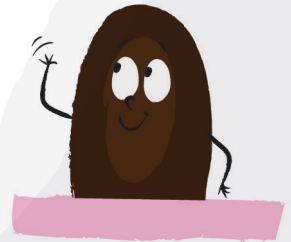
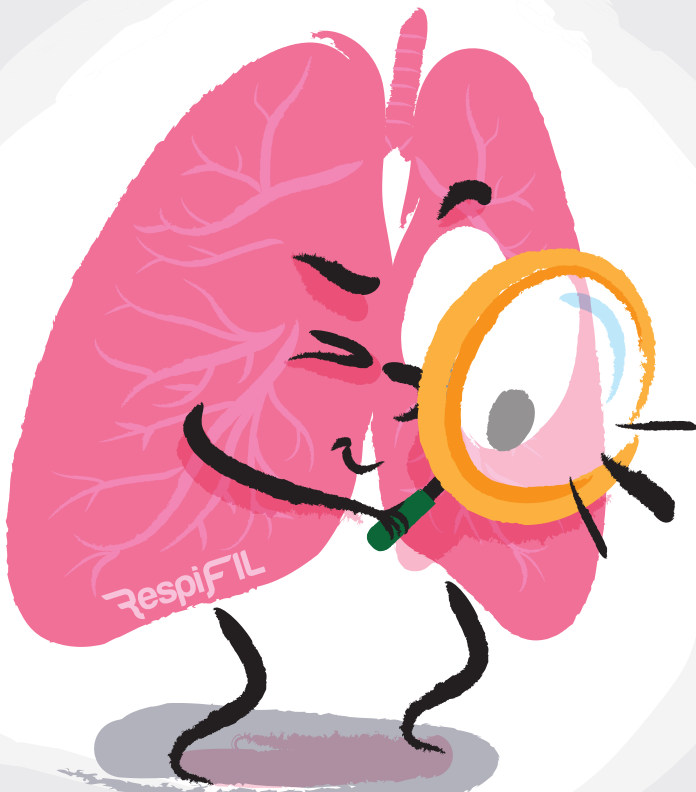


Interstitial Lung Diseases (ILDs)

NeuroEndocrine cell Hyperplasia of Infancy (NEHI)



How can this information booklet help you?

This booklet was given to you during a consultation for your child with neuroendocrine cell hyperplasia (NEHI).

It has been conceived as a guide to support you after the consultation.

It is also a tool that will help you to explain and discuss the disease with your family and relatives.

This booklet will provide you with information about neuroendocrine cell hyperplasia (NEHI): its mechanisms, symptoms, treatments and progression.

This booklet has been produced with the support of RespiFIL, the French reference network for rare respiratory diseases.

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How do we breathe?

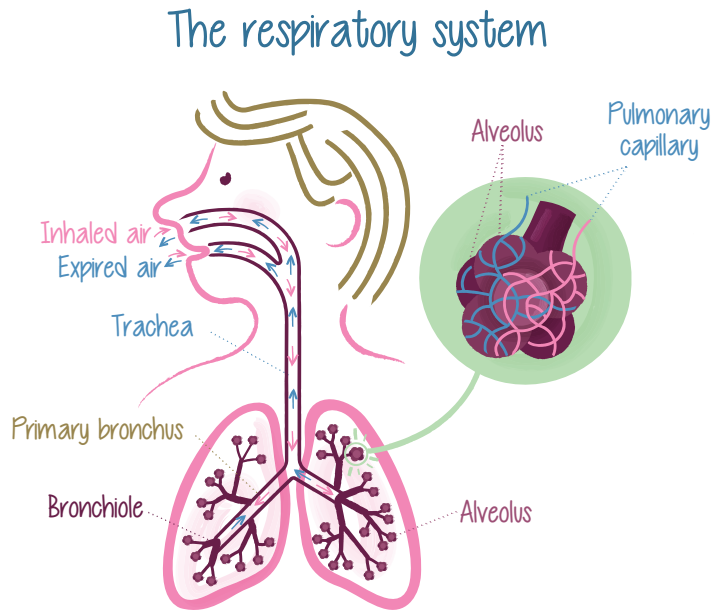
To help you better understand this pulmonary disease, it is important to know the mechanisms of breathing.

Breathing is aimed at collecting oxygen (O₂) from the air around us in order to supply the body's organs and remove their carbon dioxide (CO₂) in the air breathed out.

The respiratory system

Human beings breathe through two lungs. Each lung consists of several lobes (two on the left and three on the right).

The inhaled air enters the trachea through the nose and mouth and then reaches the primary bronchi (left and right). The bronchi branch many times to form the bronchioles and, at their extremities, terminate into the pulmonary alveoli (comparable to bunches of grapes). It is at this level that the gas exchange of O₂ and CO₂ between the air and the blood in the pulmonary capillaries takes



place.

Heart and lungs: breathing partners

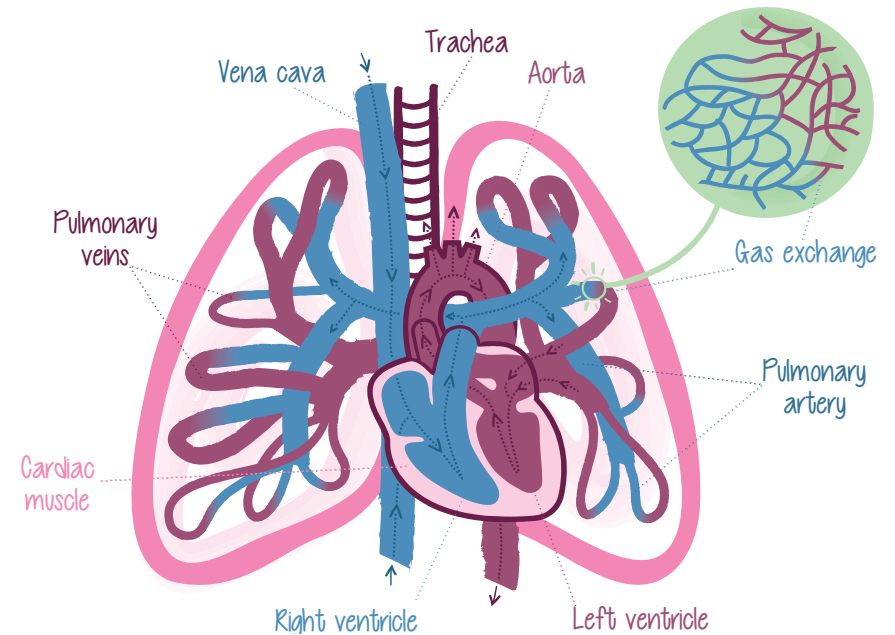
The respiratory and cardiac systems work together. The heart is a pump that enables blood circulation in the body. It is made up of four chambers: the left atrium and ventricle form the left heart; the right atrium and ventricle form the right heart.

Gas exchange takes place between the alveoli and the vessels surrounding them (the pulmonary capillaries), where the blood is enriched in O₂ and depleted of CO₂.

The left heart (in red in the diagram) ensures blood circulation from the lungs to the organs: arterial blood (in red) recharged with O₂ is thus carried throughout the body.

Blood rich in CO₂ and poor in O₂ (blue), coming from the organs, returns to

Pulmonary circulation



the right heart (blue), which in turn sends it to the lungs via the pulmonary artery (blue).

Pulmonary alveoli: centre of gas exchange between air and blood

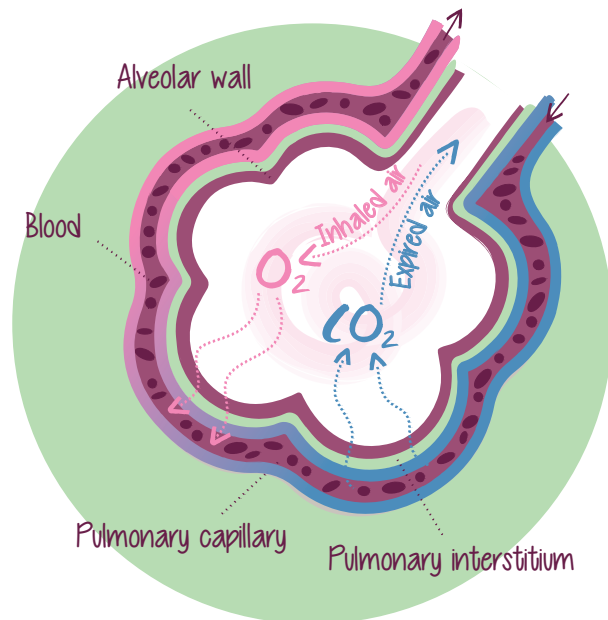
A child is born with about 100 million alveoli and has about 300 million alveoli by the age of 3-4 years. After the age of 4, the alveoli grow but no longer increase in number.

As tiny bags, the alveoli inflate with air upon inhalation and are partially emptied upon exhalation. They are coated by a supporting tissue, the pulmonary interstitium. The pulmonary capillaries run within this interstitium in the alveolar walls.

To facilitate the O_2 and CO_2 gas transfer, three conditions are crucial:

- A thin alveolar wall of a few micrometres in thickness
- A thin interstitium
- A large alveolar surface

Pulmonary alveolus and gas exchange

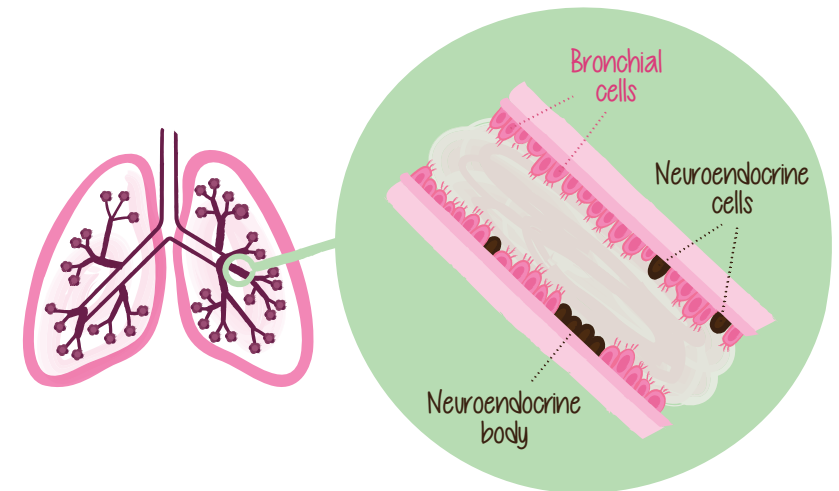


What are neuroendocrine cells?

First, let's find out where they are located!

The bronchi are lined with cells of different shapes called bronchial cells. Among them are the neuroendocrine cells. During foetal life, they are present in the bronchi and bronchioles. They are either isolated within the bronchial cells or grouped together to form neuroendocrine bodies.

Neuroendocrine cells in the lungs



The roles of neuroendocrine cells in the lungs

Neuroendocrine cells act both as nerve cells (sending signals to neighbouring cells) and as endocrine cells (releasing hormones).

During foetal life, neuroendocrine cells play an important role in the growth and development of the lungs and in the production of pulmonary surfactant (a substance that coats the alveoli and keeps them open).

After birth, the neuroendocrine cells should normally disappear almost completely.

The NeuroEndocrine cell Hyperplasia of Infancy (NEHI)

NEHI belongs to the group of child Interstitial Lung Diseases (chILD).

Children ILDs are very rare diseases. Their number is probably underestimated due to the difficulty to diagnose them.

They include a wide variety of diseases that have in common a decrease in gas exchange. This can be related to :

- A thickening of the interstitium (the space between the alveolar wall and the capillaries), due to :
 - chronic inflammation in the alveoli;
 - or poor repair of the alveoli following an aggression (by microbes, inhalation of pollutants, etc.).
- Abnormal accumulation inside the alveoli of dead cell fragments or material (such as blood), abnormal surfactant, etc.

Hyperplasia is the increase in the number of cells in an organ. In NeuroEndocrine cell Hyperplasia of Infancy (NEHI), an excessive number of neuroendocrine cells is found in the airways after birth. This excessive number probably leads to chronic inflammation of the lung and bronchoconstriction (reduction in the diameter of the bronchial tubes), which causes breathing difficulties.

What causes NEHI?

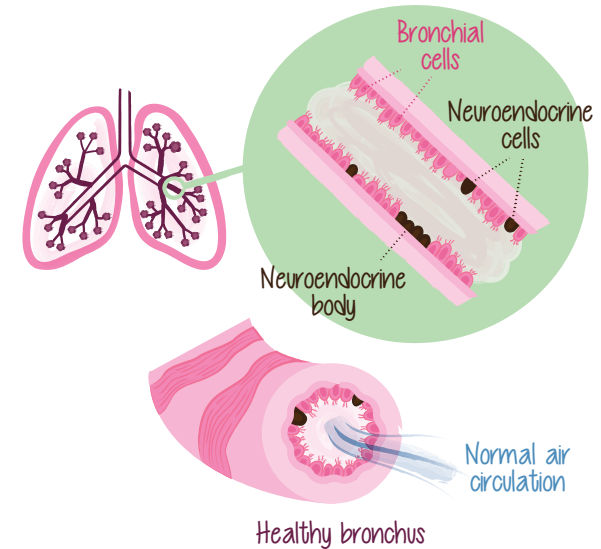
The precise cause of this rare disease (3 to 4 children in a million) is still unknown.

To date, we do not know whether these neuroendocrine cells have:

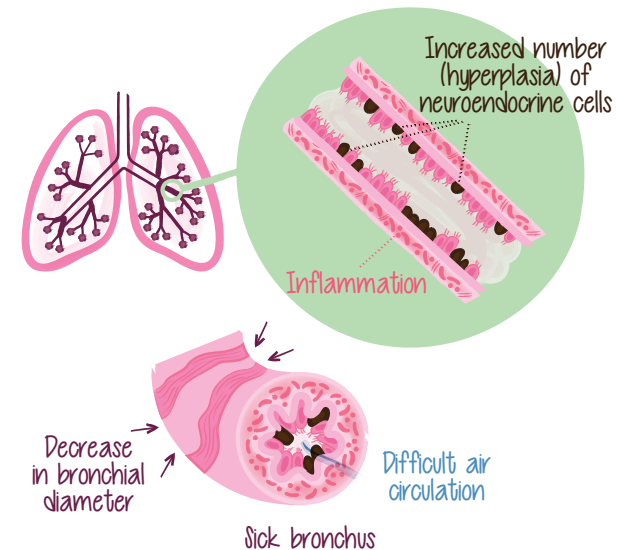
- persisted in excessive numbers since foetal life
- or decreased at birth but increased again in the first months of life.

In very few families, genetic causes of pulmonary surfactant disease have been found. For this reason and in order to progress on the understanding of this disease, a genetic study will be suggested.

Healthy bronchus



NEHI



What are the symptoms of NEHI?

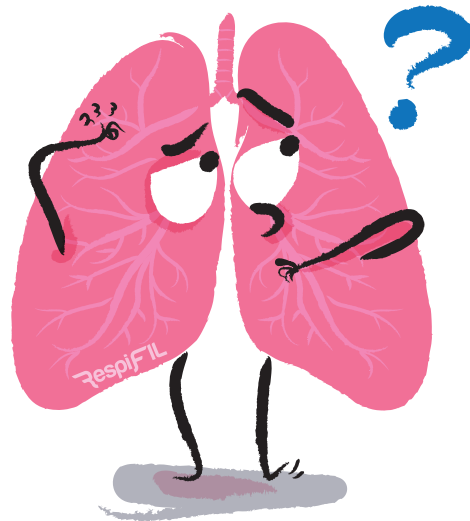
In some cases, the disease may start at birth, but most often its onset is progressive during the first months of life.

NEHI is sometimes also called 'persistent tachypnea of the infancy'.

The first symptoms are an increase in respiratory rate (tachypnoea or polypnoea) and shortness of breath (dyspnoea) during exercise, breastfeeding or bottle-feeding, and sometimes at rest.

Other symptoms may appear, such as:

- Signs of retractions when breathing: the intercostal muscles are sucked inward, between the ribs.
- Crackles and less often wheezing when breathing, which can sometimes be mistaken for signs of bronchiolitis or asthma.
- Cyanosis (bluish lips and fingertips) caused by insufficient oxygenation of the blood during sleep, wakefulness or exercise (during breastfeeding or bottle-feeding).
- Difficulties in eating and insufficient weight gain.



Current knowledge suggests that NEHI only affects the lungs.

All these symptoms can be observed in other respiratory diseases. Therefore, the diagnosis of this disease requires several examinations.

How is NEHI diagnosed?

CT scan

It can be used to detect ILDs: the lung appears in "ground glass opacities" in some parts. This is a sign of inflammation and abnormal repartition of the air in the lung. **Pulmonary ultrasonography** can also be used for the ILD follow-up.

Lung bronchoscopy

It is used to observe the bronchial tubes and analyse the alveoli contents. Analysis of the fluid collected in the alveoli helps to rule out other causes of ILD. In young children, bronchoscopy cannot be used to perform a biopsy because the diameter of the fiberscope is too small.

Blood test

It is used to perform a genetic analysis to rule out pulmonary surfactant disease.

Lung biopsy

This is a surgical procedure that removes a tiny piece of lung and counts the number of neuroendocrine cells in the bronchioles. It is not systematically performed (it is discussed on a case-by-case basis).

Lung function tests (LFTs) and blood gases

These are used to assess respiratory failure. LFTs are most often performed from the age of 3 to 6 years.

The term "NEHI syndrome" is used when the diagnosis of this disease is suspected on the basis of symptoms, CT scan and possibly respiratory function tests. The term "NEHI" is used when the diagnosis is confirmed by lung biopsy.

What are the treatments?

Depending on the individual situation, different treatments can be offered to improve symptoms, exercise tolerance and quality of life.

Medicines

Corticosteroids are the main treatment for ILDs. These anti-inflammatory drugs will help fight the inflammation of the bronchi and bronchioles. They can be given by mouth or intravenously. In NEHI, they may be less effective than in other types of ILDs. Their use has thus to be discussed on a case-by-case basis.

Other drugs may be proposed such as **hydroxychloroquine** (antimalarial) and **azithromycin** (antibiotic). These drugs also have an anti-inflammatory effect.

Oxygen

Oxygen therapy at home is often prescribed (at night and sometimes during the day or when exercising), to maintain normal organ oxygenation, necessary for the child's development.



Nutrition

ILDs, like all chronic lung diseases, involves a significant energy expenditure. This is why a prescription for **food supplements** (energy drinks or bars) or **feeding via a nasogastric tube** (through the nose) may be necessary in order to continue to gain sufficient weight and grow well.

Vaccination

In addition to the usual recommended vaccines, **supplementary vaccinations** may be offered in order to limit respiratory infections.

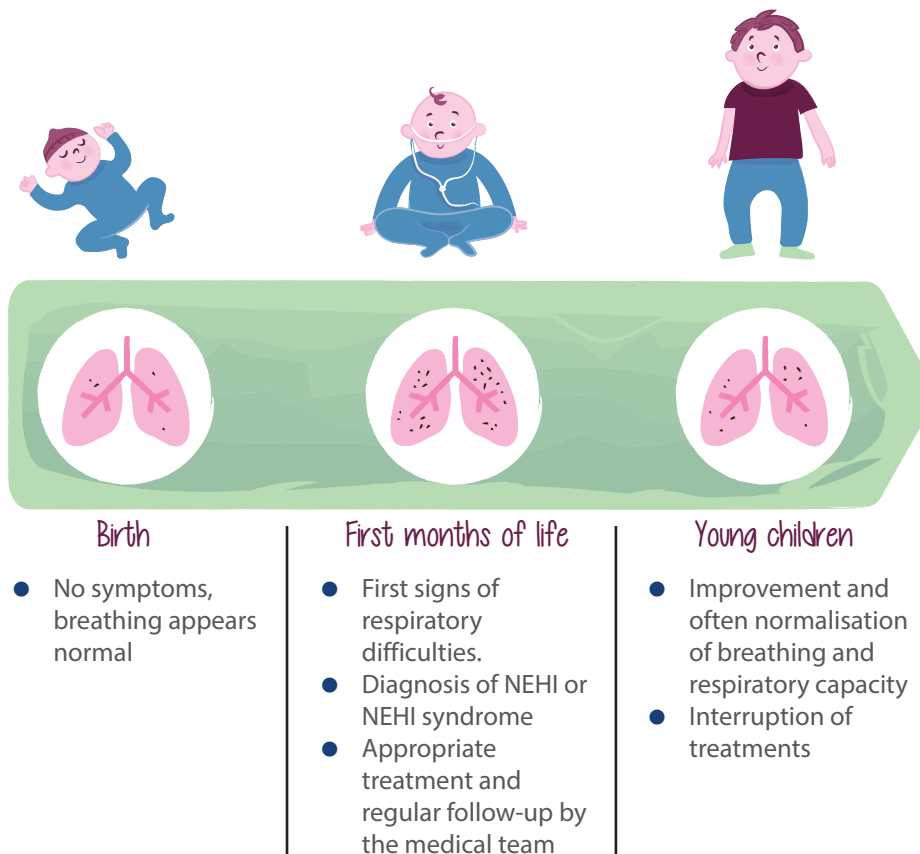
The prognosis for NEHI is usually good: the vast majority of children with this disease recover within a few months or years and sometimes even without any treatment. Regular monitoring by the medical team is essential to control the evolution of the disease.

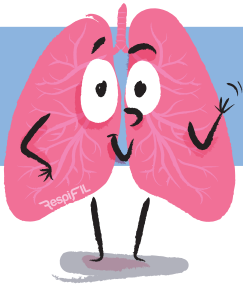
Conclusion

NEHI is a form of ILD in infants, with an unknown cause and is sometimes difficult to diagnose.

The disease may be severe at the beginning, but usually progresses favourably within a few months or years.

Studies are underway to better understand NEHI and other causes of ILDs.





Please do not hesitate to come back to us if you or someone in your family would like more information.



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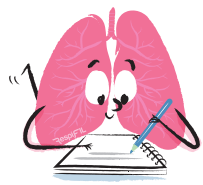
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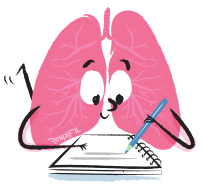
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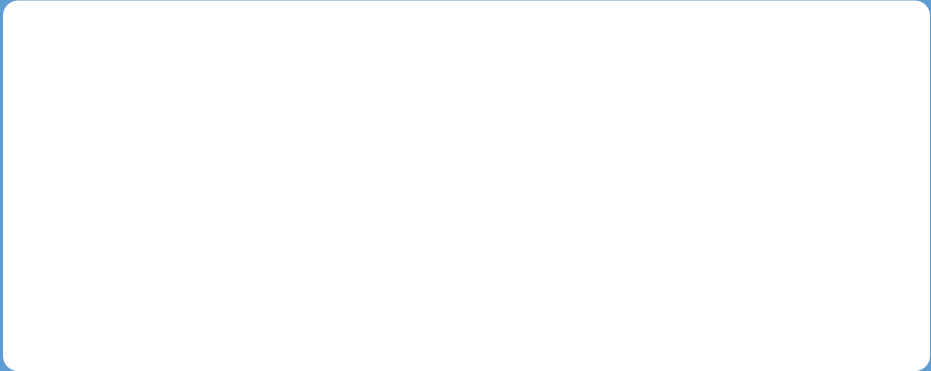








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Established in 2014, the RespiFIL
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