

## LETTER TO EDITOR

## Lung Cancer

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Dear Editor,

Lung cancer is one of the most frequent cancers of the human being.

This cancer is strongly related with the smoking habit.

The quick diagnosis of the disease is depended of the quick recognition of the clinical signs and symptoms and also of the examinations as ct of the chest bronchoscopy, cytology and biopsy.

In this letter to the editor we present the new knowledge about the symptoms and the clinical examinations for the quick diagnosis of the disease.

### Epidemiology, Risk Factors, and Prevention

According to epidemiological data, lung cancer is a serious disease that places a heavy burden on public health in most Western countries. However, developing countries are not immune to this scourge, particularly countries such as China, where smoking—the primary risk factor for lung cancer—does not appear to be curtailed by changes in relevant legislation, as is the case in the United States and Europe.<sup>1</sup>

### Epidemiological Data

Only 25% of patients survive beyond one year from the time of diagnosis, while over the last 30 years, the five-year survival rate has remained virtually unchanged at 7%.

Nevertheless, over the last fifty years, the change in attitudes towards smoking has led to a significant reduction in the average daily cigarette consumption for men, from 12 cigarettes in 1945 to 4.6 in 1992.

The incidence of lung cancer in men decreased correspondingly from 80–120 cases per 100,000 men in 1962 to 70–100 per 100,000 in 2002. In contrast, death rates among women with lung cancer have not yet begun to decline, as peak cigarette consumption was recorded in 1974. This applies to all age groups. Now, consumption has fallen by 50%, but as mortality from lung cancer lags changes in smoking habits, the mortality rate for women continues to rise.<sup>2</sup>

Lung cancer occurs at twice to three times the rate in poorer than in richer areas, with corresponding variations in mortality rates by region. Each year, approximately 243,000 deaths from lung cancer are recorded in European Union countries (188,000 men and 55,000 women). For men, despite a slight decline in the number of deaths since the peak recorded in the early 1980s, lung cancer remains the deadliest cancer, causing approximately 50 deaths per 100,000 men in 1995. In contrast, among women, the incidence of lung cancer continues to rise, leading to approximately 22 deaths per 100,000 people in 1996. The highest rates of lung cancer incidence and mortality in men have been recorded in Hungary, Poland, and Belgium, while the lowest rates have been recorded in Sweden and Portugal. Similarly, for women, the highest rates are found in Denmark, Hungary, and the United Kingdom, while the lowest are in Spain, Portugal, and Malta.<sup>3</sup>

In the US, lung cancer currently has the highest mortality rate among all cancers for both men and women. However, rates among men have declined significantly in recent years, while rates for women showed a steady upward trend until 1998, when they stabilized.

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These geographical differences reflect the varying levels of the global smoking epidemic. Although incidence and mortality are declining slowly but steadily in most Western European countries, the United States, and Australasia—especially in Asia—the increase in smoking rates will unfortunately lead to an increase in global lung cancer mortality above current levels, estimated at one million deaths per year in the 21<sup>st</sup> century.<sup>4</sup>

### Smoking

Smoking causes lung cancer. The likelihood of developing lung cancer is proportional to the dose, and quitting smoking reduces this probability, but even after quitting, the probability is increased compared to a non-smoker for at least 40 years.

The probability of developing lung cancer throughout the lifetime life of a habitual smoker is approximately 1 in 15, while for a non-smoker it is 1 in 200-300. If someone stops smoking at the age of 50, the risk is reduced to approximately 1 in 30. As a result, the incidence of lung cancer among former smokers is increasing in relation to current smokers, having reached 50% at present.

It should be emphasized that the “safe cigarette” is a big myth. The increasing use of light cigarettes, i.e., those with lower tar levels and filters may be responsible for the increase in the incidence of adenocarcinoma, as smokers tend to inhale more deeply and the smoke enters deeper into the lungs. The rate of adenocarcinoma, unlike other types of cancer, has increased in recent years from 15% to 30%. The likelihood of lung cancer for long-term pipe or cigar smokers is lower, but this does not mean that these forms of smoking are harmless, as they are responsible for other types of cancer.<sup>5</sup>

### Other Risk Factors Besides Active Smoking

Lung cancer rates increase with age and account for 10% of all cancers. Some cases of lung cancer do not appear to be related to smoking, such as bronchioloalveolar carcinoma (BAC), which mimics chronic incurable pneumonia. These tumors spread within the section or lobe of the lung, and the majority do not metastasize.

The most important risk factor, apart from smoking, are passive smoking and exposure to asbestos. Epidemiological data show that long-term passive smokers have a 20-30% increased risk of developing lung cancer when the smoker is a spouse or partner, and even higher when it comes to colleagues in the same work environment. Passive smoking causes

approximately 600 deaths from lung cancer per year in the United Kingdom.

Individuals who have symptoms of asbestosis due to occupational exposure to this harmful substance are 500% more likely to develop lung cancer.

People with COPD are clearly at greater risk of developing lung cancer.<sup>5</sup>

### Prevention

Nicotine is extremely addictive. After all, we all remember Mark Twain’s famous quote, “Quitting smoking is the easiest thing in the world—I’ve done it many times”. Although more than 70% of smokers would like to quit, the rates of long-term smoking cessation remain low. Simple advice from a doctor is heeded by 1-3% of smokers. If the advice is followed by nicotine replacement therapy and appropriate support, the success rate for quitting smoking reaches 6–8%, but this mainly concerns people over the age of 50. Young people consult their doctor less often, so the impact of medical advice on them is much smaller. Smoking cessation programs cost £800 per year of life gained (1998 data), while chemotherapy for lung cancer costs 25 times more. Lung cancer is responsible for one in five cancer deaths Lung cancer is responsible for one in five cancer deaths in the UK and is the most common cause of death from the disease in both men and women. As there are no early diagnostic tests or effective screening programs, most patients see their doctor after they have developed symptoms.

### Identification of High-Risk Patients

Most cases of lung cancer occur after the age of 60 and with increasing frequency with advancing age, while it affects men more often than women. The symptoms and signs are usually vague and general and are usually found in the context of long-term problems, such as “smoker’s cough.” Ninety percent of cases are or were smokers. The risk is cumulative and is mainly determined by the length of time spent smoking and the number of cigarettes smoked per day. Occupational factors are also very important, e.g., patient exposure to asbestos, as well as family history, especially when it includes lungs, brain, and cervical cancer.<sup>5</sup>

### Symptoms

More than three-quarters of patients with lung cancer visit their doctor for the first time because of a “different condition” or persistent cough. Some patients complain of shortness of breath or difficulty breathing and possibly some kind of chest pain. Hemoptysis is

usually a symptom that indicates extensive disease, as is hoarseness, which is often due to damage to the lower laryngeal nerve from tumor pressure. Some of the symptoms of metastatic cancer are bone pain (pathological fractures), spasms, as well as confusion or headaches (when the metastasis is in the brain). General symptoms include weight loss, fatigue, and anorexia, which are non-specific and very common. Hemoptysis, dyspnea, and abnormal spirometry values are findings more directly associated with lung cancer, immediately after ruling out the symptoms that were reported 6 months prior to diagnosis<sup>6</sup>

## Clinical Examination

Many of the symptoms and signs and clinical findings that raise suspicion of lung cancer are difficult to differentiate from those of other pathological conditions of the lungs, especially chronic obstructive pulmonary disease (COPD), which often coexists with cancer.

There may be shortness of breath at rest or after minimal exertion and heavy, labored breathing. There may also be local clinical signs in the chest, e.g., signs suggestive of atelectasis of a lung lobe, pulmonary consolidation, or pleural effusion of one hemithorax. Some more specific clinical signs are supraclavicular lymphadenopathy, clubbing of the fingers, and signs of superior vena cava obstruction—namely swelling of the neck, face, and eyelids, respiratory wheezing or persistent hemoptysis or hoarseness. Patients with lung cancer usually have a cachectic, pale, and anemic appearance and generally appear exhausted and suffering. Some clinical signs that indicate metastatic disease are usually hepatomegaly, skin metastases, or increased intracranial pressure.

## Examinations

### Chest X-ray

Nodules larger than 1 cm in diameter can be detected on a simple X-ray. Other X-rays may reveal the presence of atelectasis/consolidation or unilateral pleural effusion. However, we must bear in mind that when the cancer is very small, it may not be possible to diagnose it from a single chest X-ray. In cases, therefore, where the symptoms raise suspicion of the disease, but the X-ray is negative, we refer the patient to a pulmonologist or request a reassessment with further radiological examination within a period of a few weeks.<sup>6</sup>

### Blood Tests, Sputum Tests

Cytological examination of sputum is not common, but it is particularly indicated when the patient is

unlikely to tolerate or accept bronchoscopy or a similar procedure.

When a patient is referred to by a general practitioner, they usually see a pulmonologist. The tests recommended vary depending on the radiological findings but usually include diagnostic CT scanning with contrast medium and, on the same day, bronchoscopy with a fiberoptic bronchoscope or biopsy. On the same day, they will also meet with a specialized nurse. Further tests may follow, and the case will certainly be discussed at the oncology council of various specialties. After this council, the patient is fully informed about their health status and the findings of the evaluation, and they will be presented with a detailed treatment plan as well as other tests for any reflexes.<sup>7</sup>

### *Types of Cancer and Their Prognosis*

Lung cancer is divided into two main types: small cell and non-small cell. Overall, small cell cancer has a worse prognosis than non-small cell cancer, with an average life expectancy of 30 days if left untreated. Overall, small cell cancer has a worse prognosis than non-small cell cancer, with an average life expectancy of 30 days if left untreated from the moment it appears. In contrast, the average life expectancy for patients with untreated non-small cell cancer in stages I–III is six months. Non-small cell cancer can be further classified into adenocarcinoma and squamous cell carcinoma, but treatment is based on staging rather than cell type.<sup>7,8</sup>

### *Staging*

Small cell lung cancer is simply classified as limited or extensive stage.

Non-small cell cancer is treated according to its stage, while the results of treatment depend on the stage of the disease. Tumors are classified according to the TNM staging system. The clinical classification (cTNM) is determined by the results of imaging tests and biopsy before surgery, while the pathological classification (pTNM) is based on the examination of tissue removed during surgery. Both classifications use descriptions of the local tumor (T stage), the degree of lymph node involvement (N stage), and the presence of metastases (M stage).<sup>9,10</sup>

## Diagnostic Methods

### *Bronchoscopy*

Bronchoscopy with a flexible fiberoptic bronchoscope is often performed and has a low risk. It is the technique of choice for obtaining tissue for diagnostic purposes from tumors located centrally in the CT scan image or

from tumors accompanied by pulmonary atelectasis. Transbronchial needle aspiration biopsy (TBNA) is an increasingly used technique for the histological diagnosis of both primary cancer and lymph nodes adjacent to the airways. Endobronchial ultrasound (EBUS) will likely be quite helpful in the diagnosis and staging of patients with suspected lung cancer.<sup>11</sup>

### **Positron Emission Tomography (PET)**

Positron emission tomography (PET) is based on the increased metabolism of glucose by cancer cells. Desoxyglucose is made radioactive by attaching radioactive F to position 18 (18F-fluorodeoxyglucose or 18F-FDG) and is administered intravenously. The substance is immediately absorbed by malignant cells as glucose, but cannot be fully metabolized, so it is trapped and concentrated as 18FDG – 6 – phosphate. Computed tomography combined with PET (PET-CT) allows precise localization of areas containing the FDG derivative. PET is, among other things, a very sensitive method for evaluating lymphadenopathy. Therefore, if the suspicious lymph nodes during staging with computed tomography prove negative in PET, no further expansion is required. The specificity of PET-CT for detecting lymph node involvement is approximately 85%.

### **Ultrasound**

The role of ultrasound in the diagnosis of lung cancer is limited but extremely useful. It can be used to confirm the presence of pulmonary lesions in the chest wall, if there is doubt from the CT scan image, or to help characterize liver lesions seen on the CT scan. However, ultrasound is most often used to guide invasive procedures, such as pleural puncture, biopsy of lung tumors located very close to the chest wall, biopsy of metastases in the liver and ribs, or finally, to guide the biopsy of supraclavicular lymph nodes.<sup>12,13</sup>

### **Magnetic Resonance Imaging (MRI)**

The unique usefulness of magnetic resonance imaging lies in the evaluation of tumors at the apex of the lungs, as it provides information about the infiltration of adjacent soft tissues, mainly the brachial plexus.<sup>12,13</sup>

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