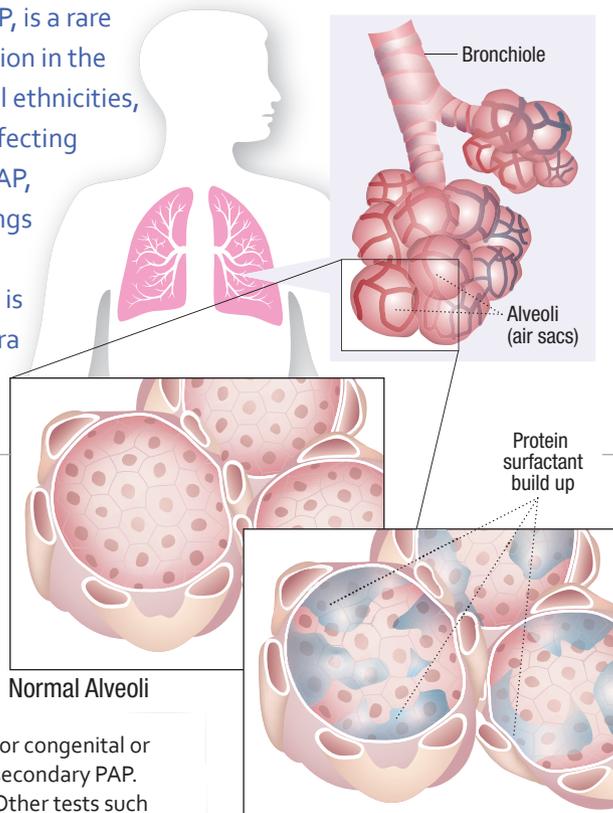


Pulmonary Alveolar Proteinosis (PAP)

Pulmonary alveolar proteinosis, commonly known as PAP, is a rare lung syndrome that occurs in about seven people per million in the general population, affecting both men and women of all ethnicities, regardless of socioeconomic class. Although primarily affecting people 30 to 50 years old, PAP can occur at any age. In PAP, there is the buildup of surfactant in the air sacs of the lungs (alveoli) that leads to problems getting oxygen into the body. Surfactant, a naturally produced fluid in the lungs, is normally present in the lungs at a certain level, yet if extra surfactant is not cleared properly, it can build up and cause difficulty breathing and other respiratory issues.



What causes PAP?

The three main causes of PAP are autoimmune, congenital, and secondary. Over ninety percent of people with PAP have the autoimmune form. In the autoimmune form, an antibody is formed that limits normal protein function (or macrophage function). This antibody is called granulocyte-macrophage colony-stimulating factor (GM-CSF). The GM-CSF antibody prevents the growth of cells called macrophages, which are responsible for removing the extra surfactant from the air sacs in the lungs. The surfactant builds up and hinders oxygen getting in and carbon dioxide getting out of the body through the air sacs.

Secondary causes of PAP include exposure to harmful toxins or dust, blood cancers, or certain infections. Congenital causes are uncommon and occur at birth due to genetic mutations.

What are the symptoms of PAP?

Symptoms of PAP are similar to other lung diseases. A third of people with PAP may not have any symptoms at all and may be detected after an abnormal chest x-ray. Sometimes people are misdiagnosed at first as having recurrent pneumonia, bronchitis, asthma or emphysema. Symptoms of PAP include:

- Shortness of breath
- Cough
- Chest pain
- Feeling tired
- Fever

How is PAP diagnosed?

There are many tests that your healthcare provider can do to help make a diagnosis of PAP and monitor for changes including:

Blood Testing (optimal method for PAP diagnosis)

A blood test will allow for a definite diagnosis of autoimmune PAP (as well as help exclude other diseases) by measuring the level of GM-CSF antibodies present in the blood. This test is useful in the autoimmune form of PAP only and does not provide a diagnosis

for congenital or secondary PAP. Other tests such as complete blood count and metabolic panel may be done to look for secondary causes of PAP. For more information about the GM-CSF test please visit: <https://www.papfoundation.org/forphysicians>.

Lung Function Testing

Pulmonary function tests measure the lungs' ability to breathe and move oxygen. Tests can include spirometry and oxygen diffusing capacity in order to determine your lungs ability to absorb oxygen. Your healthcare provider may have you do repeat lung function tests over time to track how well your disease is controlled. For more about lung function testing see the ATS Patient Information Series fact sheet at www.thoracic.org.

Imaging

A chest X-ray may show haziness over the center of the lungs. These findings are not unique to PAP and can occur with other lung problems including pneumonia.

A computed tomography (CT) scan of the chest shows better images of the lung tissue and may reveal a "crazy paving" pattern. A crazy paving pattern is the combination of enlarged pulmonary blood vessels and a hazy appearance in the lungs. These findings are characteristic but not unique to PAP.

Lung Inspection and Biopsy

A bronchoscopy and bronchoalveolar lavage may be done to collect fluid samples within the lung. A long, flexible, tube called a bronchoscope passes through your nose or mouth into the windpipe. Fluid is flushed into the airways and suctioned out and sent to the lab for analysis. With PAP, the fluid coming back from the lungs will be cloudy and show the excess surfactant level. For more information about flexible bronchoscopy, see the ATS Patient Information Series fact sheet at www.thoracic.org/patients.

A lung biopsy may be done in some cases to obtain lung tissue and help confirm the diagnosis. The biopsy is examined by a pathologist to look for changes in the lung tissue that fit with the disease. Importantly, a lung biopsy may not be needed to diagnose PAP and blood testing should be considered first. There are two ways to do a lung biopsy.

A transbronchial lung biopsy is the least invasive method but may not obtain enough tissue. The biopsy is done as part of flexible bronchoscopy. A special forceps is put through the bronchoscope to take a small sample of lung tissue through the airway wall. Usually you are asleep under anesthesia for this procedure. It can be done as an outpatient.

A video-assisted thorascopic lung biopsy is more invasive but provides more lung tissue. You are asleep under general anesthesia for this procedure. Small cuts (incisions) are made on the side of your chest. A specialist will pass a thin scope with a camera through the incision and into the chest cavity while watching on a video screen. Special forceps are passed through the scope to take pieces of tissue from the lung. This surgery is rarely needed to make a diagnosis of PAP.

How is PAP treated?

There is currently no cure for PAP, but the disease can be treated. Research is continuing to find better treatments for PAP.

People who are having breathing problems from PAP can have some relief with whole lung lavage. A whole lung lavage is a procedure where a tube with two channels is inserted through your mouth and into the windpipe (similar to bronchoscopy). This procedure is done using general anesthesia in the hospital. A specialist will put several liters of fluid into each lung separately and suction it back out in order to flush out the built-up excess surfactant. Each lung may need to have this treatment to flush it out. Sometimes you may need repeat procedures over time.

For the majority of PAP patients with autoimmune PAP, a GMCSF medication can lessen symptoms and slow, halt or even reverse disease progression by helping the body to naturally eliminate the extra surfactant. GM-CSF can be given either as an injection in the skin or (preferably) inhaled. GM-CSF works by stimulating lung macrophages to clean up the extra surfactant that builds up in PAP patients' lungs. Side effects may include fatigue, headache, fever, and pain at the site of injections.

What can you expect long term?

PAP progresses at different rates for different people. PAP may resolve without treatment in a small number of people but typically persists in most people. Despite medication and routine follow up, PAP may advance and make your breathing more difficult. In rare cases, people may develop scarring of the lung. In addition, people with PAP can be more prone to lung infections by both bacteria and fungus. Some people require supplemental

oxygen therapy. For more information about oxygen therapy, see the ATS Patient Information Fact sheet at www.thoracic.org.

PAP may progress in some people to chronic lung failure and worsening breathing problems such that they may need referral to a lung transplant center.

How will PAP affect my lifestyle?

You should follow a healthy diet just as the general population and exercise as tolerated. Like other lung diseases, avoidance of exposure to tobacco smoke or vaping will help prevent making your lung problems worse. Get a yearly influenza vaccine (flu shot) and talk to your healthcare provider about getting pneumococcal vaccine help prevent some types of bacterial pneumonia.

PAP research programs

Some people with PAP may be eligible to enroll in clinical trials that are testing new investigational therapies. More information about current trials can be found at www.clinicaltrials.gov and the PAP Foundation at www.PAPFoundation.org.

Authors: Leonard Riley, MD; Tisha Wang, MD; Ali Ataya, MD

Reviewer: Marianna Sockrider, MD, DrPH, Charlie B Strange MD

Rx Action Steps

- ✓ Let your healthcare provider know if you are having problems with exercise, shortness of breath, or worsening cough.
- ✓ Do not smoke or vape and avoid all tobacco exposure.
- ✓ Have your healthcare provider check for GM-CSF antibodies if this has not done.
- ✓ Have your lung function checked regularly.
- ✓ Talk with your healthcare provider about treatments to try to control PAP.
- ✓ Stay up to date with your immunizations, such as influenza and pneumococcal vaccinations.

Healthcare Provider's Contact Number:

For More Information

American Thoracic Society

- www.thoracic.org

PAP Foundation

- <https://www.PAPFoundation.org>
- <https://www.papfoundation.org/forpatients>

NIH U.S. National Library of Medicine Clinical research study database

- www.clinicaltrials.gov

National Organization for Rare Disorders (NORD)

- <https://rarediseases.org/rare-diseases/pulmonary-alveolar-proteinosis/>

This information is a public service of the American Thoracic Society. The content is for educational purposes only. It should not be used as a substitute for the medical advice of one's healthcare provider.

