress to life-threatening respiratory failure:

**Emergency Red Flags (Call 911)**

* **Severe respiratory distress**: Extreme difficulty breathing or inability to speak in full sentences
* **Cyanosis**: Blue discoloration of lips, face, or fingernails
* **Altered mental status**: Confusion, agitation, or decreased responsiveness
* **Apnea**: Periods of stopped breathing
* **Bradycardia**: Slow heart rate in the presence of respiratory distress (suggests impending arrest)

**Urgent Medical Attention (Emergency Department)**

* **Significant retractions**: Severe chest wall pulling with breathing
* **Persistent tachypnea**: Respiratory rate >60 in infants, >40 in children
* **Oxygen saturation <90%**: Despite supplemental oxygen
* **Grunting respirations**: Audible sounds with each breath
* **Stridor**: High-pitched breathing sounds
* **Inability to feed**: Due to respiratory distress

**Same-Day Medical Evaluation**

* **New or worsening cough**: Especially if productive or bloody
* **Exercise intolerance**: New difficulty with previously tolerated activities
* **Feeding difficulties**: Poor oral intake or failure to thrive
* **Recurrent fever**: Especially with respiratory symptoms
* **New medication side effects**: From treatments like hydroxychloroquine or corticosteroids

**Routine Follow-up Indicators**

* **Growth concerns**: Poor weight gain or linear growth
* **Developmental delays**: Missing age-appropriate milestones
* **Family planning**: Genetic counseling for future pregnancies
* **Medication monitoring**: Regular assessment of treatment efficacy and side effects

**High-Risk Situations Requiring Increased Vigilance**

* **Viral illness**: Even minor respiratory infections can cause significant deterioration
* **Procedure or surgery**: Anesthesia risks in patients with compromised lung function
* **Travel**: Changes in altitude or environment may worsen respiratory status
* **Medication changes**: Adjustments to respiratory medications require close monitoring

**Differential Diagnoses:**

**Respiratory Distress Syndrome (RDS):**

This is a common condition in premature infants due to surfactant deficiency. While surfactant metabolism dysfunction can also cause severe respiratory distress, it can have a broader age of onset and may be associated with specific genetic mutations.

**Neonatal Respiratory Distress**

* **Respiratory distress syndrome (RDS)**: Prematurity-related surfactant deficiency
* **Transient tachypnea of newborn (TTN)**: Self-resolving condition in term infants
* **Meconium aspiration syndrome**: Chemical pneumonitis from meconium
* **Congenital pneumonia**: Infectious etiology
* **Congenital heart disease**: Cyanotic heart lesions

**Chronic Lung Disease of Infancy (chILD):**

This is an umbrella term for various lung disorders presenting in infancy, often with chronic tachypnea and respiratory distress. Surfactant dysfunction can be a cause of chILD, but other conditions like cystic fibrosis, aspiration, and immunodeficiencies must be ruled out.

**Pulmonary Alveolar Proteinosis (PAP):**

PAP is characterized by an accumulation of surfactant-like material in the alveoli. While some forms of surfactant dysfunction can mimic PAP, genetic testing can differentiate between them

**Other Interstitial Lung Diseases (ILDs):**

Various other ILDs, including those caused by infections, autoimmune disorders, or environmental exposures, can present with similar symptoms to surfactant dysfunction. Genetic testing and lung biopsy can help distinguish these conditions.

**Childhood Interstitial Lung Disease**

* **Hypersensitivity pneumonitis**: Environmental antigen exposure
* **Sarcoidosis**: Multisystem granulomatous disease
* **Connective tissue diseases**: Systemic lupus erythematosus, juvenile dermatomyositis
* **Neuroendocrine cell hyperplasia of infancy (NEHI)**: Specific form of chILD
* **Pulmonary alveolar proteinosis**: Various etiologies including autoimmune

**Other genetic lung diseases:**

Several other genetic conditions, such as those involving mutations in the NKX2-1 gene, can also cause surfactant abnormalities and respiratory problems. These require specific genetic testing for diagnosis.

**Genetic/Metabolic Disorders**

* **Cystic fibrosis**: Chloride channel dysfunction
* **Primary ciliary dyskinesia**: Abnormal ciliary function
* **Alpha-1 antitrypsin deficiency**: Protease inhibitor deficiency
* **Lysosomal storage diseases**: Gaucher disease, Niemann-Pick disease

**Key Distinguishing Features:**

* **Genetic testing:**

Identifying specific mutations in surfactant protein genes (e.g., SFTPB, SFTPC, ABCA3) or NKX2-1 is crucial for confirming surfactant metabolism dysfunction

**Clinical presentation:**

While some forms of surfactant dysfunction present with severe respiratory distress at birth, others may have a more gradual onset with chronic tachypnea, hypoxemia, and failure to thrive

**Lung histology:**

Lung biopsy findings can be suggestive of surfactant dysfunction, but genetic testing is needed for definitive diagnosis

**Age of onset and family history:**

The age at which symptoms appear and whether there is a family history of lung disease can provide clues about the underlying cause

**Guidelines:**

Surfactant metabolism dysfunction (SMD) guidelines focus on early diagnosis and management of lung conditions caused by surfactant deficiency, which can lead to respiratory distress, especially in newborns. While there are no standardized treatment protocols due to the varied clinical presentations, supportive care and genetic counseling are crucial. Early diagnosis using genetic testing and lung biopsies, when necessary, is important for guiding treatment and managing complications.

Key aspects of SMD management include:

* **Early diagnosis:**

Genetic testing panels (like the Igenomix Surfactant Metabolism Dysfunction Precision Panel) can help identify the specific gene mutations causing surfactant deficiency, aiding in accurate diagnosis and prognosis.

* **Supportive care:**

This includes oxygen therapy, mechanical ventilation, and nutritional support to maintain lung function and manage respiratory distress.

* **Multidisciplinary approach:**

Effective management often involves a team of specialists, including pulmonologists, geneticists, and respiratory therapists, working together to address the various aspects of the condition.

* **Genetic counseling:**

Provides information about the inheritance patterns of SMD and helps families understand the risks of recurrence and make informed decisions about future pregnancies.

* **Experimental therapies:**

Gene therapy and lung transplantation are being explored as potential future treatments for severe cases.

* **Monitoring and follow-up:**

Regular monitoring of lung function, growth, and development is essential for managing the long-term effects of SMD.

* **Specific treatments for some subtypes:**

While no definitive treatments exist for all forms of SMD, some reports show clinical improvement with corticosteroids, azithromycin, and other medications.

Clinical manifestations of SMD can vary, ranging from severe respiratory distress syndrome in newborns to chronic interstitial lung disease in older children and adults.

In summary, surfactant metabolism dysfunction requires a comprehensive approach that includes early diagnosis through genetic testing, supportive care, and a multidisciplinary team to manage the condition and its long-term effects.

**Expert-Reviewed Q&A:**

**What is surfactant metabolism dysfunction disorder?**

It is a rare group of genetic disorders where the body cannot produce or process surfactant properly. Surfactant is a substance that coats the lungs' air sacs and is essential for breathing—without it, the lungs’ air sacs can collapse, causing severe breathing difficulties.

**How is it inherited?**

Some forms are inherited in an autosomal recessive manner (both parents must be carriers, as with SP-B and ABCA3 deficiencies), while others follow autosomal dominant patterns (only one mutated gene needed, as with some SP-C dysfunctions and NKX2.1 mutations). Genetic counseling is strongly recommended for affected families.

**What are the main symptoms in infants and children?**

* Severe or unexplained respiratory distress, especially in full-term newborns
* Rapid or labored breathing, grunting, nasal flaring, and chest retractions
* Persistent hypoxemia (low blood oxygen) not improving with regular treatment
* Chronic cough, recurrent chest infections, and poor growth in older children

**How is surfactant dysfunction diagnosed?**

**Diagnosis combines:**

* Clinical examination and history (including family/medical history)
* Chest imaging (X-rays, high-resolution CT)
* Genetic testing for mutations in surfactant-related genes
* Sometimes, specialized procedures like bronchoscopy or lung biopsy

**Is there a cure for these disorders?**

Currently, there is no cure for most forms. Management is supportive, focusing on breathing assistance (oxygen, ventilators), medications to reduce lung inflammation, nutritional support, and preventing complications. Lung transplantation is considered for severe, unresponsive cases.

**What treatments are used and what are their side effects?**

* Corticosteroids: Reduce lung inflammation but may stunt growth, weaken bones, and increase infection risk.
* Hydroxychloroquine: Modulates inflammation and metabolism with potential side effects of eye toxicity, gastrointestinal upset, and heart rhythm issues.
* Azithromycin: Used for anti-inflammatory effects but can cause stomach upset, liver enzyme elevation, and rare heart rhythm problems.
* Surfactant therapy: Can temporarily help in some cases, mostly in the neonatal period, but does not address the genetic problem.

**What is the prognosis for children with surfactant dysfunction?**

**Prognosis depends on the specific genetic mutation:**

* SP-B and ABCA3 severe deficiency: Usually poor without lung transplantation, with many infants not surviving beyond the first year.
* SP-C dysfunction/NKX2.1: Wide range—from mild symptoms to progressive lung disease.  
  Early diagnosis and comprehensive care improve outcomes in many children.

**Should families with a history of this disorder seek genetic counseling?**

Yes. Genetic counseling helps families understand inheritance risks, options for future pregnancies, and available prenatal testing or assisted reproductive choices.

**What should parents watch for/when should they seek immediate medical attention?**

**Call a doctor or visit the hospital immediately if your child has:**

* Rapid, labored, or noisy breathing
* Blue-tinged lips or skin (cyanosis)
* Lethargy or difficulty waking up
* Trouble feeding, growing, or recurrent respiratory infections

**Can these disorders be prevented?**

There is no way to prevent inherited genetic mutations, but genetic counseling and prenatal testing can guide family planning and early detection.

What research is being done for new treatments?

Studies are investigating gene therapy, new anti-inflammatory medications, and drugs targeting specific molecular pathways. Progress in genetic diagnostics has improved early detection and care.

**Summary:**

Pediatric surfactant metabolism dysfunction disorder represents a complex group of rare genetic conditions that significantly impact respiratory function and overall health outcomes. These disorders, caused by mutations in genes essential for surfactant production and function, manifest with varying degrees of severity from the neonatal period through adulthood.

The five main types include SP-B deficiency (SMDP1), SP-C dysfunction (SMDP2), ABCA3 deficiency (SMDP3), NKX2.1/TTF-1 mutations, and SP-A deficiency, each with distinct inheritance patterns, clinical presentations, and prognoses. SP-B and ABCA3 deficiencies typically present with severe neonatal respiratory distress and poor prognosis without lung transplantation, while SP-C dysfunction shows more variable presentations and outcomes.

Diagnosis requires a systematic approach combining clinical assessment, advanced imaging, genetic testing, and sometimes specialized procedures like bronchoscopy or lung biopsy. Early genetic testing is crucial for accurate diagnosis and appropriate management planning.

Treatment remains largely supportive, focusing on respiratory support, nutritional optimization, and complications prevention. Pharmacological interventions include corticosteroids, hydroxychloroquine, and azithromycin, though evidence for their efficacy is limited to case series and small studies. Lung transplantation remains the definitive treatment for end-stage disease, with outcomes similar to other pediatric lung transplant indications.

The prognosis varies significantly based on the specific genetic defect and clinical presentation. While severe forms like SP-B deficiency carry high mortality rates, some patients with milder phenotypes may experience disease stabilization or improvement with appropriate management. Early diagnosis, prompt treatment initiation, and comprehensive multidisciplinary care are essential for optimizing outcomes.

Prevention strategies focus on genetic counseling, family screening, and prenatal testing for at-risk families. Recognition of red flag symptoms and early medical intervention can prevent life-threatening complications. Ongoing research into gene therapy and novel therapeutic approaches offers hope for more effective treatments in the future.

Understanding these complex disorders is crucial for healthcare providers managing children with unexplained respiratory distress, particularly in full-term infants or children with family histories of lung disease. A high index of suspicion, appropriate diagnostic workup, and prompt referral to specialized centers are essential for optimal patient care and family support.

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1. **Bronchiolitis Obliterans**

**Definition:**

Bronchiolitis obliterans (BO) is a rare, chronic form of obstructive lung disease, often initiated with injury of the bronchiolar epithelium followed by an inflammatory response and progressive fibrosis of small airways resulting in nonuniform luminal obliteration or narrowing. The term BO comprises a group of diseases with different underlying etiologies, courses, and characteristics. The condition is distinct from common viral bronchiolitis that affects infants and resolves spontaneously.

Among the better recognized inciting stimuli leading to BO are airway pathogens such as adenovirus and mycoplasma, which, in a small percentage of infected children, will result in progressive fixed airflow obstruction, an entity referred to as postinfectious bronchiolitis obliterans (PIBO).

**Causes:**

Bronchiolitis obliterans has many possible causes, including [collagen vascular disease](https://en.wikipedia.org/wiki/Collagen_vascular_disease" \o "Collagen vascular disease), [transplant rejection](https://en.wikipedia.org/wiki/Transplant_rejection" \o "Transplant rejection) in [organ transplant](https://en.wikipedia.org/wiki/Organ_transplant" \o "Organ transplant) patients, viral infection ([adenovirus](https://en.wikipedia.org/wiki/Adenovirus" \o "Adenovirus), [respiratory syncytial virus](https://en.wikipedia.org/wiki/Respiratory_syncytial_virus" \o "Respiratory syncytial virus), [influenza](https://en.wikipedia.org/wiki/Influenza" \o "Influenza), [HIV](https://en.wikipedia.org/wiki/HIV" \o "HIV), [cytomegalovirus](https://en.wikipedia.org/wiki/Cytomegalovirus" \o "Cytomegalovirus)), [Stevens–Johnson syndrome](https://en.wikipedia.org/wiki/Stevens%E2%80%93Johnson_syndrome" \o "Stevens–Johnson syndrome), [Pneumocystis pneumonia](https://en.wikipedia.org/wiki/Pneumocystis_pneumonia" \o "Pneumocystis pneumonia), drug reaction, aspiration and complications of prematurity ([bronchopulmonary dysplasia](https://en.wikipedia.org/wiki/Bronchopulmonary_dysplasia" \o "Bronchopulmonary dysplasia)), and exposure to toxic fumes. Toxins implicated in the condition include [diacetyl](https://en.wikipedia.org/wiki/Diacetyl" \o "Diacetyl), [sulfur dioxide](https://en.wikipedia.org/wiki/Sulfur_dioxide" \o "Sulfur dioxide), [nitrogen dioxide](https://en.wikipedia.org/wiki/Nitrogen_dioxide" \o "Nitrogen dioxide), [ammonia](https://en.wikipedia.org/wiki/Ammonia" \o "Ammonia), [chlorine](https://en.wikipedia.org/wiki/Chlorine" \o "Chlorine), [thionyl chloride](https://en.wikipedia.org/wiki/Thionyl_chloride" \o "Thionyl chloride), [methyl isocyanate](https://en.wikipedia.org/wiki/Methyl_isocyanate" \o "Methyl isocyanate), [hydrogen fluoride](https://en.wikipedia.org/wiki/Hydrogen_fluoride" \o "Hydrogen fluoride), [hydrogen bromide](https://en.wikipedia.org/wiki/Hydrogen_bromide" \o "Hydrogen bromide), [hydrogen chloride](https://en.wikipedia.org/wiki/Hydrogen_chloride" \o "Hydrogen chloride), [hydrogen sulfide](https://en.wikipedia.org/wiki/Hydrogen_sulfide" \o "Hydrogen sulfide), [phosgene](https://en.wikipedia.org/wiki/Phosgene" \o "Phosgene), polyamide-amine [dyes](https://en.wikipedia.org/wiki/Dye" \o "Dye), [mustard gas](https://en.wikipedia.org/wiki/Mustard_gas" \o "Mustard gas) and [ozone](https://en.wikipedia.org/wiki/Ozone" \o "Ozone).It can also be present in patients with [IBD](https://en.wikipedia.org/wiki/Irritable_bowel_syndrome" \o "Irritable bowel syndrome), [systemic lupus erythematosus](https://en.wikipedia.org/wiki/Systemic_lupus_erythematosus" \o "Systemic lupus erythematosus), [juvenile idiopathic arthritis](https://en.wikipedia.org/wiki/Juvenile_idiopathic_arthritis" \o "Juvenile idiopathic arthritis), [rheumatoid arthritis](https://en.wikipedia.org/wiki/Rheumatoid_arthritis" \o "Rheumatoid arthritis), [GERD](https://en.wikipedia.org/wiki/GERD" \o "GERD), [IgA nephropathy](https://en.wikipedia.org/wiki/IgA_nephropathy" \o "IgA nephropathy), and [ataxia telangiectasia](https://en.wikipedia.org/wiki/Ataxia%E2%80%93telangiectasia" \o "Ataxia–telangiectasia). [Activated charcoal](https://en.wikipedia.org/wiki/Activated_carbon" \o "Activated carbon) has been known to cause it when aspirated. The ingestion of large doses of [papaverine](https://en.wikipedia.org/wiki/Papaverine" \o "Papaverine) in the vegetable [Sauropus androgynus](https://en.wikipedia.org/wiki/Sauropus_androgynus" \o "Sauropus androgynus) has caused it. Additionally, the disorder may be [idiopathic](https://en.wikipedia.org/wiki/Idiopathic" \o "Idiopathic) (without known cause).

**Lung transplant**

Bronchiolitis obliterans is a common complication in lung transplants because transplanted lungs are at greater risk of [alloimmunization](https://en.wikipedia.org/wiki/Alloimmunization" \o "Alloimmunization) as compared to healthy lungs. The disease is often termed bronchiolitis obliterans syndrome (BOS) in the setting of post lung transplantation and hematopoietic stem cell transplant (HSCT).Patients who develop BOS post lung transplant vary in disease latency and severity. Patients often initially have normal lung function on pulmonary function testing and have normal chest radiographs. As the disease progresses they begin to have symptoms of shortness of breath, cough, and wheezing as their lung function declines. The Journal of Heart and Lung Transplantation published updated guidelines in 2001 for grading the severity of BOS. The original guidelines and classification system were published in 1993 by the International Society for Heart and Lung Transplantation.Their scoring system is based on the changes in FEV1 in patients from their baseline. When patients are first diagnosed with BOS they have their baseline lung function established by doing pulmonary function testing at the time of diagnosis. The BOS scoring system is as follows:

BOS 0: FEV1 > 90% of baseline and FEF25-75 > 75% of baseline

BOS 0-p: FEV1 81-89% of baseline and/or FEF25-75 <= 75% of baseline

BOS 1: FEV1 66-80% of baseline

BOS 2: FEV1 51-65% of baseline

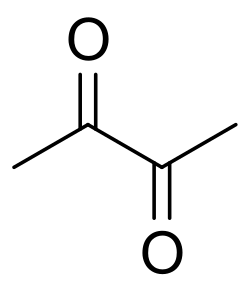
BOS 3: FEV1 50% or less of baseline

The scoring system shows an increased severity of the disease as the BOS number increases.

**Hematopoietic stem cell transplant**

Bronchiolitis obliterans affects up to 5.5% of people who have received HSCT. One of the biggest risk factors after HSCT is the development of [GVHD](https://en.wikipedia.org/wiki/Graft-versus-host_disease" \o "Graft-versus-host disease) with a 14% risk. Other risk factors post transplant including tobacco use, age of donor, age of recipient, lower baseline FEV1/FVC ratio, non-caucasian race, peripheral and lower circulating IgG levels.[[6]](https://en.wikipedia.org/wiki/Bronchiolitis_obliterans" \l "cite_note-NEJM2014-6) Studies have, however, shown mixed results regarding these other risk factors. There has been an association shown between the increased use of peripheral stem cells and the risk of developing bronchiolitis obliterans.[[6]](https://en.wikipedia.org/wiki/Bronchiolitis_obliterans" \l "cite_note-NEJM2014-6) Also, research has shown an increased risk for developing the disease within the first year of transplant if the person is infected with respiratory syncytial virus or parainfluenza virus within the first 100 days post transplant.

**Toxic exposure**

[](https://en.wikipedia.org/wiki/File:Diacetyl.svg)Diacetyl

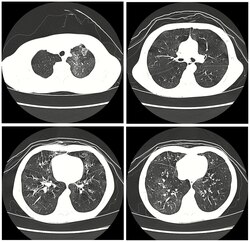
There are many industrial substances that are known to cause bronchiolitis obliterans.

Industrial workers who have presented with BO have been:

* nylon-flock workers
* workers who spray prints onto textiles with polyamide-amine dyes
* battery workers who are exposed to thionyl chloride
* workers at plants that use or manufacture diacetyl

Diacetyl is a chemical used to produce the artificial butter flavoring in many foods such as candy and microwave popcorn and occurring naturally in wines. This first came to public attention when eight former employees of the Gilster-Mary Lee popcorn plant in Jasper, Missouri developed bronchiolitis obliterans. Due to this event, bronchiolitis obliterans began to be referred to in the popular media as "popcorn lung" or "popcorn workers lung". It is also referred to as "flavorings-related lung disease".

**Post-infectious**

[](https://en.wikipedia.org/wiki/File:10.1371-journal.pone.0098381.g001.tif)High-resolution CT scan of a child with post-infectious bronchiolitis obliterans showing glass pattern with air trapping and bronchial thickening

Typically found in young children and is the most common cause at this age. Generally occurs after a viral infection of adenovirus (types 3, 7, and 21), measles (rubeola), mycoplasma, CMV, influenza, and parainfluenza.Swyer-James syndrome is a rare complication of bronchiolitis obliterans caused by measles or adenovirus. Post-infectious bronchiolitis obliterans is most common in the southern hemisphere particularly in countries such as Brazil, Argentina, Australia, Chile and New Zealand. There was a large prevalence of the disease in these areas during the 1990s and early 2000s. In one hospital in Buenos Aires, the Ricardo Gutiérrez Children's hospital, the disease accounted for 14% of their inpatient respiratory population from 1993 to 2002. As such, much of the information about post-infectious bronchiolitis obliterans has come from research out of South America. The most significant risk factors for the disease are infection with adenovirus and the need for ventilator support. In contrast with another cause of bronchiolitis obliterans in children, Steven's Johnson's syndrome, post-infectious bronchiolitis obliterans tends to be a chronic but non-progressive disease. The disease can have varying impact on children and their quality of life, which has been studied by lung function tests, as well as their exercise tolerance.Children with lower lung function based on their pulmonary function testing, have lower exercise tolerance, which compounds the impact of the disease on cardiovascular function as they are not able to maintain age appropriate aerobic fitness.This ultimately affects their activities of daily living (ADLs) and their quality of life going forward.

**Burn pits**

A form of BO is starting to present in Iraq and Afghanistan veterans. It has been attributed to veterans being exposed to trash burn pits. Veterans present with shortness of breath and other asthma-like symptoms. The only way to diagnose this condition is by doing a lung biopsy as chest X-rays and CT scans come back as normal. The US government still denies that there is any correlation between burn pits and health problems, but has started an "Airborne Hazards and Open Burn Pit Registry" to begin tracking the health of veterans who were exposed to burn pits to see if there is a connection.

**E-cigarettes**

The American Lung Association listed use of flavored e-cigarettes as a risk factor for BO in 2016.Health Canada has, however, seen no cases as of 2023.  Public Health England writes that the association has come about as "some flavourings used in e-liquids to provide a buttery flavour contain the chemical diacetyl… However, diacetyl is banned as an ingredient from e-cigarettes and e-liquids in the UK." The UK National Health Service's website states that "vaping does not cause 'popcorn lung'".

**Risk Factors:**

**Demographic Risk Factors**

* **Age**: Most cases develop in early childhood, particularly under 2 years of age
* **Geographic/ethnic predisposition**: Higher prevalence in South American populations, Asian descent, and Native American populations
* **Genetic factors**: Association with HLA haplotype DR8-DQB1.0302

**Clinical Risk Factors**

Specific risk factors for developing PIBO following adenovirus pneumonia include:

* **Hypoxemia during acute illness** (OR = 9.37)
* **Persistent wheezing** (OR = 4.65)
* **Mechanical ventilation requirement** (OR = 3.87)
* **Prolonged hospitalization** (OR = 1.25 per day)
* **Extended fever duration** (OR = 1.08 per day)

**Signs & Symptoms:**

Bronchiolitis obliterans results in worsening shortness of breath, wheezing, and a dry cough. The symptoms can start gradually, or severe symptoms can occur suddenly.These symptoms represent an obstructive pattern that is non-reversible with bronchodilator therapy, and need to be related to various lung insults. These insults include inhalation damage, post transplant auto-immune injury, post-infectious disease, drug reactions, and several auto-immune diseases.

**Physical examination findings**:

* Inspiratory crackles and expiratory wheeze
* Hyperinflated chest (barrel chest)
* Clubbing (uncommon)
* Signs of chronic respiratory insufficiency

**Disease Progression Patterns**

Three distinct progression patterns have been identified:

1. **Imperceptible onset with slow, steady deterioration**
2. **Initially rapid deterioration followed by stable state**
3. **Rapid, progressive deterioration**

**Medical Codes:**

**ICD-10 Codes**

* **J44.81**: Bronchiolitis obliterans and bronchiolitis obliterans syndrome
* **J44.1**: Chronic obstructive pulmonary disease with (acute) exacerbation (may be used for complications)

The ICD-10 code J44.81 is billable and includes obliterative bronchiolitis as a specific diagnostic classification.

**Diagnosis Mapping:**

Bronchiolitis obliterans is often diagnosed based on the symptoms of obstructive lung disease following lung injury. The definitive diagnosis is through biopsy, but due to the variable distribution of lesions, leading to falsely negative tests, and invasive nature of this procedure it is often not performed.Several tests are often needed to diagnose bronchiolitis obliterans, including spirometry, diffusing capacity of the lung tests (DLCO), lung volume tests, chest X-rays, high-resolution CT (HRCT), and lung biopsy.

**Pulmonary function testing**

Spirometry tests usually show an obstructive pattern and is the most common presentation. A slightly reduced to normal forced vital capacity (FVC), and a reduced FEV1 to FVC ratio and forced expiratory volume (FEV) with little to no correction with the use of bronchodilators are common findings.  Lung volume tests may show hyperinflation (excessive air in lungs caused by air trapping). Diffusing capacity of the lung (DLCO) tests are usually normal; people with early-stage OB are more likely to have normal DLCO. FEV1 (forced expiratory volume in 1 second) should be above 80% of predicted values to be considered normal. Bronchiolitis obliterans reduces this to between 16% and 21%.

**Medical imaging**

Early in the disease chest radiography is typically normal but may show hyperinflation. As the disease progresses a reticular pattern with thickening of airway walls may be present. HRCT can also show air trapping when the person being scanned breathes out completely; it can also show thickening in the airway and haziness in the lungs. A common finding on HRCT is patchy areas of decreased lung density, signifying reduced vascular caliber and air trapping. This pattern is often described as a "mosaic pattern", and may indicate bronchiolitis obliterans.

**Lung biopsy**

Transthoracic lung biopsies are preferable for diagnosis of constrictive BO compared to transbronchial biopsies; regardless of the type of biopsy, a diagnosis may only be achieved by examination of multiple samples. Transthoracic biopsies are preferred over transbronchial due to the heterogeneity and distribution of the lesions. OB can be further classified into two categories: constrictive or proliferative. The constrictive pattern is demonstrated by peribronchiolar cellular infiltrates which eventually causes small airway damage and leads to subepithelial fibrosis. The bronchial muscle can eventually become fibrosed which can be identified with trichrome staining. In regards to proliferative disease, intraluminal buds called "Masson bodies" fill the lumen, which results in bronchiolar plugging. Often people with proliferative disease will show butterfly wing-like appearance under microscopy. One key determinate that can be seen on biopsy to differentiate constrictive from proliferative disease is the extent of lesions. Both lesions are localized from the small bronchi to the membranous bronchi, but in constrictive disease, the lesions are intermittent while proliferative disease has a continuous distribution.

**Treatment Options:**

While the disease is not reversible, treatments can slow further worsening. This may include the use of corticosteroids or immunosuppressive medication which may have an effect on the ability to receive a lung transplant if offered. If patients have difficulty breathing (hypoxemia) oxygen can be supplemented. Routine vaccinations are recommended for patients with chronic lung disease to prevent complications from secondary infections due to pneumonia and influenza.

There is no consensus on bronchiolitis obliterans treatment. Supportive measures are important and include not smoking, vaccination against influenza, respiratory physiotherapy, supplemental oxygen at home for hypoxemic patients, and nutritional assistance. Bosa *et al.* assessed the nutritional status of 57 children with BO and found a high rate of malnutrition (21.7%) and risk of malnutrition (17.5%), indicating the need for nutritional intervention in those patients.

Bronchodilators are used to treat symptomatic wheezing, although BO has been considered a fixed obstructive disease of the small airways that does not respond or that responds poorly to bronchodilators. In a Brazilian study by Teixeira *et al.*, administration of a single dose of tiotropium to 30 patients with post-infectious BO resulted in a continued decrease in bronchial obstruction and air trapping for up to 24 hours.

Table 4. Differences in all time point assessment vs. baseline in the tiotropium vs. placebo group in the main PFT measurements (reprinted from Teixeira).

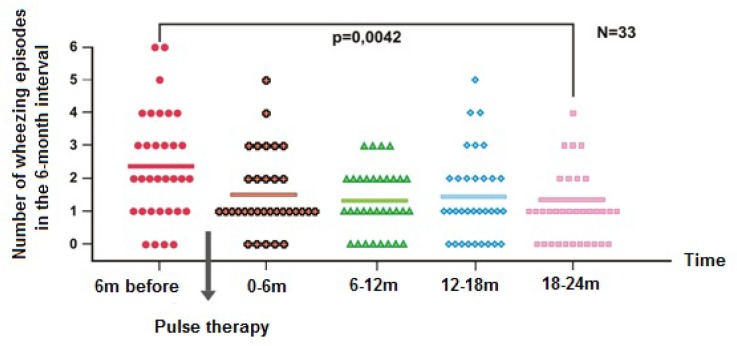
| **PFT parameter** | **Friedman Test** | ***P* value** |
| --- | --- | --- |
| FVC | 18.171 | 0.33 |
| FEV1 | 48.184 | <0.0001 |
| RV | 45.037 | <0.0001 |
| Resistance | 101.10 | <0.0001 |
| Conductance | 136.83 | <0.0001 |

The use of corticosteroids in the treatment of BO is based on the study by Moran and Hellstrom, who used a rabbit model of BO to demonstrate the natural course of the disease and that corticosteroid therapy in the early phase of illness modified fibroblastic response. However, similar studies were not performed in humans, so use of corticosteroids to treat BO remains controversial.

Zhang *et al.* (*[7](https://pmc.ncbi.nlm.nih.gov/articles/PMC4322598/" \l "bib7)*) advocated systemic use of corticosteroids, arguing that severe respiratory obstruction would prevent an aerosol spray from reaching the peripheral airways. Other clinicians prefer to use inhaled corticosteroids to minimize systemic adverse effects and to reduce bronchial hyperreactivity.

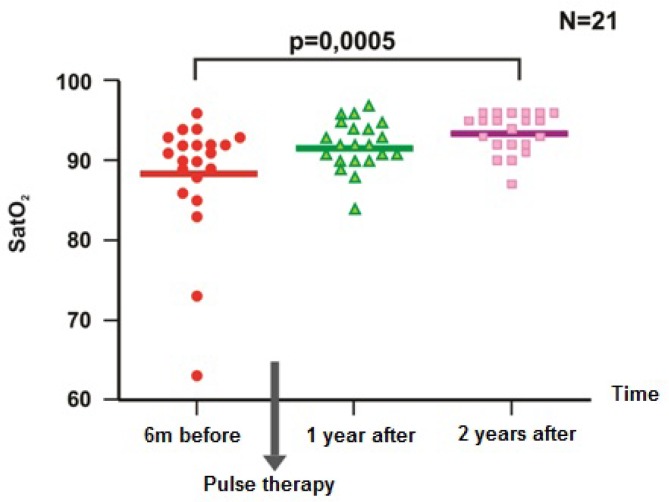
Methylprednisolone intravenous pulse therapy has been proposed to reduce adverse reactions to prolonged systemic administration of oral corticosteroids and is an alternative for patients with more severe disease. In a previous study by the current authors, 40 children with BO were treated with high-dose methylprednisolone pulse therapy, and these children exhibited clinical improvement as indicated by decreased exacerbation of wheezing and improved oxygen saturation. As a result, these patients had fewer instances of hospitalization ([Figures 2](https://pmc.ncbi.nlm.nih.gov/articles/PMC4322598/" \l "F2)–[5](https://pmc.ncbi.nlm.nih.gov/articles/PMC4322598/" \l "F5)).

Figure 2.

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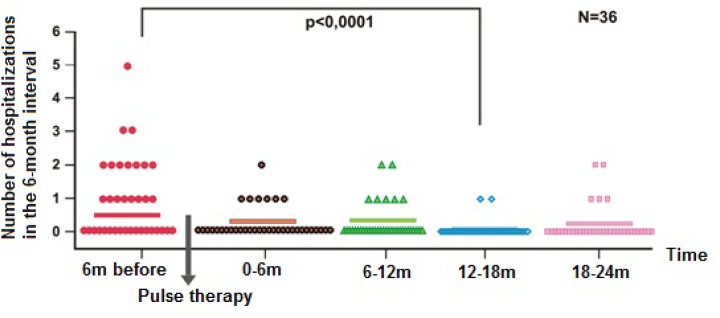
Exacerbation of wheezing before and after pulse therapy (*n* = 33).

Figure 5.

[](https://www.ncbi.nlm.nih.gov/core/lw/2.0/html/tileshop_pmc/tileshop_pmc_inline.html?title=Click%20on%20image%20to%20zoom%26p=PMC3%26id=4322598_irdr-4-7-g005.jpg)

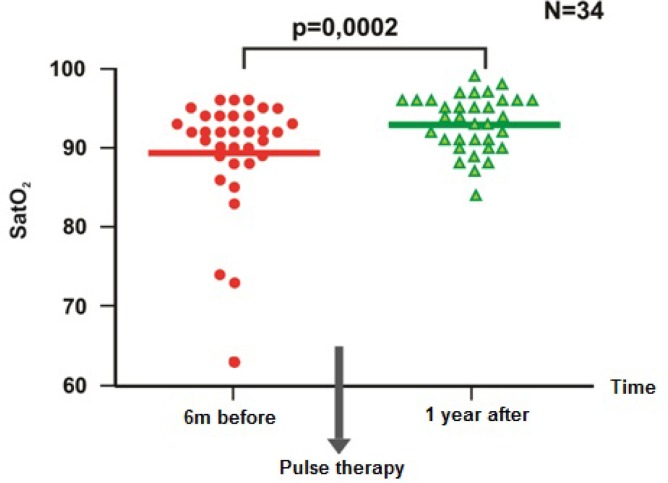
Oxygen saturation (SatO2) before and after 1 and 2 years of pulse therapy (*n* = 21).

Figure 3.



Hospitalization before and after pulse therapy (*n* = 36).

Figure 4.

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Oxygen saturation (SatO2) before and after 1 year of pulse therapy (*n* = 34).

**Anti-inflammatory Therapy**

**Systemic Corticosteroids**:

* **Pulse therapy (preferred)**: Intravenous methylprednisolone 10-30 mg/kg for 3 consecutive days, repeated monthly for 3-6 months
* **Rationale**: Should be initiated early before irreversible fibrosis develops
* **Caution**: Prolonged oral corticosteroids associated with severe complications including bone fractures and fatal infections

**Inhaled Corticosteroids**:

* **Budesonide**: 1 mg nebulized solution twice daily
* **Evidence**: Limited effectiveness as monotherapy
* **Role**: Adjunctive therapy to reduce systemic steroid exposure

**Azithromycin** (Anti-inflammatory Macrolide):

* **Dosing**: 10 mg/kg orally three times weekly (recommended standard)
* **Alternative**: 5 mg/kg once daily for first 3 days of each week
* **Mechanism**: Anti-inflammatory effects, reduces neutrophilic inflammation and IL-8 levels
* **Evidence**: Beneficial in post-transplant BO; limited data in PIBO

**Combination Therapy (FAM Protocol)**:  
Recent studies suggest benefit of combination therapy:

* **Fluticasone**: 440 mcg inhaled twice daily
* **Azithromycin**: 250 mg orally 3 times weekly (adults), 5 mg/kg (pediatric, max 250mg)
* **Montelukast**: 10 mg orally daily (adults), 4 mg daily (pediatric)
* **Evidence**: Improved pulmonary function and reduced corticosteroid exposure in post-transplant BO

**Supportive Care Measures**

**Respiratory support**:

* Supplemental oxygen for hypoxemia
* Airway clearance techniques if bronchiectasis present
* Hypertonic saline nebulization for secretion management

**Bronchodilators**:

* Limited effectiveness due to fixed obstruction
* **Tiotropium**: May provide modest benefit in some patients
* Trial of β₂-agonists reasonable if responsive

**Nutritional support**:

* High prevalence of malnutrition (21.7%) and nutritional risk (17.5%)
* Requires active nutritional intervention and monitoring

**Preventive measures**:

* Annual influenza vaccination
* Pneumococcal vaccination
* Strict avoidance of tobacco smoke exposure
* Pulmonary rehabilitation and exercise therapy

**Advanced/Experimental Therapies**

**Emerging treatments** (investigational):

* **Mesenchymal stem cell therapy**: Early-phase trials
* **Extracorporeal photopheresis**: Rescue therapy for severe cases
* **TNF-α inhibitors**: Limited case reports
* **Inhaled cyclosporine**: Investigational in severe cases

**Surgical Interventions**

**Lung transplantation**:

* Reserved for end-stage disease with severe functional impairment
* **Pediatric considerations**: May be prioritized to allow survival to adulthood
* **Outcomes**: Re-transplantation rates significant due to chronic allograft dysfunction
* **Bridge therapy**: ECMO may be used in selected critically ill candidates

**Prevention Tips:**

The primary prevention of bronchiolitis obliterans in people who have received either lung transplant or HSCT therapy is immunosuppression. In regards to post lung transplantation, the combination of calcineurin inhibitor combined with a purine synthesis inhibitor and a glucocorticoid is the general regimen used.People also have a baseline post-transplant lung function testing done in order to determine if their lung function is declining over time. People who are post-HSCT their immunosuppressive regimen typically includes methotrexate in combination with a calcineurin inhibitor to prevent GVHD, a risk factor for developing bronchiolitis obliterans.

**Vaccination programs**:

* **Adenovirus vaccination**: Not routinely available for civilians
* **Influenza vaccination**: Annual vaccination for all household members
* **Pneumococcal vaccination**: Standard pediatric schedule
* **Measles vaccination**: MMR vaccine series

**Infection control measures**:

* Proper hand hygiene techniques
* Respiratory etiquette (cough/sneeze into elbow)
* Isolation of children with respiratory symptoms
* Environmental cleaning and disinfection
* Avoiding crowded environments during viral seasons

**Secondary Prevention**

**Early recognition and treatment**:

* Prompt antiviral therapy when available
* Aggressive supportive care during acute viral illness
* Monitoring for persistent symptoms >6 weeks post-infection
* Early pulmonary function assessment if symptoms persist

**Environmental measures**:

* Strict tobacco smoke avoidance
* Air quality improvement (HEPA filtration)
* Avoidance of known toxic inhalational exposures

**Prognosis:**

During an acute adenoviral infection, mortality can be as high as 18.4%, but once an infection has been established BO has a low mortality rate. Patients with post-infectious BO, in contrast to those with post-transplant BO, usually exhibit clinical improvement after 2–3 years of supportive treatment, although clinical and radiological changes and changes in pulmonary function may persistent.

As the lungs develop, the diameter of the airways increases and the airways become less susceptible to obstruction. Thus, the clinical improvement observed may occur as a result of normal lung development and not represent a regression of lesions. In a study by Zhang *et al.* 22.6% of patients had clinical remission, 67.7% of patients continued to have symptoms, and 9.7% of patients died.

However, a study by Cazzato *et al.* yielded worrying findings indicating increased lung dysfunction (a decline in FEV1 of 1.01% and a decline in FEF25–75% of 1.04% per year) over time in patients with post-infectious BO, suggesting that BO may be a progressive lung disorder. Additional studies need to be performed to understand the process of inflammation caused by the disease and the better approaches to its treatment.

**Overall Prognosis**

**Variable outcomes** with three general patterns:

* **22.6%**: Clinical remission
* **67.7%**: Persistent symptoms with stable function
* **9.7%**: Progressive deterioration leading to death

**Prognostic Factors**

**Favorable prognostic indicators**:

* Higher post-bronchodilator FEV₁ at diagnosis
* Minimal inflammatory changes on initial CT
* Earlier age at onset (better lung growth potential)
* Response to initial corticosteroid therapy

**Poor prognostic indicators**:

* Severe initial lung function impairment
* Extensive inflammatory bronchiolitis on CT
* Need for mechanical ventilation during acute illness
* Stevens-Johnson syndrome as underlying cause

**Long-term Outcomes**

* **Functional improvement**: May occur through compensatory lung growth in children
* **Exercise capacity**: Often permanently reduced
* **Quality of life**: Variable, depending on disease severity
* **Life expectancy**: Generally good for stable disease; poor for progressive forms

**Complications:**

**Complications**

**Respiratory Complications**

* **Recurrent pneumonia**: Due to impaired clearance mechanisms
* **Pneumothorax**: From air trapping and hyperinflation
* **Chronic respiratory failure**: Progressive hypoxemia and hypercapnia
* **Pulmonary hypertension**: Secondary to chronic hypoxemia
* **Bronchiectasis**: Present in 88% of pediatric cases

**Growth and Development**

* **Failure to thrive**: Malnutrition in 21.7% of cases
* **Developmental delays**: Related to chronic hypoxemia
* **Exercise intolerance**: Reduced physical activity capacity
* **Chronic fatigue**: Impact on daily activities and school performance

**Treatment-related Complications**

**Corticosteroid complications**:

* Growth retardation
* Bone demineralization and fractures
* Increased infection susceptibility
* Adrenal suppression
* Glucose intolerance

**When to see a Doctor/Red Flags:**

**Go to A&E if:**

* your child is having difficulty breathing – you may notice grunting noises or their tummy sucking under their ribs
* there are pauses when your child breathes
* your child's skin, tongue or lips are blue
* your child is floppy and will not wake up or stay awake

As a parent, you may know if your child seems seriously unwell and should trust your own judgement.

**Emergency Warning Signs (Emergency Services)**

* **Severe respiratory distress**: Gasping, inability to speak in sentences
* **Cyanosis**: Blue coloration of lips, face, or fingernails
* **Altered mental status**: Confusion, extreme lethargy, unresponsiveness
* **Signs of respiratory failure**: Very rapid breathing (>60/min in infants), grunting, severe retractions

**Urgent Medical Attention (Same Day)**

* **Worsening dyspnea**: Increased shortness of breath at rest
* **Persistent fever**: Temperature >38.5°C (101.3°F) for >24 hours
* **Decreased oxygen saturation**: <92% on pulse oximetry
* **Signs of pneumonia**: New or increased cough with fever, chest pain
* **Feeding difficulties**: In infants, poor oral intake or vomiting

**Routine Medical Follow-up**

* **Persistent cough**: Lasting >6 weeks after respiratory infection
* **Exercise intolerance**: New limitation in physical activities
* **Recurrent wheezing**: Not responding to usual bronchodilator therapy
* **Weight loss or poor growth**: Nutritional concerns
* **Sleep disturbances**: Frequent nighttime awakening, snoring

**Differential Diagnoses:**

Other conditions that can present similarly include chronic obstructive pulmonary disease, asthma, bronchiectasis, hypersensitivity pneumonitis, and pneumonia.

**Primary Considerations**

**Asthma**:

* Key differences: Reversible airway obstruction, response to bronchodilators, allergic triggers
* **Distinguishing features**: Variable symptoms, family history of atopy, eosinophilia

**Cystic fibrosis**:

* Systematic organ involvement (pancreatic insufficiency, elevated sweat chloride)
* **Genetic testing**: CFTR mutations
* **Different pattern**: Upper lobe predominance on imaging

**Bronchopulmonary dysplasia**:

* **History**: Prematurity and prolonged mechanical ventilation
* **Timing**: Develops in neonatal period, not after normal early development

**Secondary Considerations**

**Primary ciliary dyskinesia**:

* **Clinical features**: Chronic sinusitis, situs abnormalities, male infertility
* **Diagnostic tests**: Nasal nitric oxide measurement, electron microscopy

**Immunodeficiency syndromes**:

* **Pattern**: Recurrent infections in multiple organ systems
* **Testing**: Quantitative immunoglobulins, lymphocyte subsets

**Alpha-1 antitrypsin deficiency**:

* **Laboratory**: Low alpha-1 antitrypsin levels
* **Pattern**: Early emphysema, liver involvement

**Guidelines:**

* **Early Detection and Monitoring:**
  + **Spirometry:** Regular spirometry (lung function tests) is crucial, especially after lung or stem cell transplant, to monitor for declines in FEV1 (forced expiratory volume in one second).
  + **High-Resolution CT (HRCT):** HRCT scans can detect air trapping and other changes indicative of BO.
  + **Bronchoscopy and Biopsy:** Bronchoscopy with transbronchial lung biopsy and bronchoalveolar lavage (BAL) can help identify infections or other causes of lung function decline.
* **Management of Transplant-Related BO:**
  + **Optimizing Immunosuppression:** Adjusting or adding immunosuppressive drugs like tacrolimus, cyclosporine, mycophenolate mofetil, and prednisone is a primary approach.
  + **Azithromycin:** Azithromycin has been shown to reduce the incidence and potentially improve lung function in some cases.
  + **Gastroesophageal Reflux Control:** Managing gastroesophageal reflux (GERD) is recommended as it can exacerbate BO.
  + **Extracorporeal Photopheresis:** This treatment may help slow lung function decline.
  + **Lung Retransplantation:** In severe, progressive cases, lung retransplantation may be considered.
* **Management of Non-Transplant Related BO:**
  + **Identifying and Removing Offending Agents:** If a specific cause is identified (e.g., exposure to certain chemicals), removing the exposure is crucial.
  + **Symptomatic Treatment:** Treating symptoms like cough and shortness of breath is important.

**Supportive Care:**

* **Vaccinations:** Ensuring up-to-date vaccinations (including flu, pneumonia, and COVID-19) is essential.
* **Infection Prevention:** Practicing good hygiene and avoiding exposure to infections can help.
* **Pulmonary Rehabilitation:** Encouraging regular exercise and a healthy lifestyle can improve lung function and overall well-being

Important Considerations:

* **Multidisciplinary Approach:** Managing BO often requires a team of specialists, including pulmonologists, transplant physicians, and other healthcare professionals.
* **Individualized Treatment:** Treatment plans should be tailored to the individual patient's specific situation, considering the cause of BO, severity, and overall health.
* **Ongoing Research:** Research is ongoing to develop new therapies and improve outcomes for BO.

**Expert-Reviewed Q&A:**

**"Will my child outgrow this condition?"**

**Expert response**: Unlike common childhood asthma, PIBO involves irreversible scarring of the small airways and cannot be "outgrown." However, children may experience functional improvement through compensatory lung growth as they develop. Approximately 23% of children achieve clinical remission, while 67% maintain stable symptoms. The key is optimal management to prevent progression and maximize remaining lung function.

**"Is PIBO contagious?"**

**Expert response**: PIBO itself is not contagious. It represents the aftermath of severe lung injury, typically from viral infections that have already resolved. However, children with PIBO may be more susceptible to respiratory infections due to impaired lung function, so infection prevention measures are crucial.

**"What activities can my child participate in?"**

**Expert response**: Activity levels should be individualized based on your child's functional capacity and oxygen saturation. Most children can participate in modified activities, but high-intensity sports may be limited. We recommend pulmonary rehabilitation and gradual activity progression under medical supervision. The goal is maintaining fitness while avoiding excessive respiratory stress.

**"Are there any experimental treatments available?"**

**Expert response**: Several investigational therapies are being studied, including mesenchymal stem cell therapy, extracorporeal photopheresis, and novel anti-inflammatory agents. However, these remain experimental and are typically reserved for severe, progressive cases. We monitor emerging research closely and can discuss clinical trial eligibility when appropriate.

**"How often will my child need medical monitoring?"**

**Expert response**: Regular monitoring is essential and typically includes pulmonary function testing every 3-6 months, annual CT scans to assess disease progression, nutritional assessments, and sleep studies due to increased risk of nocturnal hypoxemia. The frequency may be adjusted based on disease stability and symptoms.

**"What is the long-term outlook for children with PIBO?"**

**Expert response**: The prognosis varies significantly. Many children maintain stable lung function with appropriate treatment, allowing for relatively normal childhood activities and development. However, some may experience progressive decline requiring more intensive interventions. Early diagnosis and treatment optimization are crucial for the best possible outcomes. We work closely with families to develop individualized management plans and provide ongoing support.

**Summary:**

Pediatric bronchiolitis obliterans is a rare, chronic obstructive lung disease that predominantly affects young children following severe respiratory tract infections, particularly adenovirus pneumonia. The condition is characterized by irreversible small airway fibrosis leading to persistent airway obstruction, exercise intolerance, and chronic respiratory symptoms.

**Key clinical features** include persistent cough, wheezing, and dyspnea lasting >6 weeks after respiratory infection, with characteristic mosaic perfusion patterns on CT imaging and fixed obstructive patterns on pulmonary function testing. **Diagnosis relies** on clinical criteria combining typical history, imaging findings, lung function abnormalities, and exclusion of other chronic lung diseases.

**Treatment remains empirical** with no established protocols, focusing on anti-inflammatory therapy (pulse corticosteroids, azithromycin), supportive care (oxygen, nutrition, airway clearance), and prevention of complications. **Combination therapy** with fluticasone, azithromycin, and montelukast shows promise in reducing systemic steroid requirements.

**Prognosis is variable** with approximately one-quarter achieving clinical remission, two-thirds maintaining stable symptoms, and 10% experiencing progressive deterioration. **Early recognition and treatment** may improve outcomes, emphasizing the importance of monitoring children with persistent respiratory symptoms following severe respiratory infections.

**Prevention strategies** focus on vaccination programs, infection control measures, and avoidance of environmental toxins. **Multidisciplinary care** involving pediatric pulmonologists, respiratory therapists, nutritionists, and support services is essential for optimal management of this complex condition.

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1. **Alveolar Hemorrhage**

**Definition:**

Pediatric alveolar hemorrhage refers to bleeding from the pulmonary microvasculature into the alveolar spaces in children. This life-threatening condition is characterized by the accumulation of red blood cells originating from the alveolar capillaries, arterioles, or venules. The term encompasses both acute idiopathic pulmonary hemorrhage (AIPH) in infants and diffuse alveolar hemorrhage (DAH) in older children.

The CDC defines acute idiopathic pulmonary hemorrhage as "the sudden onset of pulmonary hemorrhage in a previously healthy infant in whom differential diagnoses and neonatal medical problems that might cause pulmonary hemorrhage have been ruled out". This condition presents with hemoptysis or blood in the airway, acute severe respiratory distress requiring mechanical ventilation, and bilateral pulmonary infiltrates on chest imaging.

**Causes:**

Etiology of DAH

In a study done with 74 patients, the causes of DAH were classified into five etiological groups (*[Table 1](https://pmc.ncbi.nlm.nih.gov/articles/PMC8649607/" \l "t1)*). Possible IPH was the most frequent cause (48 cases, 64.9%). Immune-mediated disorders were diagnosed in 7 patients: three patients with anti-neutrophil cytoplasmic antibody (ANCA)-related vasculitis, three patients with Goodpasture syndrome, and one patient with Evans syndrome (9.5%). Liver dysfunction was found in four patients: three patients with acute liver function failure and one patient with Favism (5.4%). Cardiovascular diseases were found in 3 patients: two patients with heart failure and one patient with vascular malformation (4.1%).

Table 1. Underlying etiology of DAH.

| **Etiology** | **Number (%)** |
| --- | --- |
| Idiopathic pulmonary hemosiderosis (IPH) | 48 (64.9) |
| Miscellaneous causes | 12 (16.2) |
| Sepsis | 6 |
| Pneumonia-induced acute respiratory distress syndrome (ARDS) | 3 |
| Enterovirus A71 (EV71) infection | 1 |
| Influenza B infection | 1 |
| Drowning | 1 |
| Immune-mediated disorders | 7 (9.5) |
| Anti-neutrophil cytoplasmic antibody (ANCA) associated granulomatous vasculitis | 3 |
| Goodpasture syndrome | 3 |
| Evans syndrome | 1 |
| Liver dysfunction | 4 (5.4) |
| Acute liver failure | 3 |
| Favism | 1 |
| Cardiovascular disorders | 3 (4.1) |
| Heart failure | 2 |
| Vascular malformation | 1 |

In the miscellaneous causes group (12 cases, 16.2%), the most common etiology was infection, which included pneumonia-induced acute respiratory distress syndrome (ARDS) (3 cases), sepsis (6 cases), and virus infection (2 cases). The infection group included four immunosuppressed patients (one with primary immunodeficiency; one with primary immunodeficiency who had received a stem cell transplant; one with Langerhans cell histiocytosis, who was receiving chemotherapy; and one with leukemia, who had received a bone marrow transplant). All immunocompromised patients were diagnosed with sepsis. Of the seven immunocompetent patients (aside from the drowning patient), one was diagnosed with Enterovirus A71 (EV71) infection and one was diagnosed with influenza B virus infection.

Patient characteristics with different etiologies

Demographic characteristics are shown in *[Table 2](https://pmc.ncbi.nlm.nih.gov/articles/PMC8649607/" \l "t2)*. The median age was 3.5 years (ranging from 1.5 to 7 years). The median age of the IPH group was lower than that of the immune mediated group and higher than those of the liver dysfunction and miscellaneous causes groups. There were no significant gender differences among the groups. The mean hemoglobin level was 76.8±32 g/L. The hemoglobin level was the highest in the cardiovascular disease group, and there were no significant differences among immune-mediated, liver dysfunction, and IPH groups.

Table 2. Patient characteristics and outcome according to the etiology.

| **Variables** | **All patients (n=74)** | **Immune related (n=7)** | **Liver dysfunction (n=4)** | **Cardiovascular causes (n=3)** | **Miscellaneous (infection and other conditions) (n=12)** | **IPH (n=48)** | **P value** |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Age, year | 3.5 (1.5–7) | 9 (6.0–11.0) | 0.15 (0.1–0.425) | 13 (0.6–13) | 1.5 (0.7–5.5) | 4.0 (2–6.8) | 0.001 |
| Male gender, % | 38 (51.4) | 4 (57.1) | 4 (100.0) | 3 (100.0) | 4 (33.3) | 23 (47.9) | 0.078 |
| Course, month | 1 (0.3–12.3) | 1 (1–6) | 0.7 (0.325–4.75) | 0.1 (0.075–0.55) | 0.25 (0.1–3) | 4.0 (1.0–16) | 0.006 |
| Presenting symptoms |  |  |  |  |  |  |  |
| Fever | 29 (39.2) | 2 (28.6) | 2 (50.0) | 1 (33.3) | 8 (66.7) | 16 (33.3) | 0.288 |
| Cough | 45 (60.8) | 3 (42.9) | 0 (0) | 1 (33.3) | 3 (25.0) | 38 (79.2) | <0.001 |
| Anemia | 62 (83.8) | 7 (100.0) | 3 (75.0) | 0 (0) | 7 (58.3) | 45 (93.8) | <0.001 |
| Hemoptysis | 48 (64.9) | 4 (57.1) | 1 (25.0) | 3 (100.0) | 9 (75) | 31 (64.6) | 0.280 |
| Dyspnea | 33 (44.6) | 3 (42.9) | 3 (75.0) | 3 (100.0) | 11 (91.7) | 12 (25.0) | <0.001 |
| Hypoxia | 32 (43.2) | 4 (57.1) | 4 (100.0) | 2 (66.7) | 11 (91.7) | 11 (22.9) | <0.001 |
| Clubbing | 2 (2.7) | 0 (0) | 0 (0) | 1 (33.3) | 0 (0) | 1 (2.1) | 0.024 |
| Crackles | 20 (27.0) | 0 (0) | 0 (0) | 1 (33.3) | 6 (50.0) | 13 (27.1) | 0.123 |
| Hb, g/L | 76.8±32 | 67.3±22.6 | 82.8±15.2 | 159±64.9 | 94.4±30.1 | 68.1±22.6 | 0.002 |
| Pulmonary infiltrates | 66 (89.2) | 7 (100.0) | 3 (75.0) | 3 (100.0) | 9 (75.0) | 44 (91.7) | 0.309 |
| DAH classical triad\* | 36 (48.6) | 4 (57.1) | 1 (25.0) | 0 (0) | 4 (33.3) | 27 (56.3) | 0.192 |

\*, refers to hemoptysis, anemia and pulmonary infiltrates on chest imaging.

The DAH triad of hemoptysis, iron deficiency anemia, and pulmonary infiltrates was observed in 48.6% of the patients. Ten patients in the IPH group and three patients in the immune-mediated group did not have hemoptysis. No difference was observed in the proportion of fever, hemoptysis, crackles, and pulmonary infiltrates between the IPH group and the other groups. However, in the liver dysfunction group, none of the patients had cough, and only one patient had hemoptysis. None of the patients in the cardiovascular disease group had anemia.

The proportion of dyspnea and hypoxia was lowest in the IPH group, followed by the immune-mediated group. Patients with miscellaneous causes (infection and drowning) had the highest proportions of dyspnea (91.7%) and hypoxia (91.7%).

**Risk Factors:**

**Environmental Factors:**

* Male sex
* Lack of breastfeeding
* Household smoking exposure
* Water damage in homes within previous 6 months
* Exposure to molds and fungi (including Stachybotrys)

**Medical Risk Factors:**

* Prematurity and very low birth weight
* Patent ductus arteriosus
* Coagulopathies
* Respiratory distress syndrome
* Down syndrome (increased risk)
* Prior hematopoietic stem cell transplantation

**Signs & Symptoms:**

**Clinical Presentation**

**The classic triad of pediatric alveolar hemorrhage includes:**

1. Iron deficiency anemia
2. Hemoptysis (though absent in up to 33% of cases)
3. Diffuse parenchymal infiltrates on chest imaging

**Common Symptoms:**

* Anemia (87% of patients)
* Cough (32%)
* Dyspnea (35%)
* Hemoptysis (42% - notably less common in children than adults)
* Respiratory distress or failure
* Fatigue and poor growth
* Pallor and cyanosis

**Physical Findings:**

* Tachypnea and chest retractions
* Diminished breath sounds
* Crackles may be absent
* Signs of anemia and hypoxemia

**Severity Classification**

The CDC has established severity criteria for AIPH in infants, categorizing cases as clinically confirmed, probable, or suspected based on specific clinical criteria including bleeding evidence, respiratory support requirements, and radiographic findings.

**Medical Codes:**

**Relevant ICD-10 Codes:**

* **P26.1**: Massive pulmonary hemorrhage originating in the perinatal period
* **R04.81**: Acute idiopathic pulmonary hemorrhage in infants
* **R04.2**: Hemoptysis
* **J94.2**: Hemothorax
* **D68.9**: Coagulation defect, unspecified

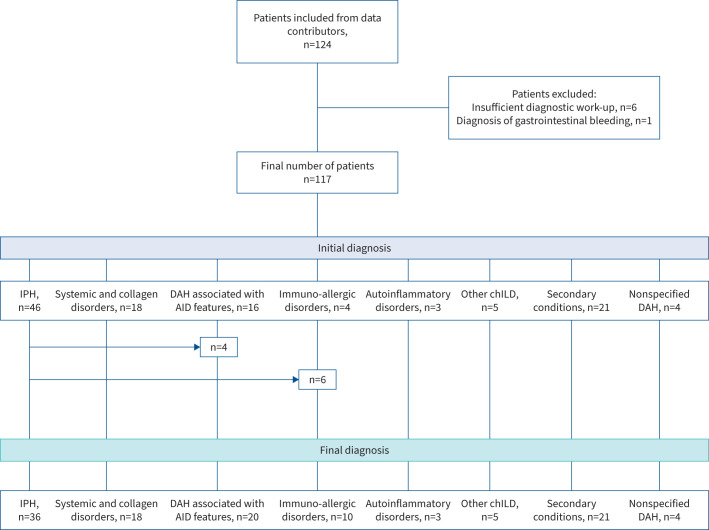
**Diagnosis Mapping:**

In a study conducted with clinicians from 26 centers in 15 countries submitted 124 patient cases of whom 117 were included. Six patients were excluded due to missing information regarding diagnostic workup and one was miscategorised. Detailed information on contributing centers is available in [supplementary table S1](http://openres.ersjournals.com/lookup/doi/10.1183/23120541.00733-2022.figures-only" \l "fig-data-supplementary-materials" \t "_blank).

**Diagnosis**

[Figure 1](https://pmc.ncbi.nlm.nih.gov/articles/PMC10123512/" \l "F1) shows the diagnosis repartition into eight subgroups: 22% (n=10) of patients were reallocated from IPH to other groups. Further details of diagnosis and baseline characteristics are presented in [tables 1](https://pmc.ncbi.nlm.nih.gov/articles/PMC10123512/" \l "TB1) and [2](https://pmc.ncbi.nlm.nih.gov/articles/PMC10123512/" \l "TB2).

FIGURE 1.

[](https://www.ncbi.nlm.nih.gov/core/lw/2.0/html/tileshop_pmc/tileshop_pmc_inline.html?title=Click%20on%20image%20to%20zoom%26p=PMC3%26id=10123512_00733-2022.01.jpg)

Inclusion process and distribution of patients with diffuse alveolar haemorrhage (DAH). IPH: idiopathic pulmonary haemosiderosis; AID: autoimmune disease; chILD: childhood interstitial lung disease.

TABLE 1.

Diagnosis in patients with diffuse alveolar haemorrhage (DAH)

| **Diagnosis** |  |
| --- | --- |
| **All DAH patients** | 117 |
| **Idiopathic pulmonary haemosiderosis** | 36 |
| **DAH associated with autoimmune features** | 20 |
| Nonspecific but ANA positive | 8 |
| Nonspecific ANCA-associated vasculitis | 9 |
| Nonspecific but SMA positive | 1 |
| Nonspecific but positive rheumatoid factor | 2 |
| **Systemic and collagen disorders** | 18 |
| Granulomatosis with polyangiitis | 6 |
| Microscopic polyangiitis | 3 |
| Polyarthritis nodosum | 1 |
| Churg–Strauss syndrome | 2 |
| Anti-glomerular basement membrane disease | 3 |
| Systemic lupus erythematosus | 1 |
| Antiphospholipid syndrome | 1 |
| Membranous glomerulopathy | 1 |
| **Immuno-allergic disorders** | 10 |
| Pulmonary haemorrhage with cow's milk antibody (IgG) | 4 |
| Lane–Hamilton syndrome | 6 |
| **Other chILD** | 5 |
| Pulmonary interstitial glycogenosis | 2 |
| Postinfectious bronchiolitis obliterans | 1 |
| SP-C disorder | 1 |
| Nonspecific lung fibrosis | 1 |
| **Autoinflammatory diseases** | 3 |
| COPA syndrome | 2 |
| STAT-3 mutation | 1 |
| **Secondary to other conditions** | 21 |
| Infectious | 7 |
| Malignancy | 1 |
| Cardiovascular disease (including pulmonary arterial hypertension) | 4 |
| Lung damage due to exogenous toxicity | 2 |
| Coagulopathy | 1 |
| Bone marrow transplant-related lung injury | 1 |
| Transfusion-related lung injury | 1 |
| Cantu syndrome with impaired lung growth and pulmonary hypertension | 1 |
| Wilson disease with acute liver failure | 1 |
| Familiar cholestasis type 1: post-liver transplantation complication | 1 |
| Wiskott–Aldrich syndrome with severe septic shock and coagulopathy | 1 |
| **Nonspecified DAH diagnosis** | 4 |

ANA: antinuclear antibodies; ANCA: anti-neutrophil cytoplasm antibodies; SMA: smooth-muscle antibodies; chILD: childhood interstitial lung disease; SP-C: surfactant protein C; COPA: COPI coat complex subunit α; STAT-3: signal transducer and activator of transcription 3.

TABLE 2.

Baseline characteristics and age at debut and diagnosis

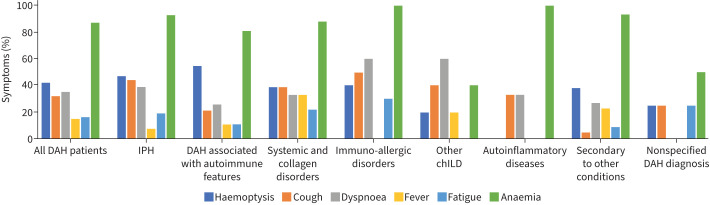
| **Diagnosis** | **Subjects n** | **Females** | **Age at debut** | **Age at diagnosis** | **Diagnostic delay** | **Trisomy 21** |
| --- | --- | --- | --- | --- | --- | --- |
| **All DAH patients** | 117 | 67 (57) | 5 (2–12.9) | 6.1 (3–13) | 2 (0–12) | 7 (6) |
| **IPH** | 36 | 21 (60) | 3.0 (1.3–5.0) | 4.2 (3.0–7.4) | 10 (2–21) | 3 (8) |
| **DAH associated with autoimmune features** | 20 | 13 (65) | 4.5 (1.8–11) | 4.8 (2.3–11) | 2 (0–11) | 0 |
| **Systemic and collagen disorders** | 18 | 12 (67) | 14.2 (12.1–15.4) | 14.2 (12.6–15.5) | 0 (0–3) | 1 (6) |
| **Immuno-allergic disorders** | 10 | 7 (70) | 5.1 (2.5–11.6) | 5.2 (3.4–12.7) | 2 (1–4) | 0 (0) |
| **Other chILD** | 5 | 2 (40) | 1.0 (0–5.8) | 1.3 (0–5.8) | 0 (0–0) | 0 (0) |
| **Autoinflammatory diseases** | 3 | 2 (67) | 2.0 (2.0–2.1) | 5.0 (4.0–9.0) | 35 (24–84) | 0 (0) |
| **Secondary to other conditions** | 21 | 9 (43) | 7.4 (1.2–14.1) | 7.6 (3.0–15.1) | 2 (0–9) | 2 (10) |
| **Nonspecified DAH diagnosis** | 4 | 1 (25) | 12 (6.8–15,3) | 10.3 (8.6–15.8) | 1 (0–1) | 1 (25) |

Data are presented as n (%) or median (IQR), unless otherwise stated. DAH: diffuse alveolar haemorrhage; IPH: idiopathic pulmonary haemosiderosis; chILD: childhood interstitial lung disease.

Clinical presentation

The median (IQR) age at presentation was 5 (2–12.9) years with a median (IQR) diagnostic delay of 2 (0–12) months ([table 2](https://pmc.ncbi.nlm.nih.gov/articles/PMC10123512/" \l "TB2)). The sex distribution was 57% females (ranging from 20% to 70%). Overall, anaemia (87%), haemoptysis (42%), dyspnoea (35%) and cough (32%) were the most frequent clinical symptoms at initial presentation with only minor differences between the subgroups ([figure 2](https://pmc.ncbi.nlm.nih.gov/articles/PMC10123512/" \l "F2)). In 20 (17%) haemoptysis was the only respiratory symptom, while respiratory symptoms were absent in 27 (23%) at initial presentation. Of those without respiratory symptoms, anaemia was described in 21 (78%) at initial presentation. Diagnostic delay was not different between patients with and without respiratory symptoms at initial presentation (p=0.67).

FIGURE 2.

[](https://www.ncbi.nlm.nih.gov/core/lw/2.0/html/tileshop_pmc/tileshop_pmc_inline.html?title=Click%20on%20image%20to%20zoom%26p=PMC3%26id=10123512_00733-2022.02.jpg)

Symptoms and clinical presentation. The proportion of symptoms in each subgroup reported as percentages. Note: one patient may have more than one symptom. DAH: diffuse alveolar haemorrhage; IPH: idiopathic pulmonary haemosiderosis; chILD; childhood interstitial lung disease.

Clinical workup

HRCT (94%), BAL (85%) and echocardiography (80%) were the most frequently performed diagnostic procedures. Lung biopsy was performed in 49 (42%) and genetic testing was performed in 52 (44%). Rheumatological workup was performed on 103 patients (88%) of whom 41 (40%) tested positive for one or more autoantibodies. Anti-transglutaminase IgA and cow's milk IgG were elevated in 17% and 14% of those who had been tested, respectively. More detailed information on diagnostic workup performed in each subgroup is available in supplementary tables S2 and S3). Pulmonary function data were available in 36 (68%) of 53 patients 6 years of age or older. Pulmonary function data demonstrated a restrictive impairment, obstructive impairment or normal pulmonary function in 22 (61%), 4 (11%) and 11 (31%) patients, respectively (supplementary table S4).

TABLE 3.

Diagnostic workup in 117 patients with diffuse alveolar haemorrhage (DAH)

|  | **Patients who were tested, n (%)** | **Of those examined who tested positive, n (%)** |
| --- | --- | --- |
| **HRCT** | 110 (94) |  |
| Ground-glass opacity |  | 78 (71) |
| **BAL** | 100 (85) |  |
| HLM |  | 74 (74) |
| Fresh bleeding |  | 28 (28) |
| Findings not described |  | 14 (14) |
| **Lung biopsy** | 49 (42) |  |
| HLM |  | 25 (51) |
| Vasculitis/capillaritis |  | 5 (10) |
| Fibrosis |  | 8 (16) |
| **Echocardiography** | 94 (80) |  |
| PAH |  | 11 (12) |
| **Genetic analysis (WES/NGS/not described)** | 52 (44) (1/8/43) |  |
| *COPA* |  | 2# |
| *STAT-3* |  | 1# |
| *APT7B* |  | 1# |
| *SFTPC* |  | 1# |
| *CYBB* |  | 1# |
| *NKX2.1* |  | 2# |
| *TBX4* |  | 1# |
| Other¶ |  | 7# |
| COPA negative |  | 12# |
| **Autoantibodies** | 103 (88) |  |
| ANCA | 100 (85) | 17 (17) |
| ANA | 96 (82) | 17 (18) |
| Anti-double-stranded DNA and anti-SMA | 74 (63) | 7 (9) |
| RF, IgM | 66 (56) | 10 (15) |
| AEA | 51 (44) | 5 (10) |
| **Specific immunoglobulins** |  |  |
| ATA, IgA | 69 (59) | 12 (17) |
| ATA, IgG | 55 (47) | 4 (7) |
| Cow's milk, IgG | 37 (32) | 6 (14) |

HRCT: high-resolution computed tomography; BAL: bronchoalveolar lavage; HLM: haemosiderin-laden macrophage; PAH: pulmonary arterial hypertension; *COPA*: COPI coat complex subunit α; *STAT-3*: signal transducer and activator of transcription 3; *ATP7B*: ATPase cobber transporting β; *SFTPC*: surfactant protein C; *CYBB*: cytochrome B-245 β chain; *NKX2.1*: NK Homeobox 1; *TBX4*: T-box transcription factor 4; ANCA: antineutrophilic cytoplasmic antibodies; ANA: antinuclear antibodies; SMA: smooth muscle antibodies; RF: rheumatoid factor; AEA: anti-endomysium antibodies; ATA: anti-transglutaminase. #: human leukocyte antigen DQ α 1 (HLA DQA1), HLA DQB1 and HLA DQ β 1, n=1. 22q11 (DiGeorge's syndrome), n=1. PFIC-1 (progressive familial intrahepatic cholestasis 1), n=1). WASp (Wiscott–Aldrich Syndrome), n=1. FLT3-ITD (fms-like tyrosine kinase 3 internal tandem duplication), n=1. WT1 (Wilms’ tumour 1), n=1. Heterozygote for *CSF2RB* (colony stimulating factor 2 receptor subunit β) (pulmonary alveolar proteinosis), n=1. ¶: percentage not reported since the number of patients who had been tested for each condition/mutation is uncertain.

Other diagnostic measures to be taken include:

**Initial Assessment**

**Essential Diagnostic Studies:**

1. **Complete Blood Count**: Assessment for anemia, thrombocytopenia
2. **Coagulation Studies**: PT, aPTT, INR, fibrinogen
3. **Chest Imaging**: X-ray and high-resolution CT
4. **Arterial Blood Gas**: Assessment of oxygenation and ventilation
5. **Urinalysis**: Evaluation for concurrent renal involvement

**Advanced Diagnostic Procedures**

**Bronchoscopy and Bronchoalveolar Lavage (BAL):**

* Gold standard for diagnosis confirmation
* Sequential BAL showing increasingly bloody return
* Identification of hemosiderin-laden macrophages (>20% diagnostic)
* Can be performed safely under general anesthesia with face mask ventilation

**Immunologic Testing:**

* ANCA (c-ANCA, p-ANCA)
* Anti-glomerular basement membrane antibodies
* Antinuclear antibodies (ANA)
* Complement levels (C3, C4)
* Anti-double-stranded DNA

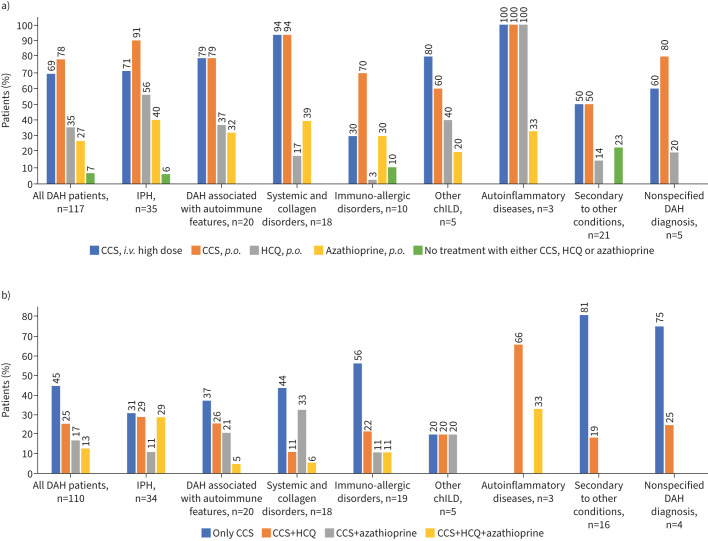
**Cardiac Evaluation:**

* Echocardiography to assess for congenital heart disease, pulmonary hypertension
* Cardiac catheterization if vascular malformations suspected

**Treatment Options:**

In the same study, systemic corticosteroids (sCCS) was the most frequently reported medical treatment (93% of patients), administered as intravenous (*i.v.*) high-dose pulse methylprednisolone (15–30 mg·kg−1 for 3 days) (69%) or oral prednisolone (78%). 72% of all patients received sCCS treatment with both *i.v.* pulses and oral prednisolone. Monotherapy with sCCS was used in 43% of patients, while sCCS were supplemented with either hydroxychloroquine, azathioprine or both in 23%, 14% and 12% of patients, respectively ([figure 3](https://pmc.ncbi.nlm.nih.gov/articles/PMC10123512/" \l "F3)). Other frequently administered medical treatments included mycophenolate mofetil, cyclosporine, cyclophosphamide and rituximab as the most frequent ([supplementary table S5](http://openres.ersjournals.com/lookup/doi/10.1183/23120541.00733-2022.figures-only" \l "fig-data-supplementary-materials" \t "_blank)). Two patients (a patient diagnosed with IPH and a patient with STAT3 mutation) required lung transplantation.

FIGURE 3.

[](https://www.ncbi.nlm.nih.gov/core/lw/2.0/html/tileshop_pmc/tileshop_pmc_inline.html?title=Click%20on%20image%20to%20zoom%26p=PMC3%26id=10123512_00733-2022.03.jpg)

Medical treatment. a) Percentage of patients in each subgroup treated with systemic corticosteroids (CCS), hydroxychloroquine (HCQ), azathioprine or none of the above. b) Percentage of patients receiving different combination of treatment in each subgroup. Only patients who have received treatment are included. DAH: diffuse alveolar haemorrhage; IPH: idiopathic pulmonary haemosiderosis; chILD: childhood interstitial lung disease.

The median (IQR) treatment duration of *i.v.* CCS pulses was 3 (1–9) months for all DAH patients whereas oral prednisolone, hydroxychloroquine and azathioprine treatment continued for 1.3 (0.5–3.5), 2.8 (1.5–4.1) and 1.7 (0.5–3.2) years, respectively. No significant difference in length of treatment was found between the largest subgroups (IPH, systemic and collagen disorders, immune-allergic conditions and secondary to other conditions).

Other managed options available include:

**Acute Management**

**Immediate Stabilization:**

1. **Airway Management**: Intubation and mechanical ventilation often required
2. **Hemodynamic Support**: IV fluids, blood products as needed
3. **Oxygen Support**: High-flow oxygen or mechanical ventilation with PEEP
4. **Coagulation Correction**: Target platelets >50,000/μL, INR <1.5

**Pharmacological Interventions**

**First-Line Therapy:**  
**High-Dose Corticosteroids:**

* Methylprednisolone 30 mg/kg/day IV (up to 2g/day) for 3-5 days
* Followed by gradual tapering over 4 weeks
* Early administration associated with improved outcomes

**Hemostatic Medications:**

**Tranexamic Acid:**

* Nebulized: 250mg (children <25kg) or 500mg (children >25kg) every 6 hours
* Systemic: 10-15 mg/kg IV every 8 hours
* Effective cessation rate: 55.6% as monotherapy

**Recombinant Factor VIIa (rFVIIa):**

* Intrapulmonary: 35-50 μg/kg per dose
* Intravenous: 90-400 μg/kg per dose
* Reserved for refractory cases
* Combined approach with nebulized TXA shows 89% overall response rate

**Additional Immunosuppressive Agents:**

* Cyclophosphamide: 2 mg/kg/day for severe autoimmune cases
* Rituximab: 375 mg/m² weekly for 4 doses
* Hydroxychloroquine: 5-7 mg/kg/day for IPH
* Azathioprine: 2-3 mg/kg/day as steroid-sparing agent

**Novel Therapeutic Approaches**

**Surfactant Therapy:**

* Intratracheal administration for neonates and infants
* Counteracts hemoglobin-induced surfactant inactivation
* Most effective when administered early

**Plasmapheresis:**

* Reserved for severe autoimmune cases
* Particularly effective in Goodpasture syndrome
* Removes circulating autoantibodies

**Prevention Tips:**

**Primary Prevention**

* Antenatal corticosteroids for preterm infants
* Prophylactic indomethacin in very low birth weight infants
* Avoidance of environmental triggers (smoking, mold exposure)
* Appropriate management of underlying conditions

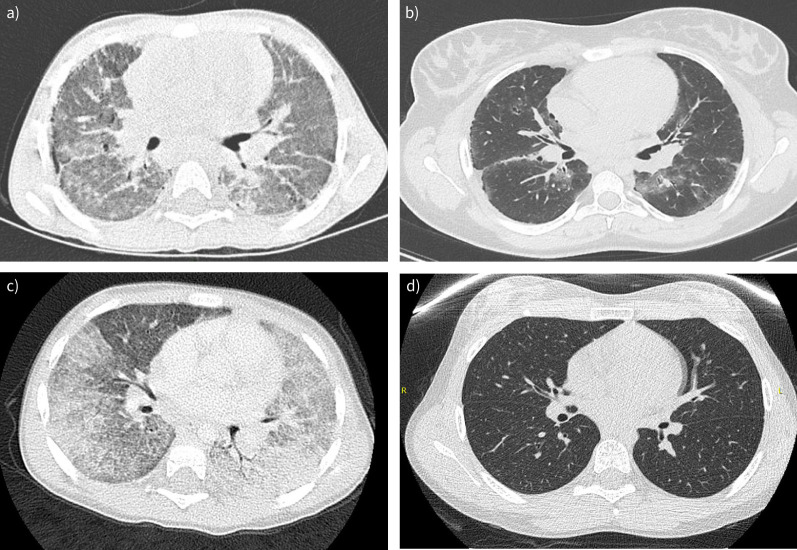
**Secondary Prevention**

* Regular monitoring in high-risk patients
* Early treatment of respiratory infections
* Compliance with maintenance immunosuppressive therapy
* Vaccination against respiratory pathogens

**Prognosis:**

Under the study mentioned earlier, the median (IQR) follow-up period was 3.2 (1.2–7.0) years from diagnosis. In patients with both baseline and long-term follow-up lung function data (n=44), there was no significant change except in FVC and total lung capacity (TLC) with an improvement of 21% and 17% (p<0.001), respectively. Follow-up HRCT or radiograph was performed in 101 patients (86%) with a median (IQR) time of 2.5 (1.0–7.0) years after the baseline radiology ([figure 4](https://pmc.ncbi.nlm.nih.gov/articles/PMC10123512/" \l "F4)). Persisting abnormal radiology was recorded in 61/101 (60%) of patients (50% of patients otherwise considered healthy; 73% of patients considered as chronic but not on medical treatment and 80% of patients with ongoing treatment) ([Table S6](http://openres.ersjournals.com/lookup/doi/10.1183/23120541.00733-2022.figures-only" \l "fig-data-supplementary-materials" \t "_blank)). Ground glass opacity (n=39), interstitial thickening (n=9) and fibrosis (n=7) were the most frequent findings described in follow-up HRCT/chest radiograph ([Table S6](http://openres.ersjournals.com/lookup/doi/10.1183/23120541.00733-2022.figures-only" \l "fig-data-supplementary-materials" \t "_blank)).

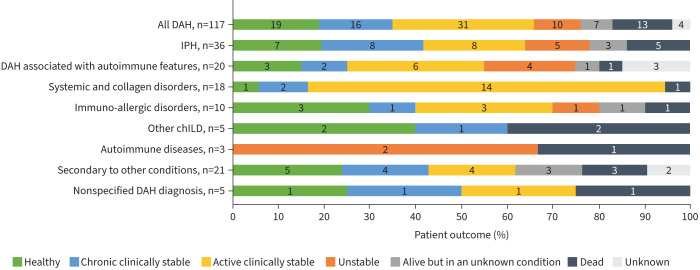
FIGURE 4.

[](https://www.ncbi.nlm.nih.gov/core/lw/2.0/html/tileshop_pmc/tileshop_pmc_inline.html?title=Click%20on%20image%20to%20zoom%26p=PMC3%26id=10123512_00733-2022.04.jpg)

Radiology and follow-up. High-resolution computed tomography (HRCT) of two patients before and after medical treatment. a) Pre-treatment HRCT of a female patient with presentation of anaemia and recurrent lower respiratory infections with first appearance at age 2.1 years. HRCT was performed at time of diagnosis at age 4.8 years. b) Latest HRCT performed on same patient after 11 years of treatment with pulse methylprednisolone and hydroxychloroquine due to several relapses. HRCT shows incomplete response to treatment. Patient is still treated with pulses of methylprednisolone and hydroxychloroquine. c) Pre-treatment HRCT of female patient with presentation of cough, dyspnoea, tachypnoea, cyanosis, haemoptysis and recurrent lower airway infection at age 6 months. HRCT was performed at time of diagnosis at 2 years of age. d) Most recent HRCT after 7 years of treatment with pulse methylprednisolone and azathioprine due to several relapses. HRCT shows almost complete regression of pathological changes. Patient is out of treatment and considered healthy.

Outcome data were available for 90%, of whom 86% were still alive: 19% were considered healthy, 16% were chronic clinical stable; 31% were active clinical stable and 12% with ongoing medical treatment and were considered unstable. 15 (13%) patients died ([figure 5](https://pmc.ncbi.nlm.nih.gov/articles/PMC10123512/" \l "F5) and supplementary table S7). Outcome in patients who tested positive for antinuclear antibodies (ANA) was not reported as either unstable or dead in any of the patients (n=17) (data not presented). The sex distribution of the 15 patients who died was 54% females. The median (IQR) time from debut of symptoms to death was 1.8 (1.3–4.0) years. The most frequent causes of death were acute bleeding (n=4), pulmonary infection (n=4), chronic respiratory failure (n=3) and complications of lung transplantation (n=2). Lung transplantation was only performed in these two patients of whom one was diagnosed with IPH and the other with STAT-3 mutation ([supplementary table S7](http://openres.ersjournals.com/lookup/doi/10.1183/23120541.00733-2022.figures-only" \l "fig-data-supplementary-materials" \t "_blank)).

FIGURE 5.

[](https://www.ncbi.nlm.nih.gov/core/lw/2.0/html/tileshop_pmc/tileshop_pmc_inline.html?title=Click%20on%20image%20to%20zoom%26p=PMC3%26id=10123512_00733-2022.05.jpg)

Patient outcome in the DAH cohort and the different subgroups presented as percentage: healthy; chronic clinically stable (chronic condition with impaired lung function and/or persistent abnormal radiology but off medication for DAH); active clinically stable (under current treatment); unstable (symptomatic and/or impaired lung function despite treatment); alive but unknown condition; unknown; and dead. DAH: diffuse alveolar haemorrhage; IPH: idiopathic pulmonary haemosiderosis; chILD; childhood interstitial lung disease.

Below are the overall survival rates for DAH:

**Survival Rates**

Overall mortality for pediatric DAH is 37%, with significant variation by etiology:

* Cardiovascular disease: 65% mortality
* Autoimmune disease: 0% mortality
* Idiopathic pulmonary hemosiderosis: 0% mortality

**Long-Term Outcomes**

* Most survivors demonstrate normal lung function
* Recurrence rates vary by underlying etiology
* IPH patients may require long-term immunosuppression
* Regular pulmonary function monitoring recommended

**Complications:**

**Acute Complications**

* Acute respiratory distress syndrome (ARDS)
* Hypoxemic respiratory failure
* Hemodynamic instability
* Cardiac arrest
* Intracranial hemorrhage (rare)

**Long-Term Complications**

* Pulmonary fibrosis
* Chronic lung disease
* Iron deficiency anemia
* Growth impairment
* Recurrent episodes

**Treatment-Related Complications**

* **Corticosteroid side effects**: Growth suppression, infection risk, bone disease
* **rFVIIa complications**: Thromboembolism (5.4% incidence), endotracheal tube obstruction
* **Mechanical ventilation**: Barotrauma, ventilator-associated pneumonia

**When to see a Doctor/Red Flags:**

**Immediate Emergency Indicators**

* Hemoptysis with respiratory distress
* Cyanosis or severe pallor
* Inability to maintain oxygen saturation >90%
* Signs of shock (hypotension, poor perfusion)
* Altered mental status
* Severe chest pain

**Clinical Warning Signs**

* Progressive dyspnea
* Recurrent epistaxis with respiratory symptoms
* Persistent cough with blood-tinged sputum
* Unexplained anemia with respiratory symptoms
* Bilateral pulmonary infiltrates on chest imaging

**Hospital Transfer Criteria**

* Need for mechanical ventilation
* Requirement for intensive care monitoring
* Massive hemoptysis (>8 mL/kg in 24 hours)
* Hemodynamic instability
* Need for specialized interventions (bronchoscopy, plasmapheresis)

**Differential Diagnoses:**

Diffuse alveolar hemorrhage (DAH) in children can be caused by various conditions, broadly categorized into immune-mediated and non-immune-mediated causes. Immune-mediated causes include:

1. Immune-Mediated:

* **ANCA-associated vasculitis:**

Conditions like microscopic polyangiitis, granulomatosis with polyangiitis (GPA), and eosinophilic granulomatosis with polyangiitis (EGPA) can cause pulmonary capillaritis and DAH.

* **Anti-glomerular basement membrane (anti-GBM) disease (Goodpasture syndrome):**

This autoimmune disease can affect the lungs and kidneys, causing DAH and glomerulonephritis.

* **Systemic lupus erythematosus (SLE):**

SLE can involve the lungs, leading to DAH and other pulmonary manifestations.

* **Idiopathic pulmonary capillaritis:**

DAH can occur without other systemic autoimmune features, but with evidence of capillaritis on lung biopsy.

* **COPA syndrome:**

A rare, inherited autoinflammatory disease causing lung and joint problems.

2. Non-Immune-Mediated:

* **Idiopathic pulmonary hemosiderosis (IPH):**

Recurrent pulmonary hemorrhages without an identified underlying cause are classified as IPH

**Coagulopathies:**

Deficiencies in clotting factors or platelet disorders can lead to bleeding, including pulmonary hemorrhage

**Cardiovascular diseases:**

Pulmonary hypertension, arteriovenous malformations, and pulmonary veno-occlusive disease can cause DAH

**Drug-induced lung injury:**

Certain medications can damage the lungs and lead to hemorrhage

**Infections:**

Pneumonia, sepsis, and other infections can sometimes cause DAH, especially in immunocompromised patients

**Foreign bodies, trauma, and airway tumors:**

These can cause focal or diffuse pulmonary hemorrhage and should be considered in the evaluation

3. Other Considerations:

* **Persistent tachypnea and failure to thrive:**

These symptoms in infants can be caused by DAH or other pulmonary or cardiovascular disorders, requiring a thorough workup

**Pulmonary-renal syndrome:**

Some conditions causing DAH can also affect the kidneys, necessitating evaluation for renal involvement

**Lung biopsy:**

In cases where a clear cause for DAH is not identified, a lung biopsy may be considered to determine the presence of capillaritis and guide treatment

**Bronchoalveolar lavage (BAL):**

BAL is a crucial diagnostic tool for DAH, helping to identify hemosiderin-laden macrophages (HLMs) and confirm the presence of alveolar hemorrhage

**Serological testing:**

Testing for antibodies related to autoimmune diseases (ANA, ANCA, anti-GBM) and other markers (e.g., milk-specific IgE) is essential.

**Guidelines:**

**Diagnostic Algorithm**

1. **Initial Assessment**: ABC approach, stabilization
2. **Imaging**: Chest X-ray, CT if indicated
3. **Laboratory**: CBC, coagulation, urinalysis, inflammatory markers
4. **Bronchoscopy**: If stable for procedure
5. **Specialized Testing**: Based on clinical suspicion

**Treatment Protocol**

1. **Stabilization**: Airway, breathing, circulation
2. **High-dose corticosteroids**: Within first 24 hours
3. **Hemostatic agents**: Nebulized TXA as first-line
4. **Advanced hemostasis**: rFVIIa for refractory cases
5. **Supportive care**: Mechanical ventilation, blood products
6. **Definitive therapy**: Based on underlying etiology

**Monitoring Guidelines**

* **Acute phase**: ICU-level monitoring, frequent assessments
* **Recovery phase**: Daily chest X-rays, serial blood counts
* **Long-term**: Pulmonary function tests, growth monitoring

**Expert-Reviewed Q&A:**

**"What causes bleeding in my child's lungs?"**

"Lung bleeding in children can result from various causes including autoimmune diseases where the body's immune system attacks lung blood vessels, heart conditions that increase pressure in lung vessels, infections, or bleeding disorders. In many cases, especially in younger children, we may not identify a specific cause initially, which we call idiopathic pulmonary hemorrhage."

**"Is this condition life-threatening?"**

"Pediatric lung hemorrhage is indeed a serious condition that requires immediate medical attention and often intensive care. However, with prompt and appropriate treatment, many children recover completely. The outlook depends on the underlying cause - children with autoimmune causes generally respond well to treatment, while those with heart-related causes may have more challenges."

**"What are the long-term effects?"**

"Most children who survive the acute episode recover with normal lung function. However, some may require long-term medications to prevent recurrence, especially if an autoimmune condition is identified. Regular follow-up with a pediatric pulmonologist is important to monitor lung function and prevent complications.”

**"How is the treatment administered?"**

"Treatment typically involves high-dose steroids given intravenously to reduce inflammation, along with medications to help stop bleeding. Some children may receive nebulized medications directly into the lungs. Most children require intensive care with mechanical ventilation initially, but many can be weaned off support as they improve."

**"Will my child need surgery?"**

"Surgery is rarely needed for lung hemorrhage itself. However, if an underlying condition like a vascular malformation is found, interventional procedures might be recommended. Most treatment is medical rather than surgical."

**"Can this happen again?"**

"Recurrence depends on the underlying cause. Children with well-controlled autoimmune conditions on appropriate medications rarely have recurrences. Those with structural problems or certain chronic conditions may have higher recurrence risks, which is why ongoing monitoring is crucial."

**"What warning signs should I watch for?"**

"Seek immediate emergency care if your child develops difficulty breathing, coughing up blood, persistent cough with blood-tinged sputum, blue coloring around the lips or face, severe paleness, or seems unusually tired or weak. Any respiratory symptoms combined with these signs warrant immediate medical attention."

**Summary:**

Pediatric alveolar hemorrhage represents a heterogeneous group of life-threatening conditions requiring prompt recognition and aggressive multidisciplinary management. The condition varies significantly by age group, with acute idiopathic pulmonary hemorrhage predominating in infants and diffuse alveolar hemorrhage from various causes affecting older children. Early diagnosis through bronchoscopy with bronchoalveolar lavage remains the gold standard, while high-dose corticosteroids constitute first-line therapy. Novel approaches including nebulized tranexamic acid and intrapulmonary recombinant factor VIIa have shown promise in refractory cases. Despite the serious nature of this condition, with appropriate intensive care management and targeted therapy, many children achieve complete recovery with normal long-term lung function. Ongoing research continues to refine treatment protocols and improve outcomes for these critically ill patients.

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1. **Connective Tissue and Immune-Mediated Lung Disorder**

**Definition:**

Pediatric connective tissue and immune-mediated lung disorders represent a heterogeneous group of autoimmune diseases that affect the lung parenchyma, interstitium, and surrounding tissues in children. These conditions, **also** **known as** childhood interstitial lung disease (chILD) associated with connective tissue diseases, are characterized by sustained inflammation, circulating autoantibodies, and progressive lung damage. The term "interstitial" refers to the tissue and space around the air sacs (alveoli) of the lungs, although other lung structures including airways, blood vessels, and pleura may also be involved.

Interstitial lung diseases (ILDs) in childhood are a diverse group of conditions that primarily involve the alveoli and perialveolar tissues, leading to derangement of gas exchange and diffuse infiltrates on radiographs. Because ILDs can involve the distal airspaces as well as the interstitium, the terms diffuse lung disease or diffuse infiltrative lung disease have been suggested. Although this nomenclature may be more accurate than ILD, childhood interstitial lung disease (chILD) has become the preferred term.

**Causes:**

Connective tissue and immune mediated lung disorders or ILD in children can be classified in many ways.In several clinical series, the diagnosis remained undetermined in approximately 25% of cases. Several important non-chILD disorders present with chronic respiratory symptoms and findings of diffuse radiographic infiltrates and must be considered in the differential diagnosis.

An etiologic classification system proposed by Griese combines pediatric and adult ILD into four main categories: lung-only disorders, systemic disease–related disorders, exposure-related disorders, and vascular disorders.ILD can also be classified based on histopathologic findings (see ILD classification systems below).

Classification systems vary internationally; however, a clinical classification of chILD is listed below.

Diffuse developmental disorders

Diffuse developmental disorders include the following:

* Acinar dysplasia
* Congenital alveolar dysplasia
* Alveolar-capillary dysplasia with pulmonary vein misalignment

Lung growth abnormalities

Lung growth abnormalities are listed below:

* Pulmonary hypoplasia
* Chronic neonatal lung disease (bronchopulmonary dysplasia [BPD])
* Associated with chromosomal disorders (ie, trisomy 21)
* Associated with congenital heart disease

Surfactant dysfunction mutations and related disorders

Surfactant dysfunction mutations and related disorders include the following:

* Mutations in *SFTPB, SFTPC, ABCA3, NKX2.1/TTF1,*and the granulocyte-macrophage colony-stimulating factor (GM-CSF) receptor
* Histology consistent with surfactant dysfunction disorder but without recognized genetic etiology

Disorders related to systemic disease processes

Disorders related to systemic disease processes are listed below:

* Autoimmune-related and connective tissue disease–related disorders (systemic lupus erythematosus [SLE], polymyositis/dermatomyositis, systemic sclerosis, sarcoidosis, mixed connective tissue disease)
* Pulmonary vasculitis (polyarteritis nodosa, Wegener granulomatosis, Churg-Strauss syndrome)
* Storage diseases (Gaucher disease, Niemann-Pick disease)
* Metabolic disorders
* Langerhans cell histiocytosis
* Malignant infiltrates (lymphoma, leukemia)
* Liver disease (chronic active hepatitis, primary biliary cirrhosis)
* Bowel disease (ulcerative colitis, Crohn disease)
* Amyloidosis
* Neurocutaneous disorders (tuberous sclerosis, neurofibromatosis, ataxia-telangiectasia)
* Lymphoproliferative disorders

Disorders with other known causes

Disorders with other known causes include the following:

* Infection
  + Viral infection (eg, adenoviral or other post-infectious bronchiolitis obliterans, cytomegalovirus [CMV] infection, infection with Epstein-Barr virus [EBV])
  + Bacterial infection (eg, pertussis or infection due to *Legionella*, *Mycoplasma*, *Chlamydia*, or Mycobacteriumspecies)
  + Fungal infection (eg, infection due to *Histoplasma*, *Aspergillus*, or Pneumocystisspecies)
  + Parasitic infection (eg, visceral larva migrans)
* Environmental conditions
  + Exposure to organic dusts (hypersensitivity pneumonitis)
  + Exposure to inorganic particulates (eg, silica, asbestos, talc, zinc)
  + Exposure to chemical fumes (eg, sulfuric acid, hydrochloric acid, methyl isocyanate)
  + Exposure to gases (eg, oxygen, chlorine, nitrogen dioxide [silo-filler disease], ammonia)
  + Exposure to radiation
* Drugs
  + Use of antineoplastic agents (eg, cyclophosphamide, nitrosoureas, methotrexate, azathioprine, cytosine arabinoside, 6-mercaptopurine, vinblastine, bleomycin, busulfan)
  + Use of other drugs or elements (eg, penicillamine, nitrofurantoin, gold)
* Post-transplantation/rejection syndromes
* Chronic aspiration pneumonitis
* Resolving acute respiratory distress syndrome (ARDS)
* Degenerative disorders (eg, pulmonary microlithiasis)
* Immunodeficiency-associated ILD
  + COPA syndrome (mutation in the *COPA*gene encoding COPα protein)
* Autoinflammatory disorder–associated ILD
  + STING (stimulator of interferon genes)-associated vasculopathy with onset in infancy (SAVI)
* Immunodeficiency-related opportunistic infections
* DNA repair defects
* Other genetic/familial disorders
  + Familial hypocalciuric hypercalcemia
  + Lysinuric protein intolerance
  + Farber lipogranulomatosis
  + Hermansky-Pudlak syndrome
  + Filamin A (FLNA) mutation
  + Pulmonary alveolar proteinosis (PAP) with known genetic associations, such as methionyl-tRNA synthetase (MARS) mutations

Disorders of uncertain etiology

Disorders of uncertain etiology are listed below:

* Neuroendocrine cell hyperplasia of infancy (NEHI)
* Pulmonary interstitial glycogenosis (PIG)
* Pulmonary alveolar proteinosis (PAP)
* Other pulmonary hemorrhage syndromes (idiopathic pulmonary hemosiderosis, capillaritis)
* Lymphocytic interstitial pneumonitis (LIP; known acquired immunodeficiency syndrome [AIDS] cases are excluded; LIP is often associated with human immunodeficiency virus [HIV] infection or AIDS but can be idiopathic)
* Lymphangiomatosis
* Bronchiolitis obliterans
* Bronchocentric granulomatosis
* Nonspecific interstitial pneumonia (this pattern has been shown to correlate with surfactant dysfunction mutations, such as ABCA3 deficiency, in older children)
* Acute interstitial pneumonitis (AIP)
* Unclassified/undetermined: conditions that do not clearly fit into a specific category (ie, end-stage disease, inadequate or nondiagnostic biopsy specimen)

Disorders with presenting features similar to those of ILD

Disorders with presenting features similar to those of ILD include the following:

* Pulmonary veno-occlusive disorders (anomalous pulmonary venous return, pulmonary hemangiomatosis, hereditary hemorrhagic telangiectasia, pulmonary venous stenosis/atresia)
* Heart disease (left ventricular failure, left-to-right shunts)
* Cystic fibrosis
* Primary ciliary dyskinesia
* Lymphatic disorders

**Risk Factors:**

**Demographic Factors**

* **Age**: Peak incidence occurs in infancy, though the condition can develop throughout childhood and adolescence
* **Gender**: More common in females for most connective tissue diseases
* **Family History**: Familial clustering suggests genetic predisposition

**Medical Risk Factors**

* Pre-existing connective tissue diseases (juvenile systemic sclerosis, dermatomyositis, systemic lupus erythematosus)
* Immunodeficiency states
* History of macrophage activation syndrome
* Chromosomal abnormalities (e.g., Trisomy 21)

**Environmental Risk Factors**

* Chronic exposure to organic dusts or environmental allergens
* Prematurity and bronchopulmonary dysplasia
* Recurrent respiratory infections

**Signs & Symptoms:**

Some patients with CT-ILD don't have symptoms. For others, common symptoms include:

* Shortness of breath with activity
* Cough
* Fatigue
* "Crackle" sound heard when listening to the chest with a stethoscope
* Symptoms of a connective tissue disease, such as joint pain and swelling, rash, dry eyes, dry mouth and acid reflux

**The clinical manifestations are often subtle and nonspecific initially. Common respiratory symptoms include:**

* Dyspnea: Progressive shortness of breath, initially with exertion, later at rest
* Tachypnea: Rapid breathing rate
* Chronic dry cough: Persistent, non-productive cough
* Exercise intolerance: Decreased ability to participate in physical activities
* Recurrent respiratory infections: Including pneumonia and bronchiolitis

**Physical Examination Findings**

* **Tachypnea and retractions**: Use of accessory muscles for breathing
* **Inspiratory crackles**: Fine, crackling sounds heard on chest auscultation
* **Cyanosis**: Blue discoloration of lips and fingernails due to low oxygen levels
* **Digital clubbing**: Enlargement of fingertips and toes
* **Failure to thrive**: Poor weight gain and growth

**Systemic Manifestations**

* Joint pain and swelling (arthritis)
* Cutaneous rashes
* Muscle weakness (in dermatomyositis)
* Raynaud's phenomenon
* Dry eyes and mouth (in Sjögren's syndrome)

**Medical Codes:**

**ICD-10-CM Diagnostic Codes**

* **M35.9**: Systemic involvement of connective tissue, unspecified
* **M35.81**: Multisystem inflammatory syndrome
* **J84**: Other interstitial pulmonary diseases
* **J98.4**: Other disorders of lung

**Specific Condition Codes**

* **J84.1**: Interstitial lung disease with mention of fume or vapor
* **J84.89**: Other specified interstitial pulmonary diseases
* **J84.9**: Interstitial pulmonary disease, unspecified

**Diagnosis Mapping:**

**Laboratory Studies**

Laboratory studies are helpful in the setting of connective tissue disease-associated (CTD) interstitial lung disease (ILD) (CTD-ILD). At least 15% of patients with ILD have evidence of underlying CTD.

**Antibody testing**

Various antibodies detected in the serum of patients with CTD help in determining the diagnosis and the prognosis (see Table 2 below).

Table 2. Autoantibodies in Connective Tissue Diseases.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Autoantibody | RA | SLE | SD | SS | PM/DM | AS | MCTD | IPAF #[[10](javascript:void(0);)] |
| RF | + | + | + | + | Rare | - | + | Possible |
| ANA | + | + | + | + | Rare | - | +  (speckled) | Possible |
| ds-DNA | - | + | - | - | - | - | - | Possible |
| Anti centromere | - | - | + (limited) | Rare | Rare | - | - | Possible |
| Scl-70 | - | - | + (diffuse) |  | Rare | - | - | Possible |
| Anti-Jo | - | - | - | Rare | + (ILD) | - | - | Possible |
| ANCA | Rare | Rare | - | - | - | - | - | - |
| Smith antibody | - | + | - | - | - | - | - | Possible |
| Anti-Ro/SSA and anti-La/SSB | - | - | - | + | - | - | - | Possible |
| Anti-U1-RNP and anti-UN-70 kd | - | - | - | - | - | - | + | Possible |
| Anti-CCP | + | - | - | - | - | - | - | Possible |
| ANA = antinuclear antibody; ANCA = antineutrophilic cytoplasmic antibody; AS = ankylosing spondylitis; CCP = cyclic citrullinated peptide; DM = dermatomyositis; ds-DNA = double-stranded DNA antibody; ILD = interstitial lung disease; IPAF = interstitial pneumonia with autoimmune features; MCTD = mixed connective-tissue disease; PM = polymyositis; RA = rheumatoid arthritis; RF = rheumatoid factor; RNP = ribonucleoprotein; SD = scleroderma; SLE = systemic lupus erythematosus; SS = Sjögren syndrome. | | | | | | | |  |

Anemia of chronic disease can be found in persons with rheumatoid arthritis (RA), whereas systemic lupus erythematosus (SLE) can cause leukopenia, lymphopenia, thrombosis, and thrombocytopenia. The erythrocyte sedimentation rate (ESR) and creatine kinase levels may be high in patients with polymyositis (PM)/dermatomyositis (DM). Total complement levels and a high ESR may be present in patients with SLE who present with an acute lupus flare.

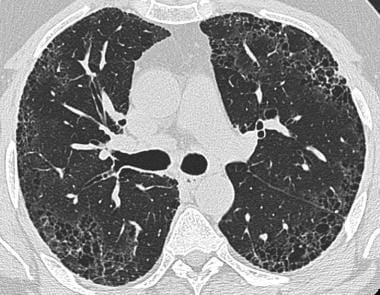
**Schirmer and Rose Bengal staining**

The Schirmer test may be used to screen for dry eyes secondary to decreased tear production in patients with Sjögren syndrome (SS). Similarly, Rose Bengal staining of the cornea can detect keratitis associated with SS.

Radiology

Radiologically, connective tissue disease (CTDs) may manifest as a focal or a diffuse pulmonary abnormality. The type and frequency of the lung abnormalities vary with the specific diseases.

Rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), scleroderma (SD), Sjögren syndrome (SS), and polymyositis/dermatomyositis (PM/DM) can cause interstitial fibrosis similar to idiopathic pulmonary fibrosis (IPF). All CTDs like IPF involve the lung bases and are subpleural, except for ankylosing spondylitis (AS), which involves the upper lobes, and RA-induced interstitial lung disease (ILD). RA-ILD is differentiated from IPF on the basis of greater upper-lobe involvement, an anterior location, and the presence of reticular infiltrates finer than those associated with IPF (see the image below).

[](javascript:refImgShow(5))

Connective Tissue Disease-Associated Interstitial Lung Disease (CTD-ILD). The high-resolution computed tomography scan of advanced-stage pulmonary fibrosis demonstrates reticular opacities with honeycombing in a predominantly subpleural distribution. This pattern can be present in rheumatoid arthritis–related interstitial lung disease, Sjögren syndrome, and scleroderma.

Radiologic features of mixed connective tissue disease (MCTD) vary across different studies. Radiologic abnormalities include subpleural honeycombing, bronchiolitis obliterans organizing pneumonia (BOOP), and pleural effusion.

**Chest radiography**

Chest radiographs can detect ILD; however, these may be normal initially.Thus, high-resolution computed tomography (CT) scanning remains the standard when it comes to the evaluation of CTD-related ILD (CTD-ILD). Depending on the type of CTD present and the extent of lung involvement, radiography may reveal a plethora of findings, including but not limited to ground-glass opacities, reticulations, pleural effusions, pulmonary nodules, bronchiectasis, volume loss, and prominent pulmonary vessels.

SS is manifested by a reticulonodular pattern of infiltrates involving lower lung zones. This finding may reflect the presence of lymphocytic interstitial fibrosis (see the image below). HRCT scans may reveal ground-glass opacities (GGOs) and bronchiolitis obliterans.

[](javascript:refImgShow(7))

Connective Tissue Disease-Associated Interstitial Lung Disease (CTD-ILD). This chest radiograph was obtained from a patient with lymphocytic interstitial pneumonia.

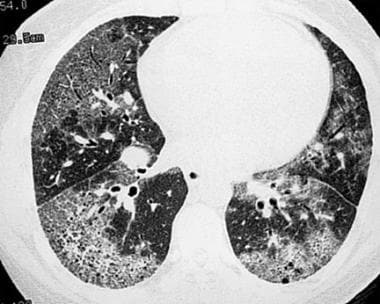
**Ultrasonography**

Although not yet adopted as a gold standard, data exists to suggest a role for the use of lung ultrasonography.

Echocardiography can help detect cardiac involvement, which is useful in patients presenting with heart failure and in patients with suspected pulmonary hypertension.

**Computed tomography (CT) scanning**

Numerous studies show high-resolution (HR) CT findings and pulmonary function test (PFT) results correlate with underlying lung histopathology in patients with CTD. GGOs and consolidation may reflect the presence of interstitial pneumonia on CT scanning of the chest (see the image below). Pulmonary fibrosis is uncommon in patients with SLE; if present, it is usually patchy. The abnormalities occur mainly at the periphery of the lung and can be associated with traction bronchiectasis and honeycombing. The HRCT findings in CTD-ILD can be indistinguishable from those found in idiopathic interstitial pneumonia.

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Connective Tissue Disease-Associated Interstitial Lung Disease (CTD-ILD). Ground-glass opacification (GGO) may correlate with active alveolitis and a favorable response to therapy. GGO is among the earliest features of rheumatoid arthritis–induced interstitial lung disease.

RA is associated with the following four CT scan patterns:

* Usual interstitial pneumonia (UIP)
* Nonspecific interstitial pneumonia (NSIP)
* Bronchiolitis
* Organizing pneumonia (OP)

The most common CT scan features of RA-related lung disease are GGOs and reticulation.RA can manifest as rheumatoid nodules, Caplan syndrome (rheumatoid nodules ≤5 cm, mostly involving the upper lungs in coal miners and resembling coal worker pneumoconiosis).In a smoker who has RA and presents with lung nodules, lung cancer should be ruled out first.

In patients with SD, HRCT scanning frequently shows evidence of interstitial pneumonitis and fibrosis, mainly involving the lower lobes, in a predominantly peripheral and posterior distribution.

PM/DM-induced lung disease is rare (5%). The most common pattern of ILD is symmetric and predominantly basal reticulation. HRCT scanning is remarkable for revealing prominent interlobular septa, patchy consolidation, and honeycombing. Patients with an acute presentation have GGOs and consolidation, in contrast to the reticulation and honeycombing seen in patients with the chronic type of ILD.

**Nuclear imaging**

Gallium scanning results may be abnormal in patients with CTDs, probably as a consequence of alveolitis. However, the role of gallium scanning in the diagnosis or prognosis of CTDs is not well established.

**Pulmonary Function Tests**

Pulmonary function testing (PFT) includes spirometry, lung volumes, diffusion capacity of the lung for carbon monoxide (DLCO), and arterial blood gas (ABG) measurements.

The American College of Rheumatology and American College of Chest Physicians recommend PFT for both screening for and monitoring ILD in patients with systemic autoimmune rheumatic diseases.[[64](javascript:void(0);)]

Most connective tissue diseases (CTDs) cause a restrictive lung disease pattern with a decrease in total lung capacity (TLC), residual volume (RV), functional residual capacity (FRC), and DLCO. Forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC) (ie, the FEV1/FVC ratio) may be normal or increased. However, bronchiolitis obliterans may cause an obstructive ventilatory defect (reduced FEV1/FVC ratio and FEV1, increased RV and RV/TLC ratio).

Arterial blood gas (ABG) analysis may reveal hypoxemia at rest. Arterial oxygen desaturation may occur with exercise. A 6-minute walk test with pulse oximetry provides a measure of oxygen desaturation and helps to detect disease progression.

**Bronchoalveolar Lavage**

Bronchoalveolar lavage (BAL) results are not diagnostic in patients with connective tissue diseases (CTDs), but they are diagnostic in excluding infections and can help narrow a differential diagnosis.

Studies have been performed to determine the importance of cell counts in BAL samples; patients with increased neutrophil counts tend to have a worse prognosis than those with increased lymphocyte counts. BAL results seem to correlate with the underlying lung pathology. Similarly, BAL lymphocytosis may predict responsiveness to corticosteroids. Most patients with underlying interstitial lung disease (ILD) have lymphocytosis in BAL fluid. Finally, BAL is valuable for excluding infections that can mimic CTDs.

**Biopsy**

As with other interstitial lung diseases (ILDs), a transbronchial biopsy is usually inadequate for diagnosis, given the often patchy distribution of histologic findings. Although lung biopsies would provide a histopathologic diagnosis, they are often not required.

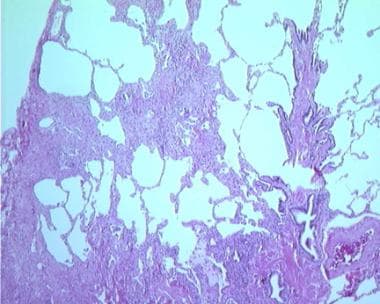
High-resolution computed tomography (HRCT) scanning results correlate well with the pathology of the underlying connective tissue disease (CTD). However, open lung biopsy is needed in atypical cases, depending on the clinical and functional status of the patient. Video-assisted thoracoscopic surgery is usually preferred.

**Histologic Findings**

The most common histopathologic findings in patients with connective disease tissues (CTDs) are interstitial pneumonia (UIP), nonspecific interstitial pneumonia (NSIP), organizing pneumonia (OP), follicular bronchiolitis, diffuse alveolar hemorrhage (DAH), and lymphoid interstitial pneumonia (LIP).

**Usual interstitial pneumonia**

Histologic findings in UIP include fibroblastic foci with alternate areas of normal lung tissue, fibrosis, and honeycombing (see the image below). The distribution is peripheral, subpleural, and basal. These findings may be seen in systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), polymyositis/dermatomyositis (DM/PM), and mixed connective tissue disease (MCTD).

[](javascript:refImgShow(8))

Connective Tissue Disease-Associated Interstitial Lung Disease (CTD-ILD). The histologic image is from a patient with usual interstitial pneumonitis. Subpleural and paraseptal inflammation are present, with the appearance of temporal heterogeneity. Patchy scarring of the lung parenchyma and normal (or nearly normal) alveoli interspersed between fibrotic areas are hallmarks of this disease. In addition, the lung architecture is completely destroyed. This pattern can be present in rheumatoid arthritis–induced interstitial lung disease and is generally associated with a poor prognosis.

**Nonspecific interstitial pneumonia**

Histologic findings in NSIP include varying proportions of interstitial inflammation and fibrosis, which may be divided into cellular and fibrosing and are patchy with intervening normal lung tissue.[[65](javascript:void(0);)]The distribution is peripheral, subpleural, basal, and symmetric. These findings may be seen in SLE, RA, DM/PM, and MCTD.

**Lymphoid interstitial pneumonia**

Histologic findings in LIP include infiltration of T cells, plasma cells, and macrophages, as well as lymphoid hyperplasia that is usually diffuse and predominantly septal. The distribution is diffuse. These findings may be seen in Sjögren syndrome (SS) and MCTD.

**Organizing pneumonia**

Histologic findings in OP include patchy intraluminal organizing fibrosis in air spaces, with preservation of lung architecture. The distribution is bronchovascular. These findings may be seen in SLE, scleroderma (SD), SS, and PM/DM.

**Diffuse alveolar hemorrhage**

Histologic findings in DAH include hyaline membrane formation, damaged type II pneumocytes, alveolar edema, and fibroblastic proliferation. Distribution is diffuse. These findings may be seen in SLE, RA, SD, and PM/DM.

**Interstitial pneumonia with autoimmune features (IPAF)**

The histopathologic features included within the morphologic domain criteria for IPAF are only those considered to be highly associated with, but not diagnostic for, the presence of CTDs. These are the primary patterns of NSIP, OP and LIP and the secondary features of interstitial lymphoid aggregates with germinal centers and diffuse lymphoplasmacytic infiltration, with or without lymphoid follicles.

**Treatment Options:**

**Approach Considerations**

In patients with suspected connective tissue disease (CTD)-associated interstitial lung disease (ILD) (CTD-ILD), referral to a center with expertise in management of CTD-ILD is recommended. A multidisciplinary approach to help guide management includes collaboration with pulmonologists, rheumatologists, radiologists, and pathologists. Furthermore, referral to centers with expertise in pulmonary hypertension on lung transplantation may be required, depending on the individual clinical context.

The treatment of CTD-ILD requires immunosuppression with either steroids or steroid-sparing agents.

Lung transplantation may be an option for those with end-stage lung disease.

**Issues to consider**

Patients with CTD-ILD often present with poor quality of life; however, therapy is also associated with severe adverse effects. Thus, treatment is generally initiated when symptoms become clinically significant or progressive. The mainstay of therapy requires immunosuppression either through steroids or steroid-sparing agents.

Prolonged treatment with corticosteroids leads to a large number of comorbidities such as diabetes mellitus, hypertension, osteoporosis, and psychiatric disease. Therefore, all efforts should be made to decrease the steroid burden as soon as possible.

However, immunosuppressive agents are not without risk either. For example, cyclophosphamide, a cytotoxic immunosuppressant, has been shown to cause hemorrhagic cystitis and is even associated with malignancy. Because the CTD-ILDs are a heterogeneous population, the addition of steroid-sparing medications should be considered, depending on the CTD being treated. Lastly, if a patient shows a progressive deterioration in lung function or shows no slowing in this decline, discontinuation of the immunosuppressive medications should be considered.

Most patients are treated in an outpatient setting. Chest radiography, the 6-minute walk test, arterial blood gas determinations (ie, arterial oxygen tension [PaO2]), and pulmonary function tests (PFTs)—especially forced vital capacity (FVC) and diffusion capacity of the lung for carbon monoxide (DLCO)—are monitored after therapy is started. Subspecialty consultations including pulmonologists and rheumatologist should be considered early in the management of these diseases. Transfer to a higher level of care is indicated if the diagnosis is in doubt or if treatment is ineffective.

Educate patients about the natural history, progression, and treatment of the disease. Before any immunosuppressive medication is started, the potential adverse effects, the duration of therapy, and the chances of success should be discussed with the patient.

**Medical Care**

As mentioned previously, immunosuppression is the cornerstone of the medical management of connective tissue disease (CTD)-associated interstitial lung disease (ILD) (CTD-ILD). These drugs include corticosteroids and corticosteroid-sparing medications, such as azathioprine, cyclosporine, cyclophosphamide, and methotrexate.

**Glucocorticoids**

Glucocorticoids have often been tried as first-line therapy for a variety of CTD-ILDs, although the optimal dose or duration of prednisone is unknown. In systemic sclerosis (SSc), glucocorticoids have been tried as monotherapy and in combination with other immunosuppression. These combinations appear to show improvement in both pulmonary and nonpulmonary complications of SSc.

Guidelines from the American College of Rheumatology (ACR) and the American College of Chest Physicians (ACCP) advise against the use of glucocorticoids as first-line therapy in patients with SSc-ILD, owing to the risk of scleroderma renal crisis. For all other CTD-ILDs, glucocorticoids are conditionally recommended as first-line treatment.

**Corticosteroid-sparing agents**

For patients with CTD-ILD other than SSc-ILD, the ACR/ACCP guidelines conditionally recommend azathioprine, mycophenolate, rituximab, and cyclophosphamide as initial corticosteroid-sparing treatments, with consideration of tocilizumab in selected conditions if progression occurs. Cyclophosphamide, once a first-line therapy, is typically reserved for refractory or rapidly progressive disease because of higher rates of intolerance and adverse effects. For SSc-ILD specifically, tocilizumab has been shown to slow disease progression and can be considered as a first-line agent.

***Cyclophosphamide,mycophenolate mofetil***

Cyclophosphamide, an alkylating agent, can be used with or without steroids in the treatment of SSc. A scleroderma lung study that compared oral cyclophosphamide and placebo showed 1 year of cyclophosphamide was associated with a significant but modest improvement in dyspnea and lung function.Common adverse effects of cyclophosphamide therapy in the study included hematuria, leukopenia, neutropenia, anemia, and pneumonia. In addition, a small prospective, multicenter, randomized control trial conducted in patients with granulomatosis with polyangiitis showed intravenous pulse cyclophosphamide may be not only as effective as oral cyclophosphamide but also may avoid some of the systemic toxicity.

In an attempt to reduce the toxicity associated with cyclophosphamide, the Scleroderma II Trial compared it with mycophenolate mofetil, an inhibitor of inosine monophosphate dehydrogenase.Mycophenolate mofetil exerts a cytostatic effect on B and T cell lymphocytes. In this trial, no significant difference was noted in forced vital capacity (FVC), the primary outcome. However, the investigators noted that although both study drugs showed an improvement in FVC (2.88% in the cyclophosphamide group and 2.19% in the mycophenolate mofetil group), those who received mycophenolate appeared have better drug tolerance as evidenced by a 43.8% withdrawal in the cyclophosphamide group and a 28.9% withdrawal in the mycophenolate group.

Mycophenolate mofetil is associated with several adverse effects, such as diarrhea (most common), bone marrow suppression, and progressive multifocal leukoencephalopathy.Nonetheless, guidelines from the American Thoracic Society strongly recommend mycophenolate for the treatment of patients with SSc-ILD.

***Tacrolimus, sirolimus***

Tacrolimus and sirolimus are calcineurin inhibitors, drugs that inhibit the action of calcineurin and thus impair T cell lymphocytes by impairing the transcription of cytokines such as interleukin (IL) 2. These agents have been used in the maintenance of immunosuppression for several years. More recently, multiple retrospective studies have evaluated their use in either steroid-resistant ILD associated with the inflammatory myopathies or as adjunctive immunosuppression with steroids in these conditions.Calcineurin inhibitors are associated with several adverse effects, including nephrotoxicity, hypertension, neurotoxicity including posterior reversible encephalopathy syndrome, increased risk for infections, and malignancy.

***Azathioprine***

Azathioprine, a generally well-tolerated immunosuppressant, exerts its effect by halting DNA replication by incorporating itself into DNA metabolism. Azathioprine has been extensively used to maintain remission in antineutrophil cytoplasmic antibody-associated (ANCA) vasculitis. In fact, in this cohort, azathioprine is considered first line after induction therapy with cyclophosphamide.Although data are limited, retrospective studies seem to suggest azathioprine is associated with the stabilization of pulmonary function in patients with CTD-ILD.

***Rituximab***

Rituximab, a monoclonal antibody that targets the CD20 antigen, is used in the treatment of several autoimmune diseases. In ANCA vasculitis, a French prospective, randomized, controlled study that compared rituximab to the first-line therapy (azathioprine) found rituximab was superior to azathioprine in maintaining remission.Another prospective, randomized, controlled trial showed rituximab to be as effective as cyclophosphamide in the induction of remission in ANCA vasculitis.In fact, in the cohort of patients with relapsing disease, rituximab may be more effective than cyclophosphamide. Similarly, rituximab may be an option in refractory CTD-ILD.

Other medications have been tried in the treatment of RA-related ILD, including methotrexate,leflunomide, and biologic inhibitors (eg, tumor necrosis factor–α [TNF-α] inhibitors). Hagiwara et al described a case in which an acute exacerbation of preexisting ILD occurred after the administration of etanercept for RA.

***Pirfenidone, nintedanib***

Pirfenidone and nintedanib are antifibrotic drugs used in the management of idiopathic pulmonary fibrosis (IPF).

In 2019, nintedanib received FDA approval in the treatment of ILD associated with SSc after being shown to slow the rate of decline in pulmonary function.Nintedanib is a tyrosine kinase inhibitor (TKI) that targets growth factors (eg, vascular endothelial growth factor receptor [VEGFR], fibroblast growth factor receptor [FGFR], platelet-derived growth factor receptor [PDGFR] 1-3, colony-stimulating factor 1 receptor [CSFIR]) that are implicated in the pathogenesis of ILDs.

Nintedanib gained approval for chronic fibrosing ILDs with a progressive phenotype in 2020. Unclassifiable ILDs, autoimmune ILDs, chronic hypersensitivity pneumonitis, sarcoidosis, myositis, Sjögren syndrome, coal worker pneumoconiosis, and idiopathic forms of interstitial pneumonias (eg, idiopathic nonspecific interstitial pneumonia) are among the diseases that may develop a progressive form of chronic fibrosing ILD.

Approval of nintedanib for chronic fibrosing ILDs was based on the INBUILD phase 3 clinical trial (N = 663). Results showed nintedanib slowed pulmonary function loss by 57% (107 mL/year) across a range of patients compared with placebo (*P*< 0.001). In patients with usual interstitial pneumonia (UIP)-like fibrotic pattern shown by high-resolution CT, nintedanib slowed the loss of pulmonary function by 61% (128.2 mL/year) compared with placebo (*P*< 0.001).

***Tocilizumab***

Tocilizumab, an anti-IL-6 inhibitor, has shown promise for the treatment of ILD due to scleroderma. In the focuSSed trial with open-label extension, the decline in forced vital capacity over 48 months was 14 mL in the tocilizumab group compared with 255 mL in the placebo group.

Hematopoietic stem cell transplantation

Hematopoietic stem cell transplantation (HSCT) has emerged as a novel approach to the management of advanced SSc.HSCT aims to reduce the activity of aberrant T cells and B cells through aggressive immunosuppression followed by transplantation of a renewed and more tolerant immune system.Three randomized controlled trials have shown survival benefit and improvement in FVC, skin thickening, and health quality of life.

**Surgical Care**

Lung transplantation is the only available treatment for refractory connective tissue disease (CTD)-associated interstitial lung disease (ILD) (CTD-ILD) related with progressive fibrosis. Despite this, many centers are reluctant to perform lung transplantations in patients with CTD because of the concern for extrapulmonary disease. However, a retrospective study from South Korea showed similar survival rates for CTD-ILD relative to idiopathic pulmonary fibrosis (IPF).[[84](javascript:void(0);)]In patients with disease refractory to treatment or who have extensive fibrosis, it is recommended that patients are referred to a transplant center for evaluation.

**Prevention Tips:**

**Primary Prevention**

* **Avoidance of environmental triggers**: Limit exposure to organic dusts, chemicals
* **Smoking cessation**: Avoid active and passive smoke exposure
* **Infection prevention**: Comprehensive vaccination including pneumococcal, influenza, and RSV

**Secondary Prevention**

* **Early recognition**: Prompt evaluation of respiratory symptoms in at-risk children
* **Regular screening**: Periodic pulmonary function testing in children with connective tissue diseases
* **Environmental modification**: Addressing known allergens or irritants

**Prognosis:**

The development of interstitial lung diseases (ILD) in connective tissue disease (CTD) is associated with substantial morbidity. However, the mortality of CTD-associated ILD (CTD-ILD) and even interstitial pneumonia with autoimmune features (IPAF) is better than that of idiopathic ILD.

CTD-ILD are a heterogeneous group of the disorder. Lung involvement in CTD ranges from asymptomatic subclinical disease to fibrotic lung disease that causes significant morbidity and mortality. Some patients develop a slow indolent course; however, others can develop rapidly progressive disease.

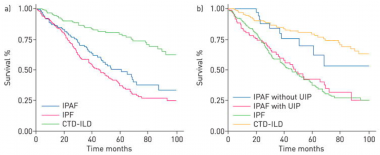
In systemic sclerosis (SSc), most cases are associated with ILD and this remains the leading cause of death.

In rheumatoid arthritis (RA), although ILD only occurs in approximately 10% of cases, the presence of ILD is associated with increased mortality. In patients with RA and systemic lupus erythematosus (SLE) who develop ILD, mortality appears to be 3-4 times higher than that in the general population, with a median survival of all patients with RA-ILD reported to be approximately 5 years.

In polymyositis/dermatomyositis (PM/DM), the presence of ILD has also been noted to have an association with poor outcomes.In fact, in Korean patients with PM/DM, Kang et al observed ILD in 40.3% of patients, with associated poor survival.

Thus, CTD-ILD has a better prognosis than idiopathic ILD. Initially, this was thought to be secondary to a higher frequency of nonspecific interstitial pneumonia (NSIP); however, a study of 362 patients in South Korea showed improved mortality in patients with usual interstitial pneumonia (UIP) in CTD when compared to idiopathic pulmonary fibrosis (IPF).

Further data supporting this finding comes from IPAF. This subset of patients has features suggestive but not diagnostic of CTD. In a retrospective study (2006-2014), patients with IPF had a worse prognosis relative to those with IPAF, who in turn had a worse prognosis than patients diagnosed with CTD-ILD.Furthermore, patients who had IPAF without the UIP pattern had improved survival compared to those who had IPAF with UIP pattern. See the image below.

[](javascript:refImgShow(9))Connective Tissue Disease-Associated Interstitial Lung Disease (CTD-ILD). In reviewing a retrospective database, Odham et al (Chicago cohort), showed a significant difference in mortality for patients with and without autoimmune features. CTD-ILD = Connective tissue disease-associated interstitial lung disease; IPAF = interstitial pneumonia with autoimmune features; IPF = idiopathic pulmonary fibrosis; UIP = usual interstitial pneumonia. Reproduced with permission of the © ERS 2019. Eur Resp J. 2016 Jun:47(6):1767-75. DOI: 10.1183/13993003.01565-2015. Published 31 May 2016. PMID: 27103387.

Finally, it appears that mortality is significantly increased in patients with CTD who develop ILD and pulmonary hypertension. Takizawa et al found that in 715 patients with CTDs, ILD and pulmonary hypertension were important causes of death (37.5% and 6%, respectively).

Tools to predict patient mortality were initially developed for IPF. More recently, however, tools such as the ILD-GAP and the Du-Bois indices have been applied to CTD-ILD as well.

**Complications:**

Superinfection can be life-threatening, particularly if the patient is receiving immunosuppressive medications, which can mask signs and symptoms of infection. Prevention and careful monitoring are crucial.

Drug toxicity causes much of the morbidity associated with ILD. Again, prevention and monitoring are the keys to management.

Hemoptysis may occur in some types of ILD and suggests vasculitis or veno-occlusive disease as possible underlying causes.

Death is usually the result of respiratory failure or cor pulmonale and right heart failure.

Pulmonary complications of CTDs include the following:

* Pulmonary infections
* Drug-induced pulmonary disease
* Pulmonary hypertension
* ILD
* Bronchiolitis
* Pleuritis
* Bronchiectasis
* Acute respiratory distress syndrome (ARDS)
* Pneumothorax
* Cor pulmonale
* Diffuse alveolar hemorrhage (DAH)

**When to see a Doctor/Red Flags:**

**Immediate Medical Attention Required**

Seek emergency care if the child experiences:

* **Severe respiratory distress**: Significant difficulty breathing, use of accessory muscles
* **Cyanosis**: Blue discoloration of lips, fingernails, or skin
* **Hemoptysis**: Coughing up blood
* **Chest pain**: Severe or persistent chest pain
* **High fever**: Especially in immunocompromised patients

**Urgent Consultation Needed**

Contact a pediatric pulmonologist for:

* **Progressive dyspnea**: Worsening shortness of breath over days to weeks
* **Persistent cough**: Chronic cough lasting more than 4 weeks
* **Exercise intolerance**: Significant decrease in activity tolerance
* **Failure to thrive**: Poor weight gain or growth retardation
* **Recurrent respiratory infections**: Multiple episodes of pneumonia or bronchitis

**Routine Follow-up Indicators**

Schedule regular visits for:

* **Known connective tissue disease**: Routine screening for pulmonary involvement
* **Family history**: Children with positive family history of ILD
* **Environmental exposure**: Chronic exposure to potential lung irritants

**Differential Diagnoses:**

As previously mentioned, a multidisciplinary approach to the diagnosis and treatment of connective tissue disease-associated interstitial lung disease (CTD-ILD) is of paramount importance. A thorough history and physical examination should be supplemented by chest radiography, serum biomarkers and, occasionally, histopathology.

It is essential to make an effort to exclude the diagnosis of underlying CTD or interstitial pneumonia with autoimmune features (IPAF) in a patient presenting with ILD, as previous data have shown improved outcomes regardless of the histopathologic diagnosis.

Differential Diagnoses

* Chronic Obstructive Pulmonary Disease (COPD)
* Coal Workers' Pneumoconiosis (Black Lung Disease)
* Cryptogenic Organizing Pneumonia
* Diaphragmatic Paralysis
* Drug-Induced Pulmonary Toxicity
* Eosinophilic Pneumonia
* Hypersensitivity Pneumonitis
* Idiopathic Nonspecific Interstitial Lung Disease
* Idiopathic Pulmonary Fibrosis (IPF)
* Lymphocytic Interstitial Pneumonia
* Idiopathic Pulmonary Arterial Hypertension
* Restrictive Lung Disease
* Sarcoidosis
* Silicosis

**Guidelines:**

Current management follows evidence-based guidelines from the American Thoracic Society, European Respiratory Society, and other international organizations. These guidelines emphasize the importance of age-appropriate classification systems, systematic diagnostic approaches, and individualized treatment plans. Expert consensus recommendations highlight the need for multidisciplinary care, regular monitoring, and family education and support.

The evolving understanding of these conditions, including genetic discoveries and improved diagnostic techniques, continues to shape clinical practice and offers hope for better outcomes for affected children and their families.

The following organizations have released guidelines for the management of connective tissue disease–associated interstitial lung disease (CTD-ILD). Key diagnostic and treatment recommendations have been reviewed and integrated throughout the article.

* 2024. American College of Rheumatology, American College of Chest Physicians. 2023 American College of Rheumatology (ACR)/American College of Chest Physicians (CHEST) guideline for the screening and monitoring of interstitial lung disease in people with systemic autoimmune rheumatic diseases
* 2024. American College of Rheumatology, American College of Chest Physicians. 2023 American College of Rheumatology (ACR)/American College of Chest Physicians (CHEST) guideline for the treatment of interstitial lung disease in people with systemic autoimmune rheumatic diseases
* 2024. American Thoracic Society. Treatment of systemic sclerosis-associated interstitial lung disease: evidence-based recommendations. An official American Thoracic Society clinical practice guideline
* 2015. European Respiratory Society, American Thoracic Society. An official European Respiratory Society/American Thoracic Society research statement: interstitial pneumonia with autoimmune features.

**Expert-Reviewed Q&A:**

**1. What are connective tissue and immune-mediated lung disorders in children?**

Connective tissue and immune-mediated lung disorders are a group of diseases where a child’s immune system incorrectly attacks the tissues within the lungs. This group includes conditions such as juvenile systemic lupus erythematosus, juvenile dermatomyositis, systemic juvenile idiopathic arthritis, and pediatric interstitial lung diseases linked to autoimmune activity. These disorders cause inflammation and scarring (fibrosis) in the lung, leading to breathing difficulties.

**2. What symptoms should parents watch for?**

Common symptoms include:

* Persistent or worsening cough
* Difficulty breathing or shortness of breath (especially during activity)
* Recurrent respiratory infections
* Fatigue, exercise intolerance
* Unexplained fevers
* Poor weight gain or growth
* Possible joint pain or swelling, skin rash, or bluish lips/fingernails in severe cases.

**3. How is this condition diagnosed?**

Diagnosis involves:

* Physical examination and detailed medical history
* Chest X-rays and high-resolution CT scans
* Blood tests for inflammation and autoantibodies
* Pulmonary function testing
* Occasionally, bronchoscopy or lung biopsy if the diagnosis remains unclear.

**4. Are these disorders treatable, and what are the main treatments?**

Yes, most are treatable though not always curable. Primary treatments include:

* Corticosteroids to reduce inflammation
* Immunosuppressive drugs (such as mycophenolate or azathioprine) for severe or steroid-resistant cases
* Hydroxychloroquine and azithromycin in some instances
* Supportive care: oxygen, nutritional support, and pulmonary rehabilitation  
  Close and regular follow-up with a multidisciplinary team (pulmonology, rheumatology, nutrition, etc.) is vital.

**5. Can my child live a normal life with this diagnosis?**

With early recognition and appropriate treatment, many children can lead fulfilling lives. Some may experience ongoing symptoms or require long-term medications and oxygen therapy. Regular medical supervision helps manage the disease, monitor for complications, and adjust treatment to optimize a child’s quality of life.

**6. What are the possible complications?**

Potential complications include:

* Progressive lung scarring leading to chronic respiratory insufficiency
* Pulmonary hypertension
* Recurrent severe lung infections
* Side effects from long-term immunosuppressive or steroid medication (growth suppression, osteoporosis, increased infection risk)
* Systemic issues like growth delay or osteoporosis.

**7. When should we urgently seek medical attention?**

Seek emergency care if your child has:

* Severe difficulty breathing
* Persistent blue color to lips or skin
* Severe chest pain
* Coughing up blood
* High fever with severe illness.

**8. Are these conditions contagious?**

No. These are autoimmune or immune-mediated disorders and are not contagious. Children cannot pass these diseases to others.

**9. What questions should families ask their healthcare team?**

* What is my child’s specific diagnosis?
* What treatments are recommended, and what are the potential side effects?
* What monitoring is needed, and how often?
* Are there signs I need to watch for at home?
* When should my child return to school or activities?
* Are there trusted resources or support groups available?

**10. Can anything be done to prevent these conditions?**

There are no proven ways to prevent these rare autoimmune lung diseases, but:

* Minimize exposure to smoke, pollution, and lung irritants
* Keep regular vaccination schedules
* Early medical evaluation for persistent cough or breathing changes can help catch complications early.

**Summary:**

Pediatric connective tissue and immune-mediated lung disorders represent a complex group of rare diseases characterized by autoimmune-mediated lung inflammation and progressive fibrosis. These conditions primarily affect the lung interstitium and surrounding structures, leading to impaired gas exchange and respiratory compromise. The pathogenesis involves dysregulated immune responses, with genetic predisposition and environmental factors contributing to disease development.

Clinical presentation typically includes progressive dyspnea, chronic cough, exercise intolerance, and failure to thrive. Diagnosis requires a systematic approach combining clinical assessment, laboratory testing, imaging studies, and sometimes invasive procedures. High-resolution computed tomography serves as the gold standard for imaging evaluation, while genetic testing has become increasingly important for specific diagnoses.

Treatment remains largely empirical, with corticosteroids serving as first-line therapy, often combined with steroid-sparing agents such as hydroxychloroquine and azithromycin. Immunosuppressive medications may be necessary for severe or progressive disease. Supportive care, including oxygen therapy, nutritional support, and infection prevention, plays a crucial role in management.

The prognosis varies significantly based on the specific diagnosis and disease severity, with overall survival rates of 83% at 24 months, 72% at 48 months, and 64% at 60 months. Many children now survive into adulthood, though they may require ongoing medical care and have persistent functional impairments.

Early recognition and prompt treatment are essential for optimal outcomes. A multidisciplinary team approach involving pediatric pulmonologists, rheumatologists, and other specialists provides the best care for these complex patients. Continued research and international collaboration are needed to improve understanding of these rare diseases and develop more effective treatments.

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