

Pulmonology and Respiratory System Procedures

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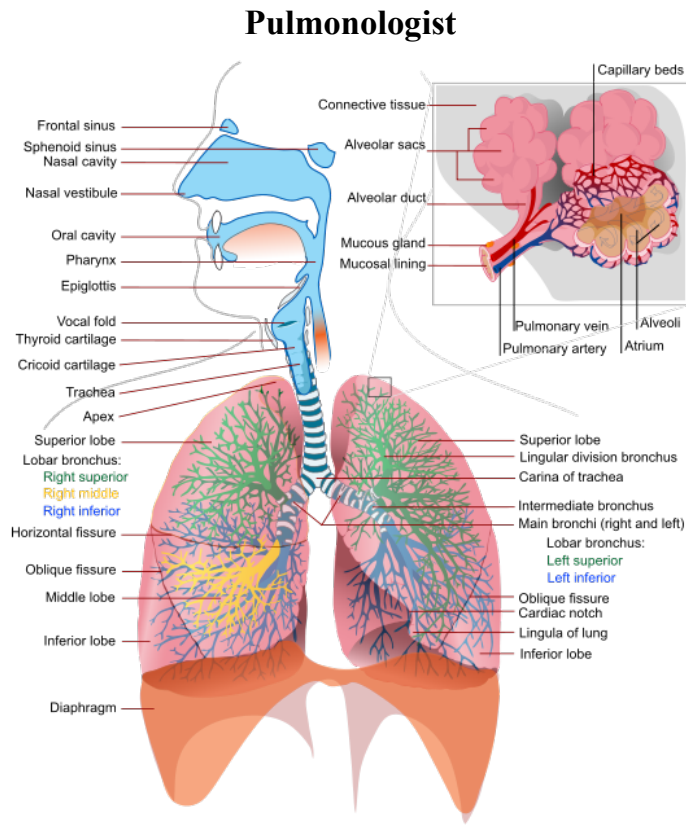
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Chapter 1

Pulmonology



A complete view of the respiratory system.

Occupation

Names	Doctor, Medical Specialist
Type	Specialty
Activity sectors	Medicine

Description

Education required	Doctor of Medicine
Fields of employment	Hospitals, Clinics

In medicine, **pulmonology** (aka **pneumology**) is the specialty that deals with diseases of the respiratory tract and respiratory disease. It is called **chest medicine** and **respiratory medicine** in some countries and areas. *Pulmonology* is generally considered a branch of internal medicine, although it is closely related to intensive care medicine (aka critical care medicine) when dealing with patients requiring mechanical ventilation. **Chest medicine** is not a specialty in itself but is an inclusive term which pertains to the treatment of diseases of the chest and contains the fields of pulmonology, thoracic surgery, and intensive care medicine. Pulmonology is concerned with the diagnosis and treatment of lung diseases, as well as secondary prevention (tuberculosis). Physicians specializing in this area are called pulmonologists. In the United Kingdom, Ireland, South Africa and Australia the term "respiratory physician" is used rather than pulmonologist. In Canada, respirology and respirologist are used. Surgery of the respiratory tract is generally performed by specialists in cardiothoracic surgery (or thoracic surgery), though minor procedures may be performed by pulmonologists. As mentioned above, pulmonology is closely related to critical care medicine when dealing with patients that require mechanical ventilation. As a result, many pulmonologists are certified to practice critical care medicine in addition to pulmonary medicine. There are fellowship programs that allow physicians to become board certified in pulmonary and critical care medicine simultaneously. Interventional pulmonology is a relatively new field within pulmonary medicine that deals with the use of procedures such as bronchoscopy to treat several pulmonary diseases. Interventional pulmonology is not its own specialty.

History of pulmonology

One of the first major discoveries pertaining to pulmonology was the discovery of pulmonary circulation. Originally, it was thought that blood reaching the right side of the heart passed through small 'pores' the septum into the left side to be oxygenated, as theorized by Galen; however, the discovery of pulmonary circulation disproves this theory, which had previously been accepted since the second century. Thirteenth century anatomist and physiologist Ibn Al-Nafis accurately theorized that there was no 'direct' passage between the two sides (ventricles) of the heart. He believed that the blood must have passed through the pulmonary artery, through the lungs, and back into the heart to be pumped around the body. This is believed by many to be the first scientific description of pulmonary circulation.

Although pulmonary medicine only began to evolve as a medical specialty in the 1950's, William Welch and William Osler founded the 'parent' organization of the American Thoracic Society, the National Association for the Study and Prevention of Tuberculosis. When the specialty did begin to evolve, several discoveries were being made linking the respiratory system and the measurement of arterial blood gases, attracting more and more physicians and researchers to the developing field.

Diagnosis

The pulmonologist begins the diagnostic process with a general review focusing on:

- hereditary diseases affecting the lungs (cystic fibrosis, alpha 1-antitrypsin deficiency)
- exposure to toxins (tobacco smoke, asbestos, exhaust fumes, coal mining fumes)
- exposure to infectious agents (certain types of birds, malt processing)
- an autoimmune diathesis that might predispose to certain conditions (pulmonary fibrosis, pulmonary hypertension)

Physical diagnostics are as important as in the other fields of medicine.

- Inspection of the hands for signs of cyanosis or clubbing, chest wall, and respiratory rate.
- Palpation of the cervical lymph nodes, trachea and chest wall movement.
- Percussion of the lung fields for dullness or hyperresonance.
- Auscultation (with a stethoscope) of the lung fields for diminished or unusual breath sounds.
 - Rales or Rhonchi heard over lung fields with a stethoscope.

As many heart diseases can give pulmonary signs, a thorough cardiac investigation is usually included.

Other tools include:

- Laboratory investigation of blood (blood tests). Sometimes arterial blood gas measurements are also required.
- Spirometry (the determination of lung volumes in time by breathing into a dedicated machine; response to bronchodilators and diffusion of carbon monoxide)
- Bronchoscopy with bronchoalveolar lavage (BAL), endobronchial and transbronchial biopsy and epithelial brushing
- Chest X-rays
- CT scanning (MRI scanning is rarely used)
- Scintigraphy and other methods of nuclear medicine
- Positron emission tomography (especially in lung cancer)
- Polysomnography (sleep studies) commonly used for the diagnosis of Sleep apnea

Treatment

Surgical treatment is generally performed by the (cardio)thoracic surgeon, generally after primary evaluation by a pulmonologist. Medication is the most important treatment of most diseases of pulmonology, either by inhalation (bronchodilators and steroids) or in oral form (antibiotics, leukotriene antagonists). A common example being the usage of inhalers in the treatment of inflammatory lung conditions such as Asthma or Chronic obstructive pulmonary disease. Oxygen therapy is often necessary in severe respiratory disease (emphysema and pulmonary fibrosis). When this is insufficient, the patient might require mechanical ventilation.

Pulmonary rehabilitation or respiratory therapy may be initiated as a treatment after all or most other treatments do little to help the patient. Pulmonary rehabilitation is for patients whose respiratory function has decreased or improved very little, even with extensive medical treatment. Pulmonary rehabilitation is intended to educate the patient, the family, and improve the overall quality of life and prognosis for the patient. Although a pulmonologist may refer a patient to therapy, the therapy is generally practiced by respiratory therapists.

Pulmonology as a career

In the United States, pulmonologists are physicians who, after receiving a medical degree (MD or DO), complete residency training in internal medicine (3 years), followed by at least 2 additional years of subspecialty fellowship training in pulmonology. After satisfactorily completing a fellowship in pulmonary medicine, he or she is permitted to take the board certification examination in pulmonary medicine. After passing this exam, he or she is now board certified. Most pulmonologists complete 3 years of combined subspecialty fellowship training in pulmonary medicine and critical care medicine.

In the United States, pediatric pulmonologists are physicians who, after receiving a medical degree (MD or DO), complete residency training in pediatrics (3 years), followed by at least 3 additional years of subspecialty fellowship training in pulmonology.

Usually, respiratory problems can be managed by a specialist in internal medicine; however, some cases require the attention of a pulmonologist. Usually, a pulmonologist will be required in advanced cases of many respiratory diseases.

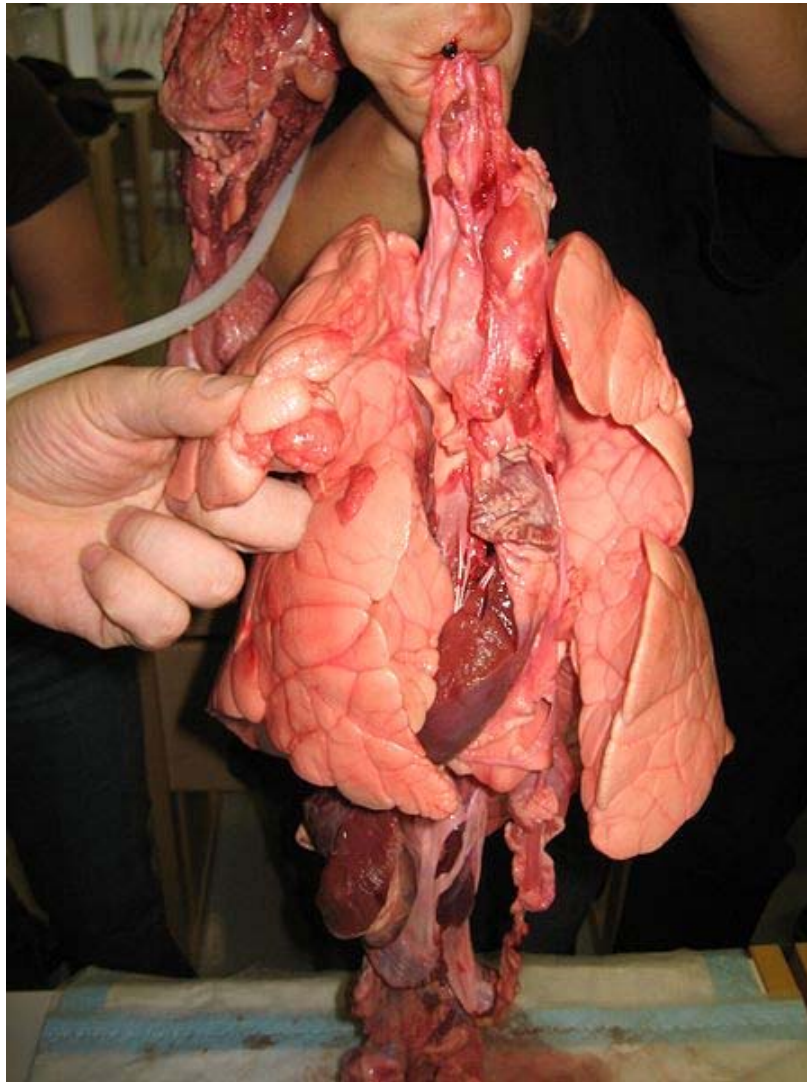
Scientific research

Pulmonologists are involved in both clinical and basic research of the respiratory system, ranging from the anatomy of the respiratory epithelium to the most effective treatment of pulmonary hypertension (a disease notoriously resistant to therapy). Scientific research also takes place to look for causes and possible treatment in diseases such as pulmonary tuberculosis and lung cancer. Several societies are dedicated to expanding the field of pulmonary medicine, some of which are listed below:

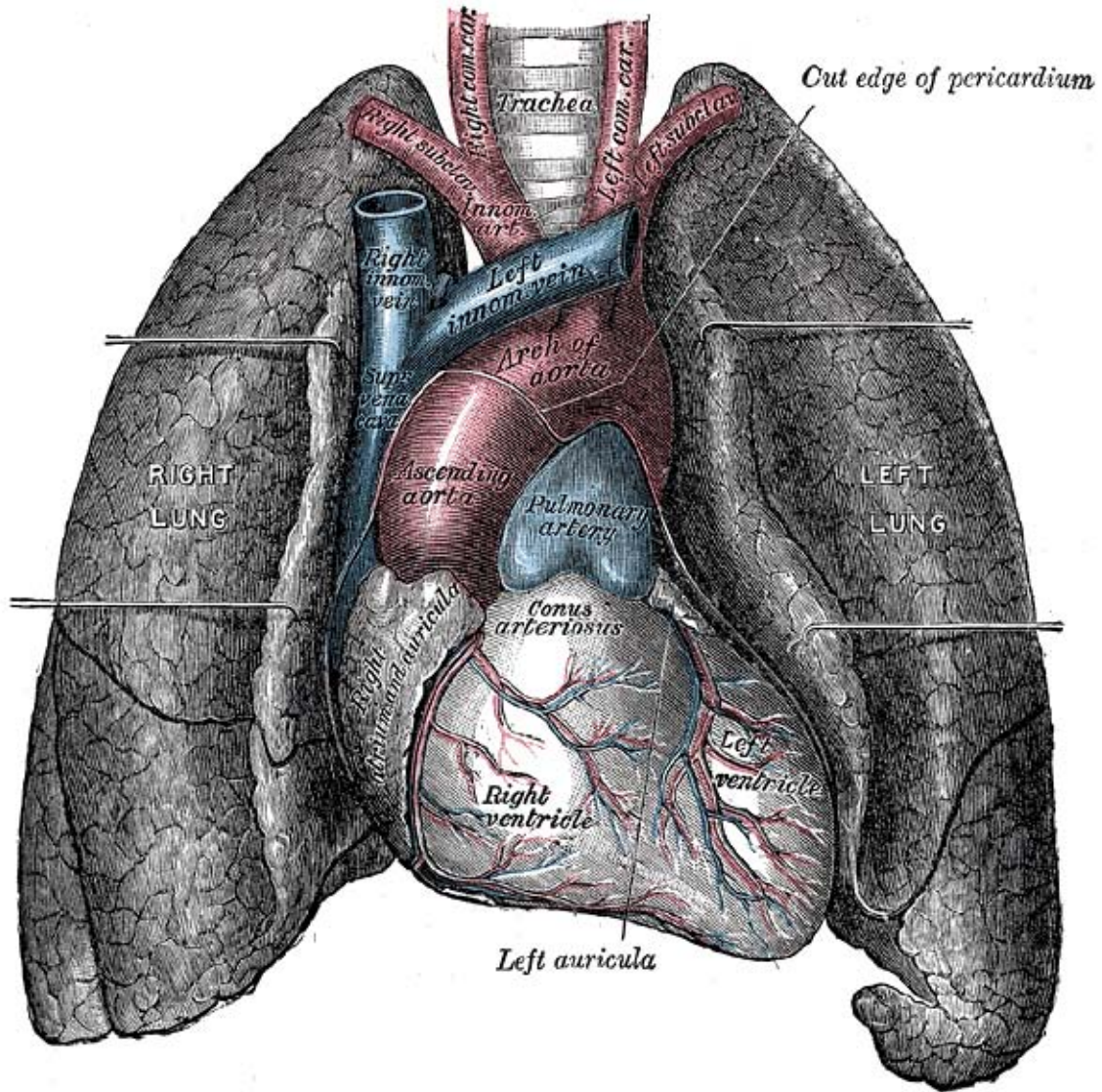
- American College of Chest Physicians
- American Lung Association
- American Thoracic Society
- British Thoracic Society
- European Respiratory Society

Chapter 2

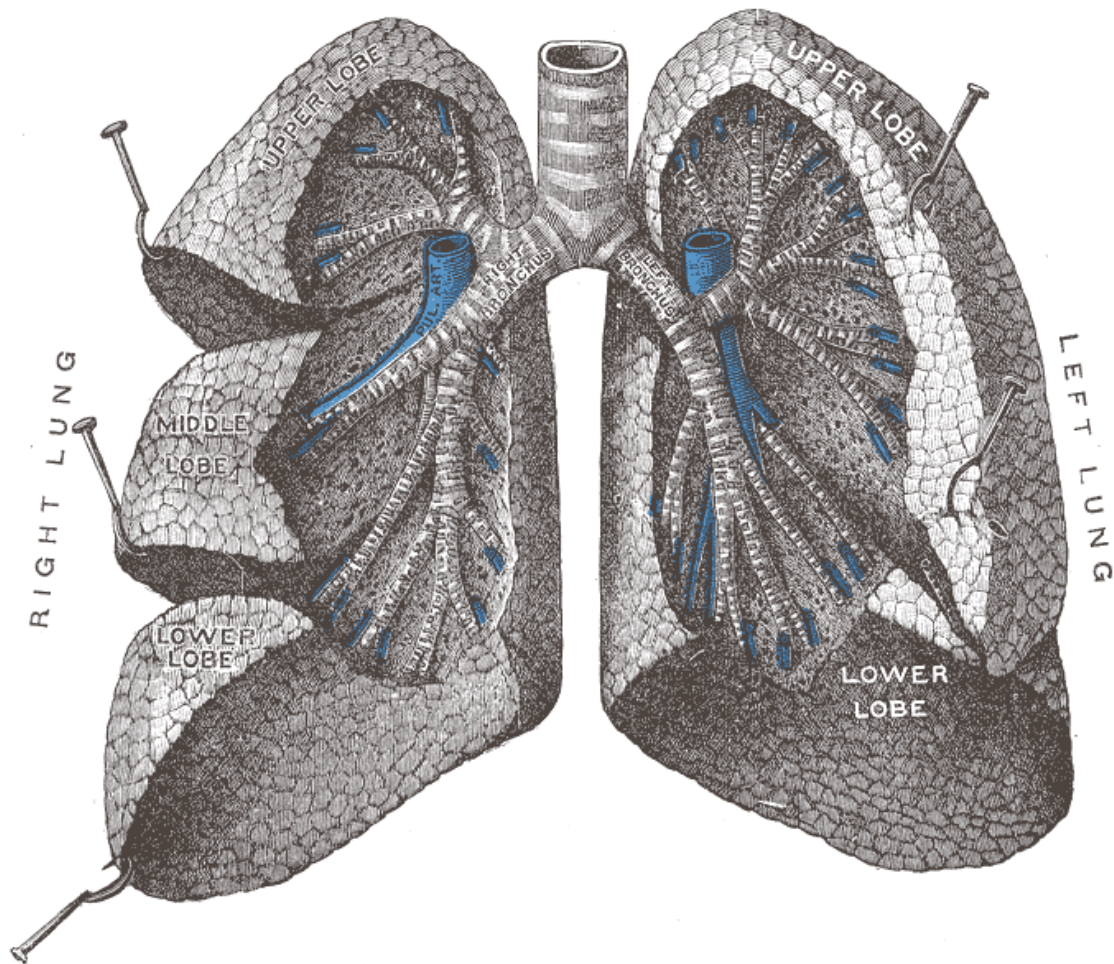
Lung



The lungs of a pig



The human lungs flank the heart and great vessels in the chest cavity



Air enters and leaves the lungs via a conduit of cartilaginous passageways—the bronchi and bronchioles. In this image, lung tissue has been dissected away to reveal the bronchioles

The **lung** (adjectival form: pulmonary) is the essential respiration organ in many air-breathing animals, including most tetrapods, a few fish and a few snails. In mammals and the more complex life forms, the two lungs are located in the chest on either side of the heart. Their principal function is to transport oxygen from the atmosphere into the bloodstream, and to release carbon dioxide from the bloodstream into the atmosphere. This exchange of gases is accomplished in the mosaic of specialized cells that form millions of tiny, exceptionally thin-walled air sacs called alveoli.

To completely explain the anatomy of the lungs, it is necessary to discuss the passage of air through the mouth to the alveoli. Once air progresses through the mouth or nose, it travels through the oropharynx, nasopharynx, the larynx, the trachea, and a progressively subdividing system of bronchi and bronchioles until it finally reaches the alveoli where the gas exchange of carbon dioxide and oxygen takes place.

The drawing and expulsion of air (ventilation) is driven by muscular action; in early tetrapods, air was driven into the lungs by the pharyngeal muscles via buccal pumping, whereas in reptiles, birds and mammals a more complicated musculoskeletal system is used.

Medical terms related to the lung often begin with *pulmo-*, from the Latin *pulmonarius* ("of the lungs"), or with *pneumo-* (from Greek πνεύμων "lung").

Mammalian lungs

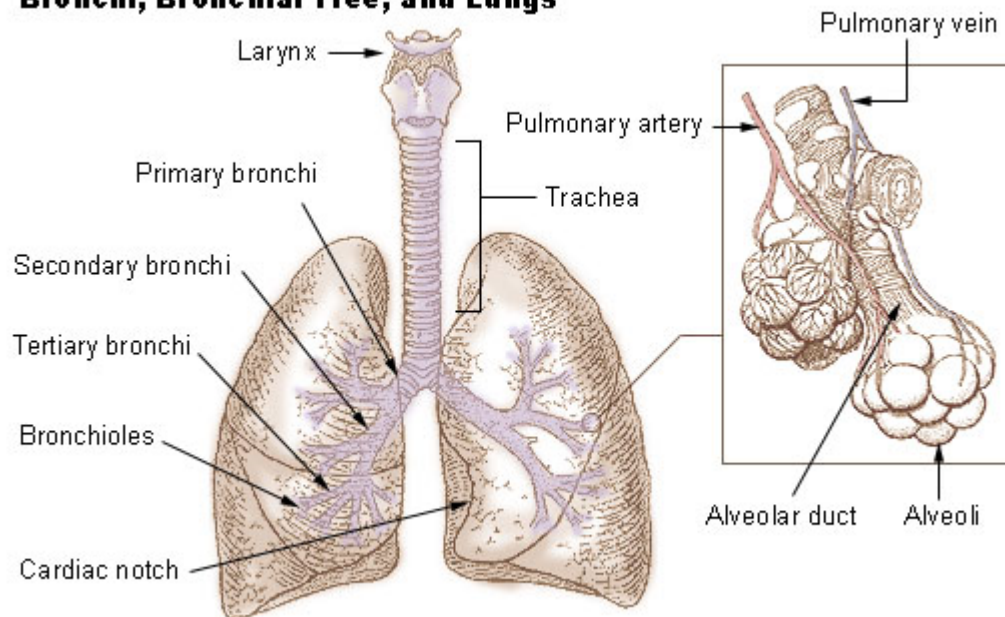
The lungs of mammals have a spongy and soft texture and are honeycombed with epithelium, having a much larger surface area in total than the outer surface area of the lung itself. The lungs of humans are a typical example of this type of lung.

Breathing is largely driven by the muscular diaphragm at the bottom of the thorax. Contraction of the diaphragm pulls the bottom of the cavity in which the lung is enclosed downward, increasing volume and thus decreasing pressure, causing air to flow into the airways. Air enters through the oral and nasal cavities; it flows through the pharynx, then the larynx and into the trachea, which branches out into the main bronchi and then subsequent divisions. During normal breathing, expiration is passive and no muscles are contracted (the diaphragm relaxes). The rib cage itself is also able to expand and contract to some degree, through the action of other respiratory and accessory respiratory muscles. As a result, air is transported into or expelled out of the lungs. This type of lung is known as a bellows lung as it resembles a blacksmith's bellows.

Anatomy

In humans, the trachea divides into the two main bronchi that enter the roots of the lungs. The bronchi continue to divide within the lung, and after multiple divisions, give rise to bronchioles. The bronchial tree continues branching until it reaches the level of terminal bronchioles, which lead to alveolar sacs. Alveolar sacs are made up of clusters of alveoli, like individual grapes within a bunch. The individual alveoli are tightly wrapped in blood vessels and it is here that gas exchange actually occurs. Deoxygenated blood from the heart is pumped through the pulmonary artery to the lungs, where oxygen diffuses into blood and is exchanged for carbon dioxide in the hemoglobin of the erythrocytes. The oxygen-rich blood returns to the heart via the pulmonary veins to be pumped back into systemic circulation.

Bronchi, Bronchial Tree, and Lungs



Human lungs are located in two cavities on either side of the heart. Though similar in appearance, the two are not identical. Both are separated into lobes by fissures, with three lobes on the right and two on the left. The lobes are further divided into segments and then into lobules, hexagonal divisions of the lungs that are the smallest subdivision visible to the naked eye. The connective tissue that divides lobules is often blackened in smokers. The medial border of the right lung is nearly vertical, while the left lung contains a cardiac notch. The cardiac notch is a concave impression molded to accommodate the shape of the heart.

Lungs are to a certain extent 'overbuilt' and have a tremendous reserve volume as compared to the oxygen exchange requirements when at rest. Such excess capacity is one of the reasons that individuals can smoke for years without having a noticeable decrease in lung function while still or moving slowly; in situations like these only a small portion of the lungs are actually perfused with blood for gas exchange. Destruction of too many alveoli over time leads to the condition emphysema, which is associated with extreme shortness of breath. As oxygen requirements increase due to exercise, a greater volume of the lungs is perfused, allowing the body to match its CO_2/O_2 exchange requirements. Additionally, due to the excess capacity, it is possible for humans to live with only one lung, with the other compensating for its loss.

The environment of the lung is very moist, which makes it hospitable for bacteria. Many respiratory illnesses are the result of bacterial or viral infection of the lungs. Inflammation of the lungs is known as pneumonia; inflammation of the pleura surrounding the lungs is known as pleurisy.

Vital capacity is the maximum volume of air that a person can exhale after maximum inhalation; it can be measured with a spirometer. In combination with other physiological measurements, the vital capacity can help make a diagnosis of underlying lung disease.

The *lung parenchyma* is strictly used to refer solely to alveolar tissue with respiratory bronchioles, alveolar ducts and terminal bronchioles. However, it often includes any form of lung tissue, also including bronchioles, bronchi, blood vessels and lung interstitium.

Non respiratory functions

In addition to their function in respiration, the lungs also:

- Alter the pH of blood by facilitating alterations in the partial pressure of carbon dioxide
- Filter out small blood clots formed in veins
- Filter out gas micro-bubbles occurring in the venous blood stream such as those created after scuba diving during decompression.
- Influence the concentration of some biologic substances and drugs used in medicine in blood
- Convert angiotensin I to angiotensin II by the action of angiotensin-converting enzyme
- May serve as a layer of soft, shock-absorbent protection for the heart, which the lungs flank and nearly enclose.
- Immunoglobulin-A is secreted in the bronchial secretion and protects against respiratory infections.
- Maintain sterility by producing mucus containing antimicrobial compounds. Mucus contains glycoproteins, e.g. mucins, lactoferrin, lysozyme, lactoperoxidase. We find also on the epithelium Dual oxidase 2 proteins generating hydrogen peroxide, useful for hypothiocyanite endogenous antimicrobial synthesis. Function not in place in cystic fibrosis patient lungs.
- Ciliary escalator action is an important defence system against air-borne infection. The dust particles and bacteria in the inhaled air are caught in the mucous layer present at the mucosal surface of respiratory passages and are moved up towards pharynx by the rhythmic upward beating action of the cilia

Avian lungs

Avian lungs do not have alveoli as mammalian lungs do, they have Faveolar lungs. They contain millions of tiny passages known as para-bronchi, connected at both ends by the dorsobronchi. The airflow through the avian lung always travels in the same direction – posterior to anterior. This is in contrast to the mammalian system, in which the direction of airflow in the lung is tidal, reversing between inhalation and exhalation. By utilizing a unidirectional flow of air, avian lungs are able to extract a greater concentration of oxygen from inhaled air. Birds are thus equipped to fly at altitudes at which mammals would succumb to hypoxia. This also allows them to sustain a higher metabolic rate than an equivalent weight mammal.

The lungs of birds are relatively small, but are connected to 8-9 air sacs that extend through much of the body, and are in turn connected to air spaces within the bones. The air sacs are smooth-walled, and do not themselves contribute much to respiration, but they do help to maintain the airflow through the lungs as air is forced through them by the movement of the ribs and flight muscles.

Because of the complexity of the system, misunderstanding is common and it is incorrectly believed that it takes two breathing cycles for air to pass entirely through a bird's respiratory system. A bird's lungs do not store air in either of the sacs between respiration cycles, air moves continuously from the posterior to anterior air sacs throughout respiration. This type of lung construction is called a circulatory lung, as distinct from the bellows lung possessed by other animals.

Reptilian lungs

Reptilian lungs are typically ventilated by a combination of expansion and contraction of the ribs via axial muscles and buccal pumping. Crocodylians also rely on the hepatic piston method, in which the liver is pulled back by a muscle anchored to the pubic bone (part of the pelvis), which in turn pulls the bottom of the lungs backward, expanding them. Turtles, which are unable to move their ribs, instead use their forelimbs and pectoral girdle to force air in and out of the lungs.

The lung of most reptiles has a single bronchus running down the centre, from which numerous branches reach out to individual pockets throughout the lungs. These pockets are similar to, but much larger and fewer in number than, mammalian alveoli, and give the lung a sponge-like texture. In tuataras, snakes, and some lizards, the lungs are simpler in structure, similar to that of typical amphibians.

Snakes and limbless lizards typically possess only the right lung as a major respiratory organ; the left lung is greatly reduced, or even absent. Amphisbaenians, however, have the opposite arrangement, with a major left lung, and a reduced or absent right lung.

Amphibian lungs

The lungs of most frogs and other amphibians are simple balloon-like structures, with gas exchange limited to the outer surface area of the lung. This is not a very efficient arrangement, but amphibians have low metabolic demands and also frequently supplement their oxygen supply by diffusion across the moist outer skin of their bodies. Unlike mammals, which use a breathing system driven by negative pressure, amphibians employ positive pressure. The majority of salamander species are lungless salamanders, which respire through their skin and tissues lining their mouth. The only other known lungless tetrapods are also amphibians; the Bornean Flat-headed Frog (*Barbourula kalimantanensis*) and *Atretochoana eiselti*, a caecilian.

The lungs of amphibians typically have a few narrow septa of soft tissue around the outer walls, increasing the respiratory surface area and giving the lung a honey-comb

appearance. In some salamanders even these are lacking, and the lung has a smooth wall. In caecilians, as in snakes, only the right lung attains any size or development.

Lungfish

The lungs of lungfish are similar to those of amphibians, with few, if any, internal septa. In *Polypterus* and the Australian lungfish, there is only a single lung, albeit divided into two lobes in the former case. Other lungfish, however, have two lungs, which are located in the upper part of the body, with the connecting duct curving round and above the esophagus. The blood supply also twists around the esophagus, suggesting that the lungs originally evolved in the ventral part of the body, as in other vertebrates.

Invertebrate lungs

Some invertebrates have "lungs" that serve a similar respiratory purpose as, but are not evolutionarily related to, vertebrate lungs. Some arachnids have structures called "book lungs" used for atmospheric gas exchange. The Coconut crab uses structures called Branchiostegal lungs to breathe air and indeed will drown in water, hence it breathes on land and holds its breath underwater. The Pulmonata are an order of snails and slugs that have developed "lungs".

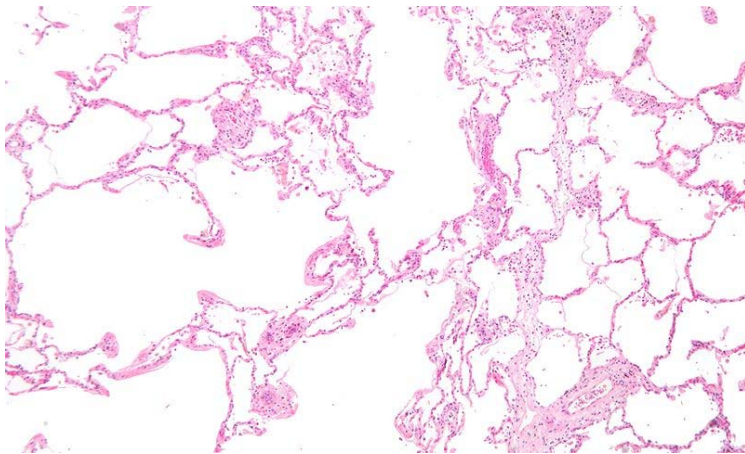
Origins of the vertebrate lung

The lungs of today's terrestrial vertebrates and the gas bladders of today's fish are believed to have evolved from simple sacs (outpocketings) of the esophagus that allowed early fish to gulp air under oxygen-poor conditions. These outpocketings first arose in the bony fish; in some of the ray-finned fish the sacs evolved into gas bladders, while in other ray-finned fish (such as the gar, bichir and amia) as well as the lobe-finned fish they evolved into lungs. The lobe-finned fish gave rise to the land-based tetrapods. Thus, the lungs of vertebrates are homologous to the gas bladders of fish (but not to their gills). This is reflected by the fact that the lungs of a fetus also develop from an outpocketing of the esophagus and in the case of gas bladders, this connection to the gut continues to exist as the pneumatic duct in more "primitive" teleosts, and is lost in the higher orders. (This is an instance of correlation between ontogeny and phylogeny.) No known animals have both a gas bladder and lungs.

Chapter 3

Respiratory Disease

Respiratory Disease



Micrograph of an emphysematous lung; emphysema is a common respiratory disease, strongly associated with smoking. H&E stain.

ICD-10 J00.-J99.

ICD-9 460-519

MeSH D012140

Respiratory disease is the term for diseases of the respiratory system. These include diseases of the lung, pleural cavity, bronchial tubes, trachea, upper respiratory tract and of the nerves and muscles of breathing. Respiratory diseases range from mild and self-limiting such as the common cold to life-threatening such as bacterial pneumonia or pulmonary embolism. They are a common and important cause of illness and death. In the US, people suffer 1 billion colds per year. One in seven people in the UK are affected by some form of chronic lung disease, most commonly chronic obstructive pulmonary disease and asthma. Respiratory disease is responsible for over 10% of hospitalizations and over 16% of deaths in Canada (including lung cancer). The study of respiratory disease is known as pulmonology. A doctor who specializes in respiratory disease is known as a pulmonologist, a chest medicine specialist, a respiratory medicine specialist, a respirologist or a thoracic medicine specialist.

Diagnostic tests

Respiratory diseases may be investigated by performing one or more of the following tests

- Chest x-ray
- Pulmonary function test
- Computed tomography scan
- Culture of microorganisms from secretions such as sputum
- Bronchoscopy
- Biopsy of the lung or pleura
- Ventilation - perfusion scan
- Ultrasound scanning can be useful to detect fluid such as pleural effusion

Treatment for respiratory diseases

Treatment of respiratory disease depends on the particular disease being treated, the severity of disease and the patient. Such as regular exercise and healthy nutrition are important in preventing and treating respiratory disease. Vaccination can prevent some respiratory diseases. In addition, the following treatments are often used for respiratory diseases:

- Medication, often given in an inhaled form
 - Corticosteroids
 - Bronchodilators
 - Antibiotics
 - Anticoagulants
 - Cancer chemotherapy
 - Immune suppressants
- Physiotherapy
- Oxygen
- Mechanical ventilation
- Liquid ventilation (or Liquid breathing)
- Surfactant Replacement Therapy
- Radiotherapy
- Surgery
 - Removal of a cancer e.g. lobectomy, pneumonectomy
 - Pleurodesis
 - Lung volume reduction surgery
 - Lung transplantation
 - Artificial lung

Respiratory diseases

Respiratory diseases can be classified in many different ways: by the organ involved, by the pattern of symptoms or by the cause of the disease. The main thing is to always be

careful around food because some foods can cause allergic reactions and incite breathing difficulties. Some common examples include sea foods prawns, some fatty fish, raddish, arrow root, ladys finger, lemon, moong dhal, peanuts, water content spinach, curd, bananas, grapes, pomegranates, berries, custard apple, ice creams, etc. In summer, bad weather condition mean sandy and dusty weather or some may affect in winter also.

Inflammatory lung disease

Characterised by a high neutrophil count, eg asthma, cystic fibrosis, emphysema, chronic obstructive pulmonary disorder or acute respiratory distress syndrome.

Obstructive lung diseases

Obstructive lung diseases are diseases of the lung where the bronchial tubes become narrowed making it hard to move air in and especially out of the lung.

Chronic Obstructive Pulmonary Disease (COPD)

Chronic Obstructive Pulmonary Disease (COPD), an example of an obstructive lung disease, is where the airways become damaged, causing them to narrow.

Asthma

Asthma is another example of an obstructive lung disease, (and of an inflammatory lung disease).

Restrictive lung diseases

Restrictive lung diseases (also known as interstitial lung diseases) are a category of respiratory disease characterized by a loss of lung compliance, causing incomplete lung expansion and increased lung stiffness. E.g. in infant respiratory distress syndrome (IRDS).

Respiratory tract infections

Infections can affect any part of the respiratory system. They are traditionally divided into upper respiratory tract infections and lower respiratory tract infections.

Upper respiratory tract infection

The most common upper respiratory tract infection is the common cold however, infections of specific organs of the upper respiratory tract such as sinusitis, tonsillitis, otitis media, pharyngitis and laryngitis are also considered upper respiratory tract infections.

Lower respiratory tract infection

The most common lower respiratory tract infection is pneumonia, a lung infection. Pneumonia is usually caused by bacteria, particularly *Streptococcus pneumoniae* in Western countries. Worldwide, tuberculosis is an important cause of pneumonia. Other pathogens such as viruses and fungi can cause pneumonia for example severe acute respiratory syndrome and pneumocystis pneumonia. A pneumonia may develop complications such as a lung abscess, a round cavity in the lung caused by the infection, or may spread to the pleural cavity.

Respiratory tumors

Tumours of the respiratory system are either malignant or benign.

Malignant tumors

Malignant tumors, or cancers of the respiratory system, particularly lung cancers, are a major health problem responsible for 15% of all cancer diagnoses and 29% of all cancer deaths. The majority of respiratory system cancers are attributable to smoking tobacco.

The major types of respiratory system cancer are:

- Small cell lung cancer
- Non-small cell lung cancer
 - Adenocarcinoma
 - Large cell undifferentiated carcinoma
- Other lung cancers (carcinoid, Kaposi's sarcoma, melanoma)
- Lymphoma
- Head and neck cancer
- Mesothelioma, usually caused by exposure to asbestos dust.

In addition, since many cancers spread via the bloodstream and the entire cardiac output passes through the lungs, it is common for cancer metastases to occur within the lung. Breast cancer may invade directly through local spread, and through lymph node metastases. After metastasis to the liver, colon cancer frequently metastasizes to the lung. Prostate cancer, germ cell cancer and renal cell carcinoma may also metastasize to the lung.

Treatment of respiratory system cancer depends on the type of cancer. Surgery (usually removal of part of the lung, a lobectomy or an entire lung, a pneumonectomy), chemotherapy and radiotherapy are all used. The chance of surviving lung cancer depends on the cancer stage at the time the cancer is diagnosed and is only about 14-17% overall. In the case of metastases to the lung, treatment can occasionally be curative but only in certain, rare circumstances.

Benign tumors

Benign tumors are relatively rare causes of respiratory disease. Examples of benign tumors are:

- Pulmonary hamartoma
- Congenital malformations such as pulmonary sequestration and congenital cystic adenomatoid malformation (CCAM).

Pleural cavity diseases

Pleural cavity diseases include emphysema and mesothelioma which are mentioned above.

A collection of fluid in the pleural cavity is known as a pleural effusion. This may be due to fluid shifting from the bloodstream into the pleural cavity due to conditions such as congestive heart failure and cirrhosis. It may also be due to inflammation of the pleura itself as can occur with infection, pulmonary embolus, tuberculosis, mesothelioma and other conditions.

A pneumothorax is a hole in the pleura covering the lung allowing air in the lung to escape into the pleural cavity. The affected lung “collapses” like a deflated balloon. A tension pneumothorax is a particularly severe form of this condition where the air in the pleural cavity cannot escape, so the pneumothorax keeps getting bigger until it compresses the heart and blood vessels, leading to a life threatening situation.

Pulmonary vascular diseases

Pulmonary vascular diseases are conditions that affect the pulmonary circulation. Examples of these conditions are

- Pulmonary embolism, a blood clot that forms in a vein, breaks free, travels through the heart and lodges in the lungs (thromboembolism). Large pulmonary emboli are fatal, causing sudden death. A number of other substances can also embolise (travel through the blood stream) to the lungs but they are much more rare: fat embolism (particularly after bony injury), amniotic fluid embolism (with complications of labour and delivery), air embolism (iatrogenic - caused by invasive medical procedures).
- Pulmonary arterial hypertension, elevated pressure in the pulmonary arteries. Most commonly it is idiopathic (i.e. of unknown cause) but it can be due to the effects of another disease, particularly COPD. This can lead to strain on the right side of the heart, a condition known as cor pulmonale.
- Pulmonary edema, leakage of fluid from capillaries of the lung into the alveoli (or air spaces). It is usually due to congestive heart failure.
- Pulmonary hemorrhage, inflammation and damage to capillaries in the lung resulting in blood leaking into the alveoli. This may cause blood to be coughed

up. Pulmonary hemorrhage can be due to auto-immune disorders such as Wegener's Granulomatosis and Goodpasture's syndrome.

Chapter 4

Acute Exacerbations of Chronic Bronchitis

Acute exacerbations of chronic bronchitis (AECB) are episodes of difficulty in breathing in a person with chronic bronchitis.

In concomitant presence of emphysema, the underlying condition can be classified as chronic obstructive pulmonary disease (COPD), and the exacerbations termed "acute exacerbation of COPD", and shares many characteristics with that of AECB.

Incidence

The incidence of AECB varies depending on which definition is used, but by AECB definitions by *Anthonisen et al.* the typical COPD patient averages two to three AECB episodes per year. With a COPD prevalence of more than 12 million (possibly 24 million including undiagnosed ones) in the United States, there are at least 30 million incidences of AECB annually in the US.

Pathogenesis

During AECB, breathing becomes much more difficult because of further narrowing of the airways, in addition to increased secretion of mucus, which often is thicker than usual.

Causes

AECB can be caused by:

- Allergens, e.g., pollens, wood or cigarette smoke, pollution
- Toxins, including a variety of different chemicals
- Acute viral or bacterial infections. The extra mucus in the airways in chronic bronchitis provides a good place for viruses and bacteria to grow. Bacterial infections are suspected when there is a yellow or greenish colour of the mucus, or it is thicker than usual. However, coloured mucus is not specific to bacterial infections. Common bacterial pathogens of acute exacerbations include *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Moraxella catarrhalis*.

Less common bacterial pathogens include *Chlamydia pneumoniae* and *MRSA*. Pathogens seen more frequently in patients with impaired lung function (FEV₁<35% of predicted) include *Haemophilus parainfluenzae* (after repeated use of antibiotics), *Mycoplasma pneumoniae* and gram-negative, opportunistic pathogens like *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*.

Although the condition of a patient with chronic bronchitis can become exacerbated by many other factors as well, the scope is generally restricted to the ones that cause the symptoms below.

Symptoms

An acute exacerbation of chronic bronchitis is associated with increased frequency and severity of coughing. It is often accompanied by worsened chest congestion and discomfort. Shortness of breath and wheezing are present in many cases.

In infection, there is often weakness, fever and chills. If due to a bacterial infection, the sputum may be slightly streaked with blood and coloured yellow or green.

Diagnosis

The diagnostic criteria for acute exacerbation of chronic bronchitis generally include an production of sputum that is purulent and may be thicker than usual, but without evidence of pneumonia (which involves mainly the alveoli rather than the bronchi). Also, diagnostic criteria may include an increased in frequency and severity of cough, as well as increased shortness of breath.

A chest X-ray is usually performed on people with fever and, especially, hemoptysis (blood in the sputum), to rule out pneumonia and get information on the severity of the exacerbation. Hemoptysis may also indicate other, potentially fatal, medical conditions.

A history of exposure to potential causes and evaluation of symptoms may help in revealing the cause of an acute exacerbation of chronic bronchitis, which helps in choosing the best treatment. A sputum culture can specify which strain is causing a bacterial AECB. An early morning sample is preferred.

Prevention

Prevention of AECB include:

- Smoking cessation and avoiding dust, passive smoking, and other inhaled irritants
- Yearly influenza and pneumococcal vaccine
- Regular exercise, appropriate rest, and healthy nutrition
- Avoiding people currently infected with e.g. cold and influenza
- Maintaining good fluid intake and humidifying the home, in order to help reduce the formation of thick sputum and chest congestion.

Treatment

Treatment is often started before the test results confirm the condition.

Treatment of AECB may include:

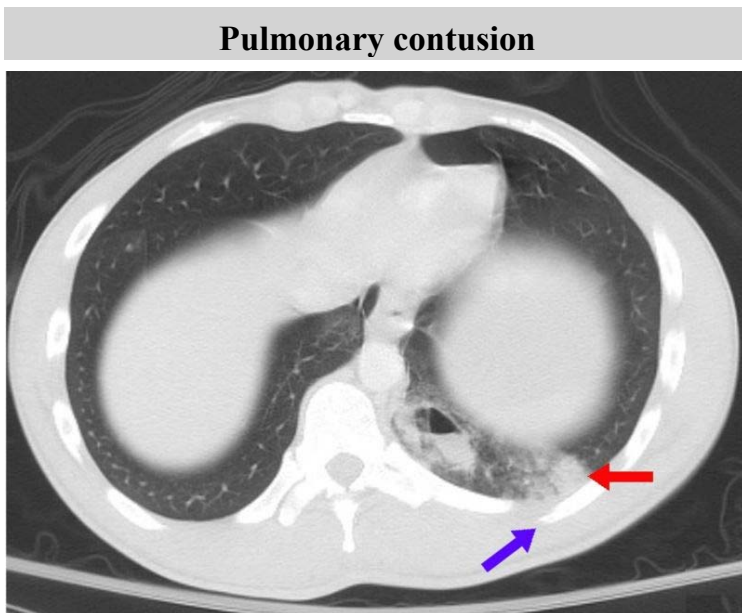
- Mucolytic agents may be used to help liquefy thick mucus, facilitating clearance from the airways. Thinning of mucus may also be done by drinking plenty of fluids.
- Inhaled bronchodilators open up the airways in the lungs. These include salbutamol and terbutaline (both β_2 -adrenergic agonists), and ipratropium (an anticholinergic).
- Antibiotics are used if a bacterial infection is the suspected cause. However, antibiotics will not treat exacerbations caused by viruses. Viral infections will usually be cured with time with the aid of proper rest and care. Still, other medications may be needed to control symptoms. Lipid-soluble antibiotics such as macrolides, tetracyclines, and quinolones penetrate the lung tissue well. Macrolides are more active against *Streptococcus pneumoniae* than the tetracyclines and the older quinolones. Within the macrolides, newer ones are more active against *Haemophilus influenzae* than the older erythromycin. Regimens should generally be given for five days. Choice of antibiotics is also dependent on the severity of chronic bronchitis:
 - "Simple" chronic bronchitis is generally where the patient is 65 years or less, has fewer than four exacerbations per year, has minimal or moderate impairment in respiratory function and no comorbid disease. In patients with "simple" chronic bronchitis, therapy should be targeted towards *Haemophilus influenzae*, *Moraxella catarrhalis*, *Streptococcus pneumoniae*, and possibly pathogens of atypical pneumonia. The first-line treatment is a beta-lactam antibiotic such as amoxicillin. The choice will depend on resistance patterns. In patients with penicillin allergy, doxycycline or trimethoprim are preferred.
 - More complicated bronchitis may be when the patient is more than 65 years old, has four or more exacerbations per year, has an FEV1/FVC ratio of less than 50% on spirometry, has failed to respond to previous antibiotic treatment, and/or has comorbidity. In these cases, treatment should be aimed at Gram-negative bacteria and the possibility of high antibiotic resistance should be considered. Sputum culture results are of great value in determining antibiotic resistance. First-line treatment is cefuroxime or co-amoxiclav. Third-line treatment, as well as treatment in penicillin-allergic patients, is a fluoroquinolone such as ciprofloxacin. An agent active against *Streptococcus pneumoniae* may have to be added.
- Corticosteroids such as prednisone reduce inflammation in the airways. They are usually used for short periods.
- Theophylline, taken orally, helps to ease the difficulty of breathing. It may be added if the patient is not already taking it for the chronic bronchitis.

- Oxygen therapy should be initiated if there is a substantial risk of hypoxia. If oxygen is required on an ongoing basis, a portable oxygen concentrator can be used.

There should also be a "care plan" in case of future exacerbations. Patients may watch for symptoms, such as shortness of breath, change in character or amount of mucus, and start self-treatment as discussed with a health care provider. This allows for treatment right away until a doctor can be seen.

Chapter 5

Pulmonary Contusion



A CT scan showing a pulmonary contusion (red arrow) accompanied by a rib fracture (blue arrow)

ICD-10 S27.3

ICD-9 861.21, 861.31

A **pulmonary contusion** (or **lung contusion**) is a contusion (bruise) of the lung, caused by chest trauma. As a result of damage to capillaries, blood and other fluids accumulate in the lung tissue. The excess fluid interferes with gas exchange, potentially leading to inadequate oxygen levels (hypoxia). Unlike pulmonary laceration, another type of lung injury, pulmonary contusion does not involve a cut or tear of the lung tissue.

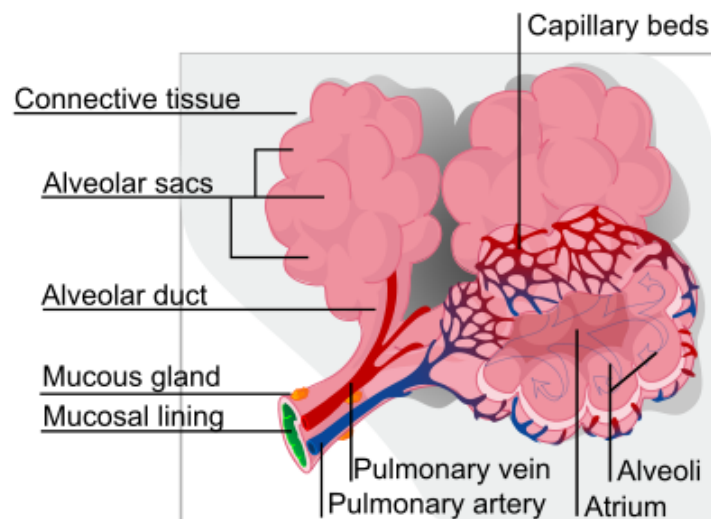
A pulmonary contusion is usually caused directly by blunt trauma but can also result from explosion injuries or a shock wave associated with penetrating trauma. With the use of explosives during World Wars I and II, pulmonary contusion resulting from blasts gained recognition. In the 1960s its occurrence in civilians began to receive wider

recognition, in which cases it is usually caused by traffic accidents. The use of seat belts and airbags reduces the risk to vehicle occupants.

Diagnosis is made by studying the cause of the injury, physical examination and chest radiography. Typical signs and symptoms include direct effects of the physical trauma, such as chest pain and coughing up blood, as well as signs that the body is not receiving enough oxygen, such as cyanosis. The contusion frequently heals on its own with supportive care. Often nothing more than supplemental oxygen and close monitoring is needed; however, intensive care may be required. For example, if breathing is severely compromised, mechanical ventilation may be necessary. Fluid replacement may be required to ensure adequate blood volume, but fluids are given carefully since fluid overload can worsen pulmonary edema, which may be lethal.

The severity ranges from mild to deadly—small contusions may have little or no impact on the patient's health—yet pulmonary contusion is the most common type of potentially lethal chest trauma. It occurs in 30–75% of severe chest injuries. With an estimated mortality rate of 14–40%, pulmonary contusion plays a key role in determining whether an individual will die or suffer serious ill effects as the result of trauma. Pulmonary contusion is usually accompanied by other injuries. Although associated injuries are often the cause of death, pulmonary contusion is thought to cause death directly in a quarter to half of cases. Children are at especially high risk for the injury because the relative flexibility of their bones prevents the chest wall from absorbing force from an impact, causing it to be transmitted instead to the lung. Pulmonary contusion is associated with complications including pneumonia and acute respiratory distress syndrome, and it can cause long-term respiratory disability.

Classification



The alveoli

Pulmonary contusion and laceration are injuries to the lung tissue. Pulmonary laceration, in which lung tissue is torn or cut, differs from pulmonary contusion in that the former involves disruption of the macroscopic architecture of the lung, while the latter does not. When lacerations fill with blood, the result is pulmonary hematoma, a collection of blood within the lung tissue. Contusion involves hemorrhage in the alveoli (tiny air-filled sacs responsible for absorbing oxygen), but a hematoma is a discrete clot of blood not interspersed with lung tissue. A collapsed lung can result when the pleural cavity (the space outside the lung) accumulates blood (hemothorax) or air (pneumothorax) or both (hemopneumothorax). These conditions do not inherently involve damage to the lung tissue itself, but they may be associated with it. Injuries to the chest wall are also distinct from but may be associated with lung injuries. Chest wall injuries include rib fractures and flail chest, in which multiple ribs are broken so that a segment of the ribcage is detached from the rest of the chest wall and moves independently.

Signs and symptoms

Presentation may be subtle; people with mild contusion may have no symptoms at all. However, pulmonary contusion is frequently associated with signs (objective indications) and symptoms (subjective states), including those indicative of the lung injury itself and of accompanying injuries. Because gas exchange is impaired, signs of low blood oxygen saturation, such as low concentrations of oxygen in arterial blood gas and cyanosis (bluish color of the skin and mucous membranes) are commonly associated. Dyspnea (painful breathing or difficulty breathing) is commonly seen, and tolerance for exercise may be lowered. Rapid breathing and a rapid heart rate are other signs. With more severe contusions, breath sounds heard through a stethoscope may be decreased, or rales (an abnormal crackling sound in the chest accompanying breathing) may be present. People with severe contusions may have bronchorrhea (the production of watery sputum). Wheezing and coughing are other signs. Coughing up blood or bloody sputum is present in up to half of cases. Cardiac output (the volume of blood pumped by the heart) may be reduced, and hypotension (low blood pressure) is frequently present. The area of the chest wall near the contusion may be tender or painful due to associated chest wall injury.

Signs and symptoms take time to develop, and as many as half of cases are asymptomatic at the initial presentation. The more severe the injury, the more quickly symptoms become apparent. In severe cases, symptoms may occur as quickly as three or four hours after the trauma. Hypoxemia (low oxygen concentration in the arterial blood) typically becomes progressively worse over 24–48 hours after injury. In general, pulmonary contusion tends to worsen slowly over a few days, but it may also cause rapid deterioration or death if untreated.

Causes



Motor vehicle accidents are the most common cause of pulmonary contusion

Pulmonary contusion, which occurs in 25–35% of all blunt chest trauma, is usually caused by the rapid deceleration that results when the moving chest strikes a fixed object. About 70% of cases result from motor vehicle collisions, most often when the chest strikes the inside of the car. Falls, assaults, and sports injuries are other causes. Pulmonary contusion can also be caused by explosions; the organs most vulnerable to blast injuries are those that contain gas, such as the lungs. Blast lung is severe pulmonary contusion, bleeding, or edema with damage to alveoli and blood vessels, or a combination of these. This is the primary cause of death among people who initially survive an explosion.

In addition to blunt trauma, penetrating trauma can cause pulmonary contusion. Contusion resulting from penetration by a rapidly moving projectile usually surrounds the path along which the projectile traveled through the tissue. The pressure wave forces tissue out of the way, creating a temporary cavity; the tissue readily moves back into place, but it is hurt. Pulmonary contusions that accompany gun and knife wounds are not usually severe enough to have a major effect on outcome; penetrating trauma causes less

widespread lung damage than does blunt trauma. An exception is shotgun wounds, which can seriously damage large areas of lung tissue through a blast injury mechanism.

Mechanism

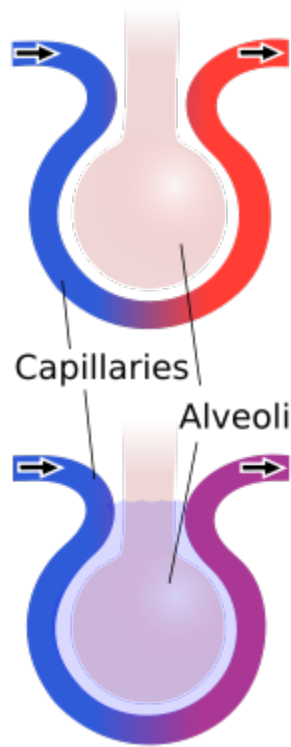
The physical processes behind pulmonary contusion are poorly understood. However, it is known that lung tissue can be crushed when the chest wall bends inward on impact. Three other possible mechanisms have been suggested: the inertial effect, the spalling effect, and the implosion effect.

- In the **inertial effect**, the lighter alveolar tissue is sheared from the heavier hilar structures, an effect similar to diffuse axonal injury in head injury. It results from the fact that different tissues have different densities, and therefore different rates of acceleration or deceleration.
- In the **spalling effect**, lung tissue bursts or is sheared where a shock wave meets the lung tissue, at interfaces between gas and liquid. The alveolar walls form such a gas-liquid interface with the air in the alveoli. The spalling effect occurs in areas with large differences in density; particles of the denser tissue are spalled (thrown) into the less dense particles.
- The **implosion effect** occurs when a pressure wave passes through a tissue containing bubbles of gas: the bubbles first implode, then rebound and expand beyond their original volume. The air bubbles cause many tiny explosions, resulting in tissue damage; the overexpansion of gas bubbles stretches and tears alveoli. This effect is thought to occur microscopically when the pressure in the airways increases sharply.

Contusion usually occurs on the lung directly under the site of impact, but, as with traumatic brain injury, a contrecoup contusion may occur at the site opposite the impact as well. A blow to the front of the chest may cause contusion on the back of the lungs because a shock wave travels through the chest and hits the curved back of the chest wall; this reflects the energy onto the back of the lungs, concentrating it. (A similar mechanism may occur at the front of the lungs when the back is struck.)

The amount of energy transferred to the lung is determined in a large part by the compliance (flexibility) of the chest wall. Children's chests are more flexible because their ribs are more elastic and there is less ossification of their intercostal cartilage. Therefore, their chest walls bend, absorbing less of the force and transmitting more of it to the underlying organs. An adult's more bony chest wall absorbs more of the force itself rather than transmitting it. Thus children commonly get pulmonary contusions without fractures overlying them, while elderly people are more likely to suffer fractures than contusions. One study found that pulmonary contusions were accompanied by fractures 62% of the time in children and 80% of the time in adults.

Pathophysiology



Normally, oxygen and carbon dioxide diffuse across the capillary and alveolar membranes and the interstitial space (top). Fluid impairs this diffusion, resulting in less oxygenated blood (bottom).

Pulmonary contusion results in bleeding and fluid leakage into lung tissue, which can become stiffened and lose its normal elasticity. The water content of the lung increases over the first 72 hours after injury, potentially leading to frank pulmonary edema in more serious cases. As a result of these and other pathological processes, pulmonary contusion progresses over time and can cause hypoxia (insufficient oxygen).

Bleeding and edema

In contusions, torn capillaries leak fluid into the tissues around them. The membrane between alveoli and capillaries is torn; damage to this capillary–alveolar membrane and small blood vessels causes blood and fluids to leak into the alveoli and the interstitial space (the space surrounding cells) of the lung. With more severe trauma, there is a greater amount of edema, bleeding, and tearing of the alveoli. Pulmonary contusion is characterized by microhemorrhages (tiny bleeds) that occur when the alveoli are traumatically separated from airway structures and blood vessels. Blood initially collects in the interstitial space, and then edema occurs by an hour or two after injury. An area of bleeding in the contused lung is commonly surrounded by an area of edema. In normal gas exchange, carbon dioxide diffuses across the endothelium of the capillaries, the interstitial space, and across the alveolar epithelium; oxygen diffuses in the other

direction. Fluid accumulation interferes with gas exchange, and can cause the alveoli to fill with proteins and collapse due to edema and bleeding. The larger the area of the injury, the more severe respiratory compromise will be.

Consolidation and collapse

Pulmonary contusion can cause parts of the lung to consolidate, alveoli to collapse, and atelectasis (partial or total lung collapse) to occur. Consolidation occurs when the parts of the lung that are normally filled with air fill with material from the pathological condition, such as blood. Over a period of hours after the injury, the alveoli in the injured area thicken and may become consolidated. A decrease in the amount of surfactant produced also contributes to the collapse and consolidation of alveoli; inactivation of surfactant increases their surface tension. Reduced production of surfactant can also occur in surrounding tissue that was not originally injured.

Inflammation of the lungs, which can result when components of blood enter the tissue due to contusion, can also cause parts of the lung to collapse. Macrophages, neutrophils, and other inflammatory cells and blood components can enter the lung tissue and release factors that lead to inflammation, increasing the likelihood of respiratory failure. In response to inflammation, excess mucus is produced, potentially plugging parts of the lung and leading to their collapse. Even when only one side of the chest is injured, inflammation may also affect the other lung. Uninjured lung tissue may develop edema, thickening of the septa of the alveoli, and other changes. If this inflammation is severe enough, it can lead to dysfunction of the lungs like that seen in acute respiratory distress syndrome.

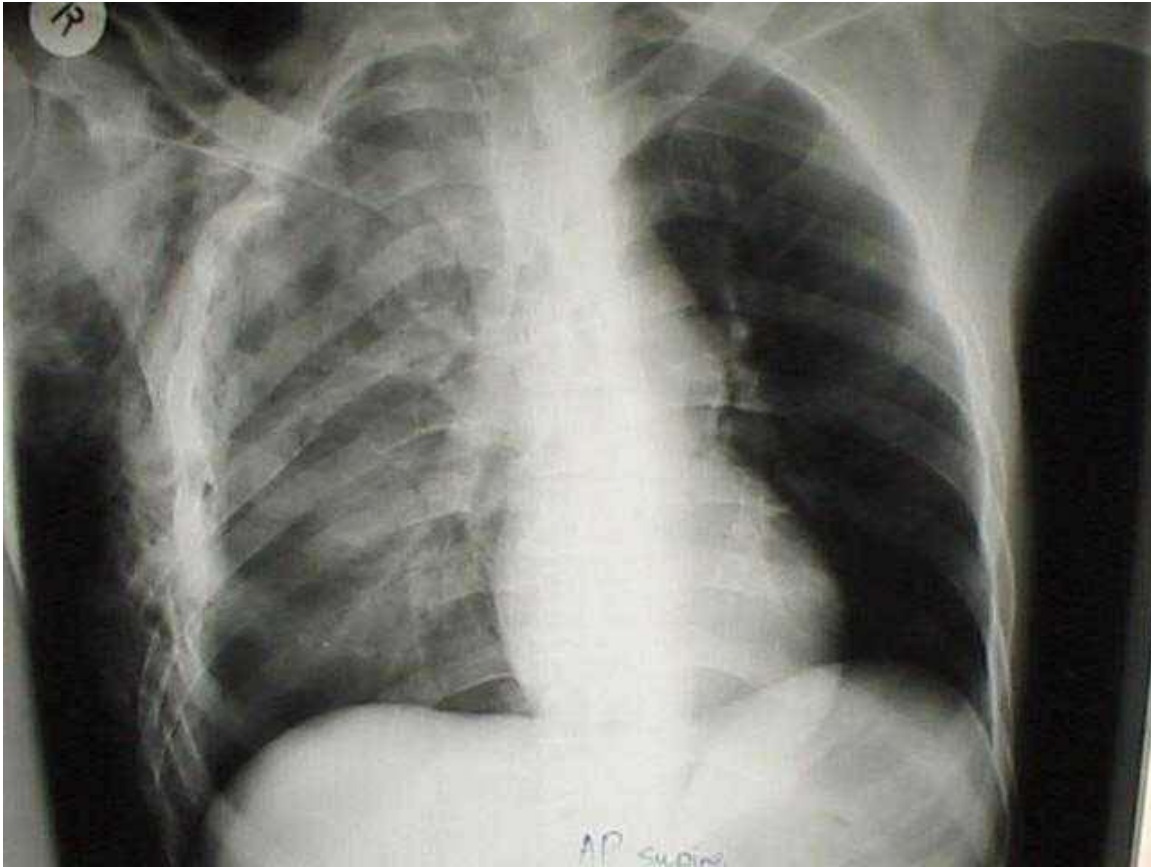
Ventilation/perfusion mismatch

Normally, the ratio of ventilation to perfusion is about one-to-one; the volume of air entering the alveoli (ventilation) is about equal to that of blood in the capillaries around them (perfusion). This ratio is reduced in pulmonary contusion; fluid-filled alveoli cannot fill with air, oxygen does not fully saturate the hemoglobin, and the blood leaves the lung without being fully oxygenated. Insufficient inflation of the lungs, which can result from inadequate mechanical ventilation or an associated injury such as flail chest, can also contribute to the ventilation/perfusion mismatch. As the mismatch between ventilation and perfusion grows, blood oxygen saturation is reduced. Pulmonary hypoxic vasoconstriction, in which blood vessels near the hypoxic alveoli constrict (narrow their diameter) in response to the lowered oxygen levels, can occur in pulmonary contusion. The vascular resistance increases in the contused part of the lung, leading to a decrease in the amount of blood that flows into it, directing blood to better-ventilated areas. Although reducing blood flow to the unventilated alveoli is a way to compensate for the fact that blood passing unventilated alveoli is not oxygenated, the oxygenation of the blood remains lower than normal. If it is severe enough, the hypoxemia resulting from fluid in the alveoli cannot be corrected just by giving supplemental oxygen; this problem is the cause of a large portion of the fatalities that result from trauma.

Diagnosis

To diagnose pulmonary contusion, health professionals use clues from a physical examination, information about the event that caused the injury, and radiography. Laboratory findings may also be used; for example, arterial blood gasses may show insufficient oxygen and excessive carbon dioxide even in someone receiving supplemental oxygen. However, blood gas levels may show no abnormality early in the course of pulmonary contusion.

X-ray

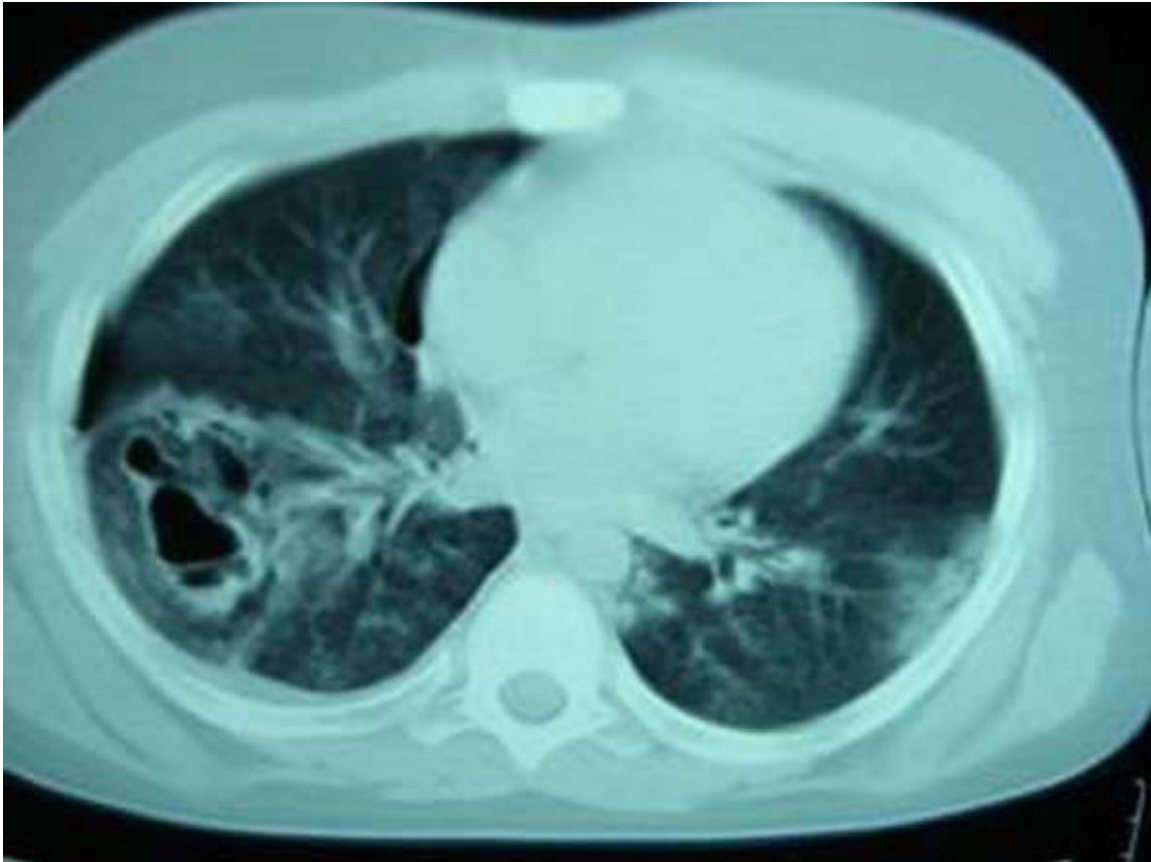


A chest X-ray showing right sided pulmonary contusion associated with rib fractures and subcutaneous emphysema

Chest X-ray is the most common method used for diagnosis, and may be used to confirm a diagnosis already made using clinical signs. Consolidated areas appear white on an X-ray film. Contusion is not typically restricted by the anatomical boundaries of the lobes or segments of the lung. The X-ray appearance of pulmonary contusion is similar to that of aspiration, and the presence of hemothorax or pneumothorax may obscure the contusion on a radiograph. Signs of contusion that progress after 48 hours post-injury are likely to be actually due to aspiration, pneumonia, or ARDS.

Although chest radiography is an important part of the diagnosis, it is often not sensitive enough to detect the condition early after the injury. In a third of cases, pulmonary contusion is not visible on the first chest radiograph performed. It takes an average of six hours for the characteristic white regions to show up on a chest X-ray, and the contusion may not become apparent for 48 hours. When a pulmonary contusion is apparent in an X-ray, it suggests that the trauma to the chest was severe and that a CT scan might reveal other injuries that were missed with X-ray.

Computed tomography

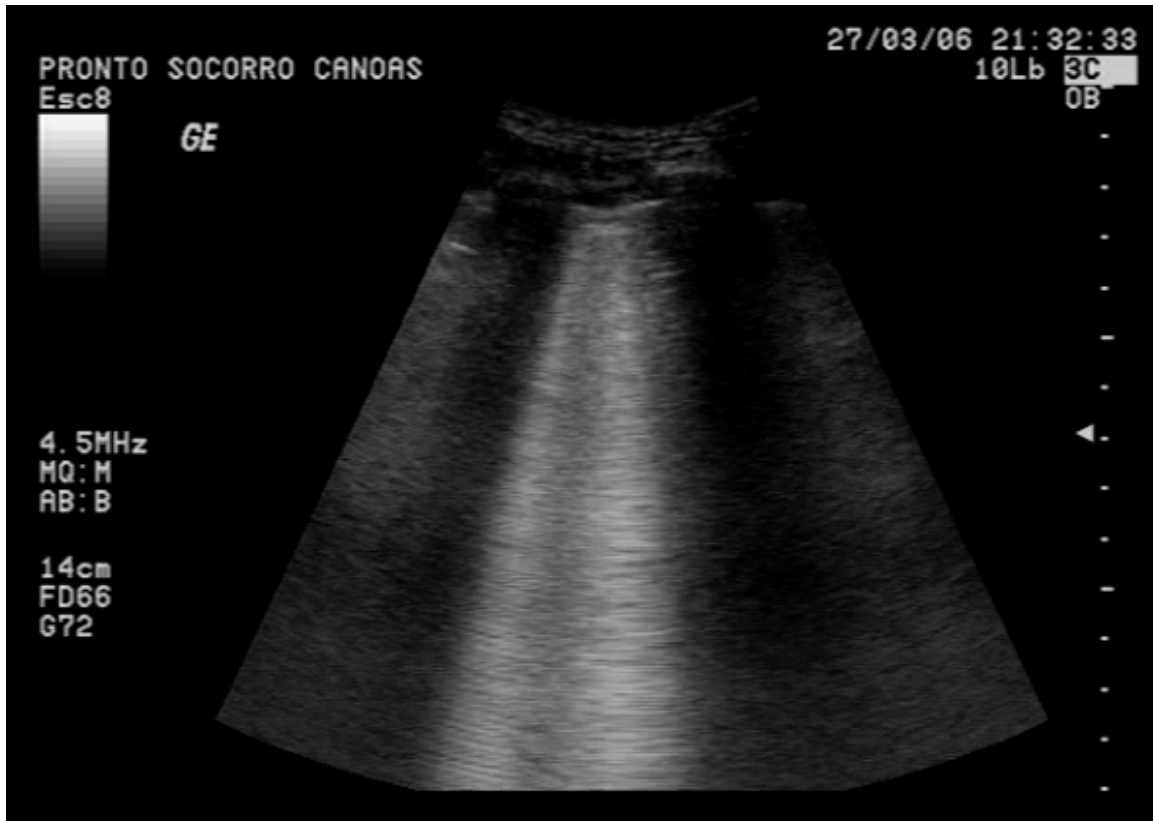


A chest CT scan revealing pulmonary contusions, pneumothorax, and pseudocysts

Computed tomography (CT scanning) is a more sensitive test for pulmonary contusion, and it can identify abdominal, chest, or other injuries that accompany the contusion. In one study, chest X-ray detected pulmonary contusions in 16.3% of people with serious blunt trauma, while CT detected them in 31.2% of the same people. Unlike X-ray, CT scanning can detect the contusion almost immediately after the injury. However, in both X-ray and CT a contusion may become more visible over the first 24–48 hours after trauma as bleeding and edema into lung tissues progress. CT scanning also helps determine the size of a contusion, which is useful in determining whether a patient needs mechanical ventilation; a larger volume of contused lung on CT scan is associated with an increased likelihood that ventilation will be needed. CT scans also help differentiate between contusion and pulmonary hematoma, which may be difficult to tell apart

otherwise. However, pulmonary contusions that are visible on CT but not chest X-ray are usually not severe enough to affect outcome or treatment.

Ultrasound



An ultrasound image showing early pulmonary contusion, at this moment not visible on radiography. Interstitial syndromes are expressed with the vertical white lines, the "B-lines".

Pulmonary ultrasound, performed at the bedside or on the accident scene, is being explored as a diagnosis for pulmonary contusion. Its use is still not widespread, being limited to facilities which are comfortable with its use for other applications, like pneumothorax, airway management, and hemothorax. Accuracy has been found to be comparable to CT scanning.

Prevention

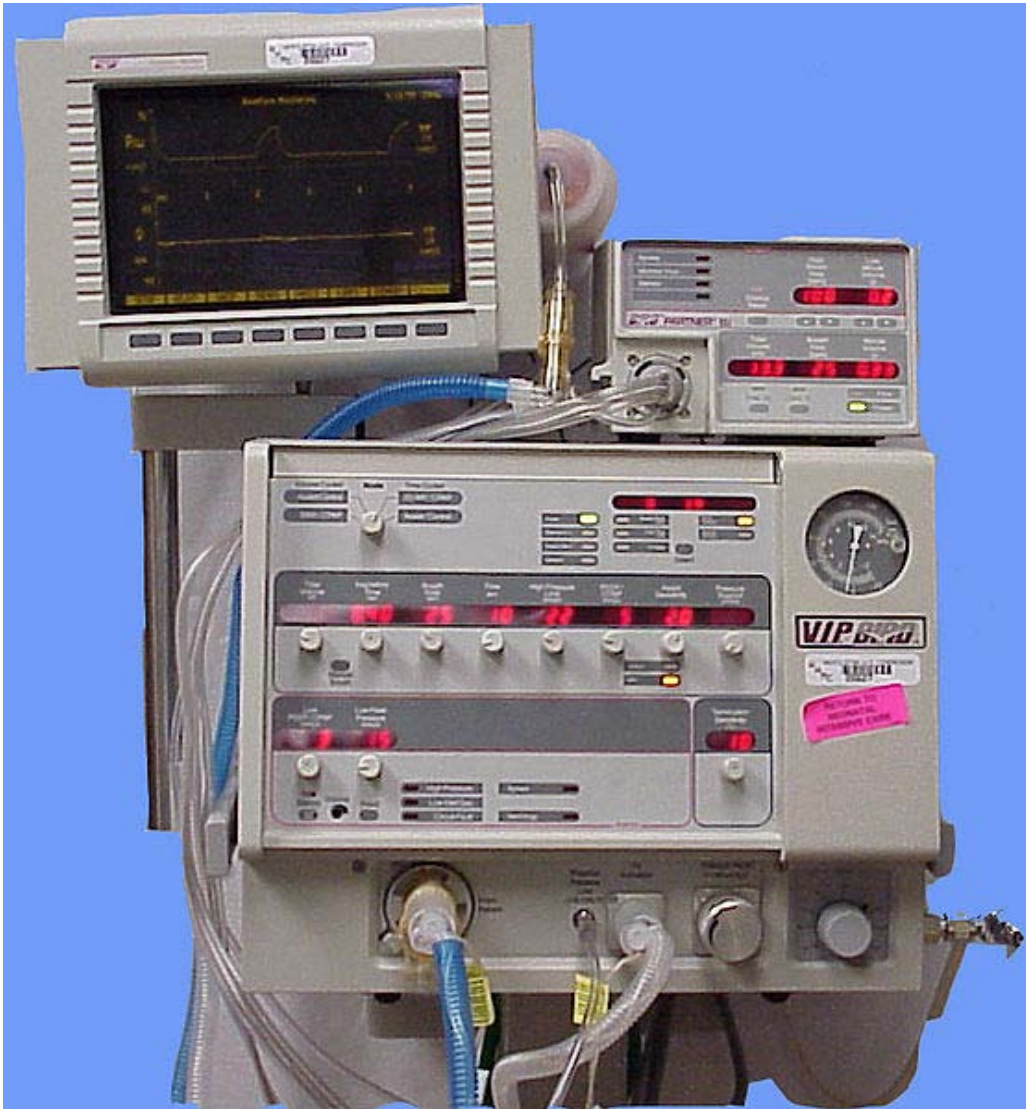
Prevention of pulmonary contusion is similar to that of other chest trauma. Airbags in combination with seat belts can protect vehicle occupants by preventing the chest from striking the interior of the vehicle during a collision, and by distributing forces involved in the crash more evenly across the body. However, in rare cases, an airbag causes pulmonary contusion in a person who is not properly positioned when it deploys. Child restraints such as carseats protect children in vehicle collisions from pulmonary contusion. Equipment exists for use in some sports to prevent chest and lung injury; for

example, in softball the catcher is equipped with a chest protector. Athletes who do not wear such equipment, such as basketball players, can be trained to protect their chests from impacts. Protective garments can also prevent pulmonary contusion in explosions. Although traditional body armor made from rigid plates or other heavy materials protects from projectiles generated by a blast, it does not protect against pulmonary contusion, because it does not prevent the blast's shock wave from being transferred to the lung. Special body armor has been designed for military personnel at high risk for blast injuries; these garments can prevent a shock wave from being propagated across the chest wall to the lung, and thus protect wearers from blast lung injuries. These garments alternate layers of materials with high and low acoustic impedance (the product of a material's density and a wave's velocity through it) in order to "decouple" the blast wave, preventing its propagation into the tissues.

Treatment

No treatment is known to speed the healing of a pulmonary contusion; the main care is supportive. Attempts are made to discover injuries accompanying the contusion, to prevent additional injury, and to provide supportive care while waiting for the contusion to heal. Monitoring, including keeping track of fluid balance, respiratory function, and oxygen saturation using pulse oximetry is also required as the patient's condition may progressively worsen. Monitoring for complications such as pneumonia and acute respiratory distress syndrome is of critical importance. Treatment aims to prevent respiratory failure and to ensure adequate blood oxygenation. Supplemental oxygen can be given and it may be warmed and humidified. When the contusion does not respond to other treatments, extracorporeal membranous oxygenation may be used, pumping blood from the body into a machine that oxygenates it and removes carbon dioxide prior to pumping it back in.

Ventilation



Mechanical ventilation may be required if pulmonary contusion causes inadequate oxygenation.

Positive pressure ventilation, in which air is forced into the lungs, is needed when oxygenation is significantly impaired. Noninvasive positive pressure ventilation including continuous positive airway pressure (CPAP) and bi-level positive airway pressure (BiPAP), may be used to improve oxygenation and treat atelectasis. In both, air is blown into the airways at a prescribed pressure via a mask fitted tightly to the face; in BiPAP the pressure changes between inhalation and exhalation, while in CPAP the pressure is the same during both. Noninvasive ventilation has advantages over invasive methods because it does not carry the risk of infection that intubation does, and it allows normal coughing, swallowing, and speech. However, the technique may cause complications; it may force air into the stomach or cause aspiration of stomach contents, especially when level of consciousness is decreased.

People with signs of inadequate respiration or oxygenation may need to be intubated and mechanically ventilated. Mechanical ventilation aims to reduce pulmonary edema and increase oxygenation. Ventilation can reopen collapsed alveoli, but it is harmful for them to be repeatedly opened, and positive pressure ventilation can also damage the lung by overinflating it. Intubation is normally reserved for when respiratory problems occur, but most significant contusions do require intubation, and it may be done early in anticipation of this need. People with pulmonary contusion who are especially likely to need ventilation include those with prior severe lung disease or kidney problems; the elderly; those with a lowered level of consciousness; those with low blood oxygen or high carbon dioxide levels; and those who are going to be operated on and need anesthesia.

Pulmonary contusion or its complications such as acute respiratory distress syndrome may cause lungs to lose compliance (stiffen), so higher pressures may be needed to give normal amounts of air and oxygenate the blood adequately. Positive end-expiratory pressure (PEEP), which delivers air at a given pressure at the end of the expiratory cycle, can reduce edema and keep alveoli from collapsing. PEEP is considered necessary with mechanical ventilation; however, if the pressure is too great it can expand the size of the contusion and injure the lung. When the compliance of the injured lung differs significantly from that of the uninjured one, the lungs can be ventilated independently with two ventilators in order to deliver air at different pressures; this helps avoid injury from overinflation while providing adequate ventilation.

Fluid therapy

The administration of fluid therapy in individuals with pulmonary contusion is controversial. Excessive fluid in the circulatory system (hypervolemia) can worsen hypoxia because it can cause fluid leakage from injured capillaries (pulmonary edema), which are more permeable than normal. However, low blood volume (hypovolemia) resulting from insufficient fluid has an even worse impact, potentially causing hypovolemic shock; for people who have lost large amounts of blood, fluid resuscitation is necessary. A lot of the evidence supporting the idea that fluids should be withheld from people with pulmonary contusion came from animal studies, not clinical trials with humans; human studies have had conflicting findings on whether fluid resuscitation worsens the condition. For people who do require large amounts of intravenous fluid, a catheter may be placed in the pulmonary artery to measure the pressure within it. Measuring pulmonary artery pressure allows the clinician to give enough fluids to prevent shock without exacerbating edema. Diuretics, drugs that increase urine output to reduce excessive fluid in the system, can be used when fluid overload does occur. Furosemide, a diuretic used in the treatment of pulmonary contusion, also relaxes the smooth muscle in the veins of the lungs, thereby decreasing pulmonary venous resistance and reducing the pressure in the pulmonary capillaries.

Supportive care

Retaining secretions in the airways can worsen hypoxia and lead to infections. Thus, an important part of treatment is pulmonary toilet, the use of suction, deep breathing,

coughing, and other methods to remove material such as mucus and blood from the airways. Chest physical therapy makes use of techniques such as breathing exercises, stimulation of coughing, suctioning, percussion, movement, vibration, and drainage to rid the lungs of secretions, increase oxygenation, and expand collapsed parts of the lungs. People with pulmonary contusion, especially those who do not respond well to other treatments, may be positioned with the uninjured lung lower than the injured one to improve oxygenation. Inadequate pulmonary toilet can result in pneumonia. People who do develop infections are given antibiotics. No studies have yet shown a benefit of using antibiotics as a preventative measure before infection occurs, although some doctors do recommend prophylactic antibiotic use even without scientific evidence of its benefit. However, this can cause the development of antibiotic resistant strains of bacteria, so giving antibiotics without a clear need is normally discouraged. For people who are at especially high risk of developing infections, the sputum can be cultured to test for the presence of infection-causing bacteria; when they are present, antibiotics are used.

Pain control is another means to facilitate the elimination of secretions. A chest wall injury can make coughing painful, increasing the likelihood that secretions will accumulate in the airways. Chest injuries also contribute to hypoventilation (inadequate breathing) because the chest wall movement involved in breathing adequately is painful. Insufficient expansion of the chest may lead to atelectasis, further reducing oxygenation of the blood. Analgesics (pain medications) can be given to reduce pain. Injection of anesthetics into nerves in the chest wall, called nerve blockade, is another approach to pain management; this does not depress respiration the way some pain medications can.

Prognosis



This CT scan, taken 22 days after pulmonary contusion with major chest trauma, shows that the contusion has completely resolved.

Pulmonary contusion usually resolves itself without causing permanent complications; however it may also have long-term ill effects on respiratory function. Most contusions resolve in five to seven days after the injury. Signs detectable by radiography are usually

gone within 10 days after the injury—when they are not, other conditions, such as pneumonia, are the likely cause. Chronic lung disease correlates with the size of the contusion and can interfere with an individual's ability to return to work. Fibrosis of the lungs can occur, resulting in dyspnea (shortness of breath), low blood oxygenation, and reduced functional residual capacity for as long as six years after the injury. As late as four years post-injury, decreased functional residual capacity has been found in most pulmonary contusion patients studied. During the six months after pulmonary contusion, up to 90% of people suffer difficulty breathing. In some cases, dyspnea persists for an indefinite period. Contusion can also permanently reduce the compliance of the lungs.

Complications

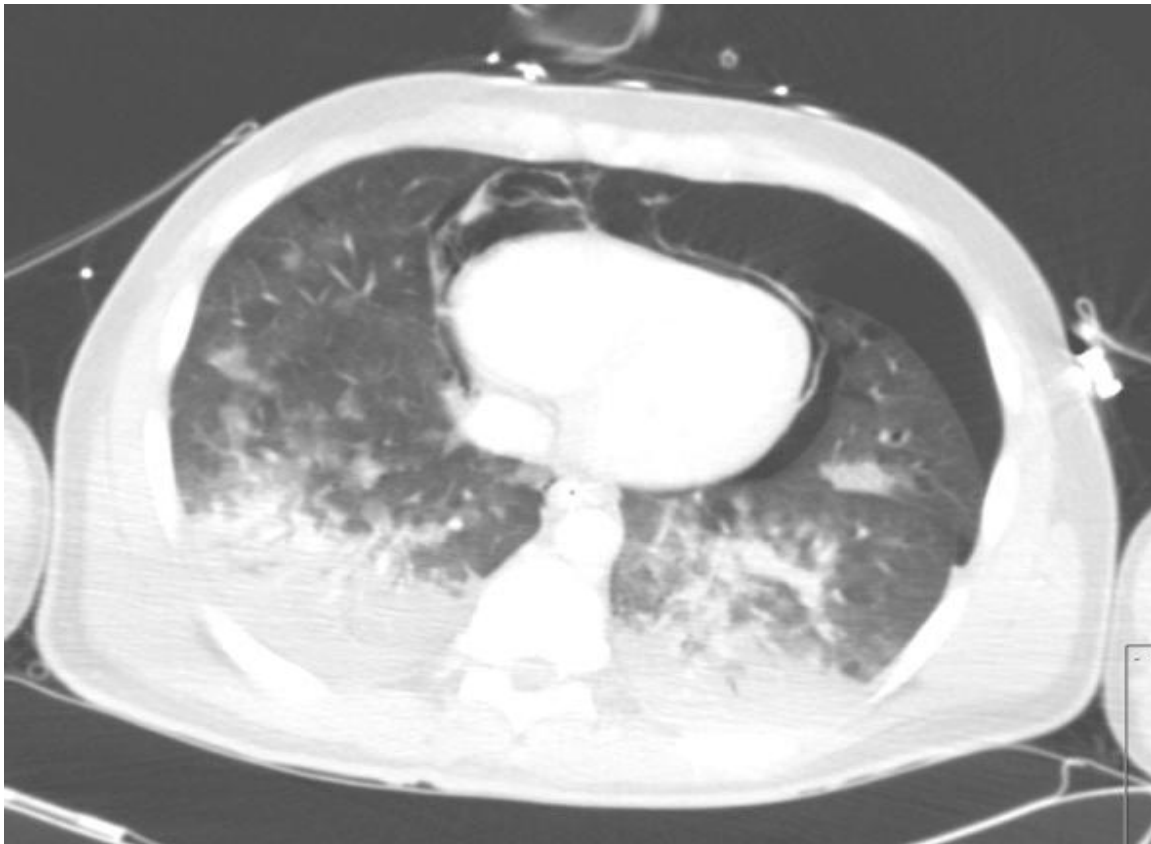


A chest X-ray showing acute respiratory distress syndrome

Pulmonary contusion can result in respiratory failure—about half of such cases occur within a few hours of the initial trauma. Other severe complications, including infections and acute respiratory distress syndrome (ARDS) occur in up to half of cases. Elderly people and those who have heart, lung, or kidney disease prior to the injury are more likely to stay longer in hospital and have complications from the injury. Complications occur in 55% of people with heart or lung disease and 13% of those without. Of people with pulmonary contusion alone, 17% develop ARDS, while 78% of people with at least two additional injuries develop the condition. A larger contusion is associated with an increased risk. In one study, 82% of people with 20% or more of the lung volume affected developed ARDS, while only 22% of people with less than 20% did so.

Pneumonia, another potential complication, develops in as many as 20% of people with pulmonary contusion. Contused lungs are less able to remove bacteria than uninjured lungs, predisposing them to infection. Intubation and mechanical ventilation further increase the risk of developing pneumonia; the tube is passed through the nose or mouth into the airways, potentially tracking bacteria from the mouth or sinuses into them. Also, intubation prevents coughing, which would clear bacteria-laden secretions from the airways, and secretions pool near the tube's cuff and allow bacteria to grow. The sooner the endotracheal tube is removed, the lower the risk of pneumonia, but if it is removed too early and has to be put back in, the risk of pneumonia rises. People who are at risk for pulmonary aspiration (e.g. those with lowered level of consciousness due to head injuries) are especially likely to get pneumonia. As with ARDS, the chances of developing pneumonia increase with the size of the contusion. Children and adults have been found to have similar rates of complication with pneumonia and ARDS.

Associated injuries



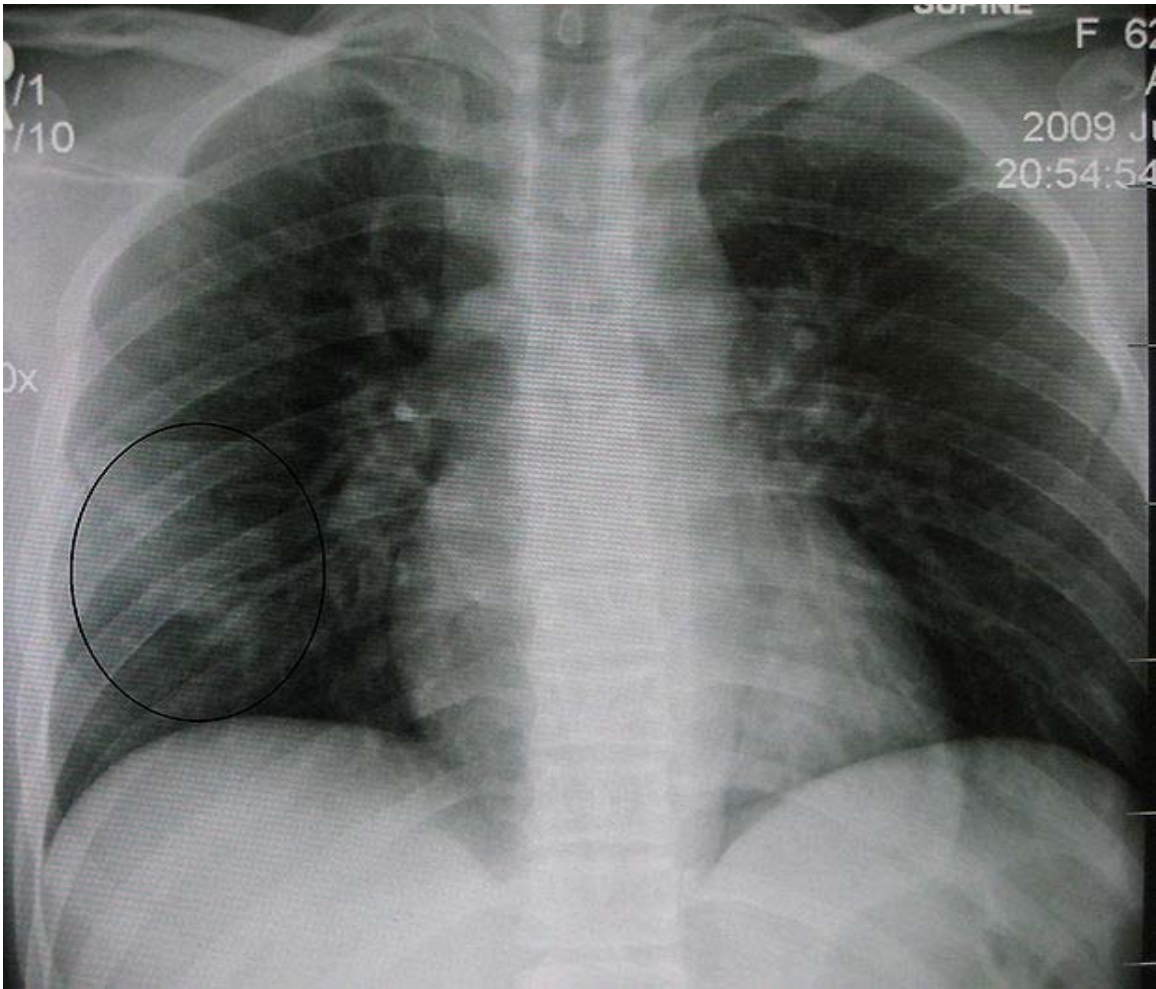
Severe pulmonary contusion with pneumothorax and hemothorax following severe chest trauma

A large amount of force is required to cause pulmonary contusion; a person injured with such force is likely to have other types of injuries as well, and pulmonary contusion can be used to gauge the severity of trauma. Up to three quarters of cases are accompanied by other chest injuries, the most common of these being hemothorax and pneumothorax.

Flail chest is usually associated with pulmonary contusion, and the contusion, rather than the chest wall injury, is often the main cause of respiratory failure in people with these injuries. Other indications of thoracic trauma may be associated, including fracture of the sternum and bruising of the chest wall. Over half of fractures of the scapula are associated with pulmonary contusion. The contusion is frequently found underlying fracture sites. When accompanied by a fracture, it is usually concentrated into a specific location—the contusion is more diffuse when there is no fracture. Pulmonary lacerations may result from the same blunt or penetrating forces that cause pulmonary contusion. Lacerations can result in pulmonary hematomas; these are reported to develop in 4–11% of pulmonary contusions.

Epidemiology

Pulmonary contusion is found in 30–75% of severe cases of chest injury, making it the most common serious injury to occur in association with thoracic trauma. Of people who have multiple injuries with an injury severity score of over 15, pulmonary contusion occurs in about 17%. It is difficult to determine the death rate (mortality) because pulmonary contusion rarely occurs by itself. Usually, deaths of people with pulmonary contusion result from other injuries, commonly traumatic brain injury. It is controversial whether pulmonary contusion with flail chest is a major factor in mortality on its own or whether it merely contributes to mortality in people with multiple injuries. The mortality rate of pulmonary contusion is estimated to range from 14–40%, depending on the severity of the contusion itself and on associated injuries. When the contusions are small, they do not normally increase the chance of death or poor outcome for people with blunt chest trauma; however, these chances increase with the size of the contusion. One study found that 35% of people with multiple significant injuries including pulmonary contusion die. In another study, 11% of people with pulmonary contusion alone died, while the number rose to 22% in those with additional injuries. An accompanying flail chest increases the morbidity and mortality to more than twice that of pulmonary contusion alone. Pulmonary contusion is thought to be the direct cause of death in a quarter to a half of people with polytrauma who die.



A right-sided pulmonary contusion post blunt chest trauma with increased opacity just below the horizontal fissure

Pulmonary contusion is the most common cause of death among vehicle occupants involved in accidents, and it is thought to contribute significantly in about a quarter of deaths resulting from vehicle collisions. As vehicle use has increased, so has the number of auto accidents, and with it the number of chest injuries. However an increase in the number of airbags installed in modern cars may be decreasing the incidence of pulmonary contusion. Use of child restraint systems has brought the approximate incidence of pulmonary contusion in children in vehicle accidents from 22% to 10%.

Since their chest walls are more flexible, children are more vulnerable to pulmonary contusion than adults are, and it is more common in children than in adults for that reason. Children in forceful impacts suffer twice as many pulmonary contusions as adults with similar injury mechanisms, yet have proportionately fewer rib fractures. Pulmonary contusion has been found in 53% of children with significant chest injuries (those requiring hospitalization). The rates of certain types of injury mechanisms differ between children and adults; for example, children are more often hit by cars when they are pedestrians. Differences in the bodies of children and adults also lead to different

manifestations of pulmonary contusion and associated injuries; for example, children have less body mass, so the same force is more likely to lead to trauma to multiple body systems. Some differences in children's physiology might be advantageous (for example they are less likely to have other medical conditions), and thus they have been predicted to have a better outcome. However, despite these differences, children with pulmonary contusion have similar mortality rates to adults.

History



Giovanni Battista Morgagni, credited with having first described lung trauma without chest wall trauma

In 1761, the Italian anatomist Giovanni Battista Morgagni was first to describe a lung injury that was not accompanied by injury to the chest wall overlying it. Nonetheless, it was the French military surgeon Guillaume Dupuytren who is thought to have coined the term *pulmonary contusion* in the 19th century. It still was not until the early 20th century that pulmonary contusion and its clinical significance began to receive wide recognition. With the use of explosives during World War I came many casualties with no external signs of chest injury but with significant bleeding in the lungs. Studies of World War I injuries by D.R. Hooker showed that pulmonary contusion was an important part of the concussive injury that results from explosions.

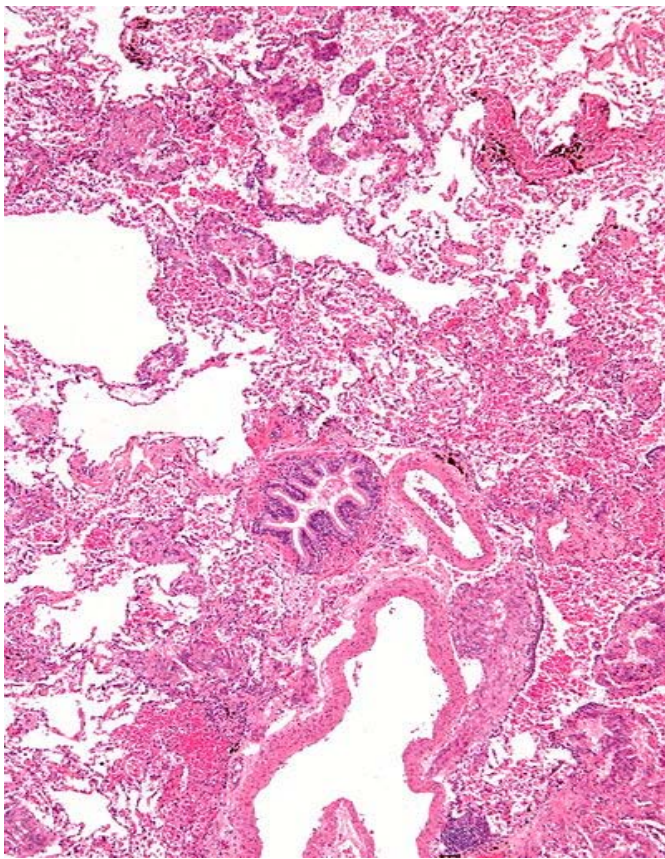
Pulmonary contusion received further attention during World War II, when the bombings of Britain caused blast injuries and associated respiratory problems in both soldiers and civilians. Also during this time, studies with animals placed at varying distances from a blast showed that protective gear could prevent lung injuries. These findings suggested that an impact to the outside of the chest wall was responsible for the internal lesions. In 1945, Buford and Burbank described what they called "wet lung", in which the lungs accumulated fluid and were simultaneously less able to remove it. They attributed the respiratory failure often seen in blunt chest trauma in part to excessive fluid resuscitation, and the question of whether and how much to administer fluids has remained controversial ever since.

During the Vietnam War, combat again provided the opportunity for study of pulmonary contusion; research during this conflict played an important role in the development of the modern understanding of its treatment. The condition also began to be more widely recognized in a non-combat context in the 1960s, and symptoms and typical findings with imaging techniques such as X-ray were described. Before the 1960s, it was believed that the respiratory insufficiency seen in flail chest was due to "paradoxical motion" of the flail segment of the chest wall (the flail segment moves in the opposite direction as the chest wall during respiration), so treatment was aimed at managing the chest wall injury, not the pulmonary contusion. For example, positive pressure ventilation was used to stabilize the flail segment from within the chest. It was first proposed in 1965 that this respiratory insufficiency is most often due to injury of the lung rather than to the chest wall, and a group led by J.K. Trinkle confirmed this hypothesis in 1975. Hence the modern treatment prioritizes the management of pulmonary contusion. Animal studies performed in the late 1960s and 1970s shed light on the pathophysiological processes involved in pulmonary contusion.

Chapter 6

Lymphangiomyomatosis

Lymphangiomyomatosis



Micrograph of lymphangiomyomatosis. H&E stain.

ICD-O:	9174/1
OMIM	606690
DiseasesDB	30755
eMedicine	med/1348 radio/415
MeSH	D018192

Lymphangiomyomatosis (LAM) is a rare lung disease that results in a proliferation of disorderly smooth muscle growth (leiomyoma) throughout the bronchioles, alveolar septa, perivascular spaces, and lymphatics, resulting in the obstruction of small airways (leading to pulmonary cyst formation and pneumothorax) and lymphatics (leading to chylous pleural effusion). LAM occurs in a sporadic form, which only affects females, who are usually of childbearing age. LAM also occurs in patients who have tuberous sclerosis.

Cause

Sporadic LAM almost always affects women.

The proliferating smooth muscle that occurs in the type of LAM seen in patients with tuberous sclerosis (TSC-LAM) has been shown to represent clones of the smooth muscle in those patients' renal angiomyolipomas. Thus it is believed to represent metastases of this "benign" tumor. There is a female preponderance to TSC-LAM. LAM occurs almost exclusively in women. The average age at onset of symptoms is approximately 34 years (5–7). The first symptoms of the disease can occur before an abnormality is detectable with chest plain radiographs or pulmonary function tests; even when such abnormalities exist, the disease may be initially misdiagnosed. There is often a delay between the onset of symptoms and correct diagnosis.

LAM commonly manifests as exertional dyspnea and recurrent pneumothorax. During the course of the illness, there may be nonproductive cough, hemoptysis, chylous pleural effusion, or chylous ascites (3,5). Obstruction of pulmonary venules causes vascular congestion and hemoptysis, and lymphatic obstruction leads to chylothorax and chylous ascites.

The clinical course of patients with LAM shows considerable variation. The disease is believed to be slowly progressive, leading to respiratory failure and death. The 10-year survival from the start of symptoms in a study at our institution was 49% (7), although reported figures range from an 8.5-year survival probability of 38% to a 10-year survival of 79% (8). Differences in survival rates may be due to improvements in diagnosis, particularly regarding the contribution of high-resolution CT, and do not mean that the progression of the disease has changed substantially. Diagnosis of mild asymptomatic forms may also have contributed to the longer survival rates (4).

Spirometry studies in LAM patients demonstrate chronic airway obstruction with increased lung volume and decreased CO₂ diffusion. The radiologic finding of an interstitial pattern with these spirometric results in a young woman narrows the differential diagnosis to some forms of emphysema, Langerhans cell histiocytosis, and sarcoidosis. The information provided by HRCT is essential for differentiating LAM from these conditions.

Numerous therapeutic strategies have been described to treat LAM (4). In light of the reports of clinical worsening of the disease during pregnancy and with use of exogenous

estrogens, many clinicians have applied therapeutic hormone manipulation. Antiestrogen therapy, first used in the early 1980s, consists of surgical castration by oophorectomy or administration of tamoxifen, progesterone, and gonadotropin-releasing hormone agonist or luteinizing hormone–releasing hormone (3,5). Several studies have reported beneficial effects of antiestrogen hormone therapies for LAM, but careful scrutiny of some of these studies reveals that the treatment improved the chylothorax or chylous ascites, whereas pulmonary involvement seemed to remain stationary or to progress. Since lung transplantation has become available for patients with poor response to therapies, certain treatments must be used with caution. In fact, castration does not clearly demonstrate a beneficial effect on the course of the disease, and the long-term effects of castration, particularly in the postoperative period of lung transplantation, can increase bone complications.

In most cases, chylothorax should be managed conservatively. Chylothorax usually appears early in the course of the disease, when the patient's functional status is good. Early application of surgical techniques such as pleural abrasion, pleurodesis, or pleurectomy must be avoided because these treatments might limit future lung transplantation. Medical treatment includes tamoxifen, progesterone, and, in some cases, a low-fat diet (4,5).

When the patient's functional status declines, bilateral lung transplantation is the best therapeutic option. The guidelines indicating transplantation include progression despite medical treatment, forced expiratory volume in 1 second (FEV1)/forced vital capacity ratio of less than 50%, total lung capacity of greater than 130%, and FEV1 of less than 30%. In the largest published series of lung transplantations in LAM patients, the average FEV1 at the time of evaluation for the procedure was 24%.

Common postoperative complications of lung transplantation are bacterial, viral, and fungal infections; acute rejection episodes; and chronic rejection. Complications specific to LAM are pneumothorax of the native lung after single-lung transplantation, chylothorax, recurrence of LAM, and abdominal complications Clinics :

Clinical Features

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Prognosis

Exact data on survival rates are difficult to collect because LAM is often misdiagnosed as asthma or other more common diseases, and may not be correctly identified until it is in an advanced condition. A comprehensive study of all known British LAM patients found that out of 21 patients that had been observed for 15 years or more since diagnosis, 18 were still alive; and 11 of 12 patients that had been observed for 20 years or more were alive, however, no data is available on respiratory disability.

Complications

- Worsening pulmonary insufficiency
- Pneumothorax, secondary to rupture of a cyst into the pleural space
- Chylous pleural effusions

Treatment

The association of LAM with women of childbearing age suggests that hormonal stimulation plays a role in the disease process, and several approaches to treatment involve diminishing the effect of estrogen. At one time or another, therapeutic approaches have included

- progesterone
- oophorectomy
- tamoxifen
- gonadotropin-releasing hormone (GnRH) agonists
- androgen therapy

No therapy is clearly efficacious, and all have undesirable side-effects. There is some evidence which shows that tamoxifen may actually cause worsening of LAM in some patients.

When pulmonary function deteriorates to the point where oxygenation is inadequate, lung transplantation is usually performed. Following lung transplant (usually unilateral), LAM patients have Kaplan-Meier estimators (survival curves) similar to other lung transplant patients. Abnormal smooth muscle may, however, also proliferate in the transplanted lung.

A single case report of an apparent response to Doxycycline has recently been reported.

Sirolimus is being tested for the treatment of LAM. The MILES Trial (Multicenter International LAM Efficacy of Sirolimus Trial) is now underway. The first site, the University of Cincinnati, is open for enrollment. The National Institutes of Health will open enrollment soon. The MILES Trial is randomized, double-blinded, and placebo-controlled. The objective of the Trial is to determine if sirolimus has a beneficial effect on lung function in LAM patients.

Chapter 7

Obstructive Lung Disease

Obstructive lung disease

MeSH

D008173

Obstructive lung disease is a category of respiratory disease characterized by airway obstruction.

MeSH includes the following in this category:

- Asthma
- Emphysema
- Bronchitis
- Chronic obstructive pulmonary disease

Cystic fibrosis is sometimes also included in this category.

FEV1/FVC ratio is usually decreased.

Overview table

Following is an overview of the main obstructive lung diseases. *Chronic obstructive pulmonary disease* is mainly a combination of chronic bronchitis and emphysema, but may be more or less overlapping with all conditions.

Condition	Main site	Major changes	Causes	Symptoms
Chronic bronchitis	Bronchus	Hyperplasia and hypersecretion of mucus glands	Tobacco smoking and air pollutants	Productive cough
Bronchiectasis	Bronchus	Dilation and scarring of airways	Persistent severe infections	Cough, purulent sputum and fever
Asthma	Bronchus	<ul style="list-style-type: none">• Smooth muscle	Immunologic or	Episodic

		hyperplasia	idiopathic	wheezing, cough and dyspnea
		<ul style="list-style-type: none"> Excessive mucus Inflammation 		
Emphysema	Acinus	Airspace enlargement and wall destruction	Tobacco smoking	Dyspnea
Bronchiolitis (subgroup of chronic bronchitis)	Bronchiole	Inflammatory scarring and bronchiole obliteration	Tobacco smoking and air pollutants	Cough, dyspnea

Scope

Chronic obstructive pulmonary disease

Chronic obstructive pulmonary disease (COPD), also known as chronic obstructive airways disease (COAD) or chronic airflow limitation (CAL), is a group of illnesses characterised by airflow limitation that is not fully reversible. The flow of air into and out of the lungs is impaired. This can be measured with breathing devices such as a peak flow meter or by spirometry. The term COPD includes the conditions emphysema and chronic bronchitis although most patients with COPD have characteristics of both conditions to varying degrees. Asthma being a reversible obstruction of airways is often considered separately, but many COPD patients also have some degree of reversibility in their airways.

In COPD, there is an increase in airway resistance, shown by a decrease in the forced expiratory volume in 1 second (FEV1) measured by spirometry. COPD is defined as a forced expiratory volume in 1 second to forced vital capacity ratio (FEV1/FVC) that is less than 0.7. The residual volume, the volume of air left in the lungs following full expiration, is often increased in COPD, as is the total lung capacity, while the vital capacity remains relatively normal. The increased total lung capacity (hyperinflation) can result in the clinical feature of a "barrel chest" - a chest with a large front-to-back diameter that occurs in some individuals with COPD. Hyperinflation can also be seen on a chest x-ray as a flattening of the diaphragm.

The most common cause of COPD is cigarette smoking. COPD is a gradually progressive condition and usually only develops after about 20 pack-years of smoking. COPD may also be caused by breathing in other particles and gases.

The diagnosis of COPD is established through spirometry although other pulmonary function tests can be helpful. A chest x-ray is often ordered to look for hyperinflation and rule out other lung conditions but the lung damage of COPD is not always visible on a chest x-ray. Emphysema, for example can only be seen on CT scan.

The main form of long term management involves the use of inhaled bronchodilators (specifically beta agonists and anticholinergics) and inhaled corticosteroids. Many

patients eventually require oxygen supplementation at home. In severe cases that are difficult to control, chronic treatment with oral corticosteroids may be necessary, although this is fraught with significant side-effects.

COPD is generally irreversible although lung function can partially recover if the patient stops smoking. Smoking cessation is an essential aspect of treatment. Pulmonary rehabilitation programmes involve intensive exercise training combined with education and are effective in improving shortness of breath. Severe emphysema has been treated with lung volume reduction surgery, with some success in carefully chosen cases. Lung transplantation is also performed for severe COPD in carefully chosen cases.

Alpha 1-antitrypsin deficiency is a fairly rare genetic condition that results in COPD (particularly emphysema) due to a lack of the antitrypsin protein which protects the fragile alveolar walls from protease enzymes released by inflammatory processes.

Asthma

Asthma is an obstructive lung disease where the bronchial tubes (airways) are extra sensitive (hyperresponsive). The airways become inflamed and produce excess mucus and the muscles around the airways tighten making the airways narrower. Asthma is usually triggered by breathing in things in the air such as dust or pollen that produce an allergic reaction. It may be triggered by other things such as an upper respiratory tract infection, cold air, exercise or smoke. Asthma is a common condition and affects over 300 million people around the world. Asthma causes recurring episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning.

Asthma is diagnosed by the characteristic pattern of symptoms.

A peak flow meter can record variations in the severity of asthma over time. Spirometry, a measurement of lung function, can provide an assessment of the severity, reversibility, and variability of airflow limitation, and help confirm the diagnosis of asthma.

Asthma is treated by identifying and removing the triggers that set it off, if possible. The main form of long term management involves the use of inhaled corticosteroids. Inhaled bronchodilators, particularly beta agonists are used to relieve and control symptoms by reducing muscle spasm around the airways. An alternative way to control mild asthma is with a leukotriene antagonist tablet.

Other obstructive lung diseases

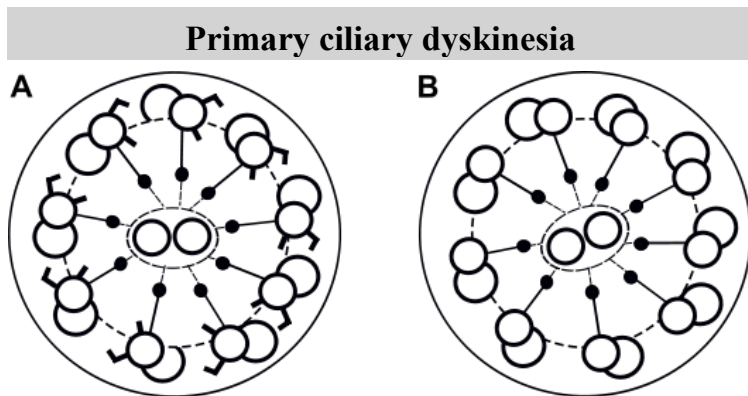
- Cystic fibrosis is an inherited disorder of the CFTR gene, a chloride ion channel. The lack of this channel causes reduced water content of secretions. This affects the mucus secreted as part of the lung's defence and creates sticky, viscous mucus. This makes the lungs more susceptible to infection, inflammation and mucous plugging.

- Bronchiectasis
- Bronchiolitis
- Allergic bronchopulmonary aspergillosis

In many parts of the world, the most common cause of obstructive lung disease is lung scarring after tuberculosis infection.

Chapter 8

Primary Ciliary Dyskinesia



Normal cilia (A) cilia in Kartagener's syndrome (B).

ICD-10	Q89.3*
ICD-9	759.3*
OMIM	244400 242650
DiseasesDB	7111 29887
eMedicine	med/1220 ped/1166
MeSH	D002925

Primary ciliary dyskinesia (PCD), also known as **immotile ciliary syndrome** or **Kartagener Syndrome (KS)**, is a rare, ciliopathic, autosomal recessive genetic disorder that causes a defect in the action of the cilia lining the respiratory tract (lower and upper, sinuses, Eustachian tube, middle ear) and fallopian tube.

Respiratory epithelial motile cilia, which resemble microscopic "hairs" (although structurally and biologically unrelated to hair), are complex organelles that beat synchronously in the respiratory tract, moving mucus toward the throat. Normally, cilia beat 7 to 22 times per second, and any impairment can result in poor mucociliary clearance, with subsequent upper and lower respiratory infection. Cilia also are involved in other biological processes (such as nitric oxide production), which are currently the

subject of dozens of research efforts. As the functions of cilia become better understood, the understanding of PCD should be expected to advance.

Genetics

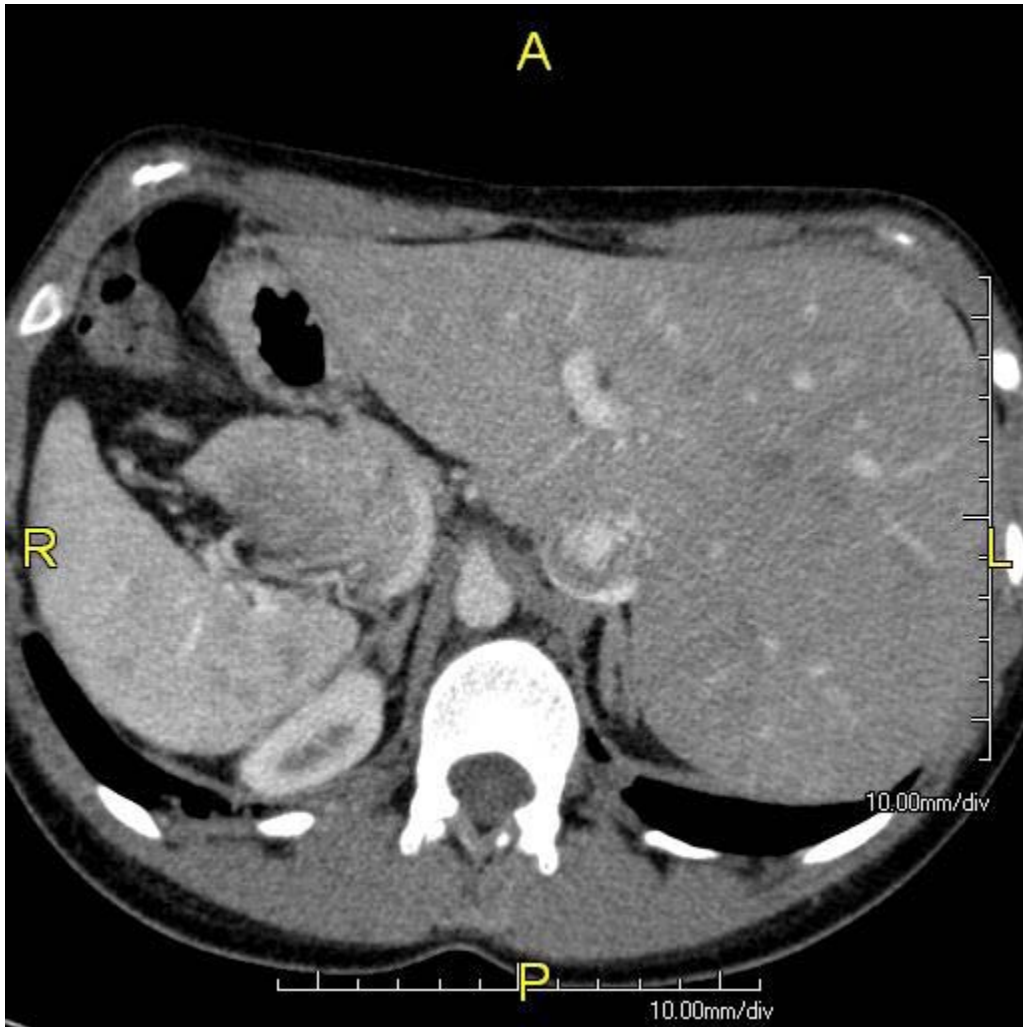
PCD is a genetically heterogeneous disorder affecting motile cilia which are made up of approximately 250 proteins. Around 90% of individuals with PCD have ultrastructural defects affecting protein(s) in the outer and/or inner dynein arms which give cilia their motility, with roughly 38% of these defects caused by mutations on two genes, DNAI1 and DNAH5, both of which code for proteins found in the ciliary outer dynein arm.

There is an international effort to identify genes that code for inner dynein arm proteins or proteins from other ciliary structures (radial spokes, central apparatus, etc.) associated with PCD. The role of DNAH5 in heterotaxy syndromes and left-right asymmetry is also under investigation.

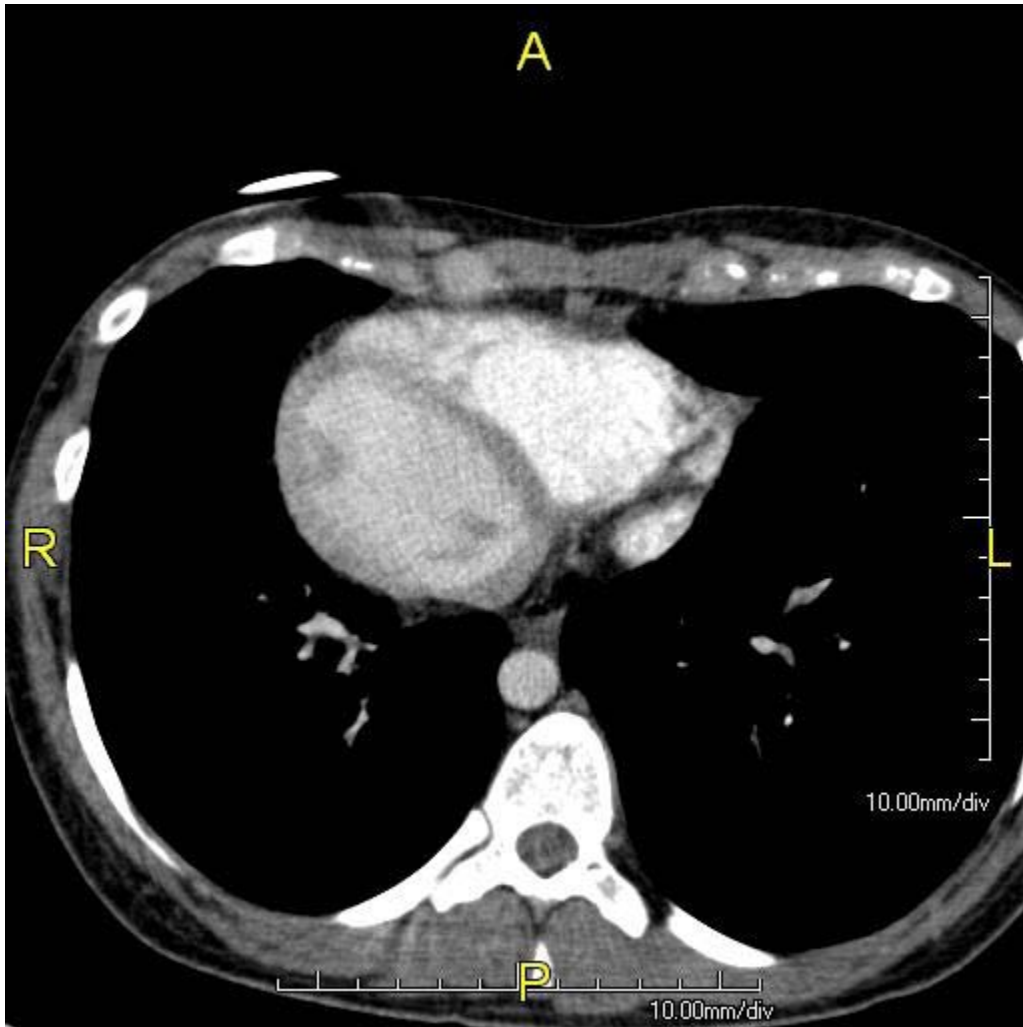
Type	OMIM	Gene	Locus
CILD1	244400	DNAI1	9p21-p13
CILD2	606763	?	19q13.3-qter
CILD3	608644	DNAH5	5p
CILD4	608646	?	15q13
CILD5	608647	?	16p12
CILD6	610852	TXNDC3	7p14-p13
CILD7	611884	DNAH11	7p21
CILD8	612274	?	15q24-q25
CILD9	612444	DNAI2	17q25
CILD10	612518	KTU	14q21.3
CILD11	612649	RSPH4A	6q22
CILD12	612650	RSPH9	6p21
CILD13	613190	LRRC50	16q24.1

Classification

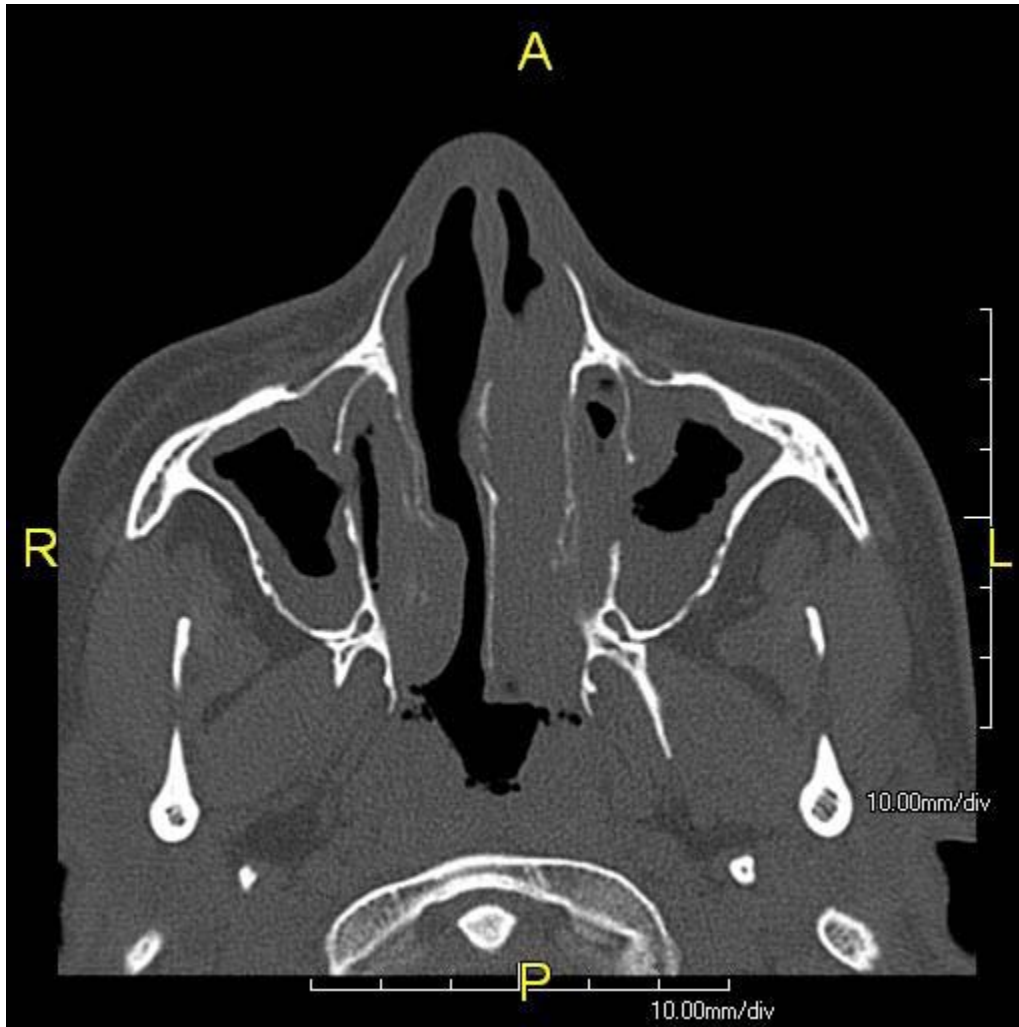
When accompanied by the combination of situs inversus (reversal of the internal organs), chronic sinusitis, and bronchiectasis, it is known as Kartagener syndrome. The phrase "immotile ciliary syndrome" is no longer favored as the cilia does have movement, but may be inefficient or unsynchronized.



Axial CT image showing situs inversus. The slice is seen from below, with the liver and IVC on the left and the spleen and aorta on the right.



Axial CT image showing dextrocardia with the IVC and morphologic right ventricle on the left and the left ventricle on the right



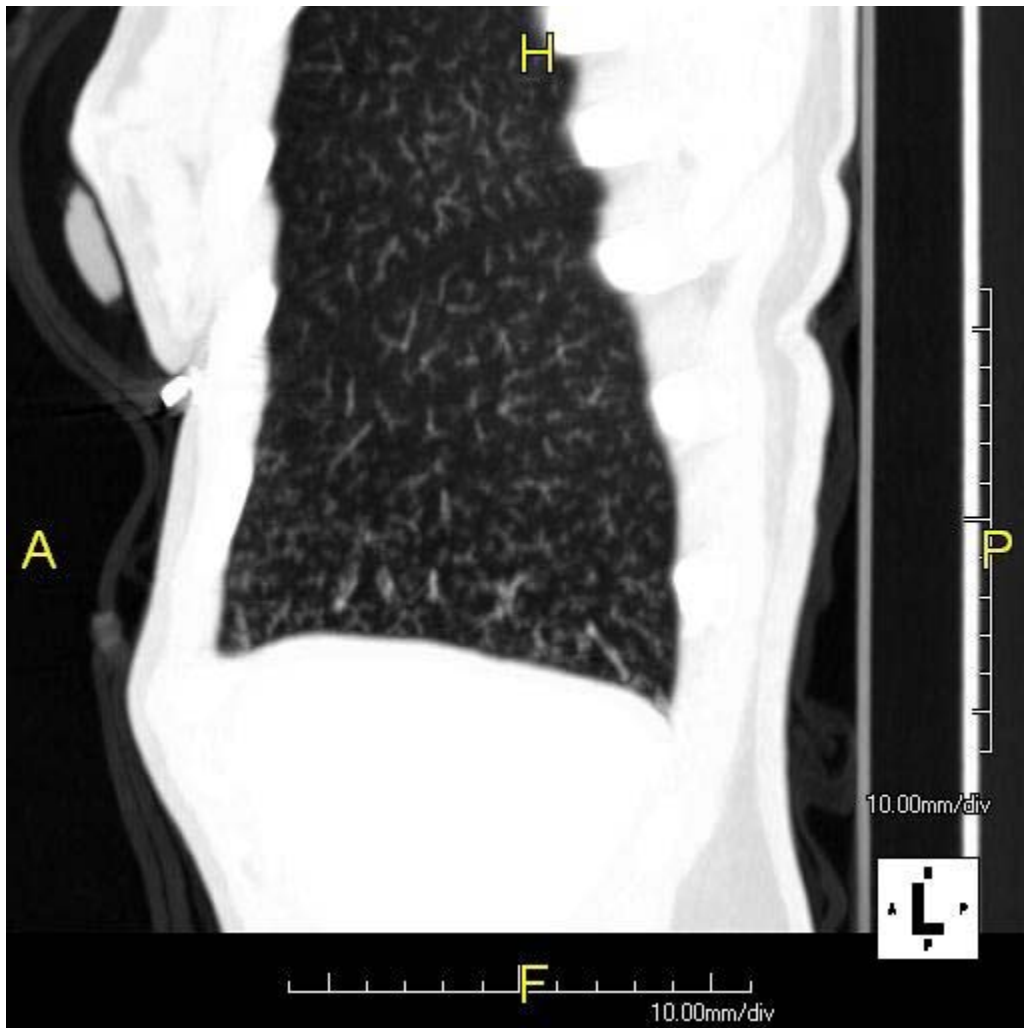
Axial CT image showing chronic sinusitis in an individual with Kartagener syndrome

Signs and symptoms

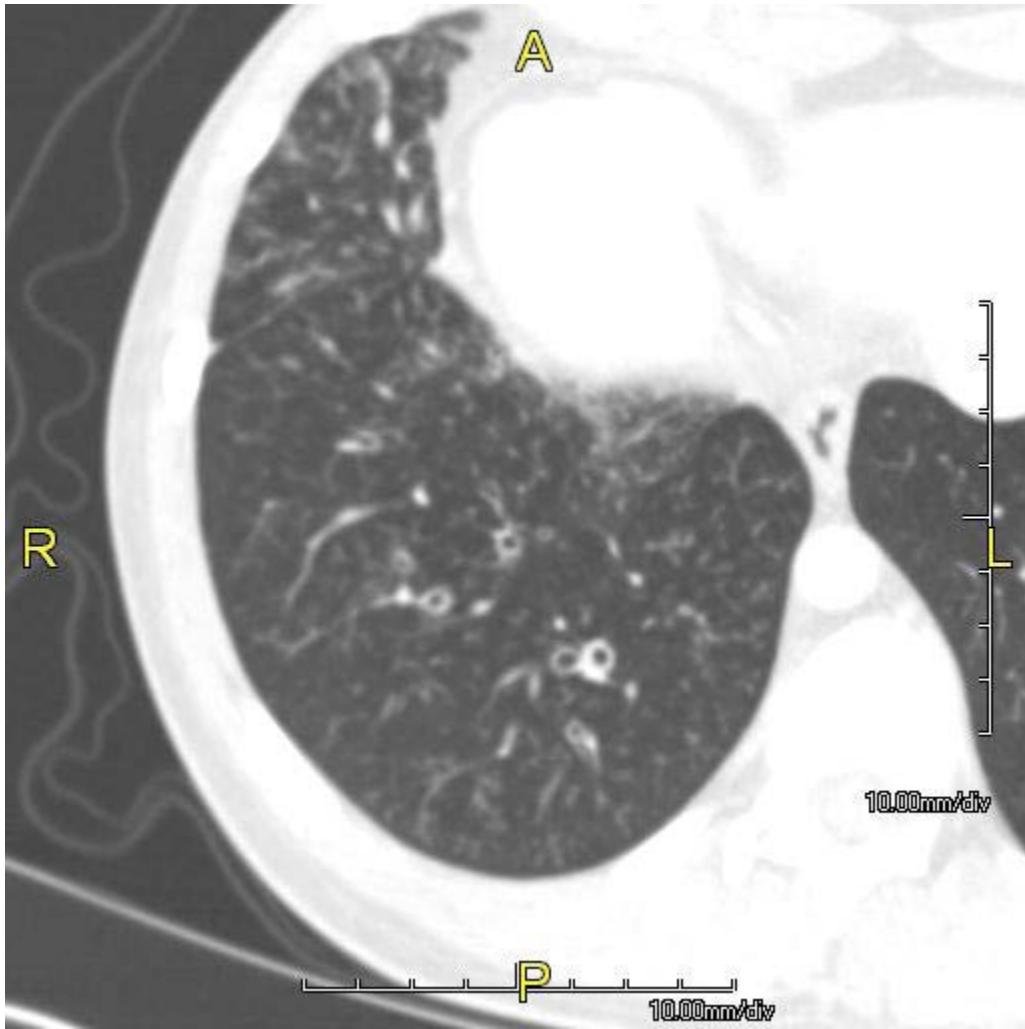
The main consequence of impaired ciliary function is reduced or absent mucus clearance from the lungs, and susceptibility to chronic recurrent respiratory infections, including sinusitis, bronchitis, pneumonia, and otitis media. Progressive damage to the respiratory system is common, including progressive bronchiectasis beginning in early childhood, and sinus disease (sometimes becoming severe in adults). However, diagnosis is often missed early in life despite the characteristic signs and symptoms.

Many affected individuals experience hearing loss and show symptoms of glue ear which demonstrate variable responsiveness to the insertion of myringotomy tubes or grommets. Some patients have been having a poor sense of smell, which is believed to accompany high mucus production in the sinuses (although others report normal - or even acute - sensitivity to smell and taste). Clinical progression of the disease is variable with lung transplantation required in severe cases. Susceptibility to infections can be drastically reduced by an early diagnosis. Treatment with various chest physiotherapy techniques

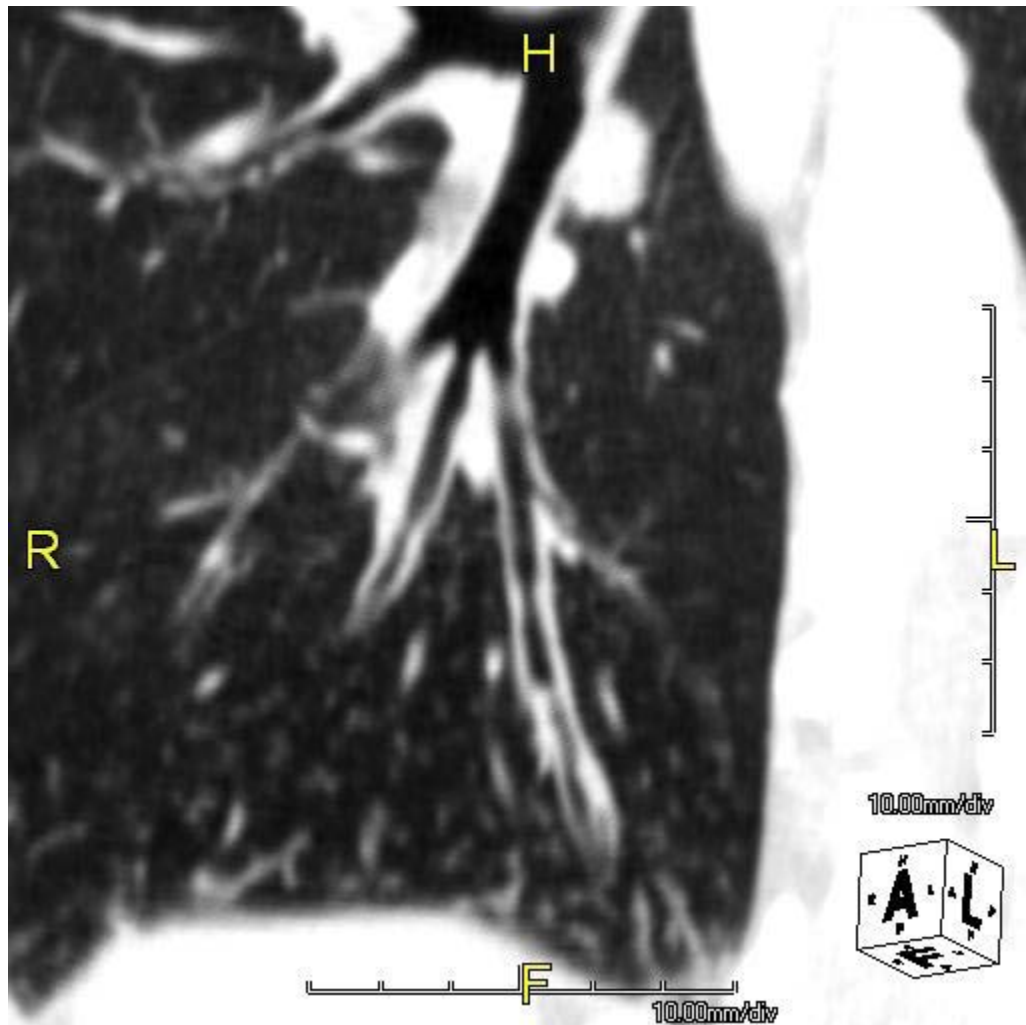
has been observed to reduce the incidence of lung infection and to slow the progression of bronchiectasis dramatically. Aggressive treatment of sinus disease beginning at an early age is believed to slow long-term sinus damage (although this has not yet been adequately documented). Aggressive measures to enhance clearance of mucus, prevent respiratory infections, and treat bacterial superinfections have been observed to slow lung-disease progression. Although the true incidence of the disease is unknown, it is estimated to be 1 in 32,000, although the actual incidence may be as high as 1 in 15,000.



Sagittal CT image showing "tree in bud" appearance of mucous impaction in distal small airways related to primary ciliary dyskinesia



CT image showing dilated and thickened medium sized airways (bronchiectasis) in a patient with Kartagener syndrome



Oblique sagittal CT image showing lower lobe cylindrical bronchiectasis in the same patient

Pathophysiology

This disease is genetically inherited. Structures that make up the cilia including inner and/or outer dynein arms, central apparatus, radial spokes, etc. are missing or dysfunctional and thus the axoneme structure lacks the ability to move. Axonemes are the elongated structures that make up cilia and flagella. Additionally, there may be chemical defects that interfere with ciliary function in the presence of adequate structure. Whatever the underlying cause, dysfunction of the cilia begins during and impacts the embryologic phase of development.

Specialised monocilia are at the heart of this problem. They lack the central-pair microtubules of ordinary motile cilia and so rotate clockwise rather than beat; in Hensen's node at the anterior end of the primitive streak in the embryo, these are angled posteriorly such that they prescribe a D-shape rather than a circle. This has been shown to generate a

net leftward flow in mouse and chick embryos, and sweeps the Sonic Hedgehog (*Shh*) protein to the left, triggering normal asymmetrical development.

However, in some individuals with PCD, mutations thought to be in the gene coding for the key structural protein left-right dynein (*Ird*) result in monocilia which do not rotate. There is therefore no flow generated in the node, *Shh* moves at random within it, and 50% of those affected develop situs inversus which can occur with or without dextrocardia, where the laterality of the internal organs is the mirror-image of normal. Affected individuals therefore have Kartagener syndrome. This is not the case with some PCD-related genetic mutations: at least 6% of the PCD population have a condition called situs ambiguus or heterotaxy where organ placement or development is neither typical (situs solitus) nor totally reversed (situs inversus totalis) but is a hybrid of the two. Splenic abnormalities such as polysplenia, asplenia and complex congenital heart defects are more common in individuals with situs ambiguus and PCD, as they are in all individuals with situs ambiguus.

The genetic forces linking failure of nodal monocilia and situs issues and the relationship of those forces to PCD are the subject of intense research interest. For now hypotheses abound—some, like the one above, are generally accepted. However, knowledge in this area is constantly advancing.

Relation to other rare genetic disorders

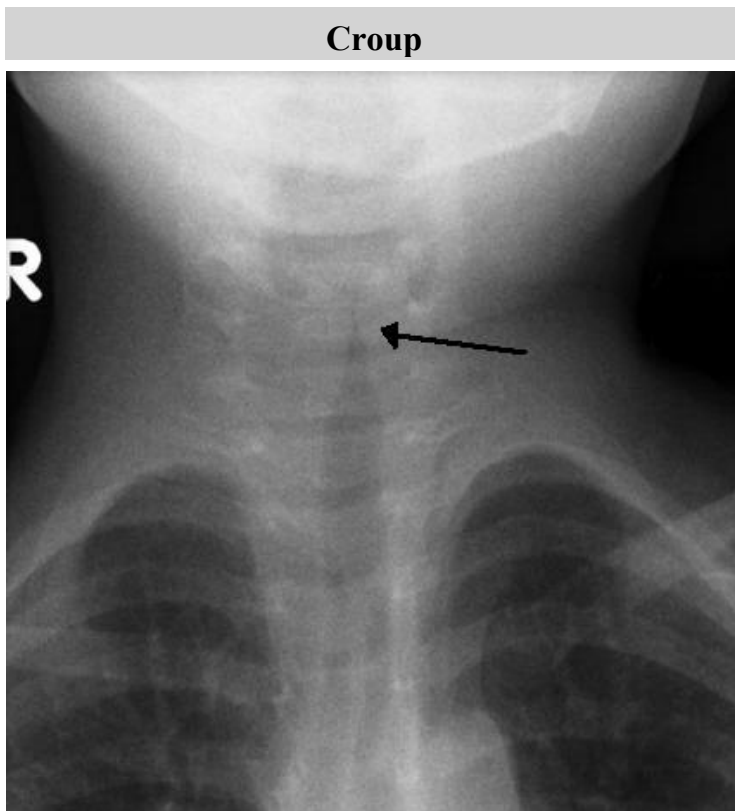
Recent findings in genetic research have suggested that a large number of genetic disorders, both genetic syndromes and genetic diseases, that were not previously identified in the medical literature as related, may be, in fact, highly related in the genotypical root cause of the widely-varying, phenotypically-observed disorders. Thus, PCD is a ciliopathy. Other known ciliopathies include Bardet-Biedl syndrome, polycystic kidney and liver disease, nephronophthisis, Alstrom syndrome, Meckel-Gruber syndrome and some forms of retinal degeneration.

History

The classic symptom combination associated with PCD was first described by A. K. Zivert in 1904, while Kartagener published his first report on the subject in 1933.

Chapter 9

Croup



The steeple sign as seen on an AP neck X-ray of a child with croup

ICD-10	J05.0
ICD-9	464.4
DiseasesDB	13233
MedlinePlus	000959
eMedicine	ped/510 emerg/370 radio/199
MeSH	D003440

Croup (or **laryngotracheobronchitis**) is a respiratory condition that is usually triggered by an acute viral infection of the upper airway. The infection leads to swelling inside the throat, which interferes with normal breathing and produces the classical symptoms of a "barking" cough, stridor, and hoarseness. It may produce mild, moderate, or severe symptoms, which often worsen at night. It is often treated with a single dose of oral steroids; occasionally epinephrine is used in more severe cases. Hospitalization is rarely required.

Croup is diagnosed on clinical grounds once potentially more severe causes of symptoms have been excluded (i.e. epiglottitis or an airway foreign body). Further investigations—such as blood tests, X-rays, and cultures—are usually not needed. It is a relatively common condition that affects about 15% of children at some point, most commonly between 6 months and 5–6 years of age. It is almost never seen in teenagers or adults.

Once due primarily to diphtheria, this cause is now primarily of historical significance in the Western world due to the success of vaccination.

Signs and symptoms

Croup is characterized by a "barking" cough, stridor, hoarseness, and difficult breathing which usually worsens at night. The "barking" cough is often described as resembling the call of a seal or sea lion. The stridor is worsened by agitation or crying, and if it can be heard at rest, it may indicate critical narrowing of the airways. As croup worsens, stridor may decrease considerably.

Other symptoms include fever, coryza (symptoms typical of the common cold), and chest wall indrawing. Drooling or a very sick appearance indicate other medical conditions.

Causes

Croup is usually deemed to be due to a viral infection. Others use the term more broadly, to include acute laryngotracheitis, spasmodic croup, laryngeal diphtheria, bacterial tracheitis, laryngotracheobronchitis, and laryngotracheobronchopneumonitis. The first two conditions involve a viral infection and are generally milder with respect to symptomatology; the last four are due to bacterial infection and are usually of greater severity.

Viral

Viral croup/acute laryngotracheitis caused by parainfluenza virus, primarily types 1 and 2, in 75% of cases. Other viral etiologies include influenza A and B, measles, adenovirus and respiratory syncytial virus (RSV). Spasmodic croup is caused by the same group of viruses as acute laryngotracheitis, but lacks the usual signs of infection (such as fever, sore throat, and increased white blood cell count). Treatment, and response to treatment, are also similar.

Bacterial

Bacterial croup may be divided into laryngeal diphtheria, bacterial tracheitis, laryngotracheobronchitis, and laryngotracheobronchopneumonitis. Laryngeal diphtheria is due to *Corynebacterium diphtheriae* while bacterial tracheitis, laryngotracheobronchitis, and laryngotracheobronchopneumonitis are usually due to a primary viral infection with secondary bacterial growth. The most common bacteria implicated are *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Hemophilus influenzae*, and *Moraxella catarrhalis*.

Pathophysiology

The viral infection that causes croup leads to swelling of the larynx, trachea, and large bronchi due to infiltration of white blood cells (especially histiocytes, lymphocytes, plasma cells, and neutrophils). Swelling produces airway obstruction which, when significant, leads to dramatically increased work of breathing and the characteristic turbulent, noisy airflow known as stridor.

Diagnosis

Feature	The Westley Score: Classification of croup severity					
	Number of points assigned for this feature					
	0	1	2	3	4	5
Chest wall retraction	None	Mild	Moderate	Severe		
Stridor	None	With agitation	At rest			
Cyanosis	None				With agitation	At rest
Level of consciousness	Normal					Disoriented
Air entry	Normal	Decreased	Markedly decreased			

Croup is a clinical diagnosis. The first step is to exclude other obstructive conditions of the upper airway, especially epiglottitis, an airway foreign body, subglottic stenosis, angioedema, retropharyngeal abscess, and bacterial tracheitis.

A frontal X-ray of the neck is not routinely performed, but if it is done, it may show a characteristic narrowing of the trachea, called the steeple sign. The steeple sign is suggestive of the diagnosis, but is absent in half of cases.

Other investigations (such as blood tests and viral culture) are discouraged as they may cause unnecessary agitation and thus worsen the stress on the compromised airway. While viral cultures, obtained via nasopharyngeal aspiration, can be used to confirm the

exact cause, these are usually restricted to research settings. Bacterial infection should be considered if a person does not improve with standard treatment, at which point further investigations may be indicated.

Severity

The most commonly used system for classifying the severity of croup is the Westley score. It is primarily used for research purposes rather than in clinical practice. It is the sum of points assigned for five factors: level of consciousness, cyanosis, stridor, air entry, and retractions. The points given for each factor is listed in the table to the right, and the final score ranges from 0 to 17.

- A total score of ≤ 2 indicates *mild* croup. The characteristic barking cough and hoarseness may be present, but there is no stridor at rest.
- A total score of 3–5 is classified as *moderate* croup. It presents with easily heard stridor, but with few other signs.
- A total score of 6–11 is *severe* croup. It also presents with obvious stridor, but also features marked chest wall indrawing.
- A total score of ≥ 12 indicates impending respiratory failure. The barking cough and stridor may no longer be prominent at this stage.

85% of children presenting to the emergency department have mild disease; severe croup is rare (<1%).

Prevention

Many cases of croup have been prevented by immunization for influenza and diphtheria. At one time, croup referred to a diphtherial disease, but with vaccination, diphtheria is now rare in the developed world.

Treatment

Children with croup are generally kept as calm as possible. Steroids are given routinely, with epinephrine used in severe cases. Children with oxygen saturations under 92% should receive oxygen, and those with severe croup may be hospitalized for observation. If oxygen is needed, "blow-by" administration (holding an oxygen source near the child's face) is recommended, as it causes less agitation than use of a mask. With treatment, less than 0.2% of people require endotracheal intubation.

Steroids

Corticosteroids, such as dexamethasone and budesonide, have been shown to improve outcomes in children with all severities of croup. However, significant relief is often not obtained for up to six hours after administration, and lasts for only about 12 hours. While effective when given orally, parenterally, or by inhalation, the oral route is preferred. A

single dose is usually all that is required, and is generally considered to be quite safe. Dexamethasone at doses of 0.15, 0.3 and 0.6 mg/kg appear to be all equally effective.

Epinephrine

Moderate to severe croup may be improved temporarily with nebulized epinephrine. While epinephrine typically produces a reduction in croup severity within 10–30 minutes, the benefits last for only about 2 hours. If the condition remains improved for 2–4 hours after treatment and no other complications arise, the child is typically discharged from the hospital.

Other

While other treatments for croup have been studied, none have sufficient evidence to support their use. Inhalation of hot steam or humidified air is a traditional self-care treatment, but clinical studies have failed to show effectiveness and currently it is rarely used. The use of cough medicines, which usually contain dextromethorphan and/or guaifenesin, are also discouraged. While breathing heliox (a mixture of helium and oxygen) to decrease the work of breathing has been used in the past, there is very little evidence to support its use. Since croup is usually a viral disease, antibiotics are not used unless secondary bacterial infection is suspected. In cases of possible secondary bacterial infection, the antibiotics vancomycin and cefotaxime are recommended. In severe cases associated with influenza A or B, the antiviral neuraminidase inhibitors may be administered.

Prognosis

Viral croup is usually a self-limited disease, but can very rarely result in death from respiratory failure and/or cardiac arrest. Symptoms usually improve within two days, but may last for up to seven days. Other uncommon complications include bacterial tracheitis, pneumonia, and pulmonary edema.

Epidemiology

Croup affects about 15% of children, and usually presents between the ages of 6 months and 5–6 years. It accounts for about 5% of hospital admissions in this population. In rare cases, it may occur in children as young as 3 months and as old as 15 years. Males are affected 50% more frequently than are females, and there is an increased prevalence in autumn (fall).

History

The word *croup* comes from the Early Modern English verb *croup*, meaning "to cry hoarsely"; the name was first applied to the disease in Scotland and popularized in the 18th century. Diphtheritic croup has been known since the time of Homer's Ancient Greece and it was not until 1826 that viral croup was differentiated from croup due to

diphtheria by Bretonneau. Viral croup was thus called "faux-croup" by the French, as "croup" then referred to a disease caused by the diphtheria bacteria. Croup due to diphtheria has become nearly unknown due to the advent of effective immunization.

Chapter 10

Eosinophilic Pneumonia

Eosinophilic pneumonia

ICD-10	J82.
ICD-9	518.3
MedlinePlus	000105
MeSH	D011657

Eosinophilic pneumonia (EP) is a disease in which a certain type of white blood cell called an eosinophil accumulates in the lung. These cells cause disruption of the normal air spaces (alveoli) where oxygen is extracted from the atmosphere. Several different kinds of eosinophilic pneumonia exist and can occur in any age group. The most common symptoms include cough, fever, difficulty breathing, and sweating at night. EP is diagnosed by a combination of characteristic symptoms, findings on a physical examination by a health provider, and the results of blood tests and x-rays. Prognosis is excellent once most EP is recognized and treatment with corticosteroids is begun.

Types of eosinophilic pneumonia

Eosinophilic pneumonia is divided into different categories depending upon whether a cause can be determined or not. Known causes include certain medications or environmental triggers, parasitic infections, and cancer. EP can also occur when the immune system attacks the lungs, a disease called Churg-Strauss syndrome. When a cause can not be found, the EP is labeled "idiopathic." Idiopathic EP can be divided into "acute eosinophilic pneumonia" (AEP) and "chronic eosinophilic pneumonia" (CEP) depending on the symptoms a person is experiencing.

Symptoms

Most causes of eosinophilic pneumonia have similar symptoms. Cough, fever, increasing breathlessness, and night sweats are prominent and almost universal. Acute eosinophilic pneumonia typically follows a rapid course. Fever and cough may develop only one or two weeks before difficulties breathing progress to the point of respiratory failure

requiring mechanical ventilation. Chronic eosinophilic pneumonia usually follows a slower course. Symptoms accumulate over several months and include fevers, cough, breathlessness, wheezing, and weight loss. Individuals with CEP are often diagnosed with asthma before CEP is finally recognized.

EP due to medications or environmental exposures is similar and occurs after an exposure to a known offending agent. EP due to parasitic infections has a similar prodrome in addition to a host of different symptoms related to the variety of underlying parasites. EP in the setting of cancer often develops in the context of a known diagnosis of lung cancer, cervical cancer, etc.

There have been cases of drug-induced eosinophilic pneumonia from daptomycin (Cubicin). Two of these cases have been noted as chronically steroid dependent. (Reference Clinical Infectious Disease 2010:50 (1 March) pp735–739.

Pathophysiology

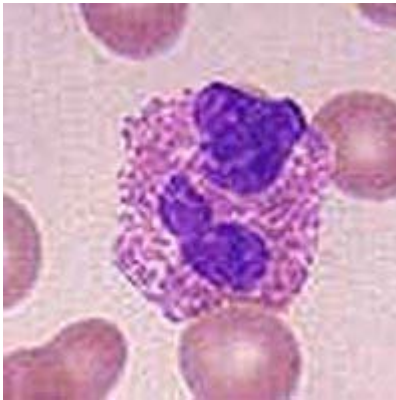


Image of an eosinophil

Eosinophilic pneumonia can develop in several different ways depending on the underlying cause of the disease. Eosinophils are thought to play a central role in defending the body against infection by parasites. Many diseases, such as asthma and eczema, are caused when eosinophils overreact to environmental triggers and release an excess of chemicals (cytokines) such as histamine. The common characteristic among different causes of EP is eosinophil overreaction or dysfunction in the lung.

Medications and environmental exposures

Medications, substance abuse, and environmental exposures may all trigger eosinophil dysfunction. Medications such NSAIDs (i.e. ibuprofen), nitrofurantoin, phenytoin, L-tryptophan, daptomycin and ampicillin and drugs of abuse such as inhaled heroin and cocaine may trigger an allergic response which results in EP. Chemicals such as sulfites, aluminum silicate, and cigarette smoke can cause EP when inhaled. A New York City firefighter developed EP after inhalation of dust from the World Trade Center on September 11, 2001.

Parasitic infections

Parasites cause EP in three different ways. Parasites can either invade the lung, live in the lung as part of their life cycle, or be spread to the lung by the bloodstream. Eosinophils migrate to the lung in order to fight the parasites and EP results. Important parasites which invade the lung include *Paragonimus* lung flukes and the tapeworms *Echinococcus* and *Taenia solium*. Important parasites which inhabit the lung as part of their normal life cycle include the worms (helminths) *Ascaris lumbricoides*, *Strongyloides stercoralis* and the hookworms *Ancylostoma duodenale* and *Necator americanus*. When EP is caused by this last group, it is often called "Löffler's syndrome". The final group of parasites cause EP when a large number of eggs are carried into the lungs by the bloodstream. This can include *Trichinella spiralis*, *Strongyloides stercoralis*, *Ascaris lumbricoides*, the hookworms, and the schistosomes.

AEP and CEP

The causes for both AEP and CEP are unknown as of 2005. There is some suspicion that at least AEP is the result of the body's response to some unidentified environmental agent.

Diagnosis

Eosinophilic pneumonia is diagnosed in one of three circumstances: when a complete blood count reveals increased eosinophils and a chest x-ray or computed tomography (CT) identifies abnormalities in the lung, when a biopsy identifies increased eosinophils in lung tissue, or when increased eosinophils are found in fluid obtained by a bronchoscopy (bronchoalveolar lavage (BAL) fluid). Association with medication or cancer is usually apparent after review of a person's medical history. Specific parasitic infections are diagnosed after examining a person's exposure to common parasites and performing laboratory tests to look for likely causes. If no underlying cause is found, a diagnosis of AEP or CEP is made based upon the following criteria. AEP is most likely with respiratory failure after an acute febrile illness of usually less than one week, changes in multiple areas and fluid in the area surrounding the lungs on a chest x-ray, and greater than 25% eosinophils on a BAL. Other typical laboratory abnormalities include an elevated white blood cell count, erythrocyte sedimentation rate, and immunoglobulin E level. Pulmonary function testing usually reveals a restrictive process with reduced diffusion capacity for carbon monoxide. CEP is most likely when the symptoms have been present for more than a month. Laboratory tests typical for CEP include increased blood eosinophils, a high erythrocyte sedimentation rate, iron deficiency anemia, and increased platelets. A chest x-ray can show abnormalities anywhere, but the most specific finding is increased shadow in the periphery of the lung, away from the heart.

Treatment

When eosinophilic pneumonia is related to an illness such as cancer or parasitic infection, treatment of the underlying cause is effective in resolving the lung disease. When due to

AEP or CEP, however, treatment with corticosteroids results in a rapid, dramatic resolution of symptoms over the course of one or two days. Either intravenous methylprednisolone or oral prednisone are most commonly used. In AEP, treatment is usually continued for a month after symptoms disappear and the x-ray returns to normal (usually four weeks total). In CEP, treatment is usually continued for three months after symptoms disappear and the x-ray returns to normal (usually four months total). Inhaled steroids such as fluticasone have been used effectively when discontinuation of oral prednisone has resulted in relapse. Because EP affects the lungs, individuals with EP have difficulty breathing. If enough of the lung is involved, it may not be possible for a person to breathe enough to live without support. Non-invasive machines such as a bilevel positive airway pressure machine may be used. Otherwise, placement of a breathing tube into the mouth may be necessary and a ventilator may be used to help the person breathe.

Prognosis

Eosinophilic pneumonia due to cancer or parasitic infection carries a prognosis related to the underlying illness. AEP and CEP, however, have very little associated mortality as long as intensive care is available and treatment with corticosteroids is given. CEP often relapses when prednisone is discontinued; therefore, some people with CEP require lifelong therapy. Chronic prednisone is associated with many side effects, including increased infections, weakened bones, stomach ulcers, and changes in appearance.

Epidemiology

Eosinophilic pneumonia is a rare disease. Parasitic causes are most common in geographic areas where each parasite is endemic. AEP can occur at any age, even in previously healthy children, though most patients are between 20 and 40 years of age. Men are affected approximately twice as frequently as women. AEP has been associated with smoking. CEP occurs more frequently in women than men and does not appear to be related to smoking. An association with radiation for breast cancer has been described.

History

Chronic eosinophilic pneumonia was first described by Carrington in 1969, and it is also known as **Carrington syndrome**. Prior to that, eosinophilic pneumonia was a well described pathologic entity usually associated with medication or parasite exposures. Acute eosinophilic pneumonia was first described in 1989

Chapter 11

Hypopnea and Infant Respiratory Distress Syndrome

Hypopnea

Hypopnea (sometimes spelled **hypopnoea**) is a medical term for a disorder which involves episodes of overly shallow breathing or an abnormally low respiratory rate. This differs from apnea in that there remains some flow of air. Hypopnea events may happen while asleep or while awake.

During sleep, hypopnea is classed as a sleep disorder. With moderate to severe hypopnea, sleep is disturbed such that patients may get a full night's sleep but still not feel rested because they did not get the right kind of sleep. The disruption in breathing causes a drop in blood oxygen level, which may in turn disrupt the stages of sleep.

Daytime hypopnea events are mostly limited to those with severely compromised respiratory muscles, as occurs in certain neuromuscular diseases. Similarly, daytime hypopnea can also cause a drop in blood oxygen level.

Etymology

Hypopnea comes from the Greek roots *hypo-* (meaning *low, under, beneath, down, below normal*) and *pnoe* (meaning *breathing*). Literally it means underbreathing.

General information

In the context of diagnosis and treatment of sleep disorders, a hypopnea event is not considered to be clinically significant unless there is a 30% (or greater) reduction in flow lasting for 10 seconds or longer and an associated 4% (or greater) desaturation in the person's O₂ levels, or if it results in arousal or fragmentation of sleep.

The direct consequence of hypopnea (as well as apnea) is that the CO₂ in the blood increases and the oxygen level in the patient's blood decrease is proportionate to the severity of the airway obstruction. This disruptive pattern of breathing generates disruptive sleep patterns, the consequences of which being that those individuals may

exhibit increased fatiguability, lethargy, decreased ability to concentrate, increased irritability, and morning headaches. Basically, those individuals are extremely tired due to their inability to get a good night's sleep.

Hypopneas can be either central (i.e., as part of a waxing and waning in breathing effort) or obstructive in origin. During an obstructive hypopnea, in comparison to an obstructive apnea, the airway is only partially closed. However, this closure is still enough to cause a physiological effect (i.e., an oxygen desaturation and/or an increase in breathing effort terminating in arousal).

A hypopnea index (HI) can be calculated by dividing the number of hypopnea events during the sleep period by the number of hours of sleep. The apnea-hypopnea index (AHI) is an index of severity that combines apneas and hypopneas. Combining them both gives an overall severity of sleep apnea including sleep disruptions and desaturations (a low level of oxygen in the blood). The apnea-hypopnea index, like the apnea index and hypopnea index, is calculated by dividing the number of apneas and hypopneas by the number of hours of sleep. Another index that is used to measure sleep apnea is the respiratory disturbance index (RDI). The respiratory disturbance index is similar to the apnea-hypopnea index; however, it also includes respiratory events that do not technically meet the definitions of apneas or hypopneas, but do disrupt sleep.

Causes

Among the causes of hypopnea are:

- anatomical defects such as nasal septum deformation or congenital narrowness of nasal meati and the gullet;
- acute tonsillitis and/or adenoiditis;
- obesity or being overweight;
- neuromuscular disease or any condition that entails weakened respiratory muscles;
- use of sedatives (sleeping pills, etc.);
- alcohol abuse;
- smoking;
- aging;
- others;

most of which are also typical causes of airway obstruction, snoring and sleep apnea.

Symptoms

The most common hypopnea symptom is excessive sleepiness, which results from constant sleep interruption. People with hypopnea often have loud, heavy snoring that is interrupted with choking sounds or loud snorts followed by periods of silence, because not enough air can flow into the lungs through the mouth and nose. The periods of silence

can last 20 seconds or longer and can happen many times each hour, resulting in poor sleep and reduced levels of oxygen in the blood.

Other symptoms of hypopnea may include depression, forgetfulness, mood or behavior changes, trouble concentrating, loss of energy, nervousness, and morning headaches. Not all people with hypopnea experience all of these symptoms and not everyone who has these symptoms has hypopnea.

Consequences

Hypopnea is a disorder that may result in excessive daytime sleepiness and compromised quality of life, including traffic accidents, diminished productivity in the work place and emotional problems.

Cardiovascular consequences of hypopnea may include myocardial infarction, stroke, psychiatric problems, impotence, cognitive dysfunction, hypertension, coronary heart disease, and memory loss.

Treatment

The most common treatment for hypopnea is continuous positive airway pressure (CPAP). CPAP is a treatment in which the patient wears a mask over the nose and/or mouth. An air blower forces air through the upper airway. The air pressure is adjusted so that it is just enough to maintain the oxygen saturation levels in the blood. For people with neuromuscular disorders, the most common treatment is the use of BIPAP or other non-invasive ventilation.

Mild hypopnea can often be treated by losing weight or by avoiding sleeping on one's back. Also quitting smoking, and avoiding alcohol, sedatives and hypnotics (soporifics) before sleep can be quite effective.

Surgery is generally a last resort in hypopnea treatment, but is a site-specific option for the upper airway. Depending on the cause of obstruction, surgery may focus on the soft palate, the uvula, tonsils, adenoids or the tongue. There are also more complex surgeries that are performed with the adjustment of other bone structures - the mouth, nose and facial bones.

Infant respiratory distress syndrome

Infant respiratory distress syndrome

ICD-10	P22.
ICD-9	769
OMIM	267450
DiseasesDB	6087
MedlinePlus	001563
eMedicine	emerg/15
MeSH	D012127

Infant respiratory distress syndrome (IRDS), also called **neonatal respiratory distress syndrome** or **respiratory distress syndrome of newborn**, previously called **hyaline membrane disease**, is a syndrome in premature infants caused by developmental insufficiency of surfactant production and structural immaturity in the lungs. It can also result from a genetic problem with the production of surfactant associated proteins. RDS affects about 1% of newborn infants and is the leading cause of death in preterm infants. The incidence decreases with advancing gestational age, from about 50% in babies born at 26–28 weeks, to about 25% at 30–31 weeks. The syndrome is more frequent in infants of diabetic mothers and in the second born of premature twins.

IRDS is distinct from pulmonary hypoplasia, another leading cause of neonatal death that involves respiratory distress.

Clinical course

Respiratory distress syndrome begins shortly after birth and is manifest by tachypnea, tachycardia, chest wall retractions (recession), expiratory grunting, flaring of the nostrils and cyanosis during breathing efforts.

As the disease progresses, the baby may develop ventilatory failure (rising carbon dioxide concentrations in the blood), and prolonged cessations of breathing ("apnea"). Whether treated or not, the clinical course for the acute disease lasts about 2 to 3 days. During the first, the patient worsens and requires more support. During the second the baby may be remarkably stable on adequate support and resolution is noted during the third day, heralded by a prompt diuresis. Despite huge advances in care, RDS remains the most common single cause of death in the first month of life of the developed world. Complications include metabolic disorders (acidosis, low blood sugar), patent ductus arteriosus, low blood pressure, chronic lung changes, and intracranial hemorrhage. The

disease is frequently complicated by prematurity and its additional defects in other organ function.

Histopathology

The characteristic histopathology seen in babies who die from RDS was the source of the name "hyaline membrane disease". These waxy-appearing layers line the collapsed tiny air sacs ("alveoli") of the lung. In addition, the lungs show bleeding, over-distention of airways and damage to the lining cells.

Pathophysiology

The lungs of infants with respiratory distress syndrome are developmentally deficient in a material called surfactant, which helps prevent collapse of the terminal air-spaces (the future site of alveolar development) throughout the normal cycle of inhalation and exhalation. Surfactant is a complex system of lipids, proteins and glycoproteins which are produced in specialized lung cells called Type II cells or Type II pneumocytes. The surfactant is packaged by the cell in structures called lamellar bodies, and extruded into the air-spaces. The lamellar bodies then unfold into a complex lining of the air-space. This layer reduces the surface tension of the fluid that lines the air-space. Surface tension is responsible for approximately 2/3 of the elastic recoil forces. In the same way that a bubble will contract to give the smallest surface area for a given volume, so the air/water interface means that the liquid surface will tend towards being as small as possible, thereby causing the air-space to contract. By reducing surface tension, surfactant prevents the air-spaces from completely collapsing on exhalation. In addition, the decreased surface tension allows re-opening of the air-space with a lower amount of force. Therefore, without adequate amounts of surfactant, the air-spaces collapse and are very difficult to expand. Microscopically, a surfactant deficient lung is characterized by collapsed air-spaces alternating with hyper-expanded areas, vascular congestion and, in time, hyaline membranes. Hyaline membranes are composed of fibrin, cellular debris, red blood cells, rare neutrophils and macrophages. They appear as an eosinophilic, amorphous material, lining or filling the air spaces and blocking gas exchange. As a result, blood passing through the lungs is unable to pick up oxygen and unload carbon dioxide. Blood oxygen levels fall and carbon dioxide rises, resulting in rising blood acid levels and hypoxia. Structural immaturity, as manifest by decreased number of gas-exchange units and thicker walls, also contributes to the disease process. Therapeutic oxygen and positive-pressure ventilation, while potentially life-saving, can also damage the lung. The diagnosis is made by the clinical picture and the chest xray, which demonstrates decreased lung volumes (bell-shaped chest), absence of the thymus (after about 6 hours), a small (0.5–1 mm), discrete, uniform infiltrate (sometimes described as a "ground glass" appearance) that involves all lobes of the lung, and air-bronchograms (i.e. the infiltrate will outline the larger airways passages which remain air-filled). In severe cases, this becomes exaggerated until the cardiac borders become inapparent (a 'white-out' appearance).

Prevention

Most cases of infant respiratory distress syndrome can be ameliorated or prevented if mothers who are about to deliver prematurely can be given glucocorticoids, one group of hormones. This 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 (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. In pregnancies of greater than 30 weeks, the fetal lung maturity may be tested by sampling the amount of surfactant in the amniotic fluid, obtained by inserting a needle through the mother's abdomen and uterus. Several tests are available that correlate with the production of surfactant. These include the lecithin-sphingomyelin ratio ("L/S ratio"), the presence of phosphatidol glycerol (PG), and more recently, the surfactant/albumin (S/A) ratio. For the L/S ratio, if the result is less than 2:1, the fetal lungs may be surfactant deficient. The presence of PG usually indicates fetal lung maturity. For the S/A ratio, the result is given as mg of surfactant per gm of protein. An S/A ratio <35 indicates immature lungs, between 35-55 is indeterminate, and >55 indicates mature surfactant production (correlates with an L/S ratio of 2.2 or greater).

Treatment

Oxygen is given with a small amount of continuous positive airway pressure ("CPAP"), and intravenous fluids are administered to stabilize the blood sugar, blood salts, and blood pressure. If the baby's condition worsens, an endotracheal tube (breathing tube) is inserted into the trachea and intermittent breaths are given by a mechanical device. An exogenous preparation of surfactant, either synthetic or extracted from animal lungs, is given through the breathing tube into the lungs. One of the most commonly used surfactants is Survanta, derived from cow lungs, which can decrease the risk of death in hospitalized very-low-birth-weight infants by 30%. Such small premature infants may remain ventilated for months. A line of research shows that an aerosol of perfluorocarbon can reduce inflammation in piglets. Chronic lung disease including bronchopulmonary dysplasia are common in severe RDS. The etiology of BPD is problematic and may be due to oxygen, overventilation or underventilation. The mortality rate for babies greater than 27 weeks gestation is less than 10%.

Extracorporeal membrane oxygenation (ECMO) is a potential treatment, providing oxygenation through an apparatus that imitates the gas exchange process of the lungs. However, newborns cannot be placed on ECMO if they are under 4.5 pounds (2 kg), because they have extremely small vessels for cannulation, thus hindering adequate flow because of limitations from cannula size and subsequent higher resistance to blood flow (compare with vascular resistance). Furthermore, in infants aged less than 34 weeks of gestation several physiologic systems are not well-developed, specially the cerebral vasculature and germinal matrix, resulting in high sensitivity to slight changes in pH, PaO₂, and intracranial pressure. Subsequently, preterm infants are at unacceptably high risk for intraventricular hemorrhage (IVH) if administered ECMO at a gestational age

less than 32 weeks. Also later, given the risk of IVH, it has become standard practice to ultrasound the brain prior to administering ECMO. Therefore, the device cannot be used for most premature newborns.

Related disorders

Acute respiratory distress syndrome (ARDS) has some similarities to IRDS.

Famous victims

- In 1963, Patrick Bouvier Kennedy, son of President John F. Kennedy and First Lady Jacqueline Kennedy, died of RDS two days after his premature birth at 34 weeks gestation.
- In 1992, Freddie Highmore survived RDS after being born at 29 weeks gestation.

Chapter 12

Lung Cancer

Lung Cancer



Cross section of a human lung. The white area in the upper lobe is cancer; the black areas are discoloration due to smoking.

ICD-10 C33.-C34.

ICD-9 162

DiseasesDB 7616

MedlinePlus	007194
eMedicine	med/1333 med/1336 emerg/335 radio/807 radio/405 radio/406
MeSH	D002283

Lung cancer is a disease which consists of uncontrolled cell growth in tissues of the lung. This growth may lead to metastasis, which is the invasion of adjacent tissue and infiltration beyond the lungs. The vast majority of primary lung cancers are carcinomas, derived from epithelial cells. Lung cancer, the most common cause of cancer-related death in men and women, is responsible for 1.3 million deaths worldwide annually, as of 2004. The most common symptoms are shortness of breath, coughing (including coughing up blood), and weight loss.

The main types of lung cancer are *small cell lung carcinoma* and *non-small cell lung carcinoma*. This distinction is important, because the treatment varies; non-small cell lung carcinoma (NSCLC) is sometimes treated with surgery, while small cell lung carcinoma (SCLC) usually responds better to chemotherapy and radiation. The most common cause of lung cancer is long-term exposure to tobacco smoke. The occurrence of lung cancer in nonsmokers, who account for as many as 15% of cases, is often attributed to a combination of genetic factors, radon gas, asbestos, and air pollution including secondhand smoke.

Lung cancer may be seen on chest radiograph and computed tomography (CT scan). The diagnosis is confirmed with a biopsy. This is usually performed by bronchoscopy or CT-guided biopsy. Treatment and prognosis depend upon the histological type of cancer, the stage (degree of spread), and the patient's performance status. Possible treatments include surgery, chemotherapy, and radiotherapy. Survival varies, depending on stage, overall health, and other factors, but the overall five-year survival rate for all persons diagnosed with lung cancer is 14%.

Signs and symptoms

Symptoms that suggest lung cancer include:

- dyspnea (shortness of breath)
- hemoptysis (coughing up blood)
- chronic coughing or change in regular coughing pattern
- wheezing
- chest pain or pain in the abdomen
- cachexia (weight loss), fatigue, and loss of appetite
- dysphonia (hoarse voice)
- clubbing of the fingernails (uncommon)
- dysphagia (difficulty swallowing).

If the cancer grows in the airway, it may obstruct airflow, causing breathing difficulties. The obstruction can lead to accumulation of secretions behind the blockage, and predispose to pneumonia. Many lung cancers have a rich blood supply. The surface of the cancer may be fragile, leading to bleeding from the cancer into the airway. This blood may subsequently be coughed up.

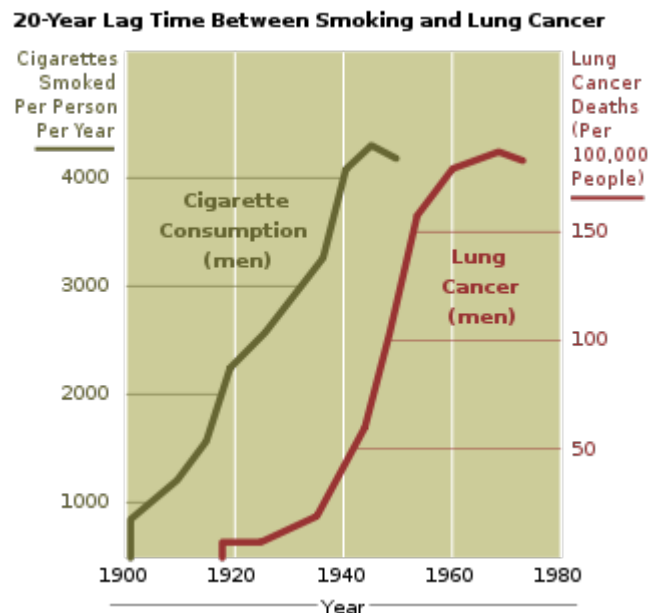
Depending on the type of tumor, so-called paraneoplastic phenomena may initially attract attention to the disease. In lung cancer, these phenomena may include Lambert-Eaton myasthenic syndrome (muscle weakness due to auto-antibodies), hypercalcemia, or syndrome of inappropriate antidiuretic hormone (SIADH). Tumors in the top (apex) of the lung, known as Pancoast tumors, may invade the local part of the sympathetic nervous system, leading to changed sweating patterns and eye muscle problems (a combination known as Horner's syndrome) as well as muscle weakness in the hands due to invasion of the brachial plexus.

Many of the symptoms of lung cancer (bone pain, fever, and weight loss) are nonspecific; in the elderly, these may be attributed to comorbid illness. In many patients, the cancer has already spread beyond the original site by the time they have symptoms and seek medical attention. Common sites of metastasis include the brain, bone, adrenal glands, contralateral (opposite) lung, liver, pericardium, and kidneys. About 10% of people with lung cancer do not have symptoms at diagnosis; these cancers are incidentally found on routine chest radiograph.

Causes

The main causes of any cancer include carcinogens (such as those in tobacco smoke), ionizing radiation, and viral infection. This exposure causes cumulative changes to the DNA in the tissue lining the bronchi of the lungs (the bronchial epithelium). As more tissue becomes damaged, eventually a cancer develops.

Smoking



NIH graph showing the correlation and time-lag between tobacco smoking and lung cancer rate in the U.S. male population

Smoking, particularly of cigarettes, is by far the main contributor to lung cancer. Cigarette smoke contains over 60 known carcinogens, including radioisotopes from the radon decay sequence, nitrosamine, and benzopyrene. Additionally, nicotine appears to depress the immune response to malignant growths in exposed tissue. Across the developed world, almost 90% of lung cancer deaths are caused by smoking. In the United States, smoking is estimated to account for 87% of lung cancer cases (90% in men and 85% in women). Among male smokers, the lifetime risk of developing lung cancer is 17.2%; among female smokers, the risk is 11.6%. This risk is significantly lower in nonsmokers: 1.3% in men and 1.4% in women.

Women who smoke (former smokers and current smokers) and take hormone therapy are at a much higher risk of dying of lung cancer. In a study by Chlebowski *et al.* published in 2009, the women taking hormones were about 60% more likely to die of lung cancer than the women taking a placebo. Not surprisingly, the risk was highest for current smokers, followed by past smokers, and lowest for never smokers. Among the women who smoked (former or current smokers), 3.4% of those taking hormone therapy died of lung cancer compared to 2.3% for women taking the placebo.

The time a person smokes (as well as rate of smoking) increases the person's chance of developing lung cancer. If a person stops smoking, this chance steadily decreases as damage to the lungs is repaired and contaminant particles are gradually removed. In addition, there is evidence that lung cancer in never-smokers has a better prognosis than in smokers, and that patients who smoke at the time of diagnosis have shorter survival times than those who have quit.

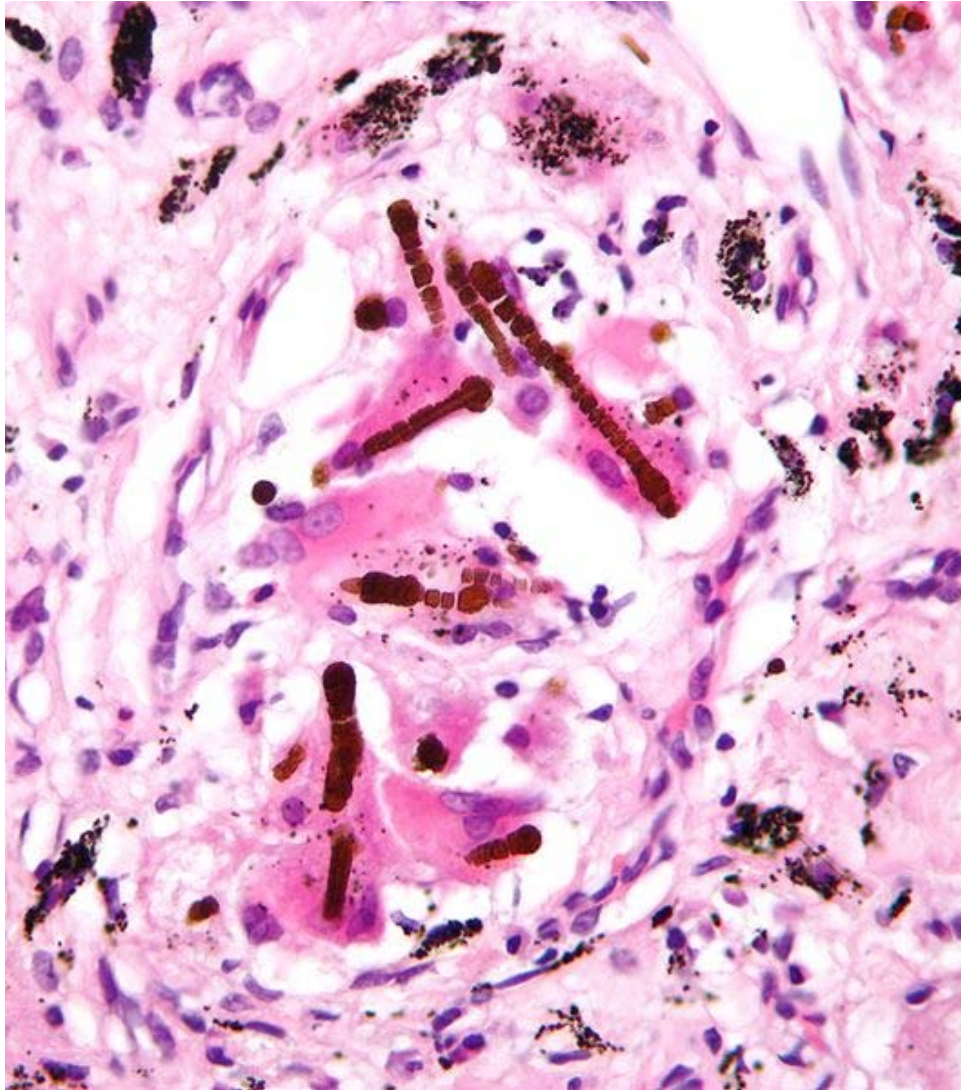
Passive smoking—the inhalation of smoke from another's smoking—is a cause of lung cancer in nonsmokers. A passive smoker can be classified as someone living or working with a smoker. Studies from the U.S., Europe, the UK, and Australia have consistently shown a significant increase in relative risk among those exposed to passive smoke. Recent investigation of sidestream smoke suggests that it is more dangerous than direct smoke inhalation.

10–15% of lung cancer patients have never smoked. That means between 20,000 to 30,000 never-smokers are diagnosed with lung cancer in the United States each year. Because of the five-year survival rate, each year in the U.S. more never-smokers die of lung cancer than do patients of leukemia, ovarian cancer, or AIDS.

Radon gas

Radon is a colorless and odorless gas generated by the breakdown of radioactive radium, which in turn is the decay product of uranium, found in the Earth's crust. The radiation decay products ionize genetic material, causing mutations that sometimes turn cancerous. Radon exposure is the second major cause of lung cancer in the general population, after smoking with the risk increasing by 8% to 16% for every 100 Bq/m³ increase in the radon concentration. Radon gas levels vary by locality and the composition of the underlying soil and rocks. For example, in areas such as Cornwall in the UK (which has granite as substrata), radon gas is a major problem, and buildings have to be force-ventilated with fans to lower radon gas concentrations. The United States Environmental Protection Agency (EPA) estimates that one in 15 homes in the U.S. has radon levels above the recommended guideline of 4 picocuries per liter (pCi/L) (148 Bq/m³). Iowa has the highest average radon concentration in the United States; studies performed there have demonstrated a 50% increased lung cancer risk, with prolonged radon exposure above the EPA's action level of 4 pCi/L.

Asbestos



Ferruginous bodies the histopathologic finding associated with asbestosis

Asbestos can cause a variety of lung diseases, including lung cancer. There is a synergistic effect between tobacco smoking and asbestos in the formation of lung cancer. In the UK, asbestos accounts for 2–3% of male lung cancer deaths. Asbestos can also cause cancer of the pleura, called mesothelioma (which is different from lung cancer).

Viruses

Viruses are known to cause lung cancer in animals, and recent evidence suggests similar potential in humans. Implicated viruses include human papillomavirus, JC virus, simian virus 40 (SV40), BK virus, and cytomegalovirus. These viruses may affect the cell cycle and inhibit apoptosis, allowing uncontrolled cell division.

Particulate matter

Studies of the American Cancer Society cohort directly link the exposure to particulate matter with lung cancer. For example, if the concentration of particles in the air increases by only 1%, the risk of developing a lung cancer increases by 14%. Further, it has been established that particle size matters, as ultrafine particles penetrate further into the lungs.

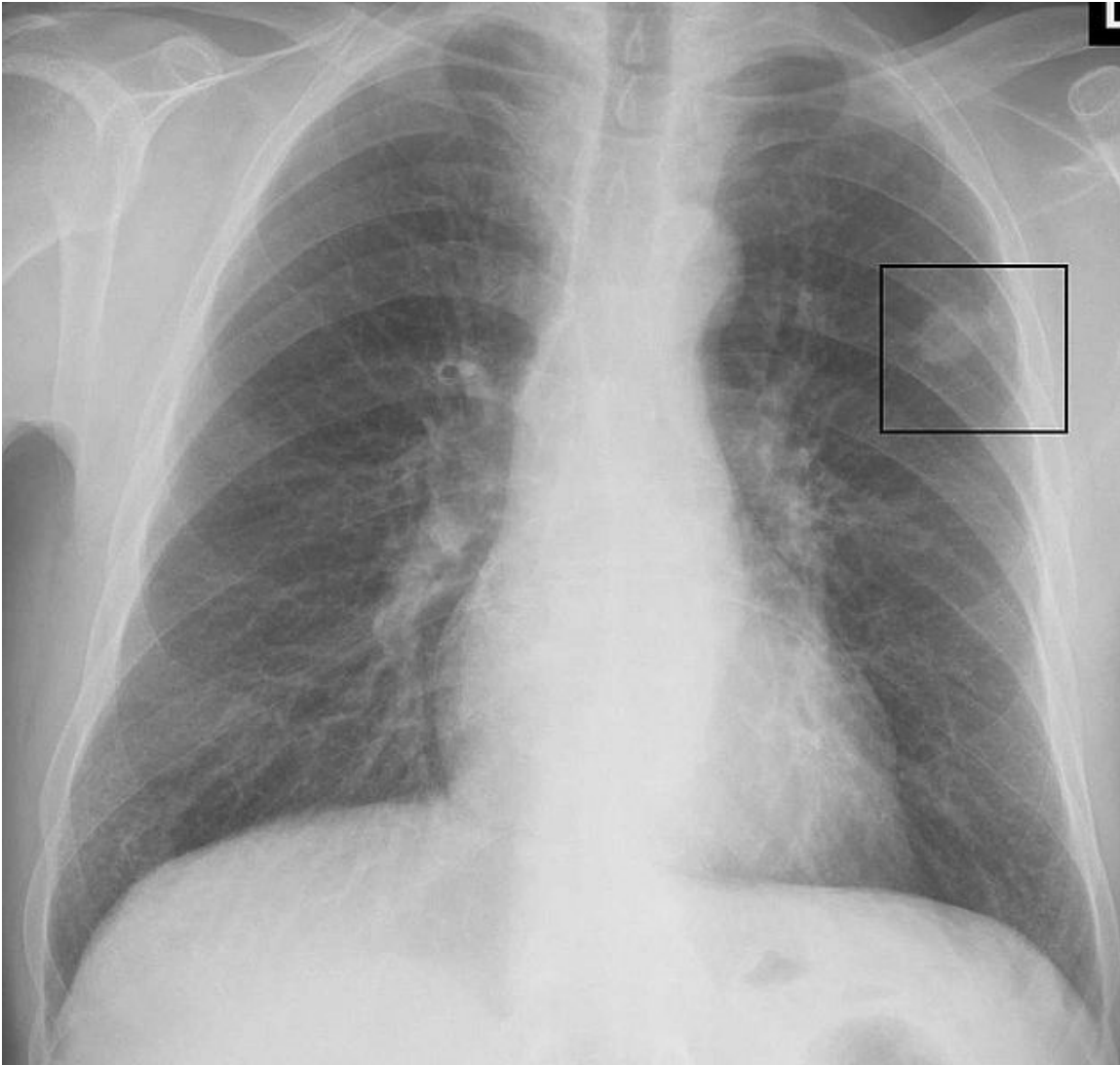
Pathogenesis

Similar to many other cancers, lung cancer is initiated by activation of oncogenes or inactivation of tumor suppressor genes. Oncogenes are genes that are believed to make people more susceptible to cancer. Proto-oncogenes are believed to turn into oncogenes when exposed to particular carcinogens. Mutations in the *K-ras* proto-oncogene are responsible for 10–30% of lung adenocarcinomas. The epidermal growth factor receptor (EGFR) regulates cell proliferation, apoptosis, angiogenesis, and tumor invasion. Mutations and amplification of EGFR are common in non-small cell lung cancer and provide the basis for treatment with EGFR-inhibitors. Her2/neu is affected less frequently. Chromosomal damage can lead to loss of heterozygosity. This can cause inactivation of tumor suppressor genes. Damage to chromosomes 3p, 5q, 13q, and 17p are particularly common in small cell lung carcinoma. The *p53* tumor suppressor gene, located on chromosome 17p, is affected in 60-75% of cases. Other genes that are often mutated or amplified are *c-MET*, *NKX2-1*, *LKB1*, *PIK3CA*, and *BRAF*.

Several genetic polymorphisms are associated with lung cancer. These include polymorphisms in genes coding for interleukin-1, cytochrome P450, apoptosis promoters such as caspase-8, and DNA repair molecules such as XRCC1. People with these polymorphisms are more likely to develop lung cancer after exposure to carcinogens.

A recent study suggested that the MDM2 309G allele is a low-penetrant risk factor for developing lung cancer in Asians.

Diagnosis



Chest radiograph showing a cancerous tumor in the left lung

Performing a chest radiograph is the first step if a patient reports symptoms that may suggest lung cancer. This may reveal an obvious mass, widening of the mediastinum (suggestive of spread to lymph nodes there), atelectasis (collapse), consolidation (pneumonia), or pleural effusion. If there are no radiographic findings but the suspicion is high (such as a heavy smoker with blood-stained sputum), bronchoscopy and/or a CT scan may provide the necessary information. Bronchoscopy or CT-guided biopsy is often used to identify the tumor type.

Abnormal findings in cells ("atypia") in sputum are associated with an increased risk of lung cancer. Sputum cytologic examination combined with other screening examinations may have a role in the early detection of lung cancer.



CT scan showing a cancerous tumor in the left lung

The differential diagnosis for patients who present with abnormalities on chest radiograph includes lung cancer as well as nonmalignant diseases. These include infectious causes such as tuberculosis or pneumonia, or inflammatory conditions such as sarcoidosis. These diseases can result in mediastinal lymphadenopathy or lung nodules, and sometimes mimic lung cancers. Lung cancer can also be an incidental finding: a solitary pulmonary nodule (also called a coin lesion) on a chest radiograph or CT scan taken for an unrelated reason. The definitive diagnosis of lung cancer and its classification (described above) is based on examination of the suspicious tissue under the microscope.

Classification

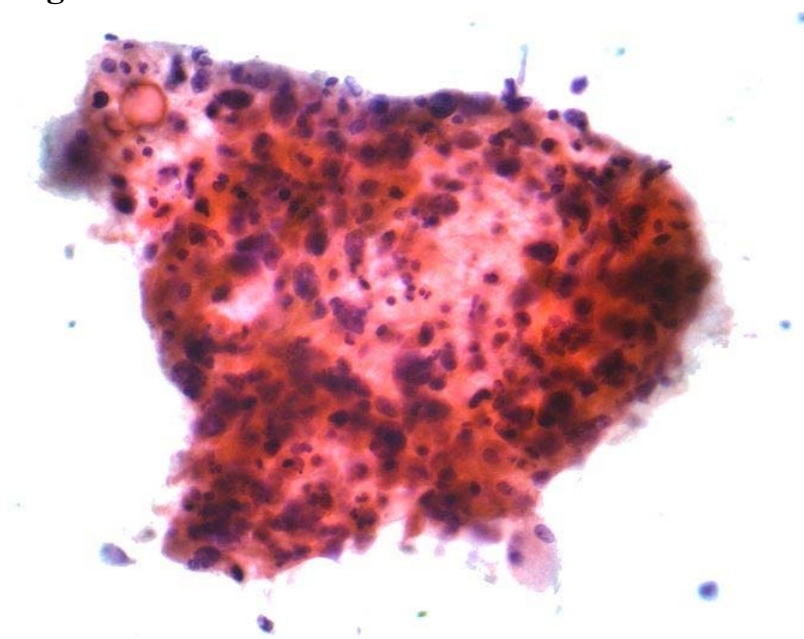
Lung cancers are classified according to histological type. This classification has important implications for clinical management and prognosis of the disease. The vast majority of lung cancers are carcinomas—malignancies that arise from epithelial cells. The two most prevalent histological types of lung carcinoma, categorized by the size and appearance of the malignant cells seen by a histopathologist under a microscope: *non-small cell* and *small-cell* lung carcinoma. The non-small cell type is the most prevalent by far (see table).

Frequency of histological types of lung cancer	
Histological type	Frequency (%)
Non-small cell lung carcinoma	80.4

Small cell lung carcinoma	16.8
Carcinoid	0.8
Sarcoma	0.1
Unspecified lung cancer	1.9

Cancer found outside of the lung may be determined to have arisen within the lung, as lung cancers that metastasize, i.e. spread, often retain a cell marker profile that allow a pathologist to say, with a good deal of certainty, that the tumor arose from the lung, i.e. is a *primary lung cancer*. Primary lung cancers of adenocarcinoma histology typically have nuclear immunostaining with TTF-1.

Non-small cell lung carcinoma



Micrograph of squamous carcinoma, a type of non-small cell carcinoma. FNA specimen. Pap stain.

The non-small cell lung carcinomas (NSCLC) are grouped together because their prognosis and management are similar. There are three main sub-types: squamous cell lung carcinoma, adenocarcinoma, and large cell lung carcinoma.

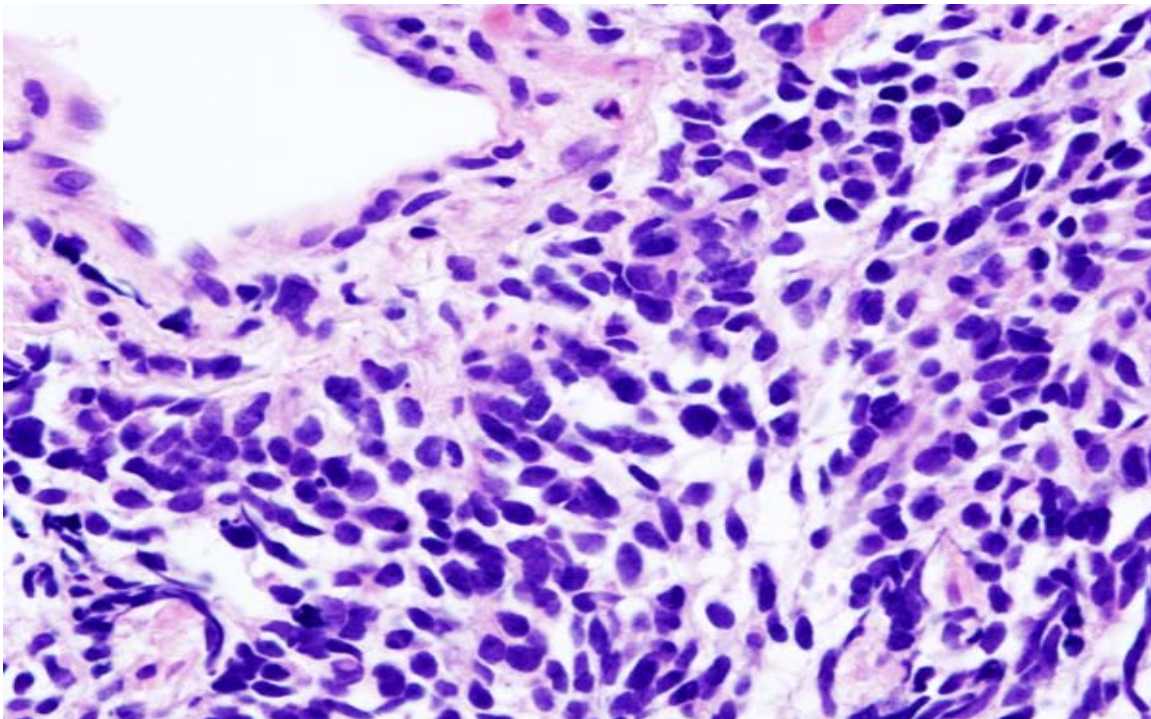
Sub-types of non-small cell lung cancer in smokers and never-smokers		
Histological sub-type	Frequency of non-small cell lung cancers (%)	
	Smokers	Never-smokers
Squamous cell lung carcinoma	42	33

Adenocarcinoma (not otherwise specified)	39	35
Bronchioloalveolar carcinoma	4	10
Carcinoid	7	16
Other	8	6

Accounting for 25% of lung cancers, squamous cell lung carcinoma usually starts near a central bronchus. A hollow cavity and associated necrosis are commonly found at the center of the tumor. Well-differentiated squamous cell lung cancers often grow more slowly than other cancer types.

Adenocarcinoma accounts for 40% of non-small cell lung cancers. It usually originates in peripheral lung tissue. Most cases of adenocarcinoma are associated with smoking; however, among people who have never smoked ("never-smokers"), adenocarcinoma is the most common form of lung cancer. A subtype of adenocarcinoma, the bronchioloalveolar carcinoma, is more common in female never-smokers, and may have different responses to treatment.

Small cell lung carcinoma



Small cell lung carcinoma (microscopic view of a core needle biopsy)

Small cell lung carcinoma (SCLC) is less common. It was formerly referred to as "oat cell" carcinoma. Most cases arise in the larger airways (primary and secondary bronchi)

and grow rapidly, becoming quite large. The small cells contain dense neurosecretory granules (vesicles containing neuroendocrine hormones), which give this tumor an endocrine/paraneoplastic syndrome association. While initially more sensitive to chemotherapy and radiation, it is often metastatic at presentation, and ultimately carries a worse prognosis. Small cell lung cancers have long been dichotomously staged into limited and extensive stage disease. This type of lung cancer is strongly associated with smoking.

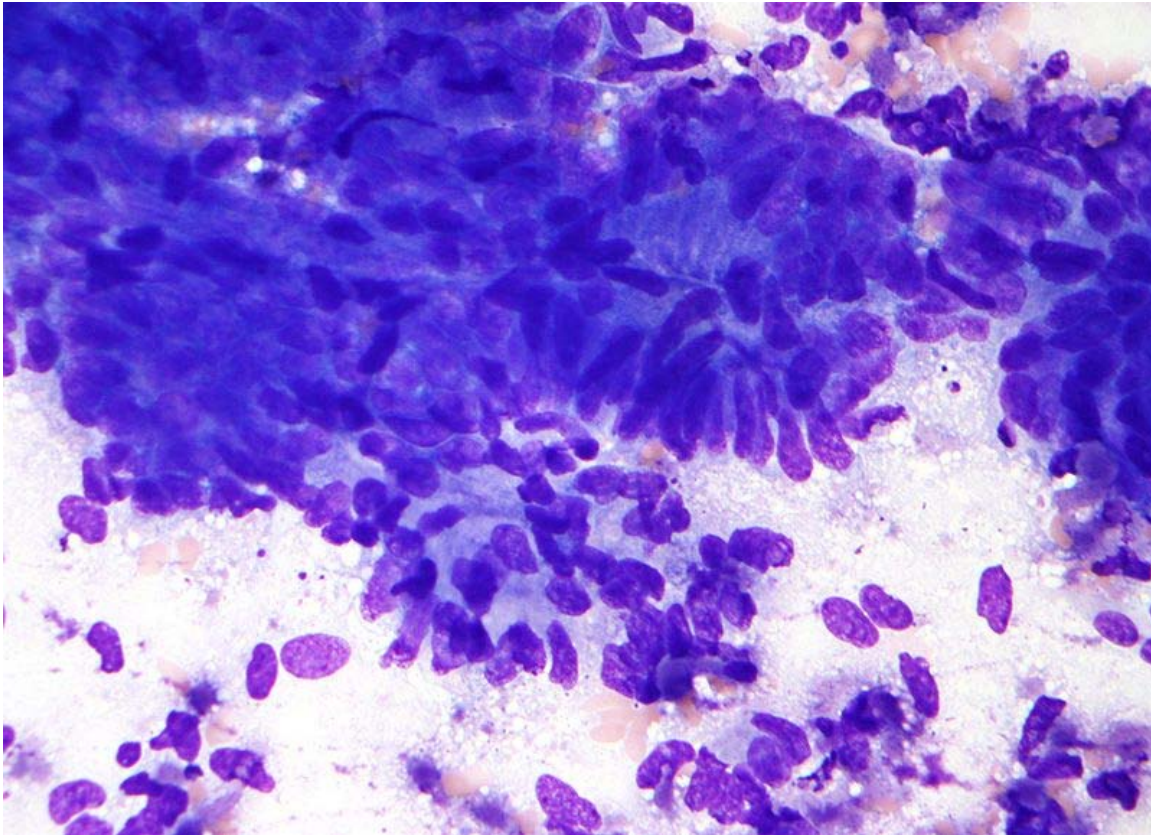
Others

Lung cancers are highly heterogeneous malignancies, with tumors containing more than one subtype being very common.

Currently, the most widely recognized and utilized lung cancer classification system is the 4th revision of the Histological Typing of Lung and Pleural Tumours, published in 2004 as a cooperative effort by the World Health Organization and the International Association for the Study of Lung Cancer. It recognizes numerous other distinct histopathological entities of non-small cell lung carcinoma, organized into several additional subtypes, including sarcomatoid carcinoma, salivary gland tumors, carcinoid tumor, and adenosquamous carcinoma. The latter subtype includes tumors containing at least 10% each of adenocarcinoma and squamous cell carcinoma. When a tumor is found to contain a mixture of both small cell carcinoma and non-small cell carcinoma, it is classified as a variant of small cell carcinoma and called a combined small cell carcinoma. Combined small cell carcinoma is the only currently recognized variant of small cell carcinoma.

In infants and children, the most common primary lung cancers are pleuropulmonary blastoma and carcinoid tumor.

Metastais



Micrograph of a lung lymph node biopsy showing metastatic colorectal adenocarcinoma. Field stain.

The lung is a common place for metastasis of tumors from other parts of the body. Secondary cancers are classified by the site of origin; e.g., breast cancer that has spread to the lung is called *breast cancer*. Metastases often have a characteristic round appearance on chest radiograph. Solitary round lung nodules are not infrequently of an uncertain etiology and may prompt a lung biopsy.

In children, the majority of lung cancers are secondary.

Primary lung cancers themselves most commonly metastasize to the adrenal glands, liver, brain, and bone.

Staging

Lung cancer staging is an assessment of the degree of spread of the cancer from its original source. It is an important factor affecting the prognosis and potential treatment of lung cancer. Non-small cell lung carcinoma is staged from IA ("one A"; best prognosis) to IV ("four"; worst prognosis). Small cell lung carcinoma is classified as *limited stage* if

it is confined to one half of the chest and within the scope of a single radiotherapy field; otherwise, it is *extensive stage*.

Prevention

Prevention is the most cost-effective means of fighting lung cancer. While in most countries industrial and domestic carcinogens have been identified and banned, tobacco smoking is still widespread. Eliminating tobacco smoking is a primary goal in the prevention of lung cancer, and smoking cessation is an important preventive tool in this process. Of utmost importance are prevention programs that target the young. In 1998 the Master Settlement Agreement entitled 46 states in the USA to an annual payout from the tobacco companies. Between the settlement money and tobacco taxes, each state's public health department funds their prevention programs, although none of the states are living up to the Center for Disease Control's recommended amount by spending 15 percent of tobacco taxes and settlement revenues on these prevention efforts.

Policy interventions to decrease passive smoking in public areas such as restaurants and workplaces have become more common in many Western countries, with California taking a lead in banning smoking in public establishments in 1998. Ireland played a similar role in Europe in 2004, followed by Italy and Norway in 2005, Scotland as well as several others in 2006, England in 2007, France in 2008 and Turkey in 2009. New Zealand has banned smoking in public places as of 2004. The state of Bhutan has had a complete smoking ban since 2005. In many countries, pressure groups are campaigning for similar bans. In 2007, Chandigarh became the first city in India to become smoke-free. India introduced a total ban on smoking at public places on Oct 2 2008.

Arguments cited against such bans are criminalisation of smoking, increased risk of smuggling, and the risk that such a ban cannot be enforced.

The long-term use of supplemental multivitamins—such as vitamin C, vitamin E, and folate—does not reduce the risk of lung cancer. Indeed long-term intake of high doses of vitamin E supplements may even increase the risk of lung cancer.

The World Health Organization has called for governments to institute a total ban on tobacco advertising to prevent young people from taking up smoking. They assess that such bans have reduced tobacco consumption by 16% where already instituted.

Screening

Screening refers to the use of medical tests to detect disease in asymptomatic people. Possible screening tests for lung cancer include chest radiograph or computed tomography (CT). As of December 2009, screening programs for lung cancer have not demonstrated any benefit.

Treatment

Treatment for lung cancer depends on the cancer's specific cell type, how far it has spread, and the patient's performance status. Common treatments include palliative care, surgery, chemotherapy, and radiation therapy.

Surgery



Pneumonectomy specimen containing a squamous cell carcinoma, seen as a white area near the bronchi

If investigations confirm lung cancer, CT scan and often positron emission tomography (PET) are used to determine whether the disease is localized and amenable to surgery or whether it has spread to the point where it cannot be cured surgically.

Blood tests and spirometry (lung function testing) are also necessary to assess whether the patient is well enough to be operated on. If spirometry reveals poor respiratory reserve (often due to chronic obstructive pulmonary disease), surgery may be contraindicated.

Surgery for lung cancer has an operative death rate of about 4.4%, depending on the patient's lung function and other risk factors. In non-small cell lung carcinoma, surgery is usually only an option if the cancer is limited to one lung, up to stage IIIA. This is assessed with medical imaging (computed tomography, positron emission tomography). A sufficient preoperative respiratory reserve must be present to allow adequate lung function after the tissue is removed.

Procedures include wedge resection (removal of part of a lobe), segmentectomy (removal of an anatomic division of a particular lobe of the lung), lobectomy (one lobe), bilobectomy (two lobes), or pneumonectomy (whole lung). In patients with adequate respiratory reserve, lobectomy is the preferred option, as this minimizes the chance of local recurrence. If the patient does not have enough functional lung for this, wedge resection may be performed. Radioactive iodine brachytherapy at the margins of wedge excision may reduce recurrence to that of lobectomy.

Video-assisted thoracoscopic surgery and VATS lobectomy have allowed for minimally invasive approaches to lung cancer surgery that may have the advantages of quicker recovery, shorter hospital stay and diminished hospital costs.

Early studies suggested that small cell lung carcinoma (SCLC) fared better when treated with chemotherapy and/or radiation than when treated surgically. While this approach to treating SCLC remains the current standard of care, the role of surgery in SCLC is being reconsidered, recent reviews indicating that surgery might improve outcomes when added to chemotherapy and radiation in early stage SCLC and combined forms of SCLC and NSCLC.

Radiotherapy

Radiotherapy is often given together with chemotherapy, and may be used with curative intent in patients with non-small cell lung carcinoma who are not eligible for surgery. This form of high intensity radiotherapy is called *radical radiotherapy*. A refinement of this technique is continuous hyperfractionated accelerated radiotherapy (CHART), in which a high dose of radiotherapy is given in a short time period. For small cell lung carcinoma cases that are potentially curable, chest radiation is often recommended in addition to chemotherapy. The use of adjuvant thoracic radiotherapy following curative intent surgery for non-small cell lung carcinoma is not well established and is

controversial. Benefits, if any, may only be limited to those in whom the tumor has spread to the mediastinal lymph nodes.

For both non-small cell lung carcinoma and small cell lung carcinoma patients, smaller doses of radiation to the chest may be used for symptom control (palliative radiotherapy). Unlike other treatments, it is possible to deliver palliative radiotherapy without confirming the histological diagnosis of lung cancer.

Brachytherapy (localized radiotherapy) may be given directly inside the airway when cancer affects a short section of bronchus. It is used when inoperable lung cancer causes blockage of a large airway.

Patients with limited stage small cell lung carcinoma are usually given prophylactic cranial irradiation (PCI). This is a type of radiotherapy to the brain, used to reduce the risk of metastasis. More recently, PCI has also been shown to be beneficial in those with extensive small cell lung cancer. In patients whose cancer has improved following a course of chemotherapy, PCI has been shown to reduce the cumulative risk of brain metastases within one year from 40.4% to 14.6%.

Recent improvements in targeting and imaging have led to the development of extracranial stereotactic radiation in the treatment of early-stage lung cancer. In this form of radiation therapy, very high doses are delivered in a small number of sessions using stereotactic targeting techniques. Its use is primarily in patients who are not surgical candidates due to medical comorbidities.

Chemotherapy

The chemotherapy regimen depends on the tumor type.

Small cell lung carcinoma

Even if relatively early stage, small cell lung carcinoma is treated primarily with chemotherapy and radiation. In small cell lung carcinoma, cisplatin and etoposide are most commonly used. Combinations with carboplatin, gemcitabine, paclitaxel, vinorelbine, topotecan, and irinotecan are also used. Celecoxib showed a potential signal of response in a small study.

Non-small cell lung carcinoma

Primary chemotherapy is also given in advanced and metastatic non-small cell lung carcinoma.

Testing for the molecular genetic subtype of non-small cell lung cancer may be of assistance in selecting the most appropriate initial therapy. For example, mutation of the epidermal growth factor receptor gene may predict whether initial treatment with a specific inhibitor or with chemotherapy is more advantageous.

Advanced non-small cell lung carcinoma is often treated with cisplatin or carboplatin, in combination with gemcitabine, paclitaxel, docetaxel, etoposide, or vinorelbine. Bevacizumab improves results in non-squamous cancers treated with paclitaxel and carboplatin in patients less than 70 years old who have reasonable general performance status.

Pemetrexed has been studied extensively in non-small cell lung cancer, with numerous studies since 1995. For adenocarcinoma and large cell lung cancer, cisplatin with pemetrexed was more beneficial than cisplatin and gemcitabine; squamous cancer had the opposite results. As a consequence, subtyping of non-small lung cancer histology has become more important.

Bronchoalveolar carcinoma is a subtype of non-small cell lung carcinoma that may respond to gefitinib and erlotinib.

Maintenance therapy

In advanced non-small cell lung cancer there are several approaches for continuing treatment after an initial response to therapy. Switch maintenance changes to different medications than the initial therapy and can use pemetrexed, erlotinib, and docetaxel, although pemetrexed is only used in non-squamous NSCLC.

Adjuvant chemotherapy

Adjuvant chemotherapy refers to the use of chemotherapy after apparently curative surgery to improve the outcome. In non-small cell lung cancer, samples are taken during surgery of nearby lymph nodes. If these samples contain cancer, the patient has stage II or III disease. In this situation, adjuvant chemotherapy may improve survival by up to 15%. Standard practice has often been to offer platinum-based chemotherapy (including either cisplatin or carboplatin). However, the benefit of platinum-based adjuvant chemotherapy was confined to patients who had tumors with low ERCC1 (excision repair cross-complementing 1) activity.

Adjuvant chemotherapy for patients with stage IB cancer is controversial, as clinical trials have not clearly demonstrated a survival benefit. Trials of preoperative chemotherapy (neoadjuvant chemotherapy) in resectable non-small cell lung carcinoma have been inconclusive.

Interventional radiology

Radiofrequency ablation should currently be considered an investigational technique in the treatment of bronchogenic carcinoma. It is done by inserting a small heat probe into the tumor to kill the tumor cells.

Palliative care

In metastatic non–small-cell lung cancer the addition of palliative care to standard treatments improved the quality of life, lessened depression, lengthened life by 3 months, and decreased the use of aggressive care at the end of life.

Other studies in advanced cancer also found benefit from palliative care, or found hospice involvement to be beneficial. These approaches allow additional discussion of treatment options and provide opportunities to arrive at well-considered decisions and may avoid unhelpful but expensive care at the end of life.

However, palliative care may often be more appropriate in conjunction with chemotherapy at some point in the treatment of the cancer, rather than on its own. Over the past 20 years, the opposite question has also been asked: does chemotherapy add to supportive care? Superior survival has been repeatedly found in advanced non-small cell lung cancer when study eligible recipients receive appropriate chemotherapy rather than supportive care alone. For example, 1994 recommendations based on reports that combined the results of several available studies found an increase in average survival from 3.9 months for best supportive care alone to 6.7 months with the addition of chemotherapy, as well as an improved quality of life. A systematic review from Sweden in 2001 looked at numerous chemotherapy reports over many years in lung cancer with adequate physical fitness. Compared to supportive care alone there was a 1.5 to 3 months prolongation of survival with chemotherapy in general, with better results seen with what were then newer agents. Symptomatic relief and an improvement in quality of life were also evident. A contemporaneous independent British review was consistent with this conclusion.

Despite a change in population demographics, this continues to hold up. A 2008 update by the NSCLC Meta-Analyses Collaborative Group looked at individual patient data from clinical trials subsequent to 1995, and recommended that chemotherapy should be considered in advanced non-small cell lung cancer provided the recipient wanted treatment and was adequately fit to be able to tolerate it. This analysis was the basis of a 2010 Cochrane Review reporting that chemotherapy improves overall survival in advanced non-small cell lung cancer, and finding a benefit in different subtypes of the cancer.

Palliative care is an essential and routine component of evidence-based, high-quality care for the management of advanced lung cancer but it is also clear that the best way to deliver palliative care is unknown. By way of emphasis, an analysis of almost 400 randomized controlled trials of palliative care concluded that the evidence for specialized palliative care as a specific intervention is limited, due to methodological shortcomings of the data. That review found that the most consistent benefit of palliative care was a increased perception by family members of good quality care. Which specific components of palliative care are of benefit is unknown, warranting further clinical assessment of different palliative approaches.

Prognosis

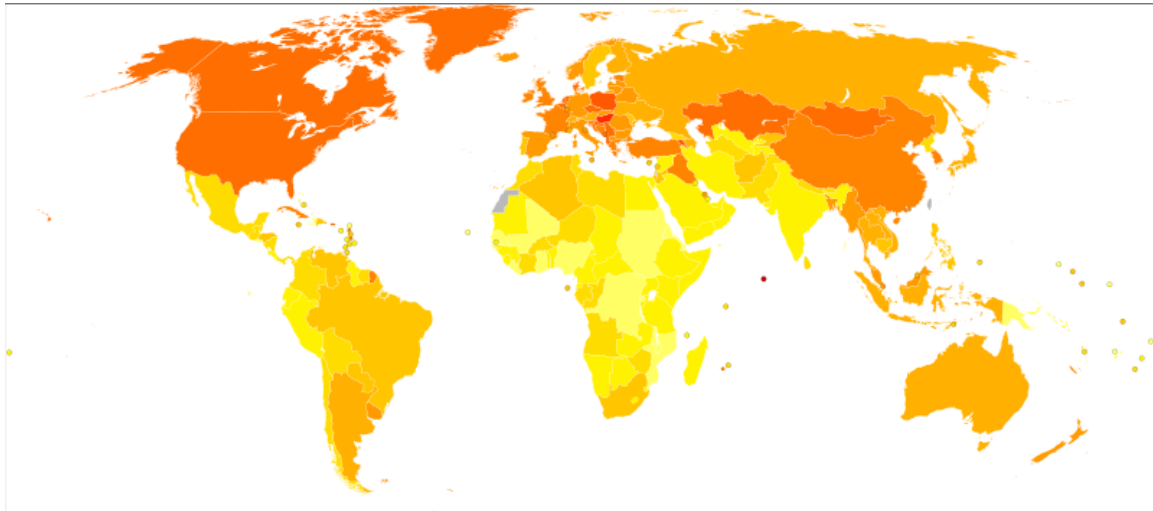
Prognostic factors in non-small cell lung cancer include presence or absence of pulmonary symptoms, tumor size, cell type (histology), degree of spread (stage) and metastases to multiple lymph nodes, and vascular invasion. For patients with inoperable disease, prognosis is adversely affected by poor performance status and weight loss of more than 10%. Prognostic factors in small-cell lung cancer include performance status, gender, stage of disease, and involvement of the central nervous system or liver at the time of diagnosis.

For non-small cell lung carcinoma (NSCLC), prognosis is generally poor. Following complete surgical resection of stage IA disease, five-year survival is 67%. With stage IB disease, five-year survival is 57%. The five-year survival rate of patients with stage IV NSCLC is about 1%.

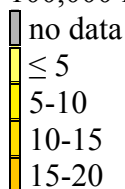
For small cell lung carcinoma, prognosis is also generally poor. The overall five-year survival for patients with SCLC is about 5%. Patients with extensive-stage SCLC have an average five-year survival rate of less than 1%. The median survival time for limited-stage disease is 20 months, with a five-year survival rate of 20%.

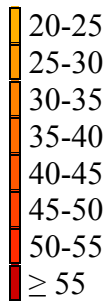
According to data provided by the National Cancer Institute, the median age at diagnosis of lung cancer in the United States is 70 years, and the median age at death is 72 years.

Epidemiology



Age-standardized death from tracheal, bronchial, and lung cancers per 100,000 inhabitants in 2004.





Worldwide, lung cancer is the most common cancer in terms of both incidence and mortality (1.1 million new cases per year and 0.95 million deaths in males and 0.51 million new cases per year and 0.43 million deaths in females). The highest rates are in Europe and North America. The population segment most likely to develop lung cancer is over-fifties who have a history of smoking. Lung cancer is the second most commonly occurring form of cancer in most Western countries, and it is the leading cancer-related cause of death. In contrast to the mortality rate in men, which began declining more than 20 years ago, women's lung cancer mortality rates have been rising for over the last decades, and are just recently beginning to stabilize. The evolution of "Big Tobacco" plays a significant role in the smoking culture. Tobacco companies have focused their efforts since the 1970s at marketing their product toward women and girls, especially with "light" and "low-tar" cigarettes. Among lifetime nonsmokers, men have higher age-standardized lung cancer death rates than women.

Not all cases of lung cancer are due to smoking, but the role of passive smoking is increasingly being recognized as a risk factor for lung cancer—leading to policy interventions to decrease undesired exposure of nonsmokers to others' tobacco smoke. Emissions from automobiles, factories, and power plants also pose potential risks.

Eastern Europe has the highest lung cancer mortality among men, while northern Europe and the U.S. have the highest mortality among women. In the United States, black men and women have a higher incidence. Lung cancer incidence is currently less common in developing countries. With increased smoking in developing countries, the incidence is expected to increase in the next few years, notably in China and India.

Lung cancer incidence (by country) has an inverse correlation with sunlight and UVB exposure. One possible explanation is a preventive effect of vitamin D (which is produced in the skin on exposure to sunlight).

From the 1950s, the incidence of lung adenocarcinoma started to rise relative to other types of lung cancer. This is partly due to the introduction of filter cigarettes. The use of filters removes larger particles from tobacco smoke, thus reducing deposition in larger airways. However the smoker has to inhale more deeply to receive the same amount of nicotine, increasing particle deposition in small airways where adenocarcinoma tends to arise. The incidence of lung adenocarcinoma in the U.S. has fallen since 1999. This may be due to reduction in environmental air pollution. However, in some developing countries like India, there has been little change in the epidemiology with squamous cell

carcinoma continuing to be the predominant histological type. An absence of change in the type of tobacco smoking or the pattern of tobacco consumption in the population could be one of the possible reasons.

History

Lung cancer was uncommon before the advent of cigarette smoking; it was not even recognized as a distinct disease until 1761. Different aspects of lung cancer were described further in 1810. Malignant lung tumors made up only 1% of all cancers seen at autopsy in 1878, but had risen to 10–15% by the early 1900s. Case reports in the medical literature numbered only 374 worldwide in 1912, but a review of autopsies showed that the incidence of lung cancer had increased from 0.3% in 1852 to 5.66% in 1952. In Germany in 1929, physician Fritz Lickint recognized the link between smoking and lung cancer, which led to an aggressive antismoking campaign. The British Doctors Study, published in the 1950s, was the first solid epidemiological evidence of the link between lung cancer and smoking. As a result, in 1964 the Surgeon General of the United States recommended that smokers should stop smoking.

The connection with radon gas was first recognized among miners in the Ore Mountains near Schneeberg, Saxony. Silver has been mined there since 1470, and these mines are rich in uranium, with its accompanying radium and radon gas. Miners developed a disproportionate amount of lung disease, eventually recognized as lung cancer in the 1870s. An estimated 75% of former miners died from lung cancer. Despite this discovery, mining continued into the 1950s, due to the USSR's demand for uranium.

The first successful pneumonectomy for lung cancer was performed in 1933. Palliative radiotherapy has been used since the 1940s. Radical radiotherapy, initially used in the 1950s, was an attempt to use larger radiation doses in patients with relatively early stage lung cancer but who were otherwise unfit for surgery. In 1997, continuous hyperfractionated accelerated radiotherapy (CHART) was seen as an improvement over conventional radical radiotherapy.

With small cell lung carcinoma, initial attempts in the 1960s at surgical resection and radical radiotherapy were unsuccessful. In the 1970s, successful chemotherapy regimens were developed.

Chapter 13

Lung Transplantation

Lung transplantation, or **pulmonary transplantation** is a surgical procedure in which a patient's diseased lungs are partially or totally replaced by lungs which come from a donor. While lung transplants carry certain associated risks, they can also extend life expectancy and enhance the quality of life for end-stage pulmonary patients.

Qualifying conditions

Lung transplantation is the therapeutic measure of last resort for patients with end-stage lung disease who have exhausted all other available treatments without improvement. A variety of conditions may make such surgery necessary. As of 2005, the most common reasons for lung transplantation in the United States were:

- 27% chronic obstructive pulmonary disease (COPD), including emphysema;
- 16% idiopathic pulmonary fibrosis;
- 14% cystic fibrosis;
- 12% idiopathic (formerly known as "primary") pulmonary hypertension;
- 5% alpha 1-antitrypsin deficiency;
- 2% replacing previously transplanted lungs that have since failed;
- 24% other causes, including bronchiectasis and sarcoidosis.

Contraindications

Despite the severity of a patient's respiratory condition, certain preexisting conditions may make a person a poor candidate for lung transplantation. These conditions include:

- concurrent chronic illness (e.g. congestive heart failure, kidney disease, liver disease);
- current infections, including HIV and hepatitis, although more and more often Hepatitis C patients are both being transplanted and are also being used as donors if the recipient is Hepatitis C positive.
- current or recent cancer;
- current use of alcohol, tobacco, or illegal drugs;
- age;
- psychiatric conditions;
- history of noncompliance with medical instructions.

History

The history of organ transplants began with several attempts that were unsuccessful due to transplant rejection. Animal experimentation by various pioneers, including Vladimir Demikhov and Dominique Metras, during the 1940s and 1950s, first demonstrated that the procedure was technically feasible. James Hardy of the University of Mississippi performed the first human lung transplant in 1963. Following a left lung transplantation, the patient survived for 18 days. From 1963-1978, multiple attempts at lung transplantation failed because of rejection and problems with anastomotic bronchial healing. It was only after the invention of the heart-lung machine, coupled with the development of immunosuppressive drugs such as cyclosporine, that organs such as the lungs could be transplanted with a reasonable chance of patient recovery.

The first successful transplant surgery involving the lungs was a heart-lung transplant, performed by Dr. Bruce Reitz of Stanford University on a woman who had idiopathic pulmonary hypertension.

- 1983: First successful single lung transplant (Tom Hall) by Joel Cooper (Toronto)
- 1986: First successful double lung transplant (Ann Harrison) by Joel Cooper (Toronto)
- 1988: First successful double lung transplant for cystic fibrosis by Joel Cooper (Toronto)

Transplant requirements

Requirements for potential donors

There are certain requirements for potential lung donors, due to the needs of the potential recipient. In the case of living donors, this is also in consideration of how the surgery will affect the donor.

- healthy;
- size match; the donated lung or lungs must be large enough to adequately oxygenate the patient, but small enough to fit within the recipient's chest cavity;
- age;
- blood type.

Requirements for potential recipients

While each transplant center is free to set its own criteria for transplant candidates, certain requirements are generally agreed upon:

- end-stage lung disease;
- has exhausted other available therapies without success;
- no other chronic medical conditions (e.g. heart, kidney, liver);

- no current infections or recent cancer. There are certain cases where preexisting infection is unavoidable, as with many patients with cystic fibrosis. In such cases, transplant centers, at their own discretion, may accept or reject patients with current infections of *B. cepacia* or *MRSA*.
- no HIV or hepatitis;
- no alcohol, smoking, or drug abuse;
- within an acceptable weight range (marked undernourishment or obesity are both associated with increased mortality);
- age (single vs. double tx);
- acceptable psychological profile;
- has social support system;
- financially able to pay for expenses; (in places where medical care is paid for directly by the patient)
- able to comply with post-transplant regimen. A lung transplant is a major operation, and following the transplant, the patient must be willing to adhere to a lifetime regimen of medications as well as continuing medical care.

Medical tests for potential transplant candidates

Patients who are being considered for placement on the organ transplant list must undergo an extensive series of medical tests in order to evaluate their overall health status and suitability for transplant surgery.

- blood typing; the blood type of the recipient must match that of the donor due to certain antigens that are present on donated lungs. A mismatch of blood type can lead to a strong response by the immune system and subsequent rejection of the transplanted organs;
- tissue typing; ideally, the lung tissue would also match as closely as possible between the donor and the recipient, but the desire to find a highly compatible donor organ must be balanced against the patient's immediacy of need;
- Chest X-ray - PA & LAT, to verify the size of the lungs and the chest cavity;
- pulmonary function tests;
- CT Scan (High Resolution Thoracic & Abdominal);
- Bone mineral density scan;
- MUGA (Gated cardiac blood pool scan);
- Cardiac stress test (Dobutamine/Thallium scan);
- ventilation/perfusion (V/Q) scan;
- electrocardiogram;
- cardiac catheterization;
- echocardiogram.

Lung allocation score

Prior to 2005, donor lungs within the United States were allocated by the United Network for Organ Sharing on a first-come, first-serve basis to patients on the transplant list. This was replaced by the current system, in which prospective lung recipients of age of 12 and

older are assigned a lung allocation score or LAS, which takes into account various measures of the patient's health. The new system allocates donated lungs according to the immediacy of need rather than how long a patient has been on the transplant list. Patients who are under the age of 12 are still given priority based on how long they have been on the transplant waitlist. The length of time spent on the list is also the deciding factor when multiple patients have the same lung allocation score.

Patients who are accepted as good potential transplant candidates must carry a pager with them at all times in case a donor organ becomes available. These patients must also be prepared to move to their chosen transplant center at a moment's notice. Such patients may be encouraged to limit their travel within a certain geographical region in order to facilitate rapid transport to a transplant center.

Types of lung transplant

Lobe

A lobe transplant is a surgery in which part of a living donor's lung is removed and used to replace part of recipient's diseased lung. This procedure usually involves the donation of lobes from two different people, thus replacing a single lung in the recipient. Donors who have been properly screened should be able to maintain a normal quality of life despite the reduction in lung volume.

Single-lung

Many patients can be helped by the transplantation of a single healthy lung. The donated lung typically comes from a donor who has been pronounced brain-dead.

Double-lung

Certain patients may require both lungs to be replaced. This is especially the case for people with cystic fibrosis, due to the bacterial colonisation commonly found within such patients' lungs; if only one lung were transplanted, bacteria in the native lung could potentially infect the newly transplanted organ.

Heart-lung

Some respiratory patients may also have severe cardiac disease which would necessitate a heart transplant. These patients can be treated by a surgery in which both lungs and the heart are replaced by organs from a donor or donors.

A particularly involved example of this has been termed a "domino transplant" in the media. First performed in 1987, this type of transplant typically involves the transplantation of a heart and lungs into recipient A, whose own healthy heart is removed and transplanted into recipient B.

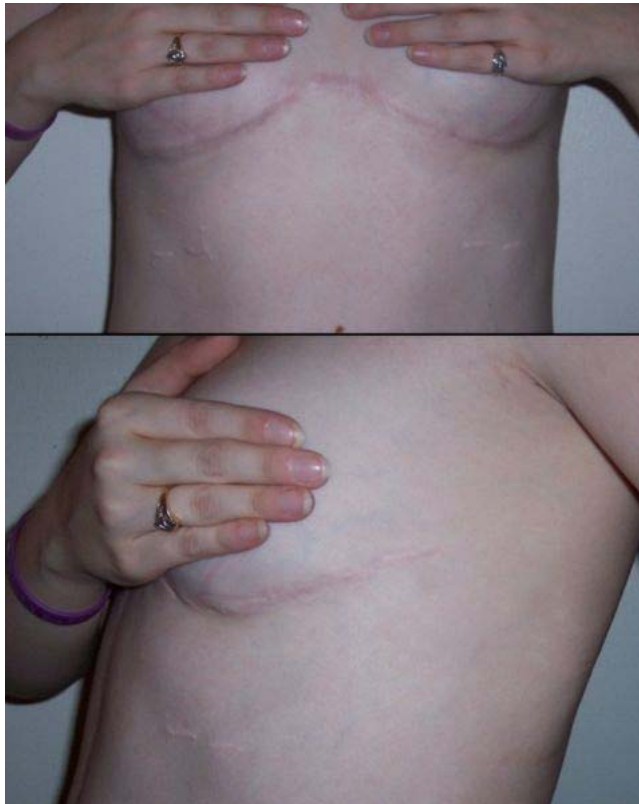
Procedure

While the precise details of surgery will depend on the exact type of transplant, there are many steps which are common to all of these procedures. Prior to operating on the recipient, the transplant surgeon inspects the donor lung(s) for signs of damage or disease. If the lung or lungs are approved, then the recipient is connected to an IV line and various monitoring equipment, including pulse oximetry. The patient will be given general anesthesia, and a machine will breathe for him or her.

It takes about one hour for the pre-operative preparation of the patient. A single lung transplant takes about four to eight hours, while a double lung transplant takes about six to twelve hours to complete. A history of prior chest surgery may complicate the procedure and require additional time.

Lobe

Single-lung



Incision scarring from a double lung transplant

In single-lung transplants, the lung with the worse pulmonary function is chosen for replacement. If both lungs function equally, then the right lung is usually favored for removal because it avoids having to maneuver around the heart, as would be required for excision of the left lung.

In a single-lung transplant the process starts out after the donor lung has been inspected and the decision to accept the donor lung for the patient has been made. An incision is generally made from under the shoulder blade around the chest, ending near the sternum. An alternate method involves an incision under the breastbone. In the case of a singular lung transplant the lung is collapsed, the blood vessels in the lung tied off, and the lung removed at the bronchial tube. The donor lung is placed, the blood vessels reattached, and the lung reinflated. To make sure the lung is satisfactory and to clear any remaining blood and mucus in the new lung a bronchoscopy will be performed. When the surgeons are satisfied with the performance of the lung the chest incision will be closed.

Double-lung

A double-lung transplant, also known as a bilateral transplant, can be executed either sequentially, en bloc, or simultaneously. Sequential is more common than en bloc. This is effectively like having two separate single-lung transplants done.

The transplantation process starts after the donor lungs are inspected and the decision to transplant has been made. An incision is then made from under the patient's armpit, around to the sternum, and then back towards the other armpit; this is known as a clamshell incision. In the case of a sequential transplant the recipient's lung with the poorest lung functions is collapsed, the blood vessels tied off, and cut at the corresponding bronchi. The new lung is then placed and the blood vessels reattached. To make sure the lung is satisfactory before transplanting the other a bronchoscopy is performed. When the surgeons are satisfied with the performance of the new lung, surgery on the second lung will proceed. In 10% to 20% of double-lung transplants the patient is hooked up to a heart-lung machine which pumps blood for the body and supplies fresh oxygen.

Post-operative care

Immediately following the surgery, the patient is placed in an intensive care unit for monitoring, normally for a period of a few days. The patient is put on a ventilator to assist breathing. Nutritional needs are generally met via total parenteral nutrition, although in some cases a nasogastric tube is sufficient for feeding. Chest tubes are put in so that excess fluids may be removed. Because the patient is confined to bed, a urinary catheter is used. IV lines are used in the neck and arm for monitoring and giving medications. After a few days, barring any complications, the patient may be transferred to a general inpatient ward for further recovery. The average hospital stay following a lung transplant is generally one to three weeks, though complications may require a longer period of time. After this stage, patients are typically required to attend rehabilitation gym for approximately 3 months to regain fitness. Light weights, exercise bike, treadmill, stretches and more are all a part of the rehabilitation programme.

There may be a number of side effects following the surgery. Because certain nerve connections to the lungs are cut during the procedure, transplant recipients cannot feel the urge to cough or feel when their new lungs are becoming congested. They must therefore

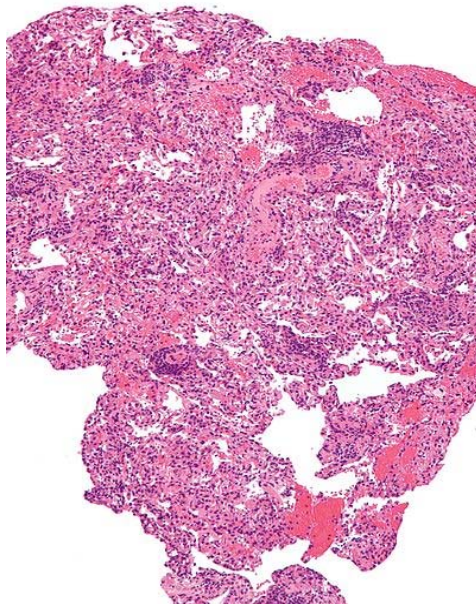
make conscious efforts to take deep breaths and cough in order to clear secretions from the lungs. Their heart rate responds less quickly to exertion due to the cutting of the vagus nerve that would normally help regulate it. They may also notice a change in their voice due to potential damage to the nerves that coordinate the vocal cords.

Miscellaneous

Post-transplant patients are held from driving for the first 3 months pending an assessment of the patient's capacity to drive; this assessment is usually performed by an occupational therapist. Eyesight, physical ability to do simple actions such as check blind spots, wear a seat belt safely without the wound site being affected and hand eye coordination are all assessed.

Hygiene becomes more important in every day living due to the Immunosuppressant drugs which are required every day to prevent transplant rejection. Lack of a strong immune system leaves transplant recipients vulnerable to infections. Care must be taken into food preparation and hygiene as gastroenteritis becomes more of a risk.

Risks



Micrograph showing lung transplant rejection. Lung biopsy. H&E stain.

As with any surgical procedure, there are risks of bleeding and infection. The newly transplanted lung itself may fail to properly heal and function. Because a large portion of the patient's body has been exposed to the outside air, sepsis is a possibility, so antibiotics will be given to try to prevent that. Other complications include Post-transplant lymphoproliferative disorder, a form of lymphoma due to the immune suppressants, and gastrointestinal inflammation and ulceration of the stomach and esophagus.

Transplant rejection is a primary concern, both immediately after the surgery and continuing throughout the patient's life. Because the transplanted lung or lungs come from another person, the recipient's immune system will "see" it as an invader and attempt to neutralize it. Transplant rejection is a serious condition and must be treated as soon as possible.

Signs of rejection:

- fever;
- flu-like symptoms, including chills, dizziness, nausea, general feeling of illness, night sweats;
- increased difficulty in breathing;
- worsening pulmonary test results;
- increased chest pain or tenderness;
- increase or decrease in body weight of more than 2 kilograms in a 24-hour period.

In order to prevent transplant rejection and subsequent damage to the new lung or lungs, patients must take a regimen of immunosuppressive drugs. Patients will normally have to take a combination of these medicines in order to combat the risk of rejection. This is a lifelong commitment, and must be strictly adhered to. The immunosuppressive regimen is begun just before or after surgery. Usually the regimen includes cyclosporine, azathioprine and corticosteroids, but as episodes of rejection may reoccur throughout a patient's life, the exact choices and dosages of immunosuppressants may have to be modified over time. Sometimes tacrolimus is given instead of cyclosporine and mycophenolate mofetil instead of azathioprine.

The immunosuppressants that are needed to prevent organ rejection also introduce some risks. By lowering the body's ability to mount an immune reaction, these medicines also increase the chances of infection. Antibiotics may be prescribed in order to treat or prevent such infections. In turn, infection may increase the risk of rejection, and generally an interaction may prevail between both risks. Certain medications may also have nephrotoxic or other potentially harmful side-effects. Other medications may also be prescribed in order to help alleviate these side effects. There is also the risk that a patient may have an allergic reaction to the medications. Close follow-up care is required in order to balance the benefits of these drugs versus their potential risks.

Chronic rejection, meaning repeated bouts of rejection symptoms beyond the first year after the transplant surgery, occurs in approximately 50% of patients. Such chronic rejection presents itself as bronchiolitis obliterans, or less frequently, atherosclerosis.

Prognosis

These statistics are based on data from 2008. The source data made no distinction between living and deceased donor organs, nor was any distinction made between lobar, single, and double lung transplants.

	1 year survival	5 years survival	10 years survival
Lung transplant	83.6%	53.4%	28.4%
Heart-lung transplant	73.8%	46.5%	28.3%

Transplanted lungs typically last three to five years before showing signs of failure.

Chapter 14

Rhinoplasty and Septoplasty

Rhinoplasty

Rhinoplasty (Greek: *Rhinos*, "Nose" + *Plassein*, "to shape"), commonly referred to as **nose reshaping** or a **nose job**, is a surgical procedure which is usually performed by either an otolaryngologist (head and neck surgeon), maxillofacial surgeon, or plastic surgeon in order to improve the function (reconstructive surgery) or the appearance (cosmetic surgery) of a human nose. Rhinoplasty can be performed to meet aesthetic goals or for reconstructive purposes to correct trauma, birth defects or breathing problems. Rhinoplasty can be combined with other surgical procedures such as chin augmentation to enhance the aesthetic results.

History

Reconstructive nose surgery was first developed by Sushruta, an important Ayurvedic physician in ancient India, who is often regarded as the "father of plastic surgery." Sushruta first described nasal reconstruction in his text *Sushruta Samhita* circa 500 BC. He and his later students and disciples used rhinoplasty to reconstruct noses that were amputated as a punishment for crimes. The techniques of forehead flap rhinoplasty he developed are practiced almost unchanged to this day. This knowledge of plastic surgery existed in India up to the late 18th century as can be seen from the reports published in *Gentleman's Magazine* (October, 1794).

A book written in Latin titled *De Curtorum Chirurgia Per Insitionem* - meaning The Surgery of Defects by Implantations - was published in 1597, and was written by Gaspare Tagliacozzi, professor of surgery and anatomy at the University of Bologna describes operations carried out to repair faces that had been wounded in battle. It is illustrated with diagrams, including the rhinoplasty, in which the patient's nose was attached to a flap of skin from his upper arm (bicep) and tells how he stayed like that for about three weeks until the skin from his arm had attached itself properly. After a further two weeks the flap of skin was shaped so it resembled a nose and the process was complete.



Patient, three days post-op. Procedures included dorsal bone reduction and re-setting and refinement of nasal tip cartilage. The typical orbital discoloration is also present due to trauma and disruption of blood vessels around the eyes. Also present is a splint.

The precursors to the modern rhinoplasty surgeons include Johann Dieffenbach (1792–1847) and Jacques Joseph (1865–1934), who used external incisions for nose reduction surgery. John Orlando Roe (1848–1915) is credited with performing the first intranasal rhinoplasty in the U.S. in 1887.

Prior to the 1970s, all rhinoplasty surgeries were performed via the intranasal approach, which is often called closed rhinoplasty. However, in 1973, Dr. Wilfred S. Goodman published an article entitled "External Approach to Rhinoplasty" which helped initiate a shift in rhinoplasty techniques to what has become known as the open rhinoplasty. The open rhinoplasty technique was further refined and popularized by Dr. Jack Anderson in his article "Open rhinoplasty: an assessment". The open approach to rhinoplasty gained in popularity during that time, but it was used mainly for first-time rhinoplasty surgery and not for revision rhinoplasty.

In 1987 Dr. Jack P. Gunter, who trained under Dr. Anderson, published an article describing the merits of the open rhinoplasty approach for secondary rhinoplasty. This was a major shift in the approach to treating nasal deformities that arose from a previous rhinoplasty.

Surgical procedures and types

Surgical approach: Open vs. closed

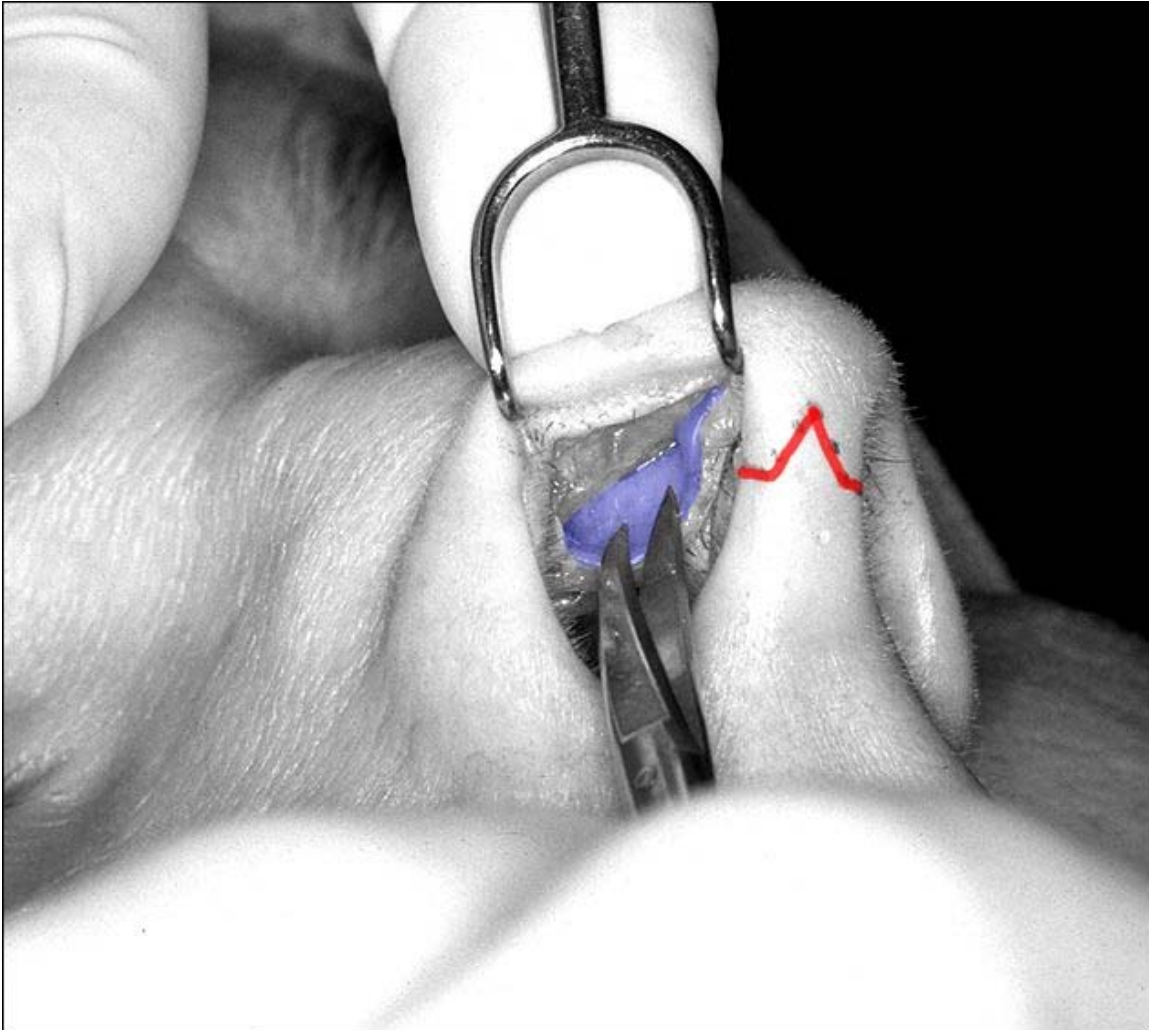
Rhinoplasty can be performed under a general anesthetic, sedation, or with local anesthetic. Initially, local anesthesia, which is a mixture of lidocaine and epinephrine, is injected to numb the area and temporarily reduce vascularity. There are two possible approaches to the nose: closed approach and open approach. In closed rhinoplasty, incisions are made inside the nostrils. In open rhinoplasty, also known as a Coronal Forehead Lift, an additional inconspicuous incision is made across the columella (the bit of skin that separates the nostrils). The surgeon first separates the skin and soft tissues of the nose from the underlying structures. The cartilage and bone are reshaped, and the incisions are sutured closed. Some surgeons use a stent or packing inside the nose, followed by tape or stent on the outside.

In some cases, the surgeon may shape a small piece of the patient's own cartilage or bone, as a graft, to strengthen or change the shape of the nose. Usually the cartilage is harvested from the septum. If there isn't enough septum cartilage, which can occur in revision rhinoplasty, cartilage can be harvested from the concha of the ear or the ribs. In the rare case where bone is required, it is harvested from the cranium, the hip, or the ribs. Sometimes a synthetic implant may be used to augment the bridge of the nose.



Skin incision for an open rhinoplasty. The incision may be “v-shaped” or a “stair-step” shaped incision. This aids the surgeon in attaining a precise closure and for camouflaging the resulting scar.

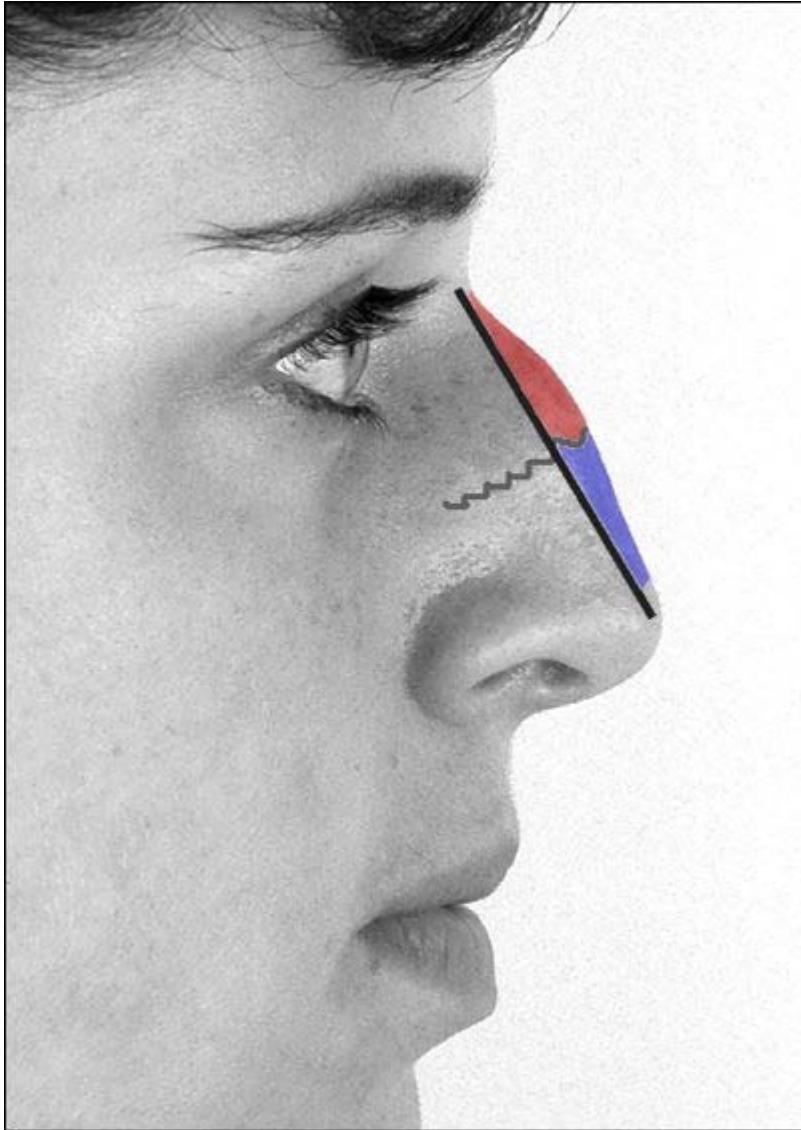
The incisions for a rhinoplasty are hidden inside the nose, with the exception of a small incision across the base of the nose, depicted by the dotted line.



Exposing the cartilages inside the nose

The incisions allow the surgeon to see the size and shape of the cartilages and bones on the inside of the nose, so that they can be altered.

Here, the scissors are pointing out the lower lateral cartilage (in blue), which is one of the cartilages that gives the tip of the nose its shape. The red line shows the location of the planned incision across the bottom of the nose.



Planning excision of a nasal hump

Once the skin has been lifted from the bone and cartilage framework of the nose, often the first task is to remove a hump, if one is present. Part of the hump is made of bone, and part of the hump is cartilage.

In the photograph, the black line shows the desired profile. The nose is made of bone above the scalloped grey line and cartilage below that line. The part of the hump made of bone is shaded red, and the part of the hump made of cartilage is shaded blue.



Rhinoplasty osteotome and hammer

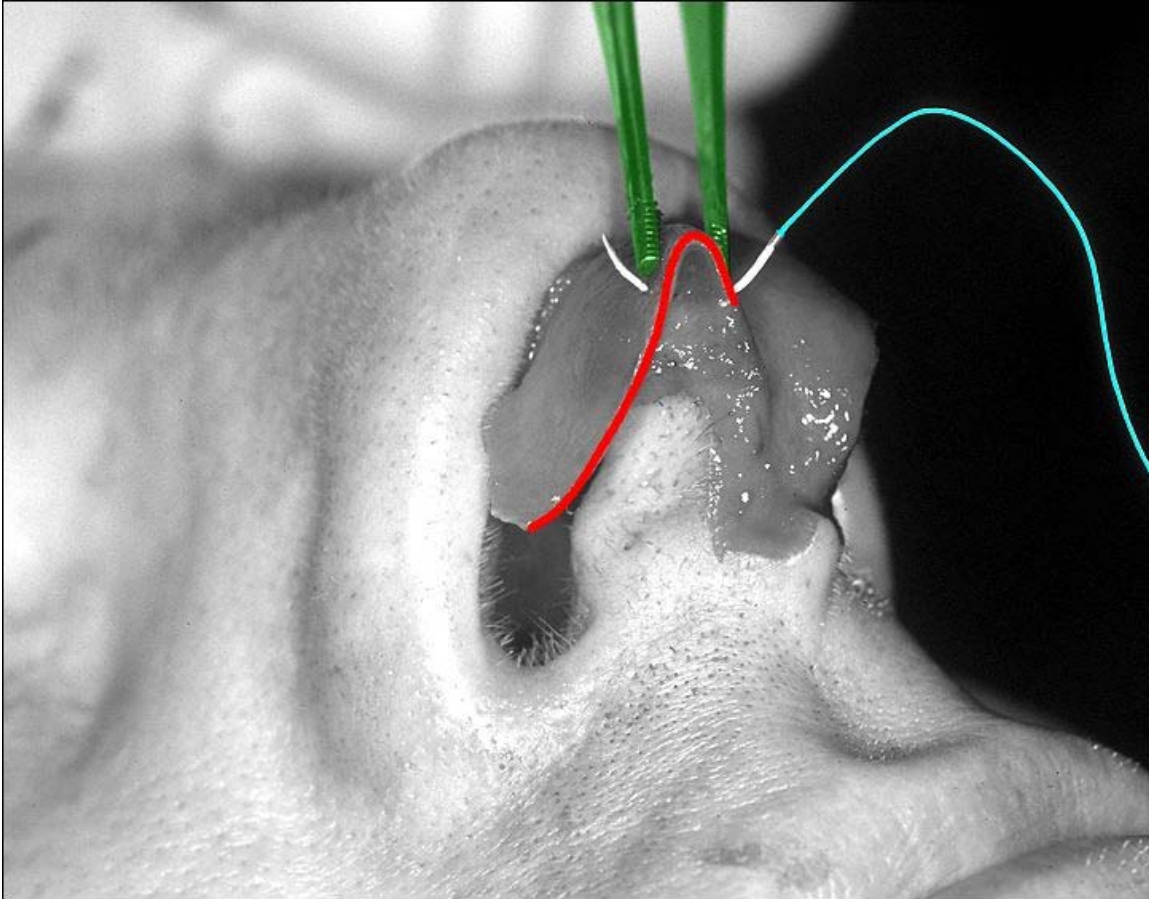
The soft cartilage of the hump is removed with a scalpel, and the bony hump is often removed with a chisel, shown at the top of this photograph. "Osteotome" is the medical term for a chisel. This photograph also shows the copper hammer that is used with the osteotome.



Rhinoplasty rasps

After the main part of the hump is removed with an osteotome, files are used to smooth out the remaining bone. The files are also called rasps, and they come in different shapes, orientations, and grades.

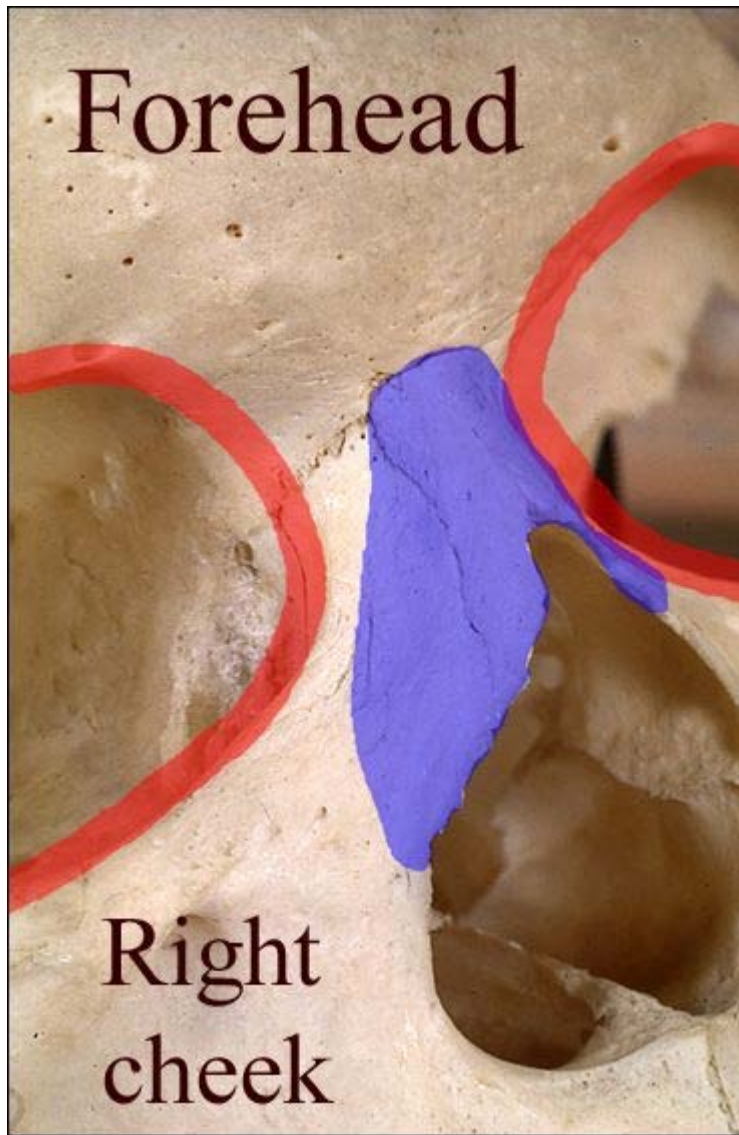
Some surgeons use rasps to remove the entire hump, foregoing use of the osteotome.



One technique to narrow the nasal tip

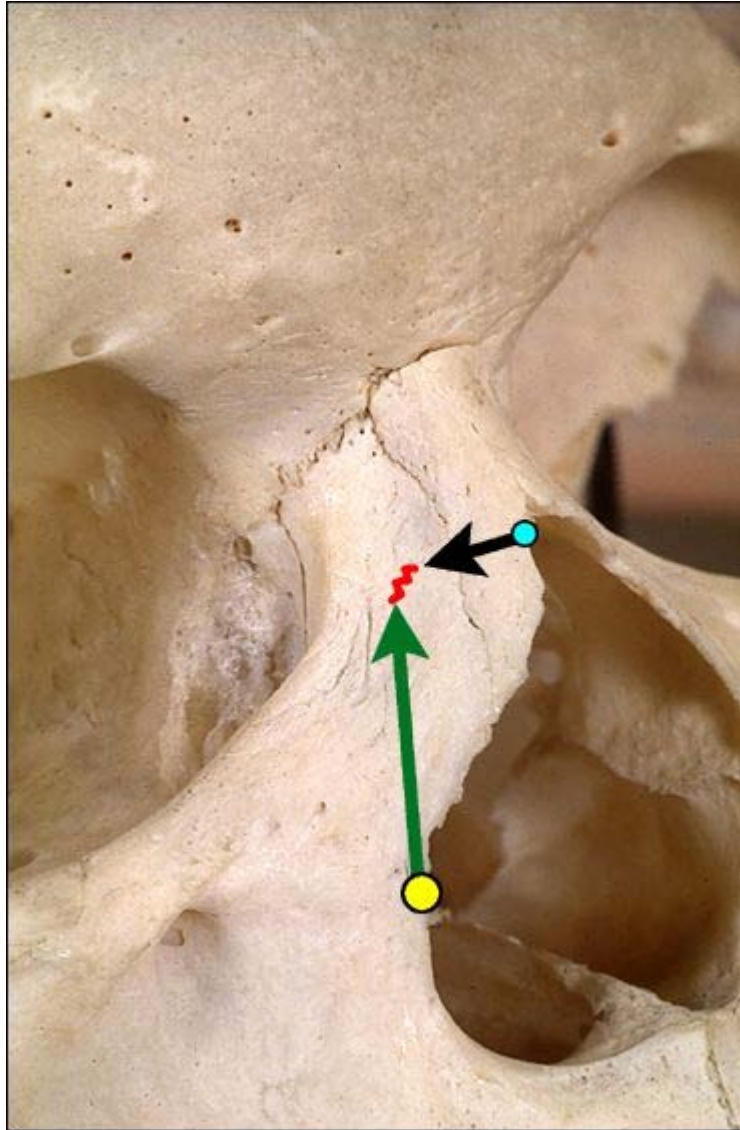
A common complaint is that the tip of the nose is too wide. Many surgical techniques are available to narrow the tip of the nose, depending on what is causing the excess width.

In this photo, a suture is being placed to narrow the tip of the nose. The red line outlines the edge of the tip cartilage, which is narrowed when the suture tightens the fold of the cartilage at its apex. The suture is in light blue, ending in the needle, which appears white in the photograph. The cartilage is being held in place with tweezers, which are shaded green.



The nasal bones

If the position of the nasal bones gives excess width to the upper part of the nose, the bones are moved inward, to a more narrow position. This skull shows in blue the position of the bones in the nose. For orientation, the eye sockets are outlined in red.



Designing the cuts in the nasal bones

To narrow a nasal bone, two cuts are made in the bone with a tiny chisel: one cut starting at the yellow dot and extending up along the green arrow, and another cut starting at the blue dot and extending out along the black arrow. The piece of bone thus loosened from the skull is pushed inward, narrowing the nose.

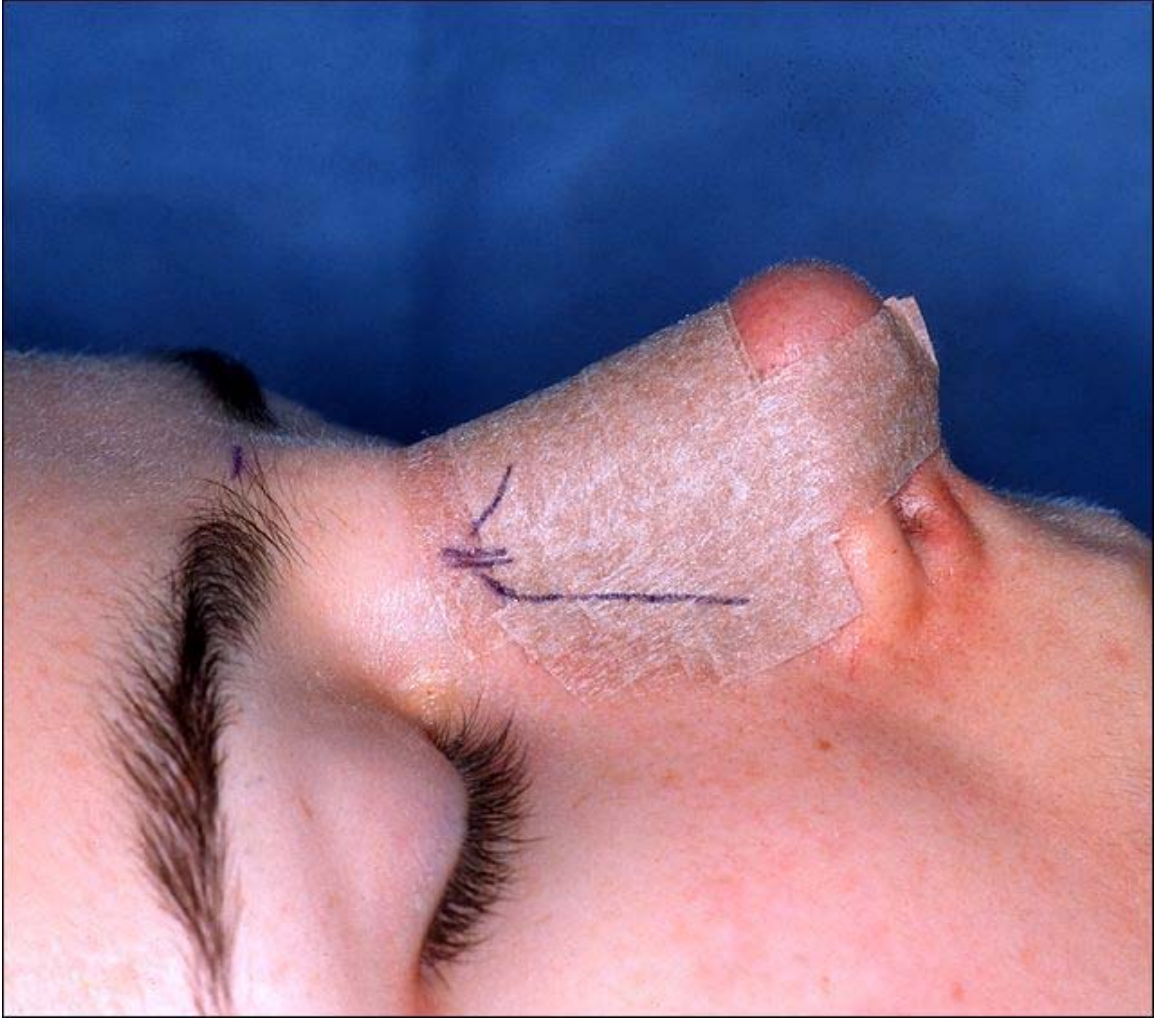
These chisel cuts are made from underneath the skin, so there is no scar in the area after healing.



At the end of the rhinoplasty

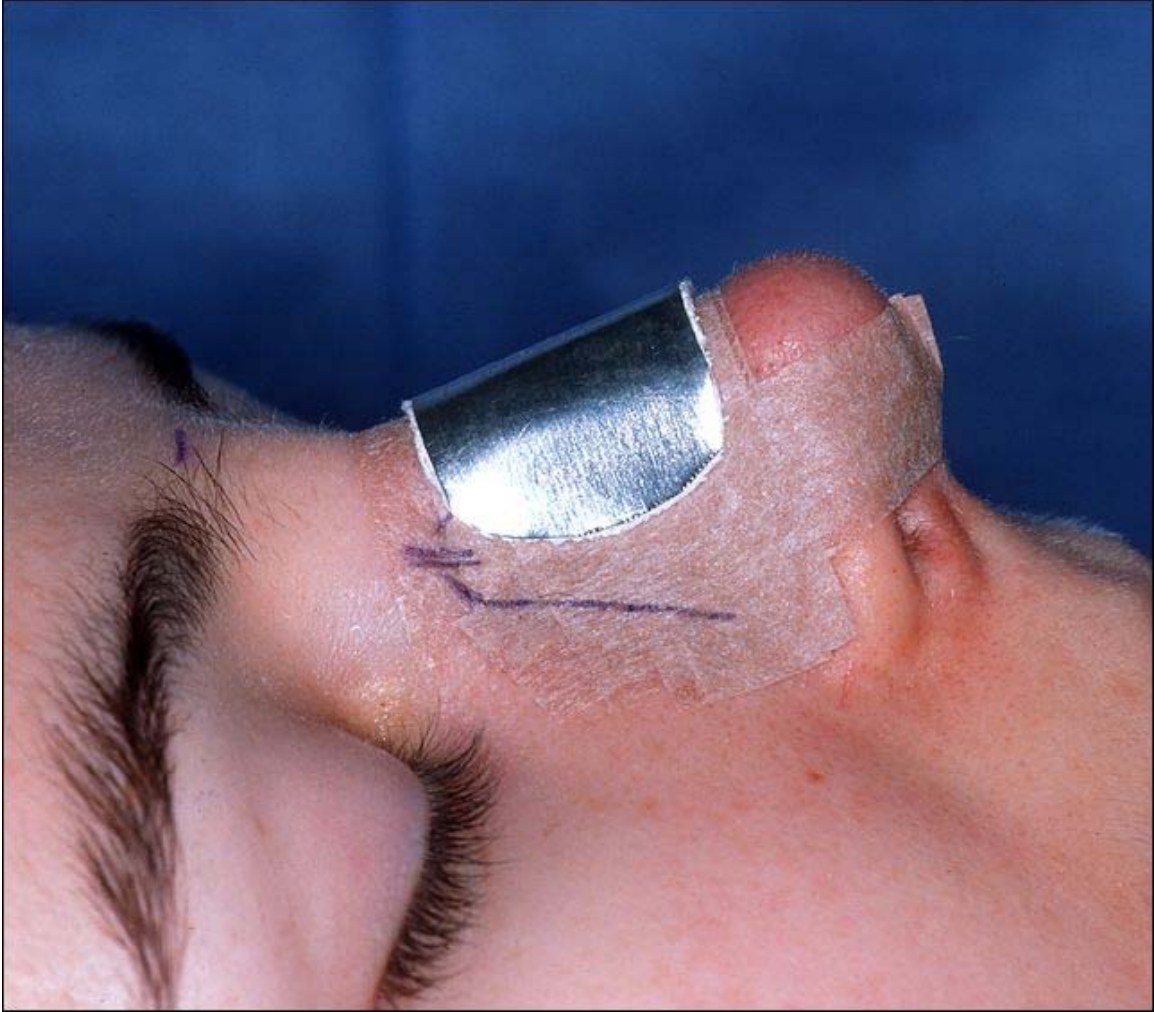
At the end of the procedure, after the incisions are closed, the nose is dressed, to hold it securely in place as it heals.

This photo shows the nose just before the dressing and splint are placed. The purple marks on the nose guided the surgeon in making accurate cuts in the bone during surgery.



Taping the nose, in preparation for the metal splint

Preparing for the metal splint: the nose is first covered with paper tape in a manner to help maintain the nose's new shape.



Metal nasal splint in place

After taping, the metal splint is designed and cut and shaped, and it is placed on the nose.



Metal nasal splint has been taped on the nose

The metal splint is then covered with the tape, to hold it in place. The operation is now completed. The dressing will be removed in one week.

Primary and secondary

Primary rhinoplasty refers to first-time rhinoplasty whether it is performed for aesthetic, functional, or reconstructive purposes.

Revision rhinoplasty, also known as secondary rhinoplasty, is a nose operation performed to correct or revise an unsatisfactory outcome from a previous rhinoplasty. An unsatisfactory outcome occurs from 5% to 20% of rhinoplasties. There are two main reasons for performing secondary rhinoplasty. Patients often seek secondary rhinoplasty to correct a cosmetic deformity of the nose. A patient may be unsatisfied with all or part of a previous "nose reshaping.". A nasal fracture may not have been reduced enough, or

too much. A prominent or bulbous nasal tip may have not been addressed appropriately, or over-aggressively. The nose may look pinched, it may look like a parrot's beak, or like a boxer's nose. There are many ways in which previous nose surgery may have left a nose aesthetically unappealing to a patient. The second reason is functional. The original nasal surgery may have been carried out to help with difficulties in breathing, and the outcome may have been unsatisfactory. Alternatively, the original surgery may have been performed for cosmetic reasons, but may have disrupted a normal physiologic mechanism involving the inspiration or expiration of air, making it difficult to breathe. Secondary rhinoplasty is a procedure often said to be extremely complicated. Because the nasal framework has often been destroyed or deformed from previous surgery, revision rhinoplasty experts frequently must reconstruct the support structures of the nose using cartilage grafts from either the ear (auricular cartilage graft) or from rib cartilage (costal cartilage graft). Most revision rhinoplasty specialists perform secondary rhinoplasty via the open approach. This allows the surgeon to directly visualize the deformity. Advances in rhinoplasty techniques, such as stabilization of rib cartilage grafts and utilization of the open approach, now allow satisfactory results in secondary rhinoplasty that were not possible in the past.

Functional and reconstructive

Reconstructive rhinoplasty refers to restoring the normal shape and function of the nose following damage from a traumatic accident, autoimmune disorder, intra-nasal drug abuse, previous injudicious cosmetic surgery, cancer involvement, or congenital abnormality. Rhinoplasty can restore skin coverage, recreate normal contours, and re-establish nasal airflow. To improve nasal breathing function, a septoplasty may also be performed. If there is turbinate hypertrophy, an inferior turbinectomy can be performed.

Rhinoplasty may be sought in the aftermath of traumatic deformity. Traumatic accidents are the most common cause of nasal deformity. Typically the nasal bones are broken and displaced. Occasionally, the nasal cartilages are disrupted or displaced, and in the worst cases the nasal dorsum is collapsed. Rhinoplasty allows shaving of the displaced bony humps, and re-alignment of the nasal bones after they are cut. When cartilage is disrupted, stitching of the cartilage for re-suspension, or use of cartilage grafts to camouflage depressions allows re-establishment of normal nasal contour. When the dorsum is collapsed, grafts of rib cartilage, ear cartilage, or cranial bone can be used to restore continuity to the dorsum. Although synthetic implants are also available for augmenting the nasal dorsum, cartilage or bone graft from the patient's own body poses fewer risks of infection or rejection.



The lower lateral cartilage (greater alar cartilage) exposed through the left nostril for modification during a rhinoplasty.

Rhinoplasty is sometimes sought for a collapsed nose due to septum perforation. Autoimmune problems such as Wegener's Granulomatosis, Sarcoidosis, Churg-Strauss Syndrome, and Relapsing Polychondritis can lead to creation of a hole in the nasal septum, and loss of support in the dorsum leading to a saddle nose deformity. Intra nasal use of drugs such as cocaine, or extreme abuse of nasal decongestant sprays can similarly cause septum perforation and nasal dorsum collapse. Dorsum reconstruction is accomplished through the use of rib cartilage or bone grafts.

Rhinoplasty to correct nasal obstruction following injudicious cosmetic surgery is common. Reconstructive rhinoplasty after injudicious cosmetic surgery allows the restoration of normal breathing. When nasal cartilages are over-aggressively trimmed during rhinoplasty, the nose can appear pinched and nasal potency compromised. Patients complain of nasal blockage that is worsened by attempts at deep inspiration. Internal cartilage grafts to support the nasal tip (batton grafts) or widen the middle vault of the nose (spreader grafts) can be quite effective in restoring normal breathing. These grafting techniques will increase the size of the nasal tip and widen the dorsum.

Rhinoplasty for skin cancer excision also exists. Excision of skin cancers from the nose can lead to loss of internal support as well as external skin coverage. Skin cancer excision in the nose is commonly accomplished via the Mohs' technique. Once the cancer is removed, reconstructive rhinoplasty aims to provide skin coverage utilizing techniques such as skin graft, local skin flaps, or pedicle flaps. If cancer resection leads to loss of tissue in the area of the nasal tip, cartilage grafts are utilized to maintain support and prevent long-term distortion, by the force of scar contracture.

Rhinophyma is the late stage manifestation of a skin condition known as Rosacea, where the skin is infected with acne roseacea. The skin in the area of the nasal tip becomes red, thickened, and enlarged as exemplified by W C Fields. Although known acne treatments such as antibiotics and Acutane can halt the progression of this disease, thickening of the skin and obscuring of the nasal tip landmarks can only be remedied by surgical correction. Currently, laser excision of thickened abnormal skin represents the best option in rhinoplasty for Rhinophyma. The CO2 laser and the Erbium YAG laser are the most effective types of laser for this disorder.

Vascular malformations and cleft lip anomalies are relatively common causes of congenital nasal deformities. In vascular malformations, the disease process can cause distortions of the skin and underlying structure of the nose. In cleft palate abnormalities, the size, position, and orientation of the nasal tip cartilages may be distorted. Rhinoplasty for reconstruction of vascular malformations can involve laser treatment of the skin and possible surgical excision. When the underlying cartilage structure is disturbed, cartilage grafts and stitching of the native nasal cartilages can help improve nasal appearance. In cleft lip patients, reconstructive rhinoplasty allows re-orientation of the nasal tip cartilages. Additional refinements with cartilage grafts to the tip are also frequently employed.

Ethnic

Although techniques and methods employed during rhinoplasty surgeries are the same regardless of ethnicity, there are some trends that apply to patients of certain ethnic backgrounds, due to their similar anatomic features. East Asian patients often want their noses to appear narrower and their bridges higher. If very little elevation of the bridge is desired, the nasal bones can be cut and moved towards the midline. This technique will narrow the bridge and also cause a slight elevation in the dorsum. East Asian patients who seek greater augmentation of the bridge of their nose require implants. A variety of alloplastic implants including Gore-Tex, Med-Por, or silicone can be used. Tissues from the patient's own body (autologous) can be used for augmentation, in order to reduce the risk of complications such as infection or extrusion. Septum cartilage, rib cartilage (costal cartilage), ear cartilage (auricular cartilage), and fascia are being often used. In non surgical rhinoplasty, filler materials such as hyaluronic acid or calcium based microspheres can be injected under the skin, in the bridge of the nose. These injections however, are non permanent lasting between six months to a year.

Patients of African descent commonly seek narrowing of wide nostrils in a procedure known as alar base reduction. This procedure may include removing sections of the base of the nostrils or sections of the nose where it meets the face. Risk of keloid scar formation is very low, if the patient has not had keloids in the past. The tip of the nose can be restructured by removing tiny sections of cartilage to give the nose more definition, or adding cartilage grafts to provide additional structure to the nasal tip.

Non-surgical

Non-surgical rhinoplasty refers to reshaping the nose with injectable substances rather than surgical means of altering the shape and structure of the nose. It is also called a "non-surgical nose job", and can be performed in the outpatient setting without anesthesia. Another non-surgical option used by some people are flexible "nose inserts" that are placed in the nostril area between the nose tip and back of the nose. The nose inserts reshape one's nose only while worn. A non-surgical nose job is not permanent and only lasts about a month.

Recovery

The patient returns home after the surgery. Most surgeons recommend antibiotics, pain medications, and steroid medication after surgery. Most people choose to remain home for a week, although it is safe to be outdoors. If there are external sutures, they are usually removed 4 to 5 days after surgery. The external cast is removed at one week. If there are internal stents, they are usually removed at four days to two weeks. The periorbital bruising usually lasts two weeks. Due to wound healing, there is moderate shifting and settling of the nose over the first year.

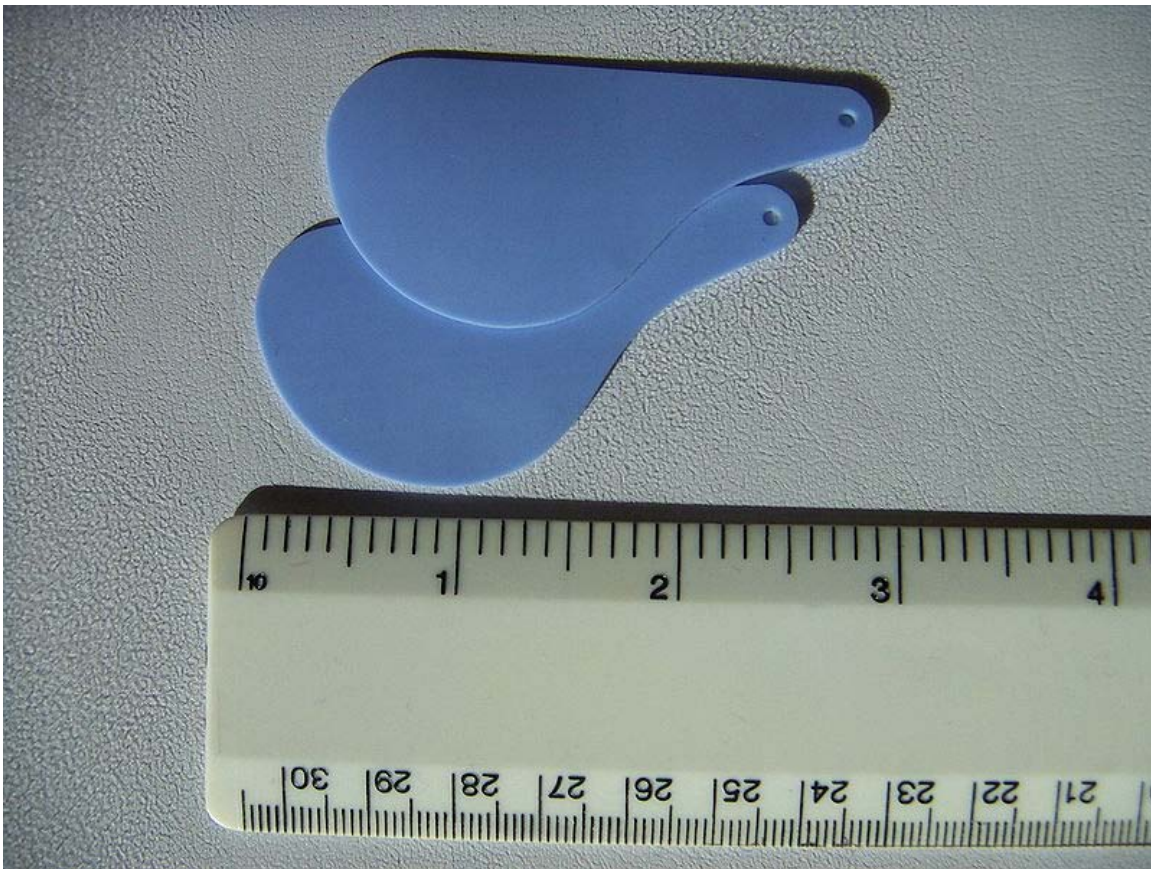
Health risks

Although rhinoplasty is usually considered to be safe and successful, several complications can arise. Post operative bleeding is uncommon and often resolves without needing treatment. Infection is rare and can occasionally progress to an abscess that requires surgical drainage under general anesthetic. Adhesions, which are scars that form to bridge across the nasal cavity from the septum to the turbinates, are also rare but cause nasal obstruction to breathing and usually need to be cut away. A hole can be inadvertently made at the time of surgery in the septum, called a septal perforation. This can cause chronic nose bleeding, crusting, difficult breathing and whistling with breathing.

If too much of the underlying structure of the nose (cartilage and/or bone) is removed, this can cause the overlying nasal skin to have little shape resulting in a "polly beak" deformity. Likewise if the septum is not supported, the bridge of the nose can sink resulting in a "saddle nose" deformity. The tip of the nose can be over-rotated causing the nostrils to be too visible and creating a pig-like look. If the cartilages of the tip of the nose are over-resected, this can cause a pinched look to the tip. If an incision is made across the collumella (open approach rhinoplasty) there can be variable degree of numbness to the nose that may take months to resolve.

Septoplasty

Septoplasty is a corrective surgical procedure done to straighten the nasal septum, the partition between the two nasal cavities. Ideally, the septum should run down the center of the nose. When it deviates into one of the cavities, it narrows that cavity and impedes airflow. Often the inferior turbinate on the opposite side enlarges, which is termed *compensatory hypertrophy*. Nasal obstructions caused by serious deviations frequently lead to chronic sinus problems. Turbinate reduction may also be advised to further enlarge the nasal cavities. If turbinate resection is indicated, special care should be taken to avoid over-resection leading to empty nose syndrome. Most surgeries are completed in 90 minutes or less, not including recovery time.



Typical flexible splints that may be used in septoplasty. They are held in place in the nose with a stitch through the hole, and are typically removed seven to 10 days after surgery.

Procedure

Because the deviation is a result of a cartilage and/or bone surplus, the procedure usually involves an excision of a portion of any of these tissues. Under general or local anesthesia, the surgeon works through the nostrils, making an incision in the lining of the septum to reach the cartilage targeted in the operation. Often an "L" strut of cartilage in

the dorsal and caudal areas (1 cm width or more) is preserved for structural support. After excess cartilage and bone have been taken out, the septum may then be stabilized with small plastic tubes, splints, or sutures.

Post-operation

Considerable swelling and bruising can be expected. The nasal cavities may or may not be packed, and a piece of gauze is taped the septal mucosa with catgut can avoid the use of nasal packing, a nasal clip or tamponade. The suturing will promptly prevent bleeding and synechiae formation as well as septal perforation due to the pressure necrosis by the pack.

Chapter 15

Tracheo-Oesophageal Puncture and Pneumonectomy

Tracheo-oesophageal puncture

A **tracheo-oesophageal puncture** (or **tracheoesophageal puncture**) is a surgically created hole between the trachea (windpipe) and the esophagus (the tubal pathway between the throat and the stomach) in a person who has had a total laryngectomy, a surgery where the larynx (voice box) is removed. The purpose of the puncture is to restore a person's ability to speak after the vocal cords have been removed. This involves creation of a fistula between trachea and oesophagus, puncturing the short segment of tissue or "common wall" that typically separates these two structures. A voice prosthesis is inserted into this puncture. The prosthesis keeps food out of the trachea but lets air into the esophagus for oesophageal speech.

A laryngectomized person is required to breathe through a permanent breathing hole in the neck, called a tracheostoma. When a laryngectomized person occludes the tracheostoma, completely blocking exhaled air to leave the body through that pathway, exhaled air is directed through the voice prosthesis. This air enters the esophagus and escapes through the mouth. During this process, as the air passes through the upper tissues of the esophagus and lower throat, it allows for vibration of the tissues of the pharyngoesophageal segment (also called PE-segment, neoglottis or pseudoglottis). This vibration creates a sound that serves to replace the sound the vocal cords previously produced. This type of speech is called tracheoesophageal speech. It is the most popular method of voice restoration after total laryngectomy. Other methods of alaryngeal speech (i.e. speech without vocal cords) are esophageal speech, and artificial larynx speech. Studies show that tracheoesophageal speech is found to be closer to normal speech than esophageal speech and is often reported to be better, both in terms of naturalness as well as how well it is understood, when compared to esophageal speech and electrolarynx speech. The first report on a tracheoesophageal puncture dates back to 1932 when a laryngectomized patient was said to use a hot ice pick to create a tracheoesophageal puncture in himself. This enabled him to speak by forcing air through the puncture when closing off the tracheostoma with a finger.

Puncture procedures

There are two tracheo-esophageal puncture procedure types: Primary and secondary puncture. Initially, the procedure was described as a secondary procedure and later also as a primary procedure.

Primary tracheoesophageal puncture: This procedure is performed during the total laryngectomy surgery. After removal of the larynx and creation of the tracheostoma, the puncture is made through the back wall of the trachea into the front wall of the esophagus. The main advantages of a primary puncture are: 1) that a second surgery to create the puncture is avoided (including the related costs and risks) and: 2) that the patient will be able to speak within a few weeks after total laryngectomy.

There are cases where a primary procedure cannot be performed. For example, this procedure cannot be used when there is complete separation of the tracheoesophageal wall where the puncture would otherwise be placed (for example, in case a portion of the esophagus is removed requiring an anastomosis, or “reconnection” of structures in the region). In that case, a sufficient period of recovery and wound healing would be required. A secondary puncture could then be placed. Secondary tracheoesophageal puncture: This procedure refers to a puncture that is placed anytime after the total laryngectomy surgery. The decision to use a primary or secondary puncture can vary greatly. Secondary puncture can be performed when: 1) primary puncture was not possible, 2) for re-puncture after closure of a previous tracheoesophageal puncture, 3) because of physician or patient preference, and 4) in case failure of esophageal or electrolarynx speech if this was chosen as the initial speech option.

Placement of the voice prosthesis

There are two different methods that can be used to place the voice prosthesis: Primary placement: A voice prosthesis is placed into the puncture immediately after it is created. During the immediate postoperative period, the patient is fed through a feeding tube, either inserted directly into the stomach or through a more temporary version that extends from the nose into the stomach. This tube is removed when the patient is able to eat enough by mouth to maintain nutritional needs; this can be as early as the second day following surgery. Speech production with the voice prosthesis is initiated when the surgical area has healed, after clearance by the surgeon. The advantages of this method are: 1) the voice prosthesis stabilizes the TE wall, 2) the flanges of the device protect the puncture against leakage of fluids, stomach acids and other stomach contents, 3) there is no irritation or pressure from a stenting catheter, used to maintain the puncture opening until a voice prosthesis can be placed, 4) patients become quickly familiar with their prosthesis care as they receive instructions while hospitalized, 5) the patient will not have to undergo an outpatient procedure during which the voice prosthesis needs to be fitted, 6) many patients can learn to speak before the start of any post-operative radiation therapy (if indicated) 7) the patient can focus on voice production immediately, as wound healing allows.

Another advantage is that generally, the voice prosthesis placed at the time of surgery lasts relatively long and requires no early frequent replacements. The only disadvantage is that the patient will need to use a feeding tube for a few days.

Delayed placement: Instead of the voice prosthesis, a catheter (red rubber, Silastic Foley catheter, Ryle's tube) is introduced through the puncture into esophagus. The tube is sometimes utilized for feeding the patient during the immediate post operative period, or the patient has a standard feeding tube for feeding. The voice prosthesis is placed after the patient is able to eat sufficiently by mouth and speech production is initiated when healing has completed, after clearance by the surgeon. The advantage of this method is that the patient may be fed through the catheter, not requiring standard tube feeding. The primary disadvantage is that the patient will have to undergo an outpatient procedure to have the voice prosthesis placed. Another disadvantage can be the need for more frequent replacements early after fitting of the voice prosthesis due to changes in the length of the puncture.

Indications

Indications include voice rehabilitation for patients who are undergoing a total laryngectomy (primary puncture) or patients who have had a total laryngectomy in the past (secondary puncture). Contra-indications are mainly related to the use of the voice prosthesis and not the puncture procedure itself. It is important to have healthy tissue at the puncture site. This will help ensure the voice prosthesis is properly supported. Poor tissue condition at the puncture site can be a contra-indication for TE puncture. It is also important that the patient candidacy be taken into account. Patients must be able to understand and manage proper prosthesis maintenance and monitor for complications or device problems. Bleeding disorders, anxiety disorders, dementia, poor vision and poor manual dexterity are all factors that may negatively interfere with successful voice restoration using tracheoesophageal techniques and should be discussed further with an appropriate healthcare provider who is knowledgeable in this topic.

Pneumonectomy



Appearance of the cut surface of a pneumonectomy specimen containing a lung cancer, here a Squamous cell carcinoma (the whitish tumor near the bronchi).

A **pneumonectomy** (or pneumectomy) is a surgical procedure to remove a lung. Removal of just one lobe of the lung is specifically referred to as a lobectomy, and that of a segment of the lung as a wedge resection (or segmentectomy).

Indications

The most common reason for a pneumonectomy is to remove tumourous tissue arising from lung cancer. In the days prior to the use of antibiotics in tuberculosis treatment, tuberculosis was sometimes treated surgically by pneumonectomy.

The operation will reduce the respiratory capacity of the patient; before conducting a pneumonectomy, the surgeon will evaluate the ability of the patient to function after the lung tissue is removed. After the operation, patients are often given an incentive spirometer to help exercise their remaining lung and to improve breathing function.

A rib or two is sometimes removed to allow the surgeon better access to the lung.

Types

There are two types of pneumonectomy:

1. **Simple pneumonectomy**: removal of just the affected lung
2. **Extrapleural pneumonectomy (EPP)**: removal of the affected lung, plus part of the diaphragm, the parietal pleura (lining of the chest) and the pericardium (lining of the heart) on that side. The linings are replaced by Gore-Tex in this radical and painful surgery that is used primarily for treatment of malignant mesothelioma. This technique produces the best long-term survival rates for this serious and fatal disease.

History

Pioneering dates

- 1895: first pneumonectomy in multiple stages by William Macewen on a patient with tuberculosis and emphysema
- 1931: first successful pneumonectomy in two stages by Rudolph Nissen on a patient with crush injury to the thorax
- 1932: first lobectomy, by Harold Brunn
- 1933: first successful single-stage total pneumonectomy by Graham and Singer
- 1939: first segmentectomy, by Churchill and Belsey

Chapter 16

Heart-Lung Transplant and Laryngectomy

Heart-lung transplant

Intervention:
Heart–lung transplant

ICD-10 code:

ICD-9 code: 33.6

MeSH D016041

Other codes:

A **heart–lung transplant** is a procedure carried out to replace both heart and lungs in a single operation. Due to a shortage of suitable donors, it is a rare procedure; only about a hundred such transplants are performed each year in the USA.

Qualifying conditions

Most candidates for heart–lung transplants have life-threatening damage to both their heart and lungs. In the US, most prospective candidates have between twelve and twenty-four months to live. At any one time, there are about 250 people registered for heart–lung transplantation at the United Network for Organ Sharing (UNOS) in the USA, of which around forty will die before a suitable donor is found.

Conditions which may necessitate a heart–lung transplant include:

- Congenital problems (defects present at birth) affecting the heart and lungs (48%);
- Pulmonary hypertension (20%);
- Cystic fibrosis (2%);
- A second transplant after the first transplant was rejected or failed to operate satisfactorily (4%).

Candidates for a heart–lung transplant are usually required to be:

- Under 55 years old;
- Have no other medical conditions (e.g. AIDS, Diabetes, Hepatitis);
- Mentally sound;
- Capable of following a post-operative regimen of exercise and immunosuppressant drugs.

History

Dr. Norman Shumway laid the groundwork for heart lung transplantation with his experiments into heart transplantation at Stanford in the mid 1960s. Shumway conducted the first adult heart transplant in the US in 1968.

Building on his research at Stanford, Dr. Bruce Reitz performed the first successful heart–lung transplant on Mary Gohlke in 1981 at Stanford Hospital. The transplant team at Stanford is the longest continuously active team performing these transplants.

Procedure

The patient is anaesthetised. When the donor organs arrive, they are checked for fitness; if any organs show signs of damage, they are discarded and the operation cancelled. Some patients are concerned that their organs will be removed and the donor organs won't be suitable. Since this is a possibility, it is standard procedure that the patient is not operated on until the donor organs arrive and are judged suitable, despite the time delay this involves.

Once suitable donor organs are present, the surgeon makes an incision starting above and finishing below the sternum, cutting all the way to the bone. The skin edges are retracted to expose the sternum. Using a bone saw, the sternum is cut down the middle. Rib spreaders are inserted in the cut, and spread the ribs to give access to the heart and lungs of the patient.

The patient is connected to a heart–lung machine, which circulates and oxygenates blood. The surgeon removes the failing heart and lungs. Most surgeons endeavour to cut blood vessels as close as possible to the heart to leave room for trimming, especially if the donor heart is of a different size than the original organ.

The donor heart and lungs are positioned and sewn into place. As the donor organs warm up to body temperature, the lungs begin to inflate. The heart may fibrillate at first – this occurs because the cardiac muscle fibres are not contracting synchronously. Internal paddles can be used to apply a small electric shock to the heart to restore proper rhythm.

Once the donor organs are functioning normally, the heart–lung machine is withdrawn, and the chest is closed.

Post-operation

Most patients spend several days in intensive care after the operation. If there are no complications (e.g. infection, rejection), some are able to return home after just two weeks in hospital. Patients will be given anti-rejection drugs, and antibiotics to prevent infection. A schedule of frequent follow up visits is necessary.

Statistics

The success rate of heart–lung transplants has improved a lot in recent years. The British National Health Service states that the survival rate is now around 85%, one year after the transplant was performed.

In 2004, there were only 39 heart–lung transplants performed in the entire United States and only 75 worldwide. By comparison, in that same year there were 2,016 heart and 1,173 lung transplants.

Laryngectomy

Intervention: Laryngectomy

ICD-10 code:

ICD-9 code: 30.2 30.3 30.4

MeSH D007825

Other codes:

Laryngectomy is the removal of the larynx and separation of the airway from the mouth, nose and esophagus. The laryngectomee breathes through an opening in the neck, a stoma. It is done in cases of laryngeal cancer. However, many laryngeal cancer cases are now treated only with radiation and chemotherapy or other laser procedures, and laryngectomy is performed when those treatments fail to conserve the larynx. laryngectomy is also performed to individuals with other types of head and neck cancer.

Voice replacement

- Voice functions are generally replaced with a voice prosthesis placed in the tracheo esophageal puncture created by the surgeon. The voice prosthesis vibrates the esophageal tissue in lieu of the larynx.

- A second method is the use of an electrolarynx. An electrolarynx is an external device that is placed against the neck and creates vibration that the speaker then articulates. The sound has been characterized as mechanical and robotic.
- A third method is called esophageal speech. The speaker pushes air into the esophagus and then pushes it back up, articulating speech sounds to speak. This method is time-consuming and difficult to learn and is seldom used by laryngectomees.

Uses

Laryngectomies number about 60,000 in the United States. Perhaps 10,000 laryngeal cancer cases are treated annually, but only about 3,000 people are laryngectomized. Because it is a relatively rare cancer and because the post-operative care is complex in achieving a functional result, laryngeal cancer patients should be treated at or at least consult a major federally designated cancer center, where the fields of surgery, radiology, chemotherapy, speech-language pathology are integrated in head and neck departments.

Most laryngeal cancers in the UK are glottic, meaning they start in the vocal cords within the larynx. Glottic cancers tend to be picked up at an early stage, as they cause a hoarse voice very quickly. About 90 out of every 100 people (90%) with T1 glottic cancers are cured with radiotherapy alone. But most of the remaining 10 out of every 100 people (10%) will be cured with surgery after their radiotherapy.

In animals

Laryngectomies may be applied to dogs as a debarking procedure.

Chapter 17

Thoracentesis

*Intervention:
Thoracentesis*



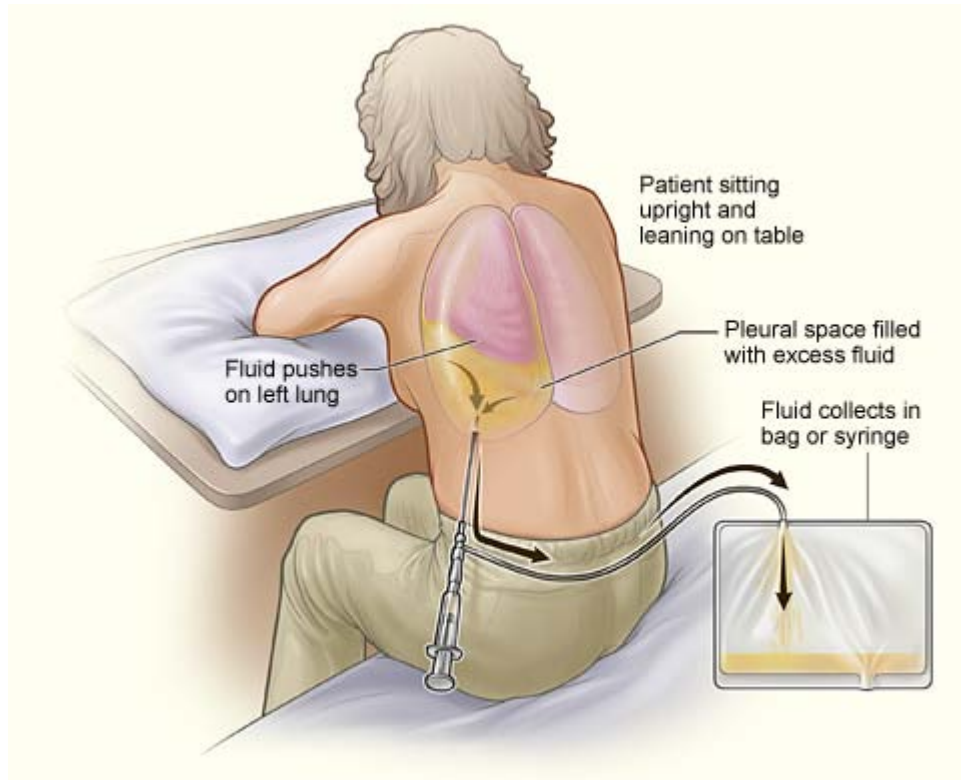
Chest X-ray showing a left-sided pleural effusion (right side of image). This can be treated with thoracentesis.

ICD-10 code:

ICD-9 code: 34.91

Other codes: **OPCS-**
4.2T12.3

Thoracentesis is an invasive procedure to remove fluid or air from the pleural space for diagnostic or therapeutic purposes. A cannula, or hollow needle, is carefully introduced into the thorax, generally after administration of local anesthesia. The procedure was first described in 1852.



The illustration shows a person having thoracentesis. The person sits upright and leans on a table. Excess fluid from the pleural space is drained into a bag.

The recommended location varies depending upon the source. It is critical that the patient hold his or her breath to avoid piercing of the lung. Some sources recommend the midaxillary line, in the ninth intercostal space.

Indications

This procedure is indicated when unexplained fluid accumulates in the chest cavity outside the lung. In more than 90% of cases analysis of pleural fluid yields clinically useful information. If a large amount of fluid is present, then this procedure can also be used therapeutically to remove that fluid and improve patient comfort and lung function.

The most common causes of pleural effusions are cancer, congestive heart failure, pneumonia, and recent surgery. In countries where tuberculosis is common, this is also a common cause of pleural effusions.

When cardiopulmonary status is compromised (i.e. when the fluid or air has its repercussions on the function of heart and lungs), due to air (significant pneumothorax), fluid (pleural fluid) or blood (hemothorax) outside the lung, then this procedure is usually replaced with tube thoracostomy, the placement of a large tube in the pleural space.

Contraindications

An uncooperative patient or a coagulation disorder that can not be corrected are absolute contraindications.

Relative contraindications include cases in which the site of insertion has known bullous disease (e.g. emphysema), use of positive end-expiratory pressure and only one functioning lung (due to diminished reserve). The aspiration should not exceed 1L as there is a risk of development of pulmonary edema.

Complications

Major complications are pneumothorax (3-30%), hemopneumothorax, hemorrhage, hypotension (low blood pressure due to a vasovagal response) and reexpansion pulmonary edema.

Minor complications include a dry tap (no fluid return), subcutaneous hematoma or seroma, anxiety, dyspnea and cough (after removing large volume of fluid).

The use of ultrasound for needle guidance can minimize the complication rate.

Interpretation of pleural fluid analysis

Several diagnostic tools are available to determine the etiology of pleural fluid.

Transudate versus exudate

First the fluid is either transudate or exudate.

A transudate is defined as pleural fluid to serum total protein ratio of less than 0.5, pleural fluid to serum LDH ratio < 0.6 , and absolute pleural fluid LDH < 200 IU or $< 2/3$ of the normal serum.

An exudate is any fluid that filters from the circulatory system into lesions or areas of inflammation. Its composition varies but generally includes water and the dissolved solutes of the main circulatory fluid such as blood. In the case of blood: it will contain some or all plasma proteins, white blood cells, platelets and (in the case of local vascular damage) red blood cells.

Exudate

- hemorrhage
- Infection
- Inflammation
- Malignancy
- Iatrogenic

- Connective tissue disease
- Endocrine disorders
- Lymphatic disorders vs Constrictive pericarditis

Transudate

- Congestive heart failure
- Nephrotic syndrome
- Hypoalbuminemia
- Cirrhosis
- Atelectasis
- trapped lung
- Peritoneal dialysis
- Superior vena cava obstruction

Amylase

A high amylase level (twice the serum level or the absolute value is greater than 160 Somogy units) in the pleural fluid is indicative of either acute or chronic pancreatitis, pancreatic pseudocyst that has dissected or ruptured into the pleural space, cancer or esophageal rupture.

Glucose

This is considered low if pleural fluid value is less than 50% of normal serum value. The differential diagnosis for this is:

- rheumatoid effusion. The levels are characteristically low (<15 mg/dL).
- lupus effusion
- bacterial empyema
- malignancy
- tuberculosis
- esophageal rupture (Boerhaave syndrome)

pH

Normal pleural fluid pH is approximately 7.60. A pleural fluid pH below 7.30 with normal arterial blood pH has the same differential diagnosis as low pleural fluid glucose.

Triglyceride and cholesterol

Chylothorax (fluid from lymph vessels leaking into the pleural cavity) may be identified by determining triglyceride and cholesterol levels, which are relatively high in lymph. A triglyceride level over 110 mg/dl and the presence of chylomicrons indicate a chylous effusion. The appearance is generally milky but can be serous.

The main cause for chylothorax is rupture of the thoracic duct, most frequently as a result of trauma or malignancy (such as lymphoma).

Cell count and differential

The number of white blood cells can give an indication of infection. The specific subtypes can also give clues as to the type of infection. The amount of red blood cells are an obvious sign of bleeding.

Cultures and stains

If the effusion is caused by infection, microbiological culture may yield the infectious organism responsible for the infection, sometimes before other cultures (e.g. blood cultures and sputum cultures) become positive. A Gram stain may give a rough indication of the causative organism. A Ziehl-Neelsen stain may identify tuberculosis or other mycobacterial diseases.

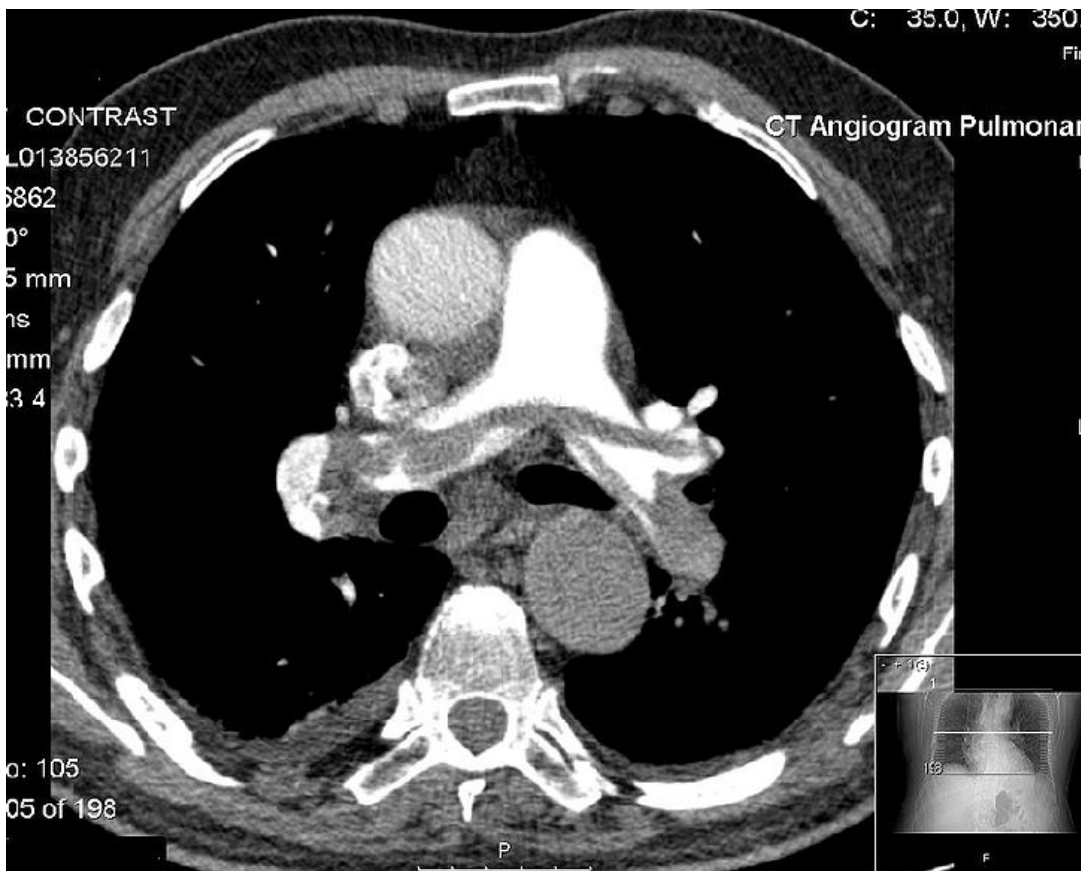
Cytology

Cytology is an important tool in identifying effusions due to malignancy. The most common causes for pleural fluid are lung cancer, metastasis from elsewhere and mesothelioma. The latter often presents with an effusion. Normal cytology results do not reliably rule out malignancy, but make the diagnosis more unlikely.

Chapter 18

CT Pulmonary Angiogram and Ventilation/Perfusion Scan

CT pulmonary angiogram



Example of a CTPA, demonstrating a saddle embolus. The white area above the center is the pulmonary artery, opacified by radiocontrast. Inside it, the grey matter is blood clot. The black areas on either side are the lungs, with around it the chest wall.

CT pulmonary angiogram (CTPA) is a medical diagnostic test that employs computed tomography to obtain an image of the pulmonary arteries. Its main use is to diagnose pulmonary embolism (PE).

Diagnostic use

CTPA was introduced in the 1990s as an alternative to ventilation/perfusion scanning, which relies on radionuclide imaging of the blood vessels of the lung. It is regarded as a highly sensitive and specific test for pulmonary embolism.

CTPA is typically only requested if pulmonary embolism is suspected clinically. If the probability of PE is considered low, a blood test called D-dimer may be requested. If this is negative and risk of a PE is considered negligible, then CTPA or other scans are generally not performed. Most patients will have undergone a chest X-ray before CTPA is requested.

After initial concern that CTPA would miss smaller emboli, a 2007 study comparing CTPA directly with ventilation/perfusion scanning found that CTPA identified more emboli without decreasing the risk of long-term complications compared to V/Q scanning.

Contraindications

CTPA is generally avoided in pregnancy due to the amount of ionizing radiation required, which may damage the fetus.

CTPA is contraindicated in known or suspected allergy to contrast media or in renal failure (where contrast agents could worsen the renal function).

Acquisition

The best results are obtained using multidetector computed tomography (MDCT) scanners.

An intravenous cannula is required for the administration of the 50-150 ml. of radiocontrast. This is injected, usually automatically, by a syringe driver, at a rate of 4 ml./second. Many hospitals use bolus tracking, where the scan commences when the contrast is detected at the level of the proximal pulmonary arteries. If this is done manually, scanning commences about 10–12 seconds after the injection has started. Slices of 1-3 mm. are performed at 1-3 mm. intervals, depending on the nature of the scanner (single- versus multidetector).

State of the art CT machines can complete a scan in approximately five seconds and it is possible to complete the entire procedure (set-up, injection and scanning) in the space of five minutes.

Interpretation

On CTPA, the pulmonary vessels are filled with contrast, and appear white. Any mass filling defects (embolus or other matter such as fat or amniotic fluid) appears darker. Generally, the scan should be complete before the contrast reaches the left side of the heart and the aorta, which could result in artifacts.

Ventilation/perfusion scan

A **ventilation/perfusion lung scan**, also called a V/Q lung scan, is a type of medical imaging using scintigraphy and medical isotopes to evaluate the circulation of air and blood within a patient's lungs, in order to determine the ventilation/perfusion ratio. The ventilation part of the test looks at the ability of air to reach all parts of the lungs, while the perfusion part evaluates how well blood circulates within the lungs.

Uses

This test is most commonly done in order to check for the presence of a blood clot or abnormal blood flow inside the lungs (such as a pulmonary embolism or PE), although computed tomography with radiocontrast is now more commonly used for this purpose. The V/Q scan may be used in some circumstances where radiocontrast would be inappropriate, as in renal failure.

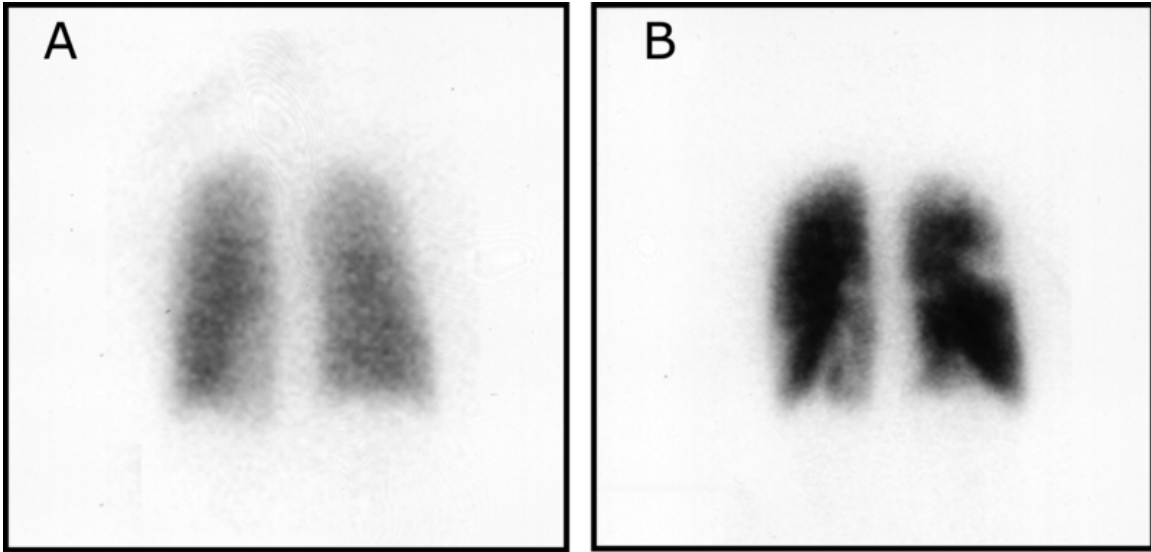
A V/Q lung scan may be performed in the case of serious lung disorders such as Chronic obstructive pulmonary disease (COPD) or pneumonia as well as a lung performance quantification tool pre- and post-lung lobectomy surgery.:

Procedure

The ventilation and perfusion phases of a V/Q lung scan are performed together and may include a chest x-ray for comparison or to look for other causes of lung disease. A defect in the perfusion images requires a mismatched ventilation defect to be indicative of pulmonary embolism.

In the ventilation phase of the test, a gaseous radionuclide such as xenon or technetium DTPA in an aerosol form is inhaled by the patient through a mouthpiece or mask that covers the nose and mouth. The perfusion phase of the test involves the intravenous injection of radioactive technetium macro aggregated albumin (Tc99m-MAA). A gamma camera acquires the images for both phases of the study.

Significance of results



Ventilation-perfusion scintigraphy in a woman taking oral contraceptives and valdecoxib with a pulmonary embolism. (A) After inhalation of 20.1 mCi of Xenon-133 gas, scintigraphic images were obtained in the posterior projection, showing uniform ventilation to lungs. (B) After intravenous injection of 4.1 mCi of Technetium-99m-labeled macroaggregated albumin, scintigraphic images were obtained, shown here in the posterior projection. This and other views showed decreased activity in the following regions: apical segment of right upper lobe, anterior segment of right upper lobe, superior segment of right lower lobe, posterior basal segment of right lower lobe, anteromedial basal segment of left lower lobe, and lateral basal segment of left lower lobe.

V/Q Scan Interpretation

Result	Interpretation	Significance
Normal	No perfusion deficit	Excludes pulmonary thromboembolism
Low probability	Perfusion deficit with matched ventilation deficit	Non diagnostic
Intermediate probability	Perfusion deficit that corresponds to parenchymal abnormality on chest x-ray	Non diagnostic
High probability	Multiple segmental perfusion deficits with normal ventilation	Diagnostic for pulmonary thromboembolism

Decreased uptake of the inhaled radioisotope may indicate an impaired ability to breathe, airway obstruction, or possible pneumonia.

Decreased circulation of the injected MAA indicates a problem with blood flow into or within the lungs. A localized area of decreased uptake, usually in a wedge shaped (or pie shaped) configuration with normal ventilation images (mismatched defect) suggests a pulmonary embolus or blood clot in the lungs, which leads to reduced perfusion.

Risks

Although this test uses radioactive materials, the total amount of radiation exposure is low. In order to decrease the radiation exposure in pregnant patients, the total radioactive dose may be decreased or the ventilation phase omitted. Computed tomography with radiocontrast can alternatively be performed. If breastfeeding, patient must be counselled to refrain from this activity for approximately 24 hours.

Chapter 19

Pneumonia Severity Index

The **pneumonia severity index [PSI]** or **PORT Score** is a clinical prediction rule that medical practitioners can use to calculate the probability of morbidity and mortality among patients with community acquired pneumonia.

Despite sometimes being used to predict the need for hospitalization in people with pneumonia, the PORT score was not developed to do so and should not be used in that way. Mortality prediction is similar to that when using CURB-65.

Development of the PSI

The rule uses demographics (whether someone is older, and is male or female), the coexistence of co-morbid illnesses, findings on physical examination and vital signs, and essential laboratory findings. This study demonstrated that patients could be stratified into five risk categories, Risk Classes I-V, and that these classes could be used to predict 30-day survival.

Data Source for Derivation & Validation

The rule was derived then validated with data from 38,000 patients from the MedisGroup Cohort Study for 1989, comprising 1 year of data from 257 hospitals across the US who used the MedisGroup patient outcome tracking software built and serviced by Mediquel Systems (Cardinal Health). One significant caveat to the data source was that patients who were discharged home or transferred from the MedisGroup hospitals could not be followed at the 30-day mark, and were therefore assumed to be "alive" at that time. Further validation was performed with the Pneumonia Patient Outcomes Research Team [PORT] (1991) cohort study. This categorization method has been replicated by others and is comparable to the CURB-65 in predicting mortality.

Usage & Application of the PSI

The purpose of the PSI is to classify the severity of a patient's pneumonia to determine the amount of resources to be allocated for care. Most commonly, the PSI scoring system has been used to decide whether patients with pneumonia can be treated as outpatients or as (hospitalized) inpatients. A **Risk Class I** pneumonia patient can be sent home on oral antibiotics. A **Risk Class II-III** pneumonia patient may be sent home with IV antibiotics

or treated and monitored for 24 hours in hospital. Patients with **Risk Class IV-V** pneumonia patient should be hospitalized for treatment.

The PSI Algorithm

The PSI Algorithm is detailed below. An online, automated PSI calculator is available on the US AHRQ website.

Step 1: Stratify to Risk Class I vs. Risk Classes II-V	
Presence of:	
Over 50 years of age	Yes/No
Altered mental status	Yes/No
Pulse \geq 125/minute	Yes/No
Respiratory rate >30/minute	Yes/No
Systolic blood pressure <90 mm Hg	Yes/No
Temperature <35°C or \geq 40°C	Yes/No
History of:	
Neoplastic disease	Yes/No
Congestive heart failure	Yes/No
Cerebrovascular disease	Yes/No
Renal disease	Yes/No
Liver disease	Yes/No
If any "Yes", then proceed to Step 2	
If all "No" then assign to Risk Class I	
Step 2: Stratify to Risk Class II vs III vs IV vs V	
Demographics	Points Assigned
If Male	+Age (yr)
If Female	+Age (yr) - 10
Nursing home resident	+10
Comorbidity	
Neoplastic disease	+30
Liver disease	+20
Congestive heart failure	+10
Cerebrovascular disease	+10
Renal disease	+10

Physical Exam Findings	
Altered mental status	+20
Pulse ≥ 125 /minute	+20
Respiratory rate >30 /minute	+20
Systolic blood pressure <90 mm Hg	+15
Temperature $<35^{\circ}\text{C}$ or $\geq 40^{\circ}\text{C}$	+10
Lab and Radiographic Findings	
Arterial pH <7.35	+30
Blood urea nitrogen ≥ 30 mg/dl (9 mmol/liter)	+20
Sodium <130 mmol/liter	+20
Glucose ≥ 250 mg/dl (14 mmol/liter)	+10
Hematocrit $<30\%$	+10
Partial pressure of arterial O ₂ <60 mmHg	+10
Pleural effusion	+10
$\Sigma <70 =$ Risk Class II	
$\Sigma 71-90 =$ Risk Class III	
$\Sigma 91-130 =$ Risk Class IV	
$\Sigma >130 =$ Risk Class V	

PSI Derivation and Validation Data

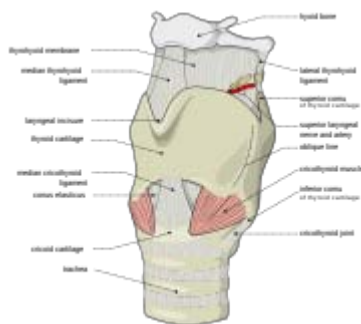
Risk Class	Medisgroup Study (1989)				PORT Validation Study (1991) Cohort					
	Derivation Cohort		Validation Cohort		Inpatients		Outpatients		All Patients	
	no. of pts	% died	no. of pts	% died	no. of pts	% died	no. of pts	% died	no. of pts	% died
I	1,372	0.4	3,034	0.1	185	0.5	587	0.0	772	0.1
II (<70)	2,412	0.7	5,778	0.6	233	0.9	244	0.4	477	0.6
III (71–90)	2,632	2.8	6,790	2.8	254	1.2	72	0.0	326	0.9
IV (91–130)	4,697	8.5	13,104	8.2	446	9.0	40	12.5	486	9.3
V (>130)	3,086	31.1	9,333	29.2	225	27.1	1	0.0	226	27.0
Total	14,199	10.2	38,039	10.6	1343	8.0	944	0.6	2287	5.2

Note: % Died refers to 30-day mortality.

Chapter 20

Cricothyrotomy

Intervention: Cricothyrotomy



In cricothyrotomy, the incision or puncture is made through the cricothyroid membrane in between the thyroid cartilage and the cricoid cartilage.

ICD-10 code:

ICD-9 code: 31.1

MeSH D014140

Other codes:

A **cricothyrotomy** (also called **thyrocricotomy**, **cricothyroidotomy**, **inferior laryngotomy**, **intercricothyrotomy**, **coniotomy** or **emergency airway puncture**) is an incision made through the skin and cricothyroid membrane to establish a patent airway during certain life-threatening situations, such as airway obstruction by a foreign body, angioedema, or massive facial trauma. Cricothyrotomy is nearly always performed as a last resort in cases where orotracheal and nasotracheal intubation are impossible or contraindicated. Cricothyrotomy is easier and quicker to perform than tracheotomy, does not require manipulation of the cervical spine, and is associated with fewer complications. However, while cricothyrotomy may be life-saving in extreme circumstances, this technique is only intended to be a temporizing measure until a definitive airway can be established.

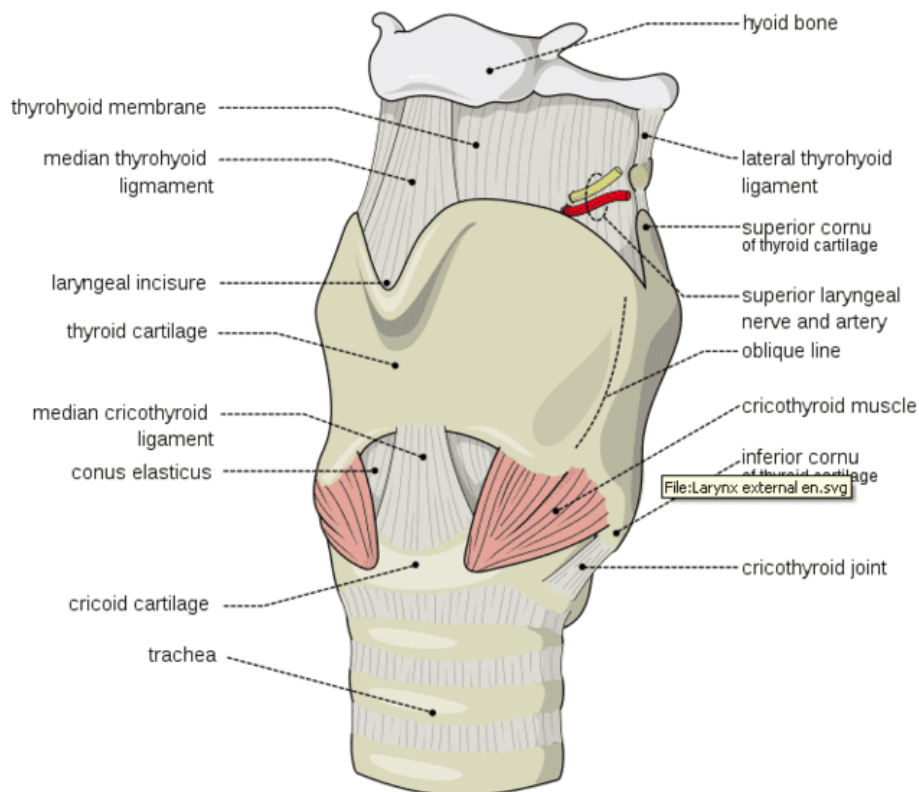
Indications

- Can't intubate
- Can't ventilate
- Severe facial or nasal injuries (that do not allow oral or nasal tracheal intubation)
- Massive midfacial trauma
- Possible cervical spine trauma preventing adequate ventilation
- Anaphylaxis
- Chemical inhalation injuries

Contraindications

- Inability to identify landmarks (cricothyroid membrane)
- Underlying anatomical abnormality (tumor)
- Tracheal transection
- Acute laryngeal disease due to infection or trauma
- Small children under 10 years old (a 12–14 gauge catheter over the needle may be safer)

Procedure



In cricothyrotomy, the incision or puncture is made through the cricothyroid membrane in between the thyroid cartilage and the cricoid cartilage.

The procedure was first described in 1805 by Vicq d'Azyr, a French surgeon and anatomist. A cricothyrotomy is generally performed by making a vertical incision on the skin of the neck just below the "Adam's apple", or thyroid cartilage, then making another transverse incision in the cricothyroid membrane which lies deep to this point. One then inserts a tube into this opening, which allows one to breathe for the patient with a machine or bag.

Technique

In a typical cricothyrotomy procedure, a scalpel is used to create a 1 cm vertical incision through the skin and the cricothyroid membrane, and the resulting hole is opened by either inserting the scalpel handle into the wound and rotating 90 degrees or by using a clamp. A tracheostomy tube or endotracheal tube with a 6 or 7 mm internal diameter is then inserted, the cuff is inflated, and the tube is secured. A bag-valve device with the highest available concentration of oxygen is used to provide ventilation, the success of which is assessed by bilateral auscultation and observation of the rise and fall of the chest. No attempts are made to remove the tracheostomy or endotracheal tube in a prehospital setting.

Cricothyrotomy in popular media

On the TV show *M*A*S*H*, Father Mulcahy performs an emergency cricothyrotomy on a patient. With the direction of Dr. Pierce via radio, he uses a pen knife and an eye dropper to perform the operation. Needless to say, this would be extremely dangerous in real life. Even under ideal, clinical conditions, a cricothyrotomy is difficult and requires specific tools, preparation and a practiced knowledge of anatomy. There are many major blood vessels and nerves in the neck and cutting there, even with the best of intentions carries a high risk of harming the patient.

In the 1980 Nicolas Roeg film "Bad Timing," Theresa Russell's character Milena Flaherty has an emergency cricothyrotomy performed following an intentional overdose.

In Grey's Anatomy, emergency cricothyrotomy is mentioned in at least three episodes:

- In "Owner of a Lonely Heart," Cristina almost performs an emergency cricothyrotomy on a patient who swallowed a light bulb. Before she is able to do so, however, Dr. Burke shows up and takes the patient to an operating room where he proceeds to perform an emergency thoracotomy.
- In "The Heart of the Matter," Izzie performs her first "emergency crike" on Camille, a niece of Chief of Surgery Dr. Richard Webber.
- In "I Saw What I Saw" Alex performs a "crike" on the patient who later dies.

In the ER episode, "Reason to Believe" Dr. Kerry Weaver performs an emergency cricothyrotomy on a student. She is shooting a news segment on childhood obesity in an elementary school cafeteria when one of the students begins to choke; after the heimlich maneuver fails, she performs a cricothyrotomy with a kitchen knife and a drinking straw.

It is also used many other times, especially in the trauma room, when an airway can't be established.

In the movie, "Playing God" (1997), David Duchovny plays a famed LA surgeon, stripped of his license due to drug abuse, who finds himself witnessing a gun fight at a bar. He saves a mafia crime figure by performing an emergency cricothyrotomy. This endears him with the mafia family and drives the plot forward.

In the BBC3 medical drama Bodies, the main protagonist Rob Lake, a newly appointed obstetrics and gynaecology registrar (played by Max Beesley), is called to a patient who is having difficulty breathing due to anaphylaxis. Lake calls for emergency assistance, but impatient and fearing for the patient's life decides to undertake a cricothyrotomy himself - a procedure he has not been trained in. The procedure is unsuccessful and the patient dies before help arrives. The guilt surrounding the event combined with the covering up by his consultant provides an important backdrop to the further development of the character and his relationship with his consultant.

Chapter 21

Bronchoscopy and Positive Pressure Ventilation

Bronchoscopy



A physician performing bronchoscopy

Bronchoscopy is a technique of visualizing the inside of the airways for diagnostic and therapeutic purposes. An instrument (bronchoscope) is inserted into the airways, usually through the nose or mouth, or occasionally through a tracheostomy. This allows the practitioner to examine the patient's airways for abnormalities such as foreign bodies, bleeding, tumors, or inflammation. Specimens may be taken from inside the lungs. The construction of bronchoscopes ranges from rigid metal tubes with attached lighting devices to flexible optical fiber instruments with realtime video equipment.

History

A German, Gustav Killian, performed the first bronchoscopy in 1897. From then until the 1970s, rigid bronchoscopes were used exclusively. Killian used rigid bronchoscopy to remove a pork bone. The procedure was done in an awake patient using topical cocaine as a local anesthetic.

An American, [Nathan Faux], refined the rigid bronchoscope in the 1920s, using this rigid tube to visually inspect the trachea and mainstem bronchi.

A Japanese, Shigeto Ikeda, invented the flexible bronchoscope in 1966. The flexible scope initially employed fiberoptic bundles requiring an external light source for illumination. These scopes had outside diameters of approximately 5 mm to 6 mm, with an ability to flex 180 degrees and to extend 120 degrees, allowing entry into lobar and segmental bronchi. More recently, fiberoptic scopes have been replaced by bronchoscopes with a charge coupled device (CCD) video chip located at their distal extremity.

Types

Rigid

Rigid bronchoscopy is used for retrieving foreign objects. Massive hemoptysis, defined as loss of >600 mL of blood in 24 hours, is a medical emergency and should be addressed with initiation of intravenous fluids and examination with rigid bronchoscopy. The larger lumen of the rigid bronchoscope versus the narrow lumen of the flexible bronchoscope allows for therapeutic approaches such as electrocautery to help control the bleeding.

Flexible (fiberoptic)

A flexible bronchoscope is longer and thinner than a rigid bronchoscope. It contains a fiberoptic system that transmits an image from the tip of the instrument to an eyepiece or video camera at the opposite end. Using Bowden cables connected to a lever at the hand piece, the tip of the instrument can be oriented, allowing the practitioner to navigate the instrument into individual lobe or segment bronchi. Most flexible bronchoscopes also include a channel for suctioning or instrumentation, but these are significantly smaller than those in a rigid bronchoscope.

Flexible bronchoscopy causes less discomfort for the patient than rigid bronchoscopy and the procedure can be performed easily and safely under moderate sedation. It is the technique of choice nowadays for most bronchoscopic procedures.

Purposes

Diagnostic

- To view abnormalities of the airway
- To obtain tissue specimens of the lung in a variety of disorders. Specimens may be taken from inside the lungs by biopsy, bronchoalveolar lavage, or endobronchial brushing.
- To evaluate a person who has bleeding in the lungs, possible lung cancer, a chronic cough, sarcoidosis

Therapeutic

- To remove secretions, blood, or foreign objects lodged in the airway
- Laser resection of tumors or benign tracheal and bronchial strictures
- Stent insertion to palliate extrinsic compression of the tracheobronchial lumen from either malignant or benign disease processes
- Bronchoscopy is also employed in percutaneous tracheostomy

- Tracheal intubation of patients with difficult airways is often performed using a flexible bronchoscope

Procedure

Bronchoscopy can be performed in a special room designated for such procedures, operating room, intensive care unit, or other location with resources for the management of airway emergencies. The patient will often be given antianxiety and antisecretory medications (to prevent oral secretions from obstructing the view), generally atropine, and sometimes an analgesic such as morphine. During the procedure, sedatives such as midazolam or propofol may be used. A local anesthetic is often given to anesthetise the mucous membranes of the pharynx, larynx, and trachea. The patient is monitored during the procedure with periodic blood pressure checks, continuous ECG monitoring of the heart, and pulse oximetry.

A *flexible* bronchoscope is inserted with the patient in a sitting or supine position. Once the bronchoscope is inserted into the upper airway, the vocal cords are inspected. The instrument is advanced to the trachea and further down into the bronchial system and each area is inspected as the bronchoscope passes. If an abnormality is discovered, it may be sampled, using a brush, a needle, or forceps. Specimen of lung tissue (transbronchial biopsy) may be sampled using a real-time x-ray (fluoroscopy). Flexible bronchoscopy can also be performed on intubated patients, such as patients in intensive care. In this case, the instrument is inserted through an adapter connected to the tracheal tube.

Rigid bronchoscopy is performed under general anesthesia. Rigid bronchoscopes are too large to allow parallel placement of other devices in the trachea; therefore the anesthesia apparatus is connected to the bronchoscope and the patient is ventilated through the bronchoscope.

Recovery

Although most patients tolerate bronchoscopy well, a brief period of observation is required after the procedure. Most complications occur early and are readily apparent at the time of the procedure. The patient is assessed for respiratory difficulty (stridor and dyspnea resulting from laryngeal edema, laryngospasm, or bronchospasm). Monitoring continues until the effects of sedative drugs wear off and gag reflex has returned. If the patient has had a transbronchial biopsy, doctors may take a chest x-ray to rule out any air leakage in the lungs (pneumothorax) after the procedure. The patient will be hospitalized if there occurs any bleeding, air leakage (pneumothorax), or respiratory distress.

Complications and Risks

Besides the risks associated with the drug used, there are also specific risks of the procedure. Although a rigid bronchoscope can scratch or tear airways or damage the vocal cords, the risk of bronchoscopy is limited. Complications from fiberoptic bronchoscopy remain extremely low. Common complications include excessive bleeding following biopsy. A lung biopsy also may cause leakage of air, called pneumothorax. Pneumothorax occurs in less than 1% of lung biopsy cases . Laryngospasm is a rare complication but may sometimes require intubation. Patients with tumors or significant bleeding may experience increased difficulty breathing after a bronchoscopic procedure, sometimes due to swelling of the mucous membranes of the airways.

Positive pressure ventilation

In emergency medicine **positive pressure ventilation (PPV)** refers to the process of forcing air into the lungs of a (usually apneic or dyspneic) patient, usually using a bag valve mask (BVM) or mechanical ventilator.

"NIPPV" is an abbreviation for "nasal intermittent positive pressure ventilation" or "non-invasive positive pressure ventilation".

During normal breathing, air is drawn into the lungs from the outside by the expansion of the chest wall and contraction of the diaphragm to increase volume inside the thoracic cavity. If the airway is sealed, the expansion of the thoracic cavity creates negative pressure inside the lungs relative to the atmospheric pressure outside the body. Hence, during normal breathing air is said to be drawn into the lungs by negative pressure.

Positive pressure ventilation, however, works by forcing air into the lungs and thereby increasing the pressure inside the airway relative to the outside. Hence the name "positive pressure." Aside from the obvious advantage of ventilating an otherwise apneic or dyspneic patient, PPV can be effectively used in the treatment of flail segments, which characteristically render negative pressure breathing ineffective, but does not impede PPV.

Positive pressure ventilation is also used in fire fighting to blow smoke out of a room or structure.

Chapter 22

Mechanical Ventilation

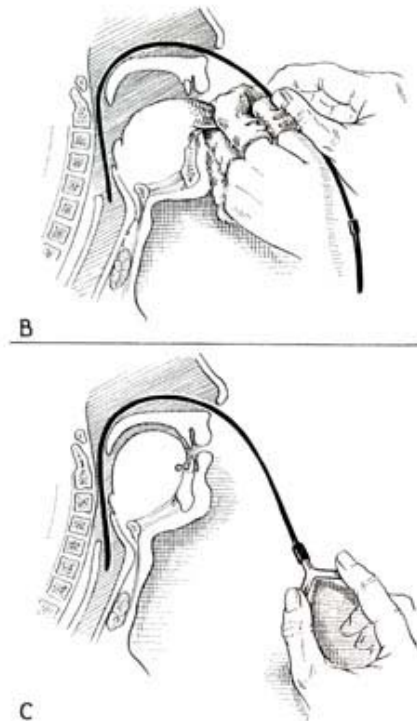


FIGURE 69.—Continued. B. Forward fixation of larynx with left hand, by holding tongue forward with gauze-covered fingers. With the right hand, the catheter is rapidly advanced through the nares and past the glottis as the patient inspires deeply. If he is comatose, a mouth gag is used, and the epiglottis is picked up with the left forefinger. The catheter is then guided through the larynx. C. Advancement of catheter into trachea by intermittent suction over Y-tube. Once it is in trachea, it is moved back and forth to stimulate coughing.

Nasotracheal intubation

In medicine, **mechanical ventilation** is a method to mechanically assist or replace spontaneous breathing.

This may involve a machine called a ventilator or the breathing may be assisted by a physician or other suitable person compressing a bag or set of bellows. Traditionally divided into negative-pressure ventilation, where air is essentially sucked into the lungs, or positive pressure ventilation, where air (or another gas mix) is pushed into the trachea.

It can be used as a short term measure, for example during an operation or critical illness (often in the setting of an intensive care unit). It may be used at home or in a nursing or rehabilitation institution if patients have chronic illnesses that require long-term ventilatory assistance.

Owing to the anatomy of the human pharynx, larynx, and esophagus and the circumstances for which ventilation is required then additional measures are often required to "secure" the airway during positive pressure ventilation to allow unimpeded passage of air into the trachea and avoid air passing into the esophagus and stomach. Commonly this is by insertion of a tube into the trachea which provides a clear route for the air. This can be either an endotracheal tube, inserted through the natural openings of mouth or nose or a tracheostomy inserted through an artificial opening in the neck. In other circumstances simple airway manoeuvres, an oropharyngeal airway or laryngeal mask airway may be employed. If the patient is able to protect their own airway such as in non-invasive ventilation or negative-pressure ventilation then no airway adjunct may be needed.

Mechanical ventilation is often a life-saving intervention, but carries many potential complications including pneumothorax, airway injury, alveolar damage, and ventilator-associated pneumonia..

In many healthcare systems prolonged ventilation as part of intensive care is a limited resource (in that there are only so many patients that can receive care at any given moment). It is used to support a single failing organ system (the lungs) and cannot reverse any underlying disease process (such as terminal cancer). For this reason there can be (occasionally difficult) decisions to be made about whether it is suitable to commence someone on mechanical ventilation. Equally many ethical issues surround the decision to discontinue mechanical ventilation.

History

The Roman physician Galen may have been the first to describe mechanical ventilation: "If you take a dead animal and blow air through its larynx [through a reed], you will fill its bronchi and watch its lungs attain the greatest distention." Vesalius too describes ventilation by inserting a reed or cane into the trachea of animals. In 1908 George Poe demonstrated his mechanical respirator by asphyxiating dogs and seemingly bringing them back to life.

Negative pressure machines



An Iron Lung

The iron lung, also known as the Drinker and Shaw tank, was developed in 1929 and was one of the first negative-pressure machines used for long-term ventilation. It was refined and used in the 20th century largely as a result of the polio epidemic that struck the world in the 1940s. The machine is effectively a large elongated tank, which encases the patient up to the neck. The neck is sealed with a rubber gasket so that the patient's face (and airway) are exposed to the room air.

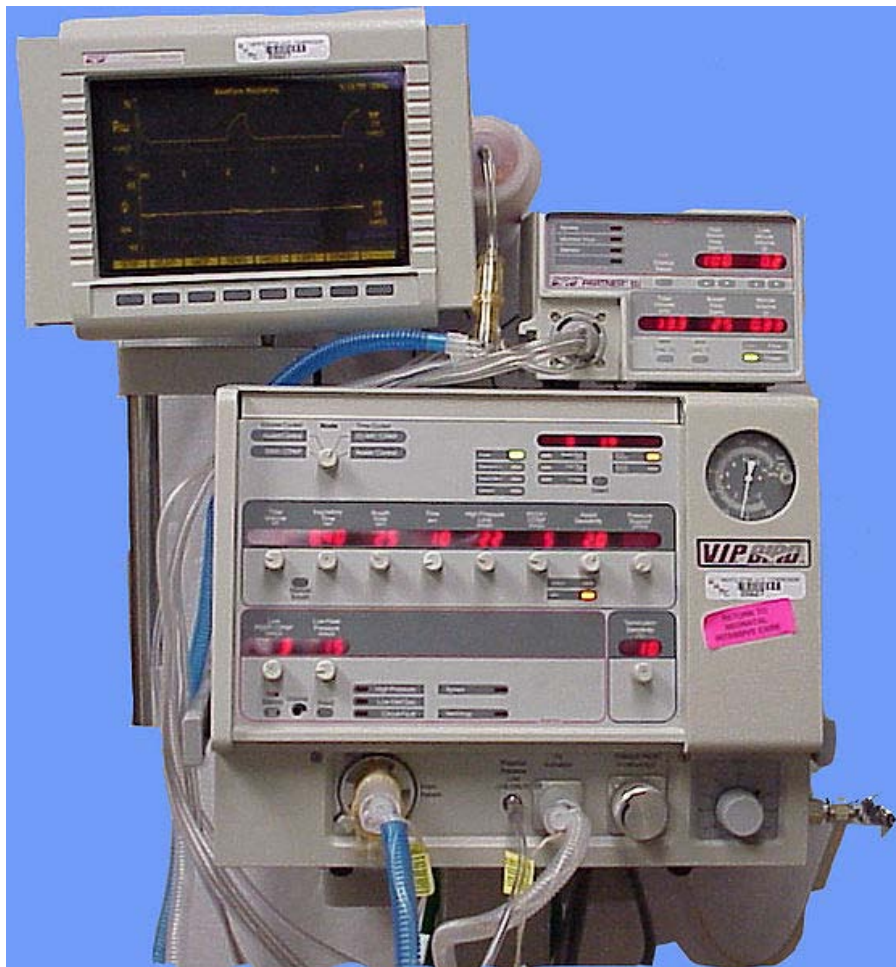
While the exchange of oxygen and carbon dioxide between the bloodstream and the pulmonary airspace works by diffusion and requires no external work, air must be moved into and out of the lungs to make it available to the gas exchange process. In spontaneous breathing, a negative pressure is created in the pleural cavity by the muscles of respiration, and the resulting gradient between the atmospheric pressure and the pressure inside the thorax generates a flow of air.

In the iron lung by means of a pump, the air is withdrawn mechanically to produce a vacuum inside the tank, thus creating negative pressure. This negative pressure leads to expansion of the chest, which causes a decrease in intrapulmonary pressure, and increases flow of ambient air into the lungs. As the vacuum is released, the pressure inside the tank equalizes to that of the ambient pressure, and the elastic coil of the chest and lungs leads to passive exhalation. However, when the vacuum is created, the abdomen also expands

along with the lung, cutting off venous flow back to the heart, leading to pooling of venous blood in the lower extremities. There are large portholes for nurse or home assistant access. The patients can talk and eat normally, and can see the world through a well-placed series of mirrors. Some could remain in these iron lungs for years at a time quite successfully.

Today, negative pressure mechanical ventilators are still in use, notably with the Polio Wing Hospitals in England such as St. Thomas' (by Westminster in London) and the John Radcliffe in Oxford. The prominent device used is a smaller device known as the cuirass. The cuirass is a shell-like unit, creating negative pressure only to the chest using a combination of a fitting shell and a soft bladder. Its main use is in patients with neuromuscular disorders who have some residual muscular function. However, it was prone to falling off and caused severe chafing and skin damage and was not used as a long term device. In recent years this device has re-surfaced as a modern polycarbonate shell with multiple seals and a high pressure oscillation pump in order to carry out biphasic cuirass ventilation.

Positive pressure machines



Neonatal mechanical ventilator

The design of the modern positive-pressure ventilators were mainly based on technical developments by the military during World War II to supply oxygen to fighter pilots in high altitude. Such ventilators replaced the iron lungs as safe endotracheal tubes with high volume/low pressure cuffs were developed. The popularity of positive-pressure ventilators rose during the polio epidemic in the 1950s in Scandinavia and the United States and was the beginning of modern ventilation therapy. Positive pressure through manual supply of 50% oxygen through a tracheostomy tube led to a reduced mortality rate among patients with polio and respiratory paralysis. However, because of the sheer amount of man-power required for such manual intervention, mechanical positive-pressure ventilators became increasingly popular.

Positive-pressure ventilators work by increasing the patient's airway pressure through an endotracheal or tracheostomy tube. The positive pressure allows air to flow into the airway until the ventilator breath is terminated. Subsequently, the airway pressure drops to zero, and the elastic recoil of the chest wall and lungs push the tidal volume -- the breath—out through passive exhalation.

Indications for use

Mechanical ventilation is indicated when the patient's spontaneous ventilation is inadequate to maintain life. It is also indicated as prophylaxis for imminent collapse of other physiologic functions, or ineffective gas exchange in the lungs. Because mechanical ventilation only serves to provide assistance for breathing and does not cure a disease, the patient's underlying condition should be correctable and should resolve over time. In addition, other factors must be taken into consideration because mechanical ventilation is not without its complications (*see below*)

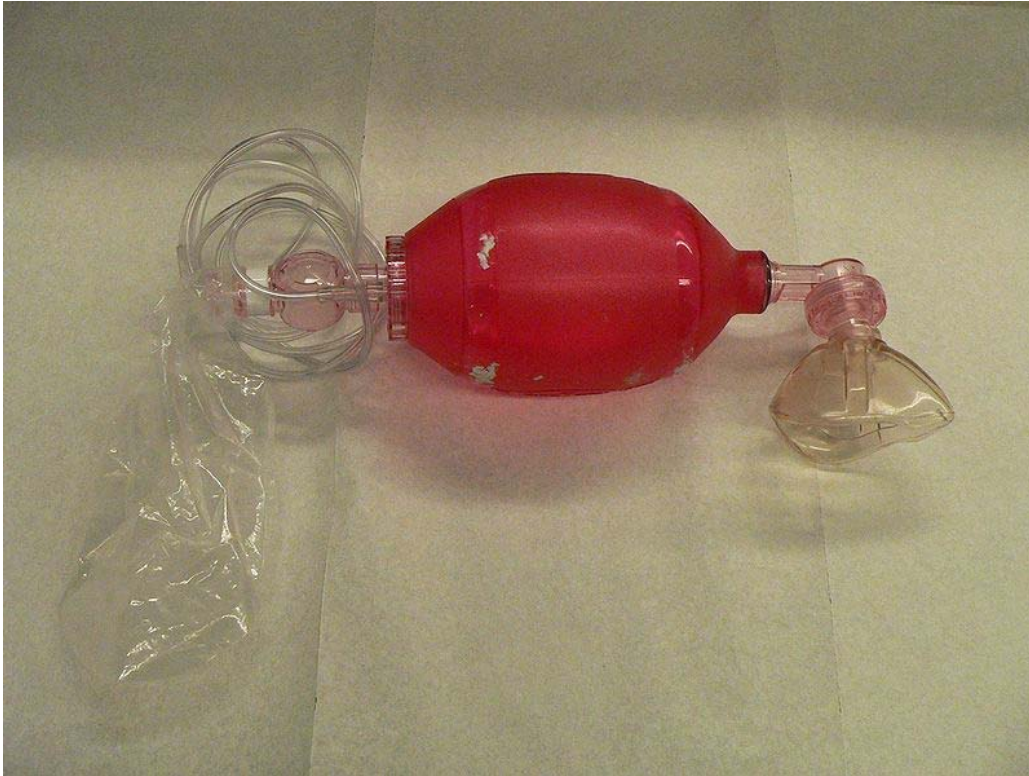
Common medical indications for use include:

- Acute lung injury (including ARDS, trauma)
- Apnea with respiratory arrest, including cases from intoxication
- Chronic obstructive pulmonary disease (COPD)
- Acute respiratory acidosis with partial pressure of carbon dioxide ($p\text{CO}_2$) > 50 mmHg and $\text{pH} < 7.25$, which may be due to paralysis of the diaphragm due to Guillain-Barré syndrome, Myasthenia Gravis, spinal cord injury, or the effect of anaesthetic and muscle relaxant drugs
- Increased work of breathing as evidenced by significant tachypnea, retractions, and other physical signs of respiratory distress
- Hypoxemia with arterial partial pressure of oxygen (PaO_2) with supplemental fraction of inspired oxygen (FiO_2) < 55 mm Hg
- Hypotension including sepsis, shock, congestive heart failure
- Neurological diseases such as Muscular Dystrophy and Amyotrophic Lateral Sclerosis

Types of ventilators

Ventilation can be delivered via:

- Hand-controlled ventilation such as:



SMART BAG MO Bag-Valve-Mask Resuscitator

- Bag valve mask
- Continuous-flow or Anaesthesia (or T-piece) bag
- A mechanical ventilator. Types of mechanical ventilators include:
 - Transport ventilators. These ventilators are small, more rugged, and can be powered pneumatically or via AC or DC power sources.
 - ICU ventilators. These ventilators are larger and usually run on AC power (though virtually all contain a battery to facilitate intra-facility transport and as a back-up in the event of a power failure). This style of ventilator often provides greater control of a wide variety of ventilation parameters (such as inspiratory rise time). Many ICU ventilators also incorporate graphics to provide visual feedback of each breath.
 - NICU ventilators. Designed with the preterm neonate in mind, these are a specialized subset of ICU ventilators which are designed to deliver the smaller, more precise volumes and pressures required to ventilate these patients.

- PAP ventilators. these ventilators are specifically designed for non-invasive ventilation. this includes ventilators for use at home, in order to treat sleep apnea.

Modes of ventilation

Conventional ventilation

The modes of ventilation can be thought of as classifications based on how to control the ventilator breath. Traditionally ventilators were classified based on how they determined when to stop giving a breath. The three traditional categories of ventilators are listed below. As microprocessor technology is incorporated into ventilator design, the distinction among these types has become less clear as ventilators may use combinations of all of these modes as well as flow-sensing, which controls the ventilator breath based on the flow-rate of gas versus a specific volume, pressure, or time.

Breath termination

Modes of ventilation are classified by the means that they determine the inspired breath is complete. This is sensed by either pressure or volume.

- Volume ventilation - A predetermined tidal volume (V_t) is set for the patient and is delivered with each inspiration. The amount of pressure necessary to deliver this volume will fluctuate from breath to breath based on the resistance and compliance of the patient and ventilator circuit. If the tidal volume is set at 500ml, the ventilator will continue to inspire gas until it reaches its goal. Upon completion of the inspired volume, the ventilator will open a valve allowing the patient to passively exhale.
- Pressure ventilation - A predetermined peak inspiratory pressure (PIP) is determined based on the patient's condition and pathophysiology. The ventilator will flow gas into the patient until this set pressure is reached. Upon reaching the preset PIP, the ventilator allows for passive exhalation. Caution and close observation must be given in this mode due to potential for either hypoventilation or hyperventilation because the tidal volume is variable.

Several manufactures have incorporated features from both of these modes in an attempt to accommodate patients needs.

These modes are flow-variable, volume-targeted, pressure-regulated, time-limited modes (for example, pressure regulated volume control - PRVC). This means that instead of providing an exact tidal volume each breath, a target volume is set and the ventilator will vary the inspiratory flow at each breath to achieve the target volume at the lowest possible peak pressure. The inspiratory time (T_i) limits the length of the inspiratory cycle and therefore the I:E ratio. Pressure regulated modes such as PRVC, Auto-flow (Draeger) or Average Volume Assured Pressure Support (AVAPS) from Philips can most

easily be thought of as turning a volume mode into a pressure mode with the added benefit of maintaining more control over tidal volume than with strictly pressure-control.

Breath initiation

The other method of classifying mechanical ventilation is based on how to determine when to start giving a breath. Similar to the termination classification noted above, microprocessor control has resulted in a myriad of hybrid modes that combine features of the traditional classifications. Note that most of the timing initiation classifications below can be combined with any of the termination classifications listed below.

- **Assist Control (AC).** In this mode the ventilator provides a mechanical breath with either a pre-set tidal volume or peak pressure every time the patient initiates a breath. Traditional assist-control used only a pre-set tidal volume—when a preset peak pressure is used this is also sometimes termed Intermittent Positive Pressure Ventilation or IPPV. However, the initiation timing is the same—both provide a ventilator breath with every patient effort. In most ventilators a back-up minimum breath rate can be set in the event that the patient becomes apnoeic. Although a maximum rate is not usually set, an alarm can be set if the ventilator cycles too frequently. This can alert that the patient is tachypneic or that the ventilator may be auto-cycling (a problem that results when the ventilator interprets fluctuations in the circuit due to the last breath termination as a new breath initiation attempt).
- **Synchronized Intermittent Mandatory Ventilation (SIMV).** In this mode the ventilator provides a pre-set mechanical breath (pressure or volume limited) every specified number of seconds (determined by dividing the respiratory rate into 60 seconds - thus a respiratory rate of 12 results in a 5 second cycle time). Within that cycle time the ventilator waits for the patient to initiate a breath using either a pressure or flow sensor. When the ventilator senses the first patient breathing attempt within the cycle, it delivers the preset ventilator breath. If the patient fails to initiate a breath, the ventilator delivers a mechanical breath at the end of the breath cycle. Additional spontaneous breaths after the first one within the breath cycle do not trigger another SIMV breath. However, SIMV may be combined with pressure support (see below). SIMV is frequently employed as a method of decreasing ventilatory support (weaning) by turning down the rate, which requires the patient to take additional breaths beyond the SIMV triggered breath.
- **Controlled Mechanical Ventilation (CMV).** In this mode the ventilator provides a mechanical breath on a preset timing. Patient respiratory efforts are ignored. This is generally uncomfortable for children and adults who are conscious and is usually only used in an unconscious patient. It may also be used in infants who often quickly adapt their breathing pattern to the ventilator timing.
- **Pressure Support Ventilation (PSV).** When a patient attempts to breathe spontaneously through an endotracheal tube, the narrowed diameter of the airway results in higher resistance to airflow, and thus a higher work of breathing. PSV was developed as a method to decrease the work of breathing in-between ventilator mandated breaths by providing an elevated pressure triggered by

spontaneous breathing that "supports" ventilation during inspiration. Thus, for example, SIMV might be combined with PSV so that additional breaths beyond the SIMV programmed breaths are supported. However, while the SIMV mandated breaths have a preset volume or peak pressure, the PSV breaths are designed to cut short when the inspiratory flow reaches a percentage of the peak inspiratory flow (e.g. 10-25%). New generation of ventilators provides user-adjustable inspiration cycling off threshold, and some even are equipped with automatic inspiration cycling off threshold function. This helps the patient ventilator synchrony. The peak pressure set for the PSV breaths is usually a lower pressure than that set for the full ventilator mandated breath. PSV can be also be used as an independent mode.

- Continuous Positive Airway Pressure (CPAP). A continuous level of elevated pressure is provided through the patient circuit to maintain adequate oxygenation, decrease the work of breathing, and decrease the work of the heart (such as in left-sided heart failure — CHF). Note that no cycling of ventilator pressures occurs and the patient must initiate all breaths. In addition, no additional pressure above the CPAP pressure is provided during those breaths. CPAP may be used invasively through an endotracheal tube or tracheostomy or non-invasively with a face mask or nasal prongs.
- Positive end-expiratory pressure (PEEP) is functionally the same as CPAP, but refers to the use of an elevated pressure during the expiratory phase of the ventilatory cycle. After delivery of the set amount of breath by the ventilator, the patient then exhales passively. The volume of gas remaining in the lung after a normal expiration is termed the *functional residual capacity* (FRC). The FRC is primarily determined by the elastic qualities of the lung and the chest wall. In many lung diseases, the FRC is reduced due to collapse of the unstable alveoli, leading to a decreased surface area for gas exchange and intrapulmonary shunting (*see above*), with wasted oxygen inspired. Adding PEEP can reduce the work of breathing (at low levels) and help preserve FRC.

APRV (Airway Pressure Release Ventilation)

APRV begins from an elevated baseline (called P_{high} or measured high pressure) and achieves tidal ventilation with a brief release of the P_{high} . This brief release allows CO_2 removal through passive exhalation secondary to elastic recoil. The exhalation time (T_{low}) is shortened to usually less than one second to prevent alveolar derecruitment and collapse - it is essentially CPAP with a brief release.

Ever increasing empirical evidence and clinical experience is showing that APRV is the primary mode to use when ventilating a patient with ARDS or ALI (Acute Lung Injury).

Advantages to APRV ventilation include: decreased airway pressures, decreased minute ventilation, decreased dead-space ventilation, promotion of spontaneous breathing, almost 24 hour a day alveolar recruitment, decreased use of sedation, near elimination of neuromuscular blockade, optimized arterial blood gas results, mechanical restoration of FRC (functional residual capacity), a positive effect on cardiac output (due to the

negative inflection from the elevated baseline with each spontaneous breath), increased organ and tissue perfusion, potential for increased urine output due to increased renal perfusion.

A patient with ARDS on average spends 8 to 11 days on a mechanical ventilator; APRV may reduce this time significantly and therefore reduce the incidence of VAP (ventilator acquired pneumonia), a risk that increases with each hour an intubated patient spends on the ventilator (VAP rate is 100% at 100 days on the vent) and carries with it a near 50% mortality rate. So, hospitals that are reporting a 0% incidence of VAP, may be improperly coding or improperly reporting.

** A controlled clinical trial testing APRV against the current ARDSNet protocol must be initiated.*

High Frequency Ventilation (HFV)



Sensormedics 3100 High Frequency ventilator

High-Frequency Ventilation refers to ventilation that occurs at rates significantly above that found in natural breathing (as high as 240-900 "breaths" per minute). Within the category of high-frequency ventilation, the three principal types are high-frequency jet ventilation (HFJV), high-frequency flow interruption (HFFI), and high-frequency oscillatory ventilation (HFOV).

High Frequency Jet Ventilation employs an endotracheal tube adaptor in place for the normal 15 mm ET tube adaptor. A high pressure "jet" of gas flows out of the adaptor and into the airway. This jet of gas occurs for a very brief duration, about 0.02 seconds, and at high frequency: 4-11 hertz. Tidal volumes ≤ 1 ml/Kg are used during HFJV. This combination of small tidal volumes delivered for very short periods of time create the lowest possible distal airway and alveolar pressures produced by a mechanical ventilator. Exhalation is passive. Jet ventilators utilize various I:E ratios--between 1:1.1 and 1:12--to help achieve optimal exhalation. Conventional mechanical breaths are sometimes used to aid in reinflating the lung. Optimal PEEP is used to maintain alveolar inflation and promote ventilation-to-perfusion matching. Jet ventilation has been shown to reduce ventilator induced lung injury by as much as 20%.

"HFFI" operates similarly to a conventional ventilator, providing increased circuit pressure during the inspiratory phase and dropping back to PEEP during the expiratory phase.

In "HFOV" the pressure wave is driven by an electromagnetically controlled diaphragm similar to a loudspeaker. Because this can rapidly change the volume in the circuit, HFOV can produce a pressure that is lower than ambient pressure during the expiratory phase. This is sometimes called "active" expiration. In both types of high-frequency ventilation the pressure wave that is generated at the ventilator is markedly attenuated by passage down the endotracheal tube and the major conducting airways. This helps protect the alveoli from volutrauma that occurs with traditional positive pressure ventilation. Although the alveoli are kept at a relatively constant volume, similar to CPAP, other mechanisms of gas exchange allow ventilation (the removal of CO₂) to occur without tidal volume exchange. Ventilation in HFOV is a function of frequency, amplitude, and I:E ratio and is best described graphically as the area under the curve of an oscillatory cycle. Amplitude is analogous to tidal volume in conventional ventilation; larger amplitudes remove more CO₂. Seemingly paradoxical, lower frequencies remove more CO₂ in HFOV whereas in conventional ventilation the opposite is true. As frequency decreases, there is less attenuation of the pressure wave transmitted to the alveoli. This results in increased mixing of gas and thus ventilation. I-time is set as a percentage of total time (usually 33%). Innovations in HFOV technology (Vision α , Novalung) facilitate a better CO₂ removal, allowing for CO₂ removal at higher oscillatory frequencies, without the need to modify I-time. Amplitude is a function of power and is subject to variability due to changes in compliance or resistance. Therefore, power requirements may vary significantly during treatment and from patient to patient. Patient characteristics and ventilator settings determine whether PaCO₂ changes may be more sensitive to amplitude or frequency manipulation. In HFOV, mean airway pressure (MAP) is delivered via a continuous flow through the patient circuit which passes

through a variable restriction valve (mushroom valve) on the expiratory limb. Increasing the flow through the circuit and/or increasing the pressure in the mushroom valve increases MAP. The MAP in HFOV functions similarly to PEEP in conventional ventilation in that it provides the pressure for alveolar recruitment.

Non-invasive ventilation (Non-invasive Positive Pressure Ventilation or NIPPV)

This refers to all modalities that assist ventilation without the use of an endotracheal tube. Non-invasive ventilation is primarily aimed at minimizing patient discomfort and the complications associated with invasive ventilation. It is often used in cardiac disease, exacerbations of chronic pulmonary disease, sleep apnea, and neuromuscular diseases. Non-invasive ventilation refers only to the patient interface and not the mode of ventilation used; modes may include spontaneous or control modes and may be either pressure or volume modes.

Some commonly used modes of NIPPV include:

- Continuous positive airway pressure (CPAP).
- Bi-level Positive Airway Pressure (BIPAP). Pressures alternate between Inspiratory Positive Airway Pressure (IPAP) and a lower Expiratory Positive Airway Pressure (EPAP), triggered by patient effort. On many such devices, backup rates may be set, which deliver IPAP pressures even if patients fail to initiate a breath.(Wheatley 2000 et al)
- Intermittent positive pressure ventilation (IPPV) via mouthpiece or mask
- Biphasic Cuirass Ventilation A form of non-invasive ventilation that uses a cuirass instead of a facemask. Allows active control of both inspiration and exhalation.

Proportional Assist Ventilation (PAV)

Proportional Assist Ventilation (PAV) is a form of synchronised ventilator support based upon the Equation of Motion in which the ventilator generates pressure in proportion to the instantaneous patient effort. Unlike other modes of partial support, there is no target flow, tidal volume or pressure. PAV's objective is to allow the patient to attain ventilation and breathing pattern his ventilatory control system desires. The main operational advantages of PAV are automatic synchrony with inspiratory efforts, exhalation and adaptability to change in ventilatory demand.

Proportional Assist Ventilation Plus — PAV+ (Puritan Bennett – 840 ventilator range, **Proportional Pressure Support — PPS** (Drager Evita series)and Respironics BiPAP Vision PAV , are commercially available implementations of PAV which automatically amplify the patient's own spontaneous effort to breathe by increasing airway pressure during inspiration proportionally to a set amplification factor.

In PAV+, the level of amplification, thus the level of work of breathing, is set through a single setting (%support) and the pressure applied is continuously and automatically

adjusted based on measures (including automatic assessment of Elastance and Resistance) taken throughout the inspiratory cycle to maintain an appropriate level of support.

Adaptive Support Ventilation (ASV)

Adaptive Support Ventilation (ASV) is a positive pressure mode of mechanical ventilation that is closed-loop controlled. In this mode, the frequency and tidal volume of breaths of a patient on the ventilator are automatically adjusted based on the patient's requirements. The lung mechanics data are used to adjust the depth and rate of breaths to minimize the work rate of breathing. In the ASV mode, every breath is synchronized with patient effort if such an effort exists, and otherwise, full mechanical ventilation is provided to the patient.

ASV technology was originally described as one of the embodiments of US Patent No. 4986268. In this invention, a modified version of an equation derived in physiology in 1950 to minimize the work rate of breathing in man, was used for the first time to find the optimum frequency of mechanical ventilation. The rationale was to make the patient's breathing pattern comfortable and natural within safe limits, and thereby stimulate spontaneous breathing and reduce the weaning time. A prototype of the system was built by the inventor in late 1980s. The inventor is Dr. Fleur T. Tehrani who is a university professor in the US. Shortly after the Patent was issued in 1991, Hamilton Medical, a ventilator manufacturing company, contacted the inventor and discussed marketing the technology with her. Some years later, Hamilton Medical marketed this closed-loop technique under license of this Patent as ASV.

Since the issuance of the Patent, a number of articles have been published by the inventor and her colleagues that are related to the invention, and some of them describe further advancements of the closed-loop techniques presented in the Patent.

Neurally Adjusted Ventilatory Assist (NAVA)

Neurally Adjusted Ventilatory Assist (NAVA) is a unique positive pressure mode to mechanical ventilation based on neural respiratory output, in connections with invasive and non-invasive NAVA.

The act of taking a breath is controlled by the respiratory center of the brain, which decides the characteristics of each breath, timing and size. The respiratory center sends a signal along the phrenic nerve, excites the diaphragm muscle cells, leading to muscle contraction and descent of the diaphragm dome. As a result, the pressure in the airway drops, causing an inflow of air into the lungs.

With NAVA, the electrical activity of the diaphragm (Edi) is captured, fed to the ventilator and used to assist the patient's breathing in synchrony with and in proportion to the patient's own efforts, regardless of patient category or size. As the work of the ventilator and the diaphragm is controlled by the same signal, coupling between the

diaphragm and the SERVO-i ventilator is synchronized simultaneously. Reference: New method permits neural control of mechanical ventilation

Choosing amongst ventilator modes

Assist-control mode minimizes patient effort by providing full mechanical support with every breath. This is often the initial mode chosen for adults because it provides the greatest degree of support. In patients with less severe respiratory failure, other modes such as SIMV may be appropriate. Assist-control mode should not be used in those patients with a potential for respiratory alkalosis, in which the patient has an increased respiratory drive. Such hyperventilation and hypocapnia (decreased systemic carbon dioxide due to hyperventilation) usually occurs in patients with end-stage liver disease, hyperventilatory sepsis, and head trauma. Respiratory alkalosis will be evident from the initial arterial blood gas obtained, and the mode of ventilation can then be changed if so desired.

Positive End Expiratory Pressure may or may not be employed to prevent atelectasis in adult patients. It is almost always used for pediatric and neonatal patients due to their increased tendency for atelectasis.

High frequency oscillation is used most frequently in neonates, but is also used as an always alternative mode in adults with severe ARDS.

Pressure Regulated Volume Control is another option.

Initial ventilator settings

The following are general guidelines that may need to be modified for the individual patient.

As a general rule, whenever possible, spontaneous breathing must be maintained or supported, to avoid muscular atrophy of the diaphragm (Ventilator Induced Dysfunction of Diaphragm, VIDDD) . To limit VALI and VILI, protective ventilation pattern should be applied to the patient. If this results in severe hypercapnia, exceeding accepted levels for permissive hypercapnia (pH below 7.2), measures for extracorporeal CO₂ removal (iLA Membranventilator, Novalung) should be installed at an early stage of mechanical ventilation, to terminate cascades of inflammatory response from the lung tissue, resulting in multiorgan failure respective.

Tidal volume, rate, and pressures

- For adult patients and older children
 - tidal volume(Vt) is calculated in milliliters per kilogram. Traditionally 10 ml/kg was used but has been shown to cause barotrauma, or injury to the lung by overextension, so 6 to 8 ml/kg is now common practice in ICU.

Hence a patient weighing 70 kg would get a V_t of 420–480 ml. In adults a rate of 12 strokes per minute is generally used.

- with acute respiratory distress syndrome (ARDS) a tidal volume of 6–8 ml/kg is used with a rate of 10–12 per minute. This reduced tidal volume allows for minimal volutrauma but may result in an elevated $p\text{CO}_2$ (due to the relative decreased oxygen delivered) but this elevation does not need to be corrected (termed *permissive hypercapnia*)
- For infants and younger children
 - without existing lung disease—a tidal volume of 4–8 ml/kg to be delivered at a rate of 30–35 breaths per minute
 - with ARDS—decrease tidal volume and increase respiratory rate sufficient to maintain $p\text{CO}_2$ between 45 and 55¹. Allowing higher $p\text{CO}_2$ (sometimes called permissive hypercapnia) may help prevent ventilator induced lung injury

As the amount of tidal volume increases, the pressure required to administer that volume is increased. This pressure is known as the *peak airway pressure*. If the peak airway pressure is persistently above 45 cmH₂O (4.4 kPa) for adults, the risk of barotrauma is increased (*see below*) and efforts should be made to try to reduce the peak airway pressure. In infants and children it is unclear what level of peak pressure may cause damage. In general, keeping peak pressures below 30 cmH₂O (2.9 kPa) is desirable.

Monitoring for barotrauma can also involve measuring the *plateau pressure*, which is the pressure *after* the delivery of the tidal volume but *before* the patient is allowed to exhale. Normal breathing pattern involves inspiration, then expiration. The ventilator is programmed so that after delivery of the tidal volume (inspiration), the patient is not allowed to exhale for a half a second. Therefore, pressure must be maintained in order to prevent exhalation, and this pressure is the plateau pressure. Barotrauma is minimized when the plateau pressure is maintained < 30–35 cmH₂O.

Sighs

An adult patient breathing spontaneously will usually sigh about 6–8 times per hour to prevent microatelectasis, and this has led some to propose that ventilators should deliver 1½–2 times the amount of the preset tidal volume 6–8 times per hour to account for the sighs. However, such high quantity of volume delivery requires very high peak pressure that predisposes to barotrauma. Currently, accounting for sighs is not recommended if the patient is receiving 10–12 mL/kg or is on PEEP. If the tidal volume used is lower, the sigh adjustment can be used, as long as the peak and plateau pressures are acceptable.

Sighs are not generally used with ventilation of infants and young children.

Initial FiO_2

Because the mechanical ventilator is responsible for assisting in a patient's breathing, it must then also be able to deliver an adequate amount of oxygen in each breath. The FiO_2

stands for *fraction of inspired oxygen*, which means the percent of oxygen in each breath that is inspired. (Note that normal room air has ~21% oxygen content). In adult patients who can tolerate higher levels of oxygen for a period of time, the initial FiO_2 may be set at 100% until arterial blood gases can document adequate oxygenation. An FiO_2 of 100% for an extended period of time can be dangerous, but it can protect against hypoxemia from unexpected intubation problems. For infants, and especially in premature infants, avoiding high levels of FiO_2 (>60%) is important.

Positive end-expiratory pressure (PEEP)

PEEP is an adjuvant to the mode of ventilation used to help maintain functional residual capacity (FRC). At the end of expiration, the PEEP exerts pressure to oppose passive emptying of the lung and to keep the airway pressure above the atmospheric pressure. The presence of PEEP opens up collapsed or unstable alveoli and increases the FRC and surface area for gas exchange, thus reducing the size of the shunt. For example, if a large shunt is found to exist based on the estimation from 100% FiO_2 (*see above*), then PEEP can be considered and the FiO_2 can be lowered (< 60%) in order to maintain an adequate PaO_2 , thus reducing the risk of oxygen toxicity.

In addition to treating a shunt, PEEP may also be useful to decrease the work of breathing. In pulmonary physiology, compliance is a measure of the "stiffness" of the lung and chest wall. The mathematical formula for compliance (C) equals change in volume divided by change in pressure. The higher the compliance, the more easily the lungs will inflate in response to positive pressure. An underinflated lung will have low compliance and PEEP will improve this initially by increasing the FRC, since the partially inflated lung takes less energy to inflate further. Excessive PEEP can however produce overinflation, which will again decrease compliance. Therefore it is important to maintain an adequate, but not excessive FRC.

Indications. PEEP can cause significant haemodynamic consequences through decreasing venous return to the right heart and decreasing right ventricular function. As such, it should be judiciously used and is indicated for adults in two circumstances.

- If a PaO_2 of 60 mmHg cannot be achieved with a FiO_2 of 60%
- If the initial shunt estimation is greater than 25%

If used, PEEP is usually set with the minimal positive pressure to maintain an adequate PaO_2 with a safe FiO_2 . As PEEP increases intrathoracic pressure, there can be a resulting decrease in venous return and decrease in cardiac output. A PEEP of less than 10 cmH₂O (1 kPa) is usually safe in adults if intravascular volume depletion is absent. Lower levels are used for pediatric patients. Older literature recommended routine placement of a Swan-Ganz catheter if the amount of PEEP used is greater than 10 cmH₂ for hemodynamic monitoring. More recent literature has failed to find outcome benefits with routine PA catheterisation when compared to simple central venous pressure monitoring. If cardiac output measurement is required, minimally invasive techniques, such as oesophageal doppler monitoring or arterial waveform contour monitoring may be

sufficient alternatives. PEEP should be withdrawn from a patient until adequate PaO₂ can be maintained with a FiO₂ < 40%. When withdrawing, it is decreased through 1–2 cmH₂O decrements while monitoring haemoglobin-oxygen saturations. Any unacceptable haemoglobin-oxygen saturation should prompt reinstatement of the last PEEP level that maintained good saturation.

Positioning

Prone (face down) positioning has been used in patients with ARDS and severe hypoxemia. It improves FRC, drainage of secretions, and ventilation-perfusion matching (efficiency of gas exchange). It may improve oxygenation in > 50% of patients, but no survival benefit has been documented.

Sedation and Paralysis

Most intubated patients receive intravenous sedation through a continuous infusion or scheduled dosing to help with anxiety or psychological stress. Sedation also helps the patient tolerate the constant irritation of the endotracheal tube in their mouth, pharynx and trachea. Without some form of sedation and analgesia, it is common for patients to "fight" the ventilator. This fighting increases work of breathing and may cause further lung injury. Daily interruption of sedation is commonly helpful to the patient for reorientation and appropriate weaning. These interruptions are frequently described as "sedation vacations" and have been shown to reduce the time patients stay on mechanical ventilation.

It is not uncommon for patients on a mechanical ventilator to be given a muscle relaxant or paralytic to aid in ventilation. These "neuromuscular blockades" prevent skeletal muscle from contracting and thereby stop all patient movement including respiratory efforts. These types of pharmaceutical agents must always be given in conjunction with sedation as the effects of the paralytics is not only uncomfortable but would cause significant psychological stress and anxiety.

Prophylaxis

- To protect against ventilator-associated pneumonia, patients' beds are often elevated to about 30°.
- Deep vein thrombosis prophylaxis with heparin or sequential compression device is important in older children and adults.
- A histamine receptor (H₂) blocker or proton-pump inhibitor may be used to prevent gastrointestinal bleeding, which has been associated with mechanical ventilation

Modification of settings

In adults when 100% FiO₂ is used initially, it is easy to calculate the next FiO₂ to be used and easy to estimate the shunt fraction. The estimated shunt fraction refers to the amount

of oxygen not being absorbed into the circulation. In normal physiology, gas exchange (oxygen/carbon dioxide) occurs at the level of the alveoli in the lungs. The existence of a shunt refers to any process that hinders this gas exchange, leading to wasted oxygen inspired and the flow of un-oxygenated blood back to the left heart (which ultimately supplies the rest of the body with unoxygenated blood).

When using 100% F_{iO_2} , the degree of shunting is estimated by subtracting the measured PaO_2 (from an arterial blood gas) from 700 mmHg. For each difference of 100 mmHg, the shunt is 5%. A shunt of more than 25% should prompt a search for the cause of this hypoxemia, such as mainstem intubation or pneumothorax, and should be treated accordingly. If such complications are not present, other causes must be sought after, and PEEP should be used to treat this intrapulmonary shunt. Other such causes of a shunt include:

- Alveolar collapse from major atelectasis
- Alveolar collection of material other than gas, such as pus from pneumonia, water and protein from acute respiratory distress syndrome, water from congestive heart failure, or blood from haemorrhage

When to withdraw mechanical ventilation

Withdrawal from mechanical ventilation—also known as weaning—should not be delayed unnecessarily, nor should it be done prematurely. Patients should have their ventilation considered for withdrawal if they are able to support their own ventilation and oxygenation, and this should be assessed continuously. There are several objective parameters to look for when considering withdrawal, but there is no specific criteria that generalizes to all patients.

Trials of spontaneous breathing have been shown to accurately predict the success of spontaneous breathing. (Yang K, Tobin MJ. A prospective study of indexes predicting the outcome of weaning from mechanical ventilation. *N Engl J Med* 1991;324:1445–1450).

Connection to ventilators

There are various procedures and mechanical devices that provide protection against airway collapse, air leakage, and aspiration:

- Face mask - In resuscitation and for minor procedures under anaesthesia, a face mask is often sufficient to achieve a seal against air leakage. Airway patency of the unconscious patient is maintained either by manipulation of the jaw or by the use of *nasopharyngeal* or *oropharyngeal airway*. These are designed to provide a passage of air to the pharynx through the nose or mouth, respectively. Poorly fitted masks often cause nasal bridge ulcers, a problem for some patients. Face masks are also used for non-invasive ventilation in conscious patients. A full face mask does not, however, provide protection against aspiration.

- Laryngeal mask airway - The laryngeal mask airway (LMA) causes less pain and coughing than a tracheal tube. However, unlike tracheal tubes it does not seal against aspiration, making careful individualised evaluation and patient selection mandatory.
- *Tracheal intubation* is often performed for mechanical ventilation of hours to weeks duration. A tube is inserted through the nose (nasotracheal intubation) or mouth (orotracheal intubation) and advanced into the trachea. In most cases tubes with inflatable cuffs are used for protection against leakage and aspiration. Intubation with a cuffed tube is thought to provide the best protection against aspiration. Tracheal tubes inevitably cause pain and coughing. Therefore, unless a patient is unconscious or anaesthetized for other reasons, sedative drugs are usually given to provide tolerance of the tube. Other disadvantages of tracheal intubation include damage to the mucosal lining of the nasopharynx or oropharynx and subglottic stenosis.
- Esophageal obturator airway - sometimes used by emergency medical technicians and basic EMS providers not trained to intubate. It is a tube which is inserted into the esophagus, past the epiglottis. Once it is inserted, a bladder at the tip of the airway is inflated, to block ("obturate") the esophagus, and oxygen is delivered through a series of holes in the side of the tube which is then forced into the lungs.
- *Cricothyrotomy* - Patients who require emergency airway management, in whom tracheal intubation has been unsuccessful, may require an airway inserted through a surgical opening in the cricothyroid membrane. This is similar to a tracheostomy but a cricothyrotomy is reserved for emergency access.
- *Tracheostomy* - When patients require mechanical ventilation for several weeks, a tracheostomy may provide the most suitable access to the trachea. A tracheostomy is a surgically created passage into the trachea. Tracheostomy tubes are well tolerated and often do not necessitate any use of sedative drugs. Tracheostomy tubes may be inserted early during treatment in patients with pre-existing severe respiratory disease, or in any patient who is expected to be difficult to wean from mechanical ventilation, i.e., patients who have little muscular reserve.
- *Mouthpiece* - Less common interface, does not provide protection against aspiration. There are lipseal mouthpieces with flanges to help hold them in place if patient is unable.

Terminology

Terminology used in the field of mechanical ventilation and respiratory support:

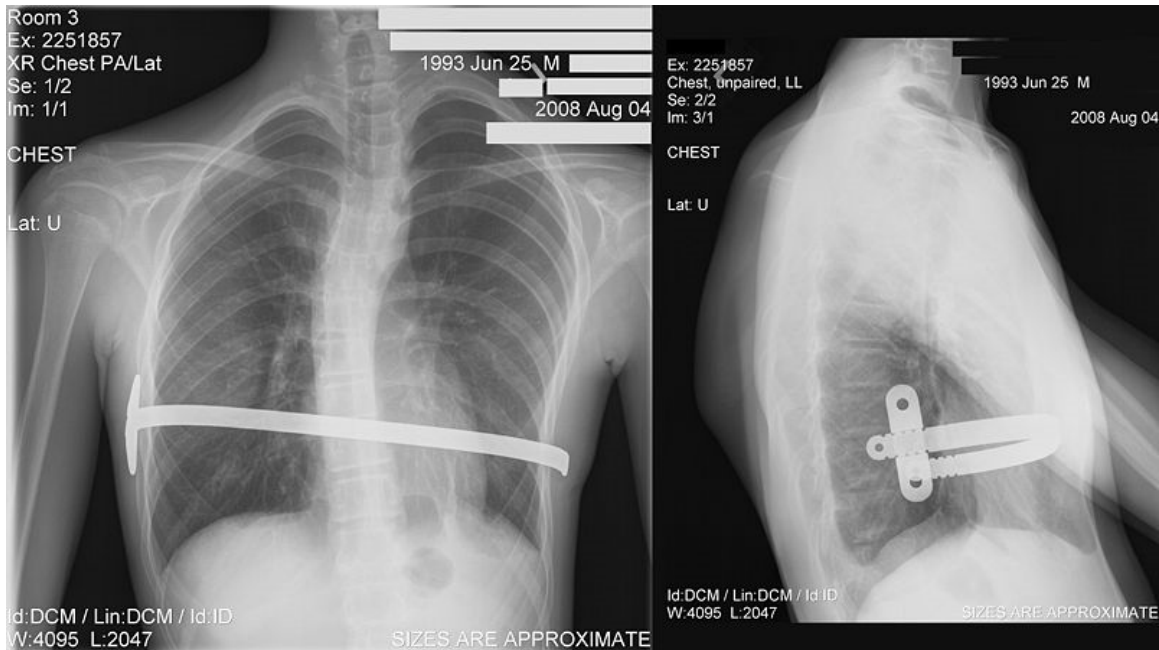
- APRV Airway pressure release ventilation
- ASB Assisted spontaneous breathing—also *ASV* = assisted spontaneous ventilation
- ASV Adaptive support ventilation—a patented technology—closed-loop mechanical respiration, a further development of MMV. Can also stand for assisted spontaneous ventilation.
- ATC Automatic tube compensation
- Automode Automode

- BCV Biphasic Cuirass Ventilation
- BIPAP Bilevel Positive Airway Pressure
- CMV Continuous mandatory ventilation
- CPAP Continuous positive airway pressure
- CPPV Continuous positive pressure ventilation
- EPAP Expiratory positive airway pressure
- HFV High frequency ventilation
 - HFFI High frequency flow interruption
 - HFJV High frequency jet ventilation
 - HFOV High frequency oscillatory ventilation
 - HFPPV High frequency positive pressure ventilation
- ILV Independent lung ventilation—separate sides positive pressure ventilation.
- IPAP Inspiratory positive airway pressure
- IPPV Intermittent positive pressure ventilation
- IRV Inversed ratio ventilation— mechanical ventilation with switched respiration phases/time rate.
- LFPPV Low frequency positive pressure ventilation
- MMV Mandatory minute volume
- NAVA Neurally Adjusted Ventilatory Assist
- NIF Negative inspiratory force—amount of force generated by a patient against a closed valve; greater than 20 cmH₂O indicates an adequately strong diaphragm.
- NIV Non-invasive ventilation
- PAP Positive airway pressure
- PAV and PAV+ Proportional assist ventilation and proportional assist ventilation plus
- *P/F* ratio Ratio of *PaO₂* off an ABG and *FiO₂* off the ventilator. *P/F* < 200 indicates ARDS, *P/F* < 300 indicates ALI
- PCMV (P-CMV) Pressure controlled mandatory ventilation
- PCV Pressure controlled ventilation or PC Pressure control—pressure-controlled, fully mechanical ventilation.
- PEEP Positive end-expiratory pressure
- PNPV Positive negative pressure ventilation—switching pressure mechanical ventilation
- PPS Proportional pressure support
- PRVC Pressure regulated volume controlled ventilation
- PSV Pressure Support Ventilation or PS—supported spontaneous respiration
- RSBI Rapid shallow breathing index—ratio of breath rate divided by the tidal volume. RSBI<105 declares a patient can be extubated and maintain themselves. Also indicates patient has a good chance of staying extubated.
- (S) IMV (Synchronized) intermittent mandatory ventilation
- S-CPPV Synchronized continuous positive pressure ventilation
- S-IPPV Synchronized intermittent positive pressure ventilation
- TNI Therapy with nasal insufflation—nasal high-flow mechanical ventilation for respiration support.
- VCMV (V-CMV) Volume controlled mandatory ventilation

- VCV Volume controlled ventilation or VC, Volume Control—volume-controlled, fully mechanical ventilation.
- VS Volume Support
- ZAP Zero airway pressure—spontaneous respiration under atmospheric pressure.

Chapter 23

Nuss Procedure



X-Ray of a 15 year old male after undergoing the procedure

The **Nuss procedure** is a minimally-invasive procedure, invented by Dr. Donald Nuss for treating pectus excavatum. He developed it at Children's Hospital of The King's Daughters, in Norfolk, Virginia. The operation typically takes approximately two hours.

Through two small incisions in the side of the chest, an introducer is pushed along posterior to the sternum and ribs, and anterior to the heart and lungs. Then a concave stainless steel bar is slipped under the sternum, through the incisions in the side of the chest. A third, smaller incision is made to insert a thoracoscope (small camera) used to help guide the bar. Taller patients, older patients, or patients requiring extensive correction may receive two or more bars. All bars may be placed through two incisions or additional incisions may be made. The bar is then flipped, and the sternum pops out. To support the bar and keep it in place a metal plate called a stabilizer may be inserted with the bar on one side of the torso. PDS sutures may also be used in addition to the stabilizer. The stabilizer fits around the bar and into the ribcage. The bar and stabilizer are secured with sutures that dissolve in about six months.

Some surgeons have achieved excellent results using only pericostal sutures, without the use of stabilizers. For older children who have more ossified bones, an additional option the surgeon has is to make an incision across the sternum so the bar is attached with a wire to the sternum to avoid bar displacement. Older children's bones do not conform as easily to the bar, thus increasing the risk of bar displacement, so the wire attaching the bar directly to the sternum may help avoid a second surgery to correct bar displacement.

Eventually, the bar is secured with muscle tissue that regrows during the recovery time. Although initially recommended only for younger patients, the Nuss procedure is now commonly used on patients in their thirties and forties with excellent results.

Postoperative evaluation indicates a significant improvement in pulmonary function studies and a high proportion of patients report improvements in well being and an increase in exercise tolerance.

Although this procedure is categorized as "minimally invasive", one must not infer that recovery from this procedure is minimal. Post-operative pain control can be quite challenging thus requiring multi-modal pain management, such as epidural. Nurses who attend these patients post operation generally concur that this operation is one of the more difficult recoveries of any operations for children.

Recovery

Recovery time is generally four to five days as an in-patient, depending on the patient age, activity level, co-morbidities and post-operative complications (if any), followed by time at home to overcome the pain and to let the bar settle into place. Patients younger than fifteen often require only two to four weeks at home after being discharged from the hospital for recovery. However, older children and adults typically require a greater recovery time due to the increased ossification (and thus decreased flexibility) of their bones.

In this case, the difficulty and length of recovery should be carefully considered prior to making the decision to undergo the operation, as the limitations to lifestyle, functionality and comfort can be dramatic for many months. This cannot be understated for older children, which is why many doctors do not recommend this procedure unless medically necessary (i.e. not for cosmetic reasons). Fully grown adults may require from four weeks to many months before they can resume normal activities, including work. For six to twenty-four hours after the operation, the patient generally will have a Foley catheter to minimize risk of movement that could displace bar, and because the epidural can interfere with normal urination. The patient may also receive thoracic epidural analgesia in the back for two to five days depending on patient recovery.

For six weeks, physical activity should be limited (i.e. no running or strenuous physical activity, and lifting is limited to ten pounds or less). Walking for exercise and breathing exercises aid in recovery. It is sometimes suggested that weight-training should be limited or eliminated for up to three months. It is also recommended that any sports

where contact may occur should be avoided. However, aerobic sports are encouraged, as results after bar removal are best maintained in patients who have stimulated their cardiopulmonary systems while the bar is in place. After a period of six to ten months the athletic skills are almost completely recovered

Bar removal

After a period of two to four years, the surgical stainless steel bar is removed from the patient's chest. This outpatient procedure lasts approximately ninety minutes. The patient stays at the hospital for a few hours.

Complications

Iatrogenic damage to the heart and lungs during the procedure is a concern. Scopes (cameras) are often utilized by the surgical team to minimize this risk. There is still an extremely minor risk of abrasion or puncture.

Air in the chest (pneumothorax) is one of the more frequent complications. A chest tube may be required or aggressive breathing exercises and close monitoring may be adequate.

With the use of stabilizers and PDS sutures, bar displacement rarely occurs. If these methods of bar fixation are not used, bar displacement may occur. This can be quite painful and requires some sort of intervention: either bar removal, or repositioning of the bar with some sort of bar fixation. Patients should understand prior to the surgery that if bar displacement occurs soon after surgery, a second surgery will be immediately required which is even a more difficult recovery as the patient is already weakened and in pain. High impact trauma, such as car accidents can dislodge the bars, causing extreme pain. This is the reason for the restriction on driving, because a sudden defensive maneuver, such as a jerk of the steering wheel, could dislodge the bar up to six weeks directly after the surgery.

Other complications which may occur include hemothorax, pleural effusion, pericarditis, wound infection and pneumonia and acquired scoliosis. Vigorous incentive spirometry is used to prevent pneumonia. Some patients are allergic to one of the components of stainless steel. As a result, allergy testing is now routinely done prior to surgery. In the event of an allergy, a titanium bar will be used.

Older children may also struggle with adjusting to living in their changed bodies during the several months of healing due to the pain and limitations.

Again, it is very important to be fully aware that although the surgery may be minimally invasive, the recovery process and risks of complications (and consequences thereof) are not minimal.