

## **Trailer**

My grandfather was a cigarette smoker, since the time he was 15 or 16 years old, and so is my dad. Most Vietnamese males are smokers. It is just like a culture thing in Vietnam. Offering a cigarette is a way of greeting, like shaking hands to start a friendly conversation, or to conduct business. After 60 pack years in smoking, my grandfather started coughing and developed chest pain. He lost a lot of weight in a few months. The coughing got worse, but he insisted that he did not have any problems, until he coughed out blood and fainted. My parents called 911 to take him to the hospital. The doctor ordered a lung scan, and found a mass in his right lung. After a complete checkup, the doctor concluded that my grandfather had advanced stage lung cancer. The tumor was inoperable. My grandfather passed away a few months later. I would like to find out more about this deadly disease, and its relationship to smoking.

## **Medical Experience Sharing Paper**

Lungs are major organs of the respiratory system. The two lungs are located in the thoracic cavity, and covered by a double-layered serous membrane called the pleura. The air passes from the atmosphere through the nose, pharynx, larynx, and trachea into the lungs. Just before entering the lungs, the trachea branches into the left and right bronchi. In the lungs, primary bronchi continue to branch off into the secondary bronchi, tertiary bronchi, bronchioles, respiratory bronchioles, alveolar ducts, alveolar sacs, and alveoli. Alveoli are the functional units of the lungs that allow the greatest gas exchange. The lungs are made up of many different types of cells. Most of these cells are epithelial cells that line the airways and the alveoli. Some of the cells lining the alveoli secrete a substance called surfactant to protect the lungs, while other cells serve as gas exchange sites (McKinley, 2013).

The major function of the respiratory system is the exchange of respiratory gases (oxygen and carbon dioxide) between the atmosphere and blood. This exchange involves four processes: pulmonary ventilation, alveolar gas exchange, gas transport, and systemic gas exchange.

Pulmonary ventilation is the movement of respiratory gases between the atmosphere and the alveoli of the lungs. Pulmonary ventilation includes inhalation and exhalation. Alveolar gas exchange (external respiration) is the exchange of respiratory gases between alveoli in lungs and pulmonary capillaries. Oxygen diffuses from the alveoli into the blood in the pulmonary capillaries. Carbon dioxide simultaneously diffuses in the opposite direction. Within the plasma, 97% of oxygen binds to iron molecules of hemoglobin, and is transported to tissues for cellular respiration. On the other hand, carbon dioxide, the cellular metabolic waste, diffuses from the tissue cells into venous capillaries. About 70% of carbon dioxide is transported in plasma, mainly in the form of bicarbonate ions. Systemic gas exchange (internal respiration) is the gas exchange between systemic cells and systemic capillaries. Oxygen diffuses from the blood in the systemic capillaries into tissue cells, while carbon dioxide diffuses in the opposite direction (McKinley 2013).

Cancer is an uncontrolled cell growth. Lung cancer begins with mutation in a lung cell's DNA. The mutated cells divide and pass along the mutation to new daughter cells. The new mutated daughter cells continue dividing to make more new mutated cells. During the precancerous stage, mutated cells are still able to perform their functions, but after many cell divisions, mutated cancer cells gradually lose their ability to carry out their normal functions. This uncontrolled cell growth results in a tumor.

Based on morphological classification, lung cancers are of two types - small cell (SCLC) and non-small cell lung cancers (NSCLC). The NSCLC is further classified into squamous cell carcinoma (SCC) and adenocarcinoma (ADC). The most common lung cancer is NSCLC, but SCLC is an

aggressive type of lung cancer. SCLC is a neuroendocrine carcinoma, associated with several endocrine conditions, such as Syndrome of Inappropriate Antidiuretic hormone secretion (SIADH) or syndrome of ectopic adrenocorticotrophic hormone secretion, or hypercalcemia, or many others.

Studies have found many factors that contribute to the development of lung cancer. Cigarette smoke is a well-known factor in literature. Studies show that 85% of lung cancers are caused by tobacco smoke (Lubin, 2006). Review of other contributing factors like diet and food supplements, alcohol, exercise and physical activity, have revealed no association with increased lung cancer risk (Molina, 2008). Asbestos exposure has been recognized as being carcinogenic, increasing the risk of lung cancer, especially mesothelioma, which is a cancer of the pleura. Retroviruses are not widely considered as carcinogens of lung cancer (York, 2005).

Tobacco consumption is no doubt a culprit for lung cancer; however, worldwide, the incidence of lung cancer has been shown to increase among female non-smokers, especially in Asian countries, which raises an alarm for the possibility of a new etiology for lung cancer. An inherited genetic susceptibility to lung cancer has also been suggested in literature. Some studies have found an association between tobacco smokers and an inherited susceptibility for developing addiction to nicotine, which is a potential carcinogen for lung cancer. Family history of lung cancer is a strong risk factor for lung cancer development. Molecular studies have found a difference in KRAS and EGFR genes between lung cancers in nonsmokers and smokers. This may entail an added investigation methodology for lung cancer in future (Brambilla, 2009).

Most lung cancer cases are at stage III or IV (metastasis to distant body organs) at the time of diagnosis, because lung cancer symptoms do not appear early, or the symptoms are often misdiagnosed. Most early stage lung cancers are found incidentally while treating other medical conditions. Patients normally seek medical attention for persistent cough or chest pain, or difficulty in breathing (dyspnea), which is often mistaken for arising from other more common conditions. History of cigarette smoke or family history of lung cancer needs to be taken into consideration.

Chest X-ray or CT scan or PET/CT scan can reveal a mass or an abnormality of the chest. A biopsy can be done to remove tissue samples for cancer testing. MRI is needed if the patient seeks medical attention on account of symptoms relating to other body organs such as brain (headache, dizziness, confusion, and/or coma), liver (jaundice or a liver mass), bone (fractures), or adrenal gland (SIADH, or ectopic secretion of ACTH). Besides imaging for metastatic cancer, pulmonary function tests are also required. Molecular testing can be used to look for gene changes, like the overactive EGFR mutations and ALK gene rearrangement. These gene changes, when present, cause new cancer cells to grow quicker.

Treatment options for lung cancer are based on many factors. Staging is very important for treatment planning, because the purpose of cancer staging is to evaluate the extent of the disease. The T (tumor) N (node) M (metastasis) staging is based on the extent of tumor (T in situ, T1-4), the spread of cancer cells throughout the body via lymph nodes (N0-N3), and metastasis of the disease to distant sites such as bone, brain, liver, adrenal gland (M0-1). The early stages of all cancers, including lung cancers, often have better survival rates.

Treatment for lung cancer includes surgery to remove the tumor. Lung surgery includes wedge resection, segmentectomy, lobectomy, or pneumonectomy. Radiation might be another option - to use high energy rays to locally treat or control lung cancer. Chemotherapy is the use of drugs to kill cancer cells by damaging their DNA or disrupting the making of DNA. Based on the result of EGFR and ALK molecular testing, targeted therapy is an option. Targeted therapy involves using a class of

drugs that stop the action of molecules that help cancer cells grow. These drugs will block the signal from EGFRs or from ALKs that stimulate the cancer cells to grow. Immunotherapy involves using drugs that increase the activity of the patient's immune system to kill cancer cells.

According to American Cancer Society (ACS), there has been an estimated 221,000 new cases of lung cancer diagnosed in the U.S. in 2015. Lung cancer is the second most common cancer in both sexes in the US compared to prostate cancer and breast cancer. However, it is the leading cause of cancer death in the U.S. compared to colon, breast, and prostate cancers combined. Lung cancer mainly occurs in older people. The average age at the time of diagnosis is about 70. More black men are likely to develop lung cancer than white men.

Survival rate of lung cancer (percentage of patients who live at least 5 years after diagnosis) varies depending on the TNM stage at the time of diagnosis. The National Cancer Institute's Surveillance Epidemiology and End Results (SEER) database reveals the trend for a 5-year relative survival rate for lung and bronchial cancer patients after diagnosis: a slight increased rate from 11.4% in 1975 to 18.2% in 2007. This 5-year survival rate is still very low, which makes lung cancer one of the most fatal diseases. This low survival rate can be explained by the advanced stage at the time of diagnosis, as described by Nichols et al in 2012 that the immediate cause of death is due to the complications of metastatic lung cancer.

The National Lung Screening Trial (NLST), a large clinical trial, used low-dose CT scan to screen 50,000 people aged 55 to 74 with a high risk for lung cancer. The study group included people who had been or who were currently smoking (30 pack years), but were not yet diagnosed with lung cancer. Individuals in the study underwent either 3 LDCT (Low Dose Computed Tomography) scans or 3 chest X-rays, each a year apart. The results showed a 16% lower chance of dying from lung cancer for individuals in the LDCT group compared to individuals in the chest x-ray group. There are many questions that still need to be answered from this study, but based on the findings of this study, ACS has issued guidelines for using LDCT as the primary lung cancer screening tool for high risk populations.

My grandfather passed away a few months later after the diagnosis from advanced stage lung cancer. It was a shock to my family, and it also affected my dad who is a smoker. My dad has since quit smoking. Hopefully, he will be able to overcome the nicotine withdrawal symptoms, and stop smoking for good.

## References

McKinley, M., O'Loughlin, V., and Bidle, T. (2013, 2<sup>th</sup> Ed) *Anatomy & Physiology: An Integrative Approach*. The McGraw Hill Education Inc.

Lubin JH and Caporaso NE. (2006). Cigarette smoking and lung cancer: modeling total exposure and intensity. *Cancer Epidemiology Biomarkers Prev.* Mar; 15(3): 517-23. Abstract. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/16537710>

York, M. (2005). Pathogenesis of lung cancer. *American Journal of Respiratory Cell and Molecular Biology Am J Respir Cell Mol Biol.* Sep; 33(3): 216-223. Retrieved from <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2715312/>

Brambilla, E. and Gazdar, A. Pathogenesis of lung cancer signaling pathways: roadmap for therapies (2009). Eur Respir J. Jun: 33(6): 1485-1497. Retrieved from <http://erj.ersjournals.com/content/33/6/1485.long>

Molina, JR, Yang, P, Sassivi, SD et.al. (2008) Non-small cell lung cancer: Epidemiology, Risk Factors, Treatment, and Survivorship. Mayo Clin Proc. 2008 May; 83(5): 584-594. Retrieved from <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2718421/>

Nichols, L; Saunders, R; and Knollmann, F. (2012). Causes of Death of Patients with Lung Cancer. Arch Pathol Lab Med. 136:1552-1557. Retrieved from <http://www.archivesofpathology.org/doi/pdf/10.5858/arpa.2011-0521-OA>  
American Cancer Society (ACS) Lung Cancer. Retrieved from <http://www.cancer.org/cancer/lungcancer-non-smallcell/?gclid=CNWopvTQ8MkCFU6QHwodpBYNnA>

NCCN Guidelines for Patients-Non-Small Cell Lung Cancer. Retrieved from <http://www.nccn.org/patients/guidelines/nscl/#55/z>

The National Cancer Institute's Surveillance Epidemiology and End Results (SEER) database. Retrieved from <http://seer.cancer.gov/statfacts/html/lungb.html>

American Cancer Society (ACS) Lung Cancer. Retrieved from <http://www.cancer.org/cancer/lungcancer-non-smallcell/?gclid=CNWopvTQ8MkCFU6QHwodpBYNnA>

American Cancer Society (ACS) Lung Cancer. Retrieved from <http://www.cancer.org/cancer/lungcancer-non-smallcell/detailedguide/non-small-cell-lung-cancer-detection>