= Lung cancer =

Lung cancer , also known as lung carcinoma , is a malignant lung tumor characterized by uncontrolled cell growth in tissues of the lung . If left untreated , this growth can spread beyond the lung by the process of metastasis into nearby tissue or other parts of the body . Most cancers that start in the lung , known as primary lung cancers , are carcinomas . The two main types are small @-@ cell lung carcinoma (SCLC) and non @-@ small @-@ cell lung carcinoma (NSCLC) . The most common symptoms are coughing (including coughing up blood) , weight loss , shortness of breath , and chest pains .

The vast majority (85 %) of cases of lung cancer are due to long @-@ term tobacco smoking . About 10 ? 15 % of cases occur in people who have never smoked . These cases are often caused by a combination of genetic factors and exposure to radon gas , asbestos , second @-@ hand smoke , or other forms of air pollution . Lung cancer may be seen on chest radiographs and computed tomography (CT) scans . The diagnosis is confirmed by biopsy which is usually performed by bronchoscopy or CT @-@ guidance .

Prevention is by avoiding risk factors including smoking and air pollution . Treatment and long @-@ term outcomes depend on the type of cancer , the stage (degree of spread) , and the person 's overall health . Most cases are not curable . Common treatments include surgery , chemotherapy , and radiotherapy . NSCLC is sometimes treated with surgery , whereas SCLC usually responds better to chemotherapy and radiotherapy .

Worldwide in 2012 , lung cancer occurred in 1 @.@ 8 million people and resulted in 1 @.@ 6 million deaths . This makes it the most common cause of cancer @-@ related death in men and second most common in women after breast cancer . The most common age at diagnosis is 70 years . Overall , 17 @.@ 4 % of people in the United States diagnosed with lung cancer survive five years after the diagnosis , while outcomes on average are worse in the developing world .

= = Signs and symptoms = =

Signs and symptoms which may suggest lung cancer include :

Respiratory symptoms : coughing , coughing up blood , wheezing , or shortness of breath

Systemic symptoms : weight loss , weakness , fever , or clubbing of the fingernails

Symptoms due to the cancer mass pressing on adjacent structures : chest pain , bone pain , superior vena cava obstruction , or difficulty swallowing

If the cancer grows in the airways , it may obstruct airflow , causing breathing difficulties . The obstruction can lead to accumulation of secretions behind the blockage , and predispose to pneumonia .

Depending on the type of tumor , paraneoplastic phenomena ? symptoms not due to the local presence of cancer ? may initially attract attention to the disease . In lung cancer , these phenomena may include hypercalcemia , syndrome of inappropriate antidiuretic hormone (SIADH , abnormally concentrated urine and diluted blood) , ectopic ACTH production , or Lambert ? Eaton myasthenic syndrome (muscle weakness due to autoantibodies) . Tumors in the top of the lung , known as Pancoast tumors , may invade the local part of the sympathetic nervous system , leading to Horner 's syndrome (dropping of the eyelid and a small pupil on that side) , as well as damage to the brachial plexus .

Many of the symptoms of lung cancer (poor appetite , weight loss , fever , fatigue) are not specific . In many people , the cancer has already spread beyond the original site by the time they have symptoms and seek medical attention . Symptoms that suggest the presence of metastatic disease include weight loss , bone pain and neurological symptoms (headaches , fainting , convulsions , or limb weakness) . Common sites of spread include the brain , bone , adrenal glands , 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 radiography .

= = Causes = =

Cancer develops following genetic damage to DNA and epigenetic changes . These changes affect the normal functions of the cell , including cell proliferation , programmed cell death (apoptosis) and DNA repair . As more damage accumulates , the risk of cancer increases .

= = = Smoking = = =

Smoking , particularly of cigarettes , is by far the main contributor to lung cancer . Cigarette smoke contains at least 73 known carcinogens , including benzo [a] pyrene , NNK , 1 @,@ 3 @-@ butadiene and a radioactive isotope of polonium , polonium @-@ 210 . Across the developed world , 90 % of lung cancer deaths in men during the year 2000 were attributed to smoking (70 % for women) . Smoking accounts for about 85 % of lung cancer cases .

Passive smoking ? the inhalation of smoke from another 's smoking ? is a cause of lung cancer in nonsmokers . A passive smoker can be defined as someone living or working with a smoker . Studies from the US , Europe and the UK have consistently shown a significantly increased risk among those exposed to passive smoke . Those who live with someone who smokes have a 20 ? 30 % increase in risk while those who work in an environment with secondhand smoke have a 16 ? 19 % increase in risk . Investigations of sidestream smoke suggest it is more dangerous than direct smoke . Passive smoking causes about 3 @,@ 400 deaths from lung cancer each year in the USA .

Marijuana smoke contains many of the same carcinogens as those in tobacco smoke . However , the effect of smoking cannabis on lung cancer risk is not clear . A 2013 review did not find an increased risk from light to moderate use . A 2014 review found that smoking cannabis doubled the risk of lung cancer .

= = = Radon gas = = =

Radon is a colourless 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 is the second @-@ most common cause of lung cancer in the USA , causing about 21 @,@ 000 deaths each year . The risk increases 8 ? 16 % for every 100 Bq / m^3 increase in the radon concentration . Radon gas levels vary by locality and the composition of the underlying soil and rocks . About one in 15 homes in the US has radon levels above the recommended guideline of 4 picocuries per liter (pCi / l) (148 Bq / m^3) .

= = = Asbestos = = =

Asbestos can cause a variety of lung diseases , including lung cancer . Tobacco smoking and asbestos have a synergistic effect on the formation of lung cancer . In smokers who work with asbestos , the risk of lung cancer is increased 45 @-@ fold compared to the general population . Asbestos can also cause cancer of the pleura , called mesothelioma (which is different from lung cancer) .

= = = Air pollution = = =

Outdoor air pollution has a small effect on increasing the risk of lung cancer . Fine particulates (PM2.5) and sulfate aerosols , which may be released in traffic exhaust fumes , are associated with slightly increased risk . For nitrogen dioxide , an incremental increase of 10 parts per billion increases the risk of lung cancer by 14 % . Outdoor air pollution is estimated to account for 1 ? 2 % of lung cancers .

Tentative evidence supports an increased risk of lung cancer from indoor air pollution related to the burning of wood , charcoal , dung or crop residue for cooking and heating . Women who are

exposed to indoor coal smoke have about twice the risk and a number of the by @-@ products of burning biomass are known or suspected carcinogens . This risk affects about 2 @.@ 4 billion people globally , and is believed to account for 1 @.@ 5 % of lung cancer deaths .

= = = Genetics = = =

About 8 % of lung cancer is due to inherited factors . In relatives of people with lung cancer , the risk is doubled . This is likely due to a combination of genes . Polymorphisms on chromosomes 5 , 6 and 15 are known to affect the risk of lung cancer .

= = = Other causes = = =

Numerous other substances , occupations , and environmental exposures have been linked to lung cancer . The International Agency for Research on Cancer (IARC) states there is " sufficient evidence " to show the following are carcinogenic in the lungs :

Some metals (aluminum production , cadmium and cadmium compounds , chromium (VI) compounds , beryllium and beryllium compounds , iron and steel founding , nickel compounds , arsenic and inorganic arsenic compounds , underground hematite mining)

Some products of combustion (incomplete combustion , coal (indoor emissions from household coal burning) , coal gasification , coal @-@ tar pitch , coke production , soot , diesel engine exhaust)

Ionizing radiation (X @-@ radiation , gamma radiation , plutonium)

Some toxic gases (methyl ether (technical grade) , Bis- (chloromethyl) ether , sulfur mustard , MOPP (vincristine @-@ prednisone @-@ nitrogen mustard @-@ procarbazine mixture) , fumes from painting)

Rubber production and crystalline silica dust

= = Pathogenesis = =

Similar to many other cancers , lung cancer is initiated by activation of oncogenes or inactivation of tumor suppressor genes . Carcinogens cause mutations in these genes which induce the development of cancer .

Mutations in the K @-@ ras proto @-@ oncogene are responsible for 10 ? 30 % of lung adenocarcinomas . About 4 % of non @-@ small @-@ cell lung carcinomas involve an EML4 @-@ ALK tyrosine kinase fusion gene .

Epigenetic changes ? such as alteration of DNA methylation , histone tail modification , or microRNA regulation ? may lead to inactivation of tumor suppressor genes .

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 carcinoma and provide the basis for treatment with EGFR @-@ inhibitors . Her2 / neu is affected less frequently . Other genes that are often mutated or amplified are c @-@ MET , NKX2 @-@ 1 , LKB1 , PIK3CA , and BRAF .

The cell lines of origin are not fully understood . The mechanism may involve abnormal activation of stem cells . In the proximal airways , stem cells that express keratin 5 are more likely to be affected , typically leading to squamous @-@ cell lung carcinoma . In the middle airways , implicated stem cells include club cells and neuroepithelial cells that express club cell secretory protein . Small @-@ cell lung carcinoma may be derived from these cell lines or neuroendocrine cells , and may express CD44 .

Metastasis of lung cancer requires transition from epithelial to mesenchymal cell type . This may occur through activation of signaling pathways such as Akt / GSK3Beta , MEK @-@ ERK , Fas , and Par6 .

= = Diagnosis = =

Performing a chest radiograph is one of the first investigative steps if a person 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 . CT imaging is typically used to provide more information about the type and extent of disease . Bronchoscopy or CT @-@ guided biopsy is often used to sample the tumor for histopathology .

Lung cancer often appears as a solitary pulmonary nodule on a chest radiograph . However , the differential diagnosis is wide . Many other diseases can also give this appearance , including metastatic cancer , hamartomas , and infectious granulomas such as tuberculosis , histoplasmosis and coccidioidomycosis . Lung cancer can also be an incidental finding , as a solitary pulmonary nodule on a chest radiograph or CT scan done for an unrelated reason . The definitive diagnosis of lung cancer is based on histological examination of the suspicious tissue in the context of the clinical and radiological features .

Clinical practice guidelines recommend frequencies for pulmonary nodule surveillance . CT imaging should not be used for longer or more frequently than indicated as extended surveillance exposes people to increased radiation .

= = = Classification = = =

Lung cancers are classified according to histological type . This classification is important for determining management and predicting outcomes of the disease . Lung cancers are carcinomas ? malignancies that arise from epithelial cells . Lung carcinomas are categorized by the size and appearance of the malignant cells seen by a histopathologist under a microscope . For therapeutic purposes , two broad classes are distinguished : non @-@ small @-@ cell lung carcinoma and small @-@ cell lung carcinoma .

= = = = Non @-@ small @-@ cell lung carcinoma = = = =

The three main subtypes of NSCLC are adenocarcinoma , squamous @-@ cell carcinoma and large @-@ cell carcinoma .

Nearly 40 % of lung cancers are adenocarcinoma , which usually originates in peripheral lung tissue . Although most cases of adenocarcinoma are associated with smoking , adenocarcinoma is also the most common form of lung cancer among people who have smoked fewer than 100 cigarettes in their lifetimes (" never @-@ smokers ") and ex @-@ smokers with a modest smoking history . A subtype of adenocarcinoma , the bronchioloalveolar carcinoma , is more common in female never @-@ smokers , and may have a better long @-@ term survival .

Squamous @-@ cell carcinoma accounts for about 30 % of lung cancers . They typically occur close to large airways . A hollow cavity and associated cell death are commonly found at the centre of the tumor . About 9 % of lung cancers are large @-@ cell carcinoma . These are so named because the cancer cells are large , with excess cytoplasm , large nuclei and conspicuous nucleoli .

= = = = Small @-@ cell lung carcinoma = = = =

In small @-@ cell lung carcinoma (SCLC) , the cells contain dense neurosecretory granules (vesicles containing neuroendocrine hormones) , which give this tumor an endocrine / paraneoplastic syndrome association . Most cases arise in the larger airways (primary and secondary bronchi) . Sixty to seventy percent have extensive disease (which cannot be targeted within a single radiation therapy field) at presentation .

= = = = Others = = = =

Four main histological subtypes are recognised , although some cancers may contain a

combination of different subtypes , such as adenosquamous carcinoma . Rare subtypes include carcinoid tumors , bronchial gland carcinomas and sarcomatoid carcinomas .

= = = Metastasis = = =

The lung is a common place for the spread 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 metastatic breast cancer . Metastases often have a characteristic round appearance on chest radiograph .

Primary lung cancers themselves most commonly metastasize to the brain , bones , liver and adrenal glands . Immunostaining of a biopsy is often helpful to determine the original source . The presence of Napsin @-@ A , TTF @-@ 1 , CK7 and CK20 are helpful in confirming the subtype of lung carcinoma . SCLC derived from neuroendocrine cells may express CD56 , neural cell adhesion molecule , synaptophysin or chromogranin .

= = = Staging = = =

Lung cancer staging is an assessment of the degree of spread of the cancer from its original source . It is one of the factors affecting the prognosis and potential treatment of lung cancer .

The evaluation of non @-@ small @-@ cell lung carcinoma (NSCLC) staging uses the TNM classification . This is based on the size of the primary tumor , lymph node involvement , and distant metastasis .

Using the TNM descriptors , a group is assigned , ranging from occult cancer , through stages 0 , IA (one @-@ A) , IB , IIA , IIB , IIIA , IIIB and IV (four) . This stage group assists with the choice of treatment and estimation of prognosis .

Small @-@ cell lung carcinoma (SCLC) has traditionally been classified as " limited stage " (confined to one half of the chest and within the scope of a single tolerable radiotherapy field) or " extensive stage " (more widespread disease) . However , the TNM classification and grouping are useful in estimating prognosis .

For both NSCLC and SCLC , the two general types of staging evaluations are clinical staging and surgical staging . Clinical staging is performed prior to definitive surgery . It is based on the results of imaging studies (such as CT scans and PET scans) and biopsy results . Surgical staging is evaluated either during or after the operation , and is based on the combined results of surgical and clinical findings , including surgical sampling of thoracic lymph nodes .

Diagrams of main features of staging

= = Prevention = =

Smoking prevention and smoking cessation are effective ways of preventing the development of lung cancer .

= = = Smoking ban = = =

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 .

Policy interventions to decrease passive smoking in public areas such as restaurants and workplaces have become more common in many Western countries . Bhutan has had a complete smoking ban since 2005 while India introduced a ban on smoking in public in October 2008 . 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 instituted .

= = = Screening = = =

Cancer screening uses medical tests to detect disease in large groups of people who have no symptoms . For individuals with high risk of developing lung cancer , computed tomography (CT) screening can detect cancer and give a person options to respond to it in a way that prolongs life . This form of screening reduces the chance of death from lung cancer by an absolute amount of 0 @.@ 3 % (relative amount of 20 %) . High risk people are those age 55 @-@ 74 who have smoked equivalent amount of a pack of cigarettes daily for 30 years including time within the past 15 years .

CT screening is associated with a high rate of falsely positive tests which may result in unneeded treatment . For each true positive scan there are about 19 falsely positives scans . Other concerns include radiation exposure and the cost of testing along with follow up . Research has not found two other available tests ? sputum cytology or chest radiograph (CXR) screening tests ? to have any benefit .

The U.S. Preventative Services Task Force (USPSTF) recommends yearly screening using low @-@ dose computed tomography in those who have a total smoking history of 30 pack @-@ years and are between 55 and 80 years old until a person has not been smoking for more than 15 years . Screening should not be done in those with other health problems that would make treatment of lung cancer if found not an option . The English National Health Service was in 2014 re @-@ examining the evidence for screening .

= = = Other prevention strategies = = =

The long @-@ term use of supplemental vitamin A , vitamin C , vitamin D or vitamin E does not reduce the risk of lung cancer . Some studies suggest that people who eat diets with a higher proportion of vegetables and fruit tend to have a lower risk , but this may be due to confounding ? with the lower risk actually due to the association of a high fruit / vegetables diet with less smoking . More rigorous studies have not demonstrated a clear association between diet and lung cancer risk .

= = Management = =

Treatment for lung cancer depends on the cancer 's specific cell type , how far it has spread , and the person 's performance status . Common treatments include palliative care , surgery , chemotherapy , and radiation therapy . Targeted therapy of lung cancer is growing in importance for advanced lung cancer .

= = = Surgery = = =

If investigations confirm NSCLC , the stage is assessed to determine whether the disease is localized and amenable to surgery or if it has spread to the point where it cannot be cured surgically . CT scan and positron emission tomography are used for this determination . If mediastinal lymph node involvement is suspected , the nodes may be sampled to assist staging . Techniques used for this include transthoracic needle aspiration , transbronchial needle aspiration (with or without endobronchial ultrasound) , endoscopic ultrasound with needle aspiration , mediastinoscopy , and thoracoscopy . Blood tests and pulmonary function testing are used to assess whether a person is well enough for surgery . If pulmonary function tests reveal poor respiratory reserve , surgery may not be possible .

In most cases of early @-@ stage NSCLC , removal of a lobe of lung (lobectomy) is the surgical treatment of choice . In people who are unfit for a full lobectomy , a smaller sublobar excision (wedge resection) may be performed . However , wedge resection has a higher risk of recurrence than lobectomy . Radioactive iodine brachytherapy at the margins of wedge excision may reduce the risk of recurrence . Rarely , removal of a whole lung (pneumonectomy) is performed . Video @-@

assisted thoracoscopic surgery (VATS) and VATS lobectomy use a minimally invasive approach to lung cancer surgery . VATS lobectomy is equally effective compared to conventional open lobectomy , with less postoperative illness .

In SCLC , chemotherapy and / or radiotherapy is typically used . However the role of surgery in SCLC is being reconsidered . Surgery might improve outcomes when added to chemotherapy and radiation in early stage SCLC .

= = = Radiotherapy = = =

Radiotherapy is often given together with chemotherapy , and may be used with curative intent in people with NSCLC 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 . Postoperative thoracic radiotherapy generally should not be used after curative intent surgery for NSCLC . Some people with mediastinal N2 lymph node involvement might benefit from post @-@ operative radiotherapy .

For potentially curable SCLC cases , chest radiotherapy is often recommended in addition to chemotherapy .

If cancer growth blocks a short section of bronchus , brachytherapy (localized radiotherapy) may be given directly inside the airway to open the passage . Compared to external beam radiotherapy , brachytherapy allows a reduction in treatment time and reduced radiation exposure to healthcare staff . Evidence for brachytherapy , however , is less than that for external beam radiotherapy .

Prophylactic cranial irradiation (PCI) is a type of radiotherapy to the brain , used to reduce the risk of metastasis . PCI is most useful in SCLC . In limited @-@ stage disease , PCI increases three @-@ year survival from 15 % to 20 % ; in extensive disease , one @-@ year survival increases from 13 % to 27 % .

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

For both NSCLC and SCLC patients , smaller doses of radiation to the chest may be used for symptom control (palliative radiotherapy) .

= = = Chemotherapy = = =

The chemotherapy regimen depends on the tumor type . Small @-@ cell lung carcinoma (SCLC) , even relatively early stage disease , is treated primarily with chemotherapy and radiation . In SCLC , cisplatin and etoposide are most commonly used . Combinations with carboplatin , gemcitabine , paclitaxel , vinorelbine , topotecan , and irinotecan are also used . In advanced non @-@ small cell lung carcinoma (NSCLC) , chemotherapy improves survival and is used as first @-@ line treatment , provided the person is well enough for the treatment . Typically , two drugs are used , of which one is often platinum @-@ based (either cisplatin or carboplatin) . Other commonly used drugs are gemcitabine , paclitaxel , docetaxel , pemetrexed , etoposide or vinorelbine .

Adjuvant chemotherapy refers to the use of chemotherapy after apparently curative surgery to improve the outcome . In NSCLC , samples are taken of nearby lymph nodes during surgery to assist staging . If stage II or III disease is confirmed , adjuvant chemotherapy improves survival by 5 % at five years . The combination of vinorelbine and cisplatin is more effective than older regimens . Adjuvant chemotherapy for people with stage IB cancer is controversial , as clinical trials have not clearly demonstrated a survival benefit . Chemotherapy before surgery in NSCLC that can be removed surgically also appears to improve outcomes .

Chemotherapy may be combined with palliative care in the treatment of the NSCLC . In advanced cases , appropriate chemotherapy improves average survival over supportive care alone , as well as improving quality of life . With adequate physical fitness maintaining chemotherapy during lung

cancer palliation offers 1 @.@ 5 to 3 months of prolongation of survival , symptomatic relief , and an improvement in quality of life , with better results seen with modern agents . The NSCLC Meta @-@ Analyses Collaborative Group recommends if the recipient wants and can tolerate treatment , then chemotherapy should be considered in advanced NSCLC .

= = = = Targeted therapy = = = =

Several drugs that target molecular pathways in lung cancer are available , especially for the treatment of advanced disease . Erlotinib , gefitinib and afatinib inhibit tyrosine kinase at the epidermal growth factor receptor . Denosumab is a monoclonal antibody directed against receptor activator of nuclear factor kappa @-@ B ligand . It may be useful in the treatment of bone metastases .

= = = Bronchoscopy = = =

Several treatments can be administered via bronchoscopy for the management of airway obstruction or bleeding . If an airway becomes obstructed by cancer growth , options include rigid bronchoscopy , balloon bronchoplasty , stenting , and microdebridement . Laser photosection involves the delivery of laser light inside the airway via a bronchoscope to remove the obstructing tumor .

= = = Palliative care = = =

Palliative care when added to usual cancer care benefits people even when they are still receiving chemotherapy . These approaches allow additional discussion of treatment options and provide opportunities to arrive at well @-@ considered decisions . Palliative care may avoid unhelpful but expensive care not only at the end of life , but also throughout the course of the illness . For individuals who have more advanced disease , hospice care may also be appropriate .

= = Prognosis = =

Of all people with lung cancer in the US , 16 @.@ 8 % survive for at least five years after diagnosis . In England , between 2005 and 2009 , overall five @-@ year survival for lung cancer was less than 10 % . Outcomes are generally worse in the developing world . Stage is often advanced at the time of diagnosis . At presentation , 30 ? 40 % of cases of NSCLC are stage IV , and 60 % of SCLC are stage IV . Survival for lung cancer falls as the stage at diagnosis becomes more advanced : the English data suggest that around 70 % of patients survive at least a year when diagnosed at the earliest stage , but this falls to just 14 % for those diagnosed with the most advanced disease .

Prognostic factors in NSCLC include presence of pulmonary symptoms , large tumor size (> 3 cm) , nonsquamous cell type (histology) , degree of spread (stage) and metastases to multiple lymph nodes , and vascular invasion . For people with inoperable disease , outcomes are worse in those with 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 NSCLC , the best prognosis is achieved with complete surgical resection of stage IA disease , with up to 70 % five @-@ year survival . People with extensive @-@ stage SCLC have an average five @-@ year survival rate of less than 1 % . The average 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 . In the US , people with medical insurance are more likely to have a better outcome .

= = Epidemiology = =

Worldwide , lung cancer is the most common cancer among men in terms of both incidence and mortality , and among women has the third highest incidence , and is second after breast cancer in mortality . In 2012 , there were 1 @.@ 82 million new cases globally , and 1 @.@ 56 million deaths due to lung cancer , representing 19 @.@ 4 % of all deaths from cancer . The highest rates are in North America , Europe and East Asia , with over a third of new cases in 2012 in China . Rates in Africa and South Asia are much lower .

The population segment most likely to develop lung cancer is people aged over 50 who have a history of smoking . 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 over the last decades , and are just recently beginning to stabilize . In the USA , the lifetime risk of developing lung cancer is 8 % in men and 6 % in women .

For every 3 ? 4 million cigarettes smoked , one lung cancer death occurs . The influence of " Big Tobacco " plays a significant role in the smoking culture . Young nonsmokers who see tobacco advertisements are more likely to take up smoking . 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 .

In the United States , black men and women have a higher incidence . Lung cancer rates are currently lower in developing countries . With increased smoking in developing countries , the rates are expected to increase in the next few years , notably in China and India .

In the United States military veterans have a 25 @-@ 50 % higher rate of lung cancer primarily due to higher rates of smoking . During World War Two and the Korean War asbestos also played a part and Agent Orange may have caused some problems during the Vietnam War .

Lung cancer is the second most common cancer in the UK (around 43 @,@ 500 people were diagnosed with the disease in 2011) , and it is the most common cause of cancer death (around 35 @,@ 400 people died in 2012) .

From the 1960s , the rates 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 continues to rise .

= = 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 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 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 . Despite this discovery , mining continued into the 1950s , due to the USSR 's demand for uranium . Radon was confirmed as a cause of lung cancer in the 1960s .

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 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 .

= = Research directions = =

Current research directions for lung cancer treatment include immunotherapy , which encourages the body 's immune system to attack the tumor cells , epigenetics , and new combinations of chemotherapy and radiotherapy , both on their own and together . Many of these new treatments work through immune checkpoint blockade , disrupting cancer 's ability to evade the immune system .

Ipilimumab blocks signaling through a receptor on T cells known as CTLA @-@ 4 which dampens down the immune system . It has been approved by the U.S. Food and Drug Administration (FDA) for treatment of melanoma and is undergoing clinical trials for both non @-@ small cell lung cancer (NSCLC) and small cell lung cancer (SCLC) .

Other immunotherapy treatments interfere with the binding of programmed cell death 1 (PD @-@ 1) protein with its ligand PD @-@ 1 ligand 1 (PD @-@ L1) . Signaling through PD @-@ 1 inactivates T cells . Some cancer cells appear to exploit this by expressing PD @-@ L1 in order to switch off T cells that might recognise them as a threat . Monoclonal antibodies targeting both PD @-@ 1 and PD @-@ L1 , such as pembrolizumab and nivolumab are currently in clinical trials for treatment for lung cancer .

Epigenetics is the study of small , usually heritable , molecular modifications ? or " tags " ? that bind DNA and modify gene expression levels . Targeting these tags with drugs can kill cancer cells . Early @-@ stage research in NSCLC using drugs aimed at epigenetic modifications shows that blocking more than one of these tags can kill cancer cells with fewer side effects . Studies also show that giving patients these drugs before standard treatment can improve its effectiveness . Clinical trials are underway to evaluate how well these drugs kill lung cancer cells in humans . Several drugs that target epigenetic mechanisms are in development . Histone deacetylase inhibitors in development include valproic acid , vorinostat , belinostat , panobinostat , entinostat , and romidepsin . DNA methyltransferase inhibitors in development include decitabine , azacytidine , and hydralazine .

The TRACERx project is looking at how NSCLC develops and evolves , and how these tumors become resistant to treatment . The project will look at tumor samples from 850 NSCLC patients at various stages including diagnosis , after first treatment , post @-@ treatment , and relapse . By studying samples at different points of tumor development , the researchers hope to identify the changes that drive tumor growth and resistance to treatment . The results of this project will help scientists and doctors gain a better understanding of NSCLC and potentially lead to the development of new treatments against the disease .

For lung cancer cases that develop resistance to epidermal growth factor receptor (EGFR) and anaplastic lymphoma kinase (ALK) tyrosine kinase inhibitors , new drugs are in development . New EGFR inhibitors include afatinib and dacomitinib . An alternative signaling pathway , c @-@ Met , can be inhibited by tivantinib and onartuzumab . New ALK inhibitors include crizotinib and ceritinib .