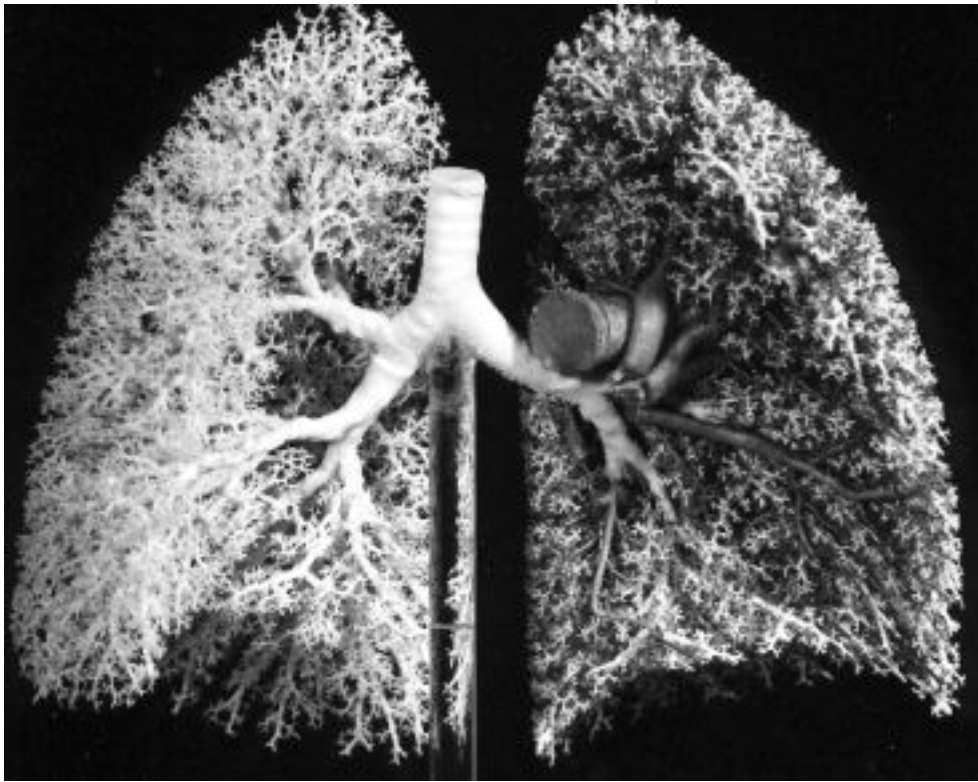


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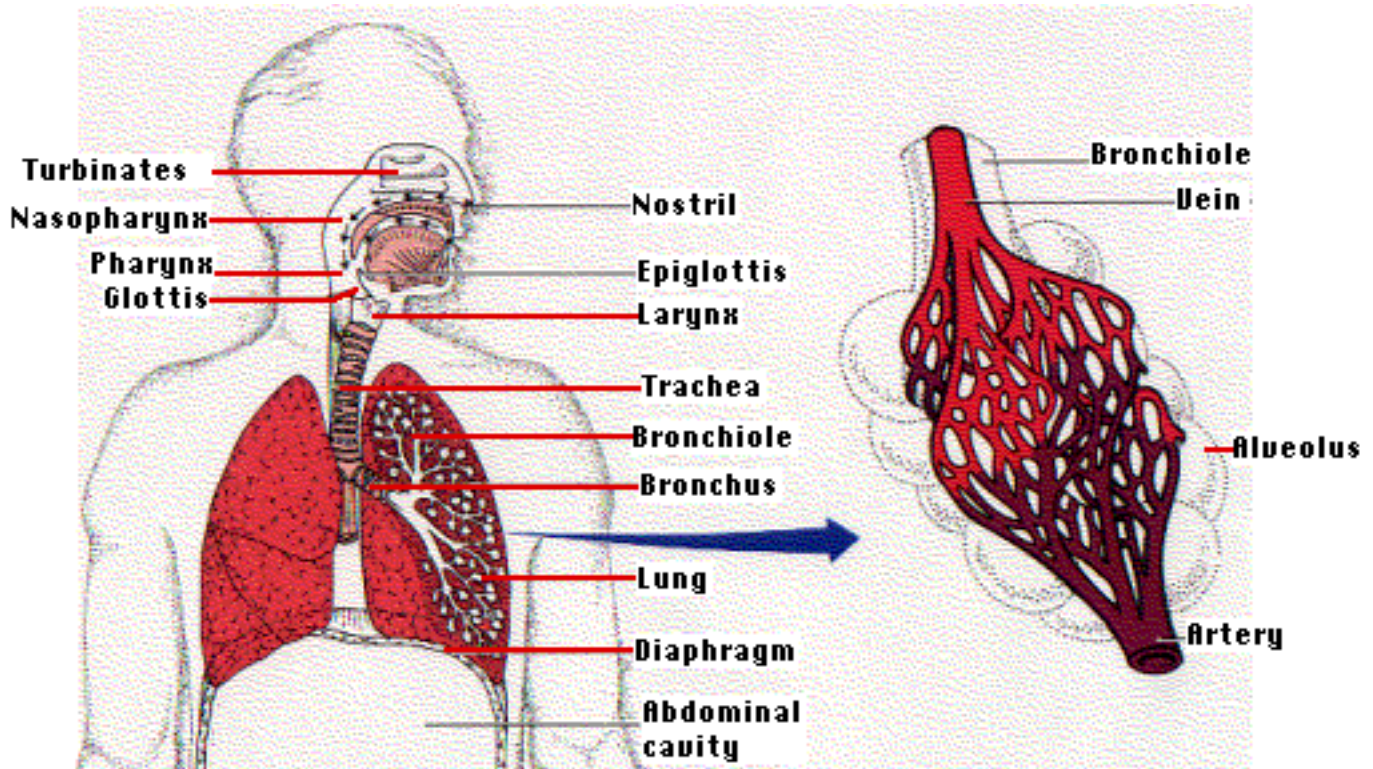
[Lung Cancer](#)

This photo (courtesy of the Anatomical Institute, Bern) shows a rubber cast of human lungs.

The Human Respiratory System

The Pathway

- Air enters the



nostrils

- passes through the **nasopharynx**,
- the **oral pharynx**
- through the **glottis**
- into the **trachea**
- into the right and left **bronchi**, which branches and rebranches into
- **bronchioles**, each of which terminates in a cluster of
- **alveoli**

Only in the alveoli does actual gas exchange takes place. There are some 300 million alveoli in two adult lungs. These provide a surface area of some 160 m² (almost equal to the singles area of a tennis court and 80 times the area of our skin!).

Breathing

In mammals, the diaphragm divides the body cavity into the

- **abdominal cavity**, which contains the viscera (e.g., stomach and intestines) and the
- **thoracic cavity**, which contains the heart and lungs.

The inner surface of the thoracic cavity and the outer surface of the lungs are lined with **pleural membranes** which adhere to each other. If air is introduced between them, the adhesion is broken and the natural elasticity of the lung causes it to collapse. This can occur from trauma. And it is sometimes induced deliberately to allow the lung to rest. In either case, reinflation occurs as the air is gradually

absorbed by the tissues.

Because of this adhesion, any action that increases the volume of the thoracic cavity causes the lungs to expand, drawing air into them.

- During inspiration (inhaling),
 - The external intercostal muscles contract, lifting the ribs up and out.
 - The diaphragm contracts, drawing it down .
- During expiration (exhaling), these processes are reversed and the natural elasticity of the lungs returns them to their normal volume. At rest, we breath 15-18 times a minute exchanging about 500 ml of air.
- In more vigorous expiration,
 - The internal intercostal muscles draw the ribs down and inward
 - The wall of the abdomen contracts pushing the stomach and liver upward.

Under these conditions, an average adult male can flush his lungs with about 4 liters of air at each breath. This is called the **vital capacity**. Even with maximum expiration, about 1200 ml of **residual air** remain.

The table shows what happens to the composition of air when it reaches the alveoli. Some of the oxygen dissolves in the film of moisture covering the epithelium of the alveoli. From here it diffuses into the blood in a nearby capillary. It enters a red blood cell and combines with the hemoglobin therein.

At the same time, some of the carbon dioxide in the blood diffuses into the alveoli from which it can be exhaled.

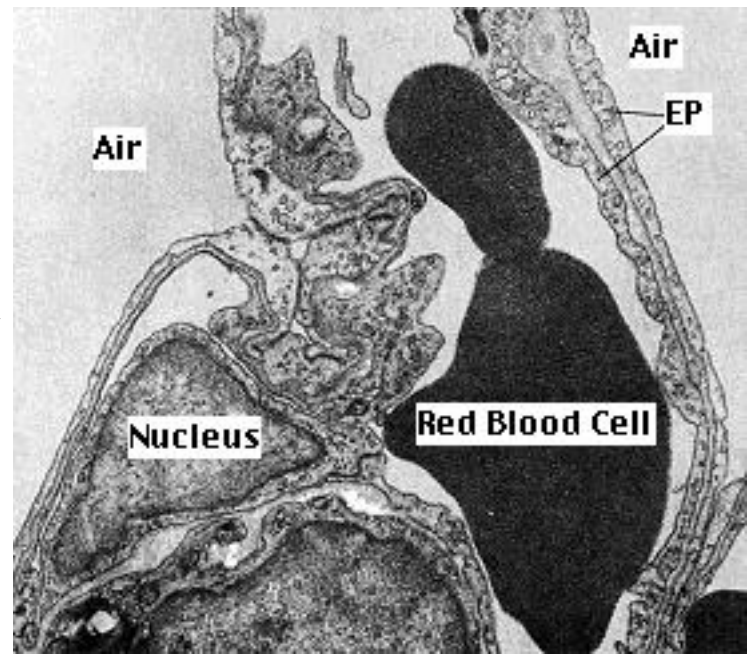
[Link to discussion of gas transport in the blood.](#)

Composition of atmospheric air and expired air in a typical subject.

Note that only a fraction of the oxygen inhaled is taken up by the lungs.

Component	Atmospheric Air (%)	Expired Air (%)
N ₂ (plus inert gases)	78.62	74.9
O ₂	20.85	15.3
CO ₂	0.03	3.6
H ₂ O	0.5	6.2
	100.0%	100.0%

The ease with which oxygen and carbon dioxide can pass between air and blood is clear from this electron micrograph of two alveoli (**Air**) and an adjacent capillary from the lung of a laboratory mouse. Note the thinness of the epithelial cells (**EP**) that line the alveoli and capillary (except where the nucleus is located). At the closest point, the surface of the red blood cell is only 0.7 μm away from the air in the alveolus. (Reproduced with permission from Keith R. Porter and Mary A. Bonneville, **An Introduction to the Fine Structure of Cells and Tissues**, 4th. ed., Lea & Febiger, 1973.)



Central Control of Breathing

The rate of cellular respiration (and hence oxygen consumption and carbon dioxide production) varies with level of activity. Vigorous exercise can increase by 20-25 times the demand of the tissues for oxygen. This is met by increasing the rate and depth of breathing.

It is a rising concentration of **carbon dioxide** — not a declining concentration of oxygen — that plays the major role in regulating the ventilation of the lungs. The concentration of CO_2 is monitored by cells in the [medulla oblongata](#). If the level rises, the medulla responds by increasing the activity of the motor nerves that control the intercostal muscles and diaphragm.

However, the medulla oblongata also has receptors that respond to a drop in oxygen.

These receptors are actually detecting [nitric oxide](#) (NO). Hemoglobin transports NO at the same time it carries oxygen [[Link to discussion of oxygen transport](#)]. When it unloads oxygen in the tissues, it also releases NO.

In severe deoxygenation, NO-sensitive cells in the medulla oblongata respond to this release by increasing the rate and depth of breathing.

Local Control of Breathing

The smooth muscle in the walls of the bronchioles is very sensitive to the concentration of carbon dioxide. A rising level of CO₂ causes the bronchioles to dilate. This lowers the resistance in the airways and thus increases the flow of air in and out.

Diseases of the Lungs

Pneumonia

Pneumonia is an infection of the alveoli. It can be caused by many kinds of both bacteria (e.g., [Streptococcus pneumoniae](#)) and viruses. Tissue fluids accumulate in the alveoli reducing the surface area exposed to air. If enough alveoli are affected, the patient may need supplemental oxygen.

Asthma

In asthma, periodic constriction of the bronchi and bronchioles makes it more difficult to breathe in and, especially, out. Attacks of asthma can be

- triggered by airborne irritants such as chemical fumes and cigarette smoke
- airborne particles to which the patient is **allergic**.

[Link to discussion of allergic asthma.](#)

Emphysema

In this disorder, the delicate walls of the alveoli break down, reducing the gas exchange area of the lungs. The condition develops slowly and is seldom a direct cause of death. However, the gradual loss of gas exchange area forces the heart to pump ever-larger volumes of blood to the lungs in order to satisfy the body's needs. The added strain can lead to heart failure.

The immediate cause of emphysema seems to be the release of proteolytic enzymes as part of the inflammatory process that follows irritation of the lungs. Most people avoid this kind of damage during infections, etc. by producing an enzyme inhibitor (a [serpin](#)) called **alpha-1 antitrypsin**. Those rare people who inherit two defective genes for alpha-1 antitrypsin are particularly susceptible to developing emphysema.

Chronic Bronchitis

Any irritant reaching the bronchi and bronchioles will stimulate an increased secretion of mucus. In

chronic bronchitis the air passages become clogged with mucus, and this leads to a persistent cough. Chronic bronchitis is usually associated with [cigarette smoking](#).

Chronic Obstructive Pulmonary Disease (COPD)

Irritation of the lungs can lead to asthma, emphysema, and chronic bronchitis. And, in fact, many people develop two or three of these together. This constellation is known as **chronic obstructive pulmonary disease (COPD)**.

Among the causes of **COPD** are

- cigarette smoke (often)
- cystic fibrosis (rare)

Cystic fibrosis is a genetic disorder caused by inheriting two defective genes for [CFTR](#), a [transmembrane protein](#) needed for the transport of Cl^- ions. The lungs produce copious amounts of a heavy mucus that plugs the airways interfering with breathing and causing a persistent cough. Cystic fibrosis is the most common inherited disease in the U.S. white population.

[Some mutations that cause cystic fibrosis.](#)

Lung Cancer

Lung cancer is the most common cancer and the most common cause of cancer deaths in U.S. males. Although more women develop breast cancer than lung cancer, since 1987 U.S. women have been dying in larger numbers from lung cancer than from breast cancer.

[Link to lung cancer data.](#)

Lung cancer, like all cancer, is an uncontrolled proliferation of cells. There are several forms of lung cancer, but the most common (and most rapidly increasing) types are those involving the epithelial cells lining the bronchi and bronchioles.

Ordinarily, the lining of these airways consists of two layers of cells. Chronic exposure to irritants

- causes the number of layers to increase. This is especially apt to happen at forks where the bronchioles branch.
- The ciliated and mucus-secreting cells disappear and are replaced by a disorganized mass of cells

with abnormal nuclei.

- If the process continues, the growing mass penetrates the underlying basement membrane.

[Link to illustrations of the cellular changes in developing lung cancer.](#)

- At this point, malignant cells can break away and be carried in lymph and blood to other parts of the body where they may lodge and continue to proliferate.
- It is this [metastasis](#) of the primary tumor that eventually kills the patient.

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12 September 2003