

USA Incidence and mortality

Lung cancer is the **leading cause of cancer-related death** in both genders worldwide. In 2019, it is expected to account for 228 150 new cases and 142 670 deaths in the USA.

It is the second most common solid tumour type in both genders, after prostate cancer in men and breast cancer in women.

Lung cancer is the cause of 24% and 23% of all male and female cancer-related deaths, respectively, exceeding prostate and breast cancer mortality.



Fig. 1.1

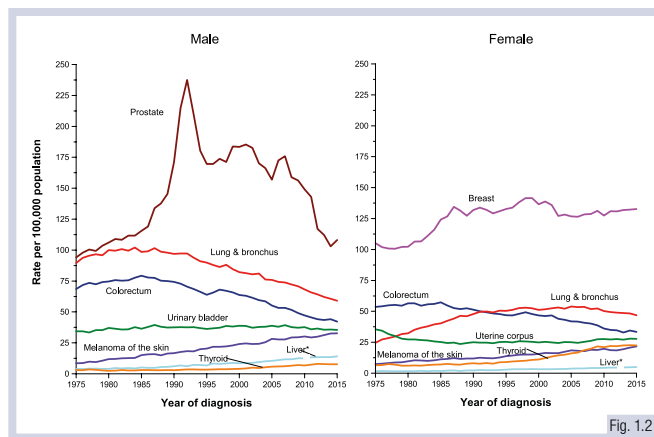


Fig. 1.2

In both genders, USA lung cancer incidence rates increased from the 1970s, until the mid 1980s in men and the late 1990s in women.

Incidence is now beginning to decline, possibly due to the reduction in smoking prevalence. Differences in lung cancer incidence patterns between men and women reflect mainly historical disparities in smoking habits.

Cigarette smoking prevalence peaked about 20 years later in women than in men.

The USA lung cancer death rate rose for most of the 20th century, peaking at the beginning of the 1990s for men, and almost two decades later for women.

Lung cancer death rates have followed the same trend as smoking prevalence and incidence rates, demonstrating the strong correlation between the major risk factor and the disease and the poor prognosis of this malignancy, respectively.

Recently, a steady decline in lung cancer death rates has been observed in both sexes, as a result of combined improvements in primary prevention, control of associated risk factors, and treatment.

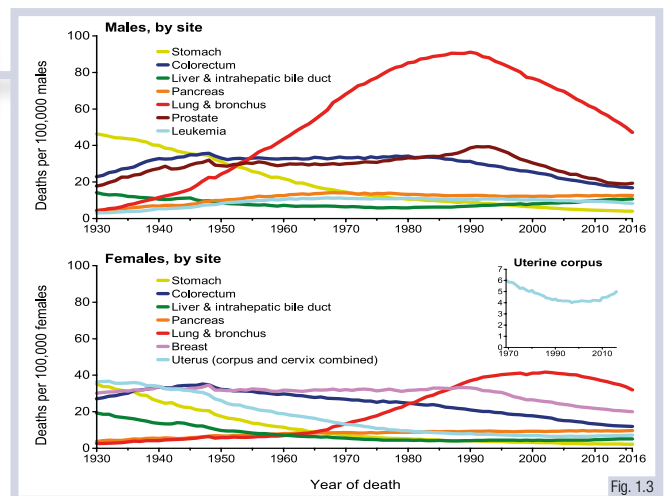


Fig. 1.3

REVISION QUESTIONS

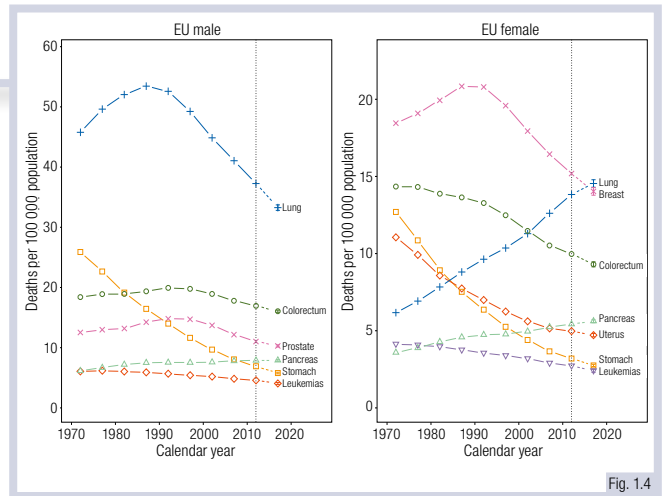
1. What is the lung cancer incidence trend in the USA over the last 20 years?
2. Is there a difference in lung cancer mortality rates between men and women?
3. What is the percentage of deaths due to lung cancer among all cancer-related deaths?

European scenario

European predictions for the year 2018 in men and women, estimated 267 000 and 121 000 lung cancer-related deaths, respectively, corresponding to about 20% of total cancer deaths in both sexes combined.

Lung cancer is the primary cause of cancer-related deaths in men in Europe and is second only to breast cancer in women, with a very slight difference in the number of expected deaths.

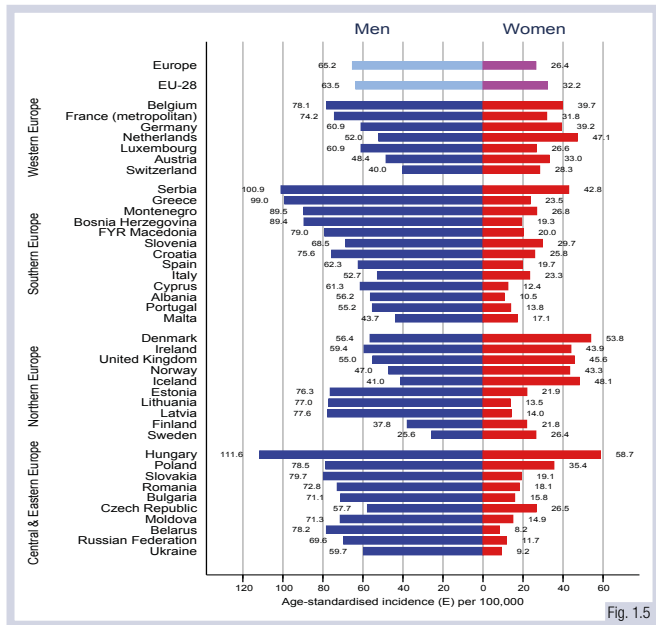
European mortality for lung cancer peaked in the late 1980s in men and began declining later, while in women, in contrast to the USA scenario, mortality continues to increase with 26.4 cases/100 000 in 2018. An opposite trend has been observed in breast cancer.



An evaluation performed in 2018 revealed that the lung cancer incidence rate for men was highest in Central and Eastern European countries and lowest in Northern Europe.

On the contrary, with the exception of Hungary, the incidence rate for women was highest in Northern European countries and lowest in Eastern Europe.

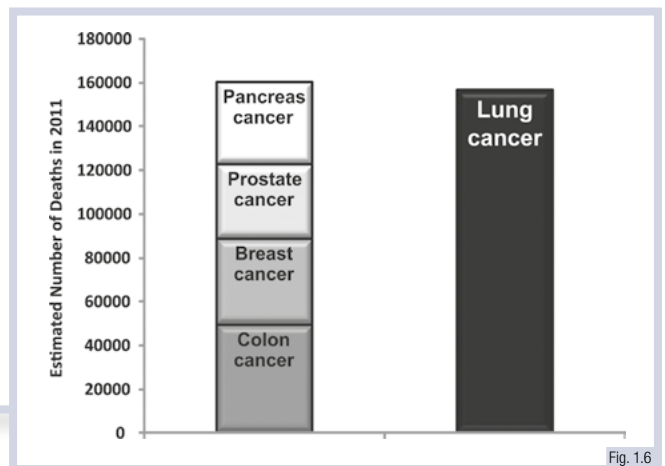
Considering both sexes combined, the highest incidence rates were seen in Hungary (incidence rate 111.6 cases/100 000 for men and 58.7 cases/100 000 for women).



Lung cancer rates in underdeveloped countries are lower than in developed ones, although incidence and mortality are slowly increasing.

The World Health Organization estimates that lung cancer deaths worldwide will continue to rise, largely as a result of an increase in global tobacco consumption (over one billion smokers worldwide).

Worldwide, every year, as many people die from lung cancer as the cumulative number resulting from prostate, breast and colon cancers.



REVISION QUESTIONS

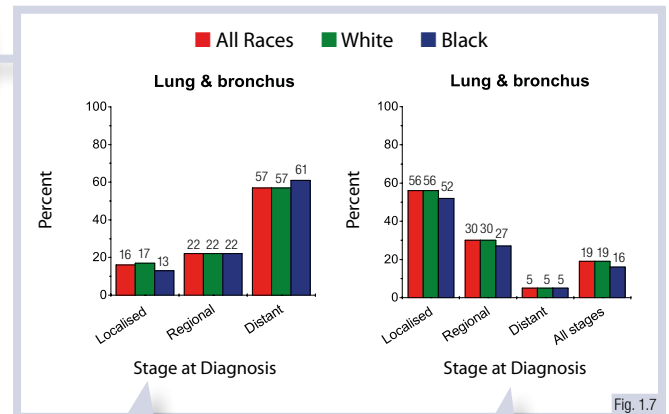
1. Are there differences in the lung cancer mortality rates between the USA and Europe?
2. Is lung cancer incidence homogeneous throughout Europe?
3. What is the mortality rate due to lung cancer compared with other 'big killers'?

Clinical features and survival expectancy

Around only 15% of all lung cancer cases are diagnosed at an early stage, with a 5-year survival rate >50%.

In a large percentage of cases, lung cancer is diagnosed at an advanced stage with distant metastases and a 5-year survival rate of about 5%.

The 5-year survival rate for all lung cancer stages combined is about 18%.



Stage distribution by race, United States, 2008-2014

5-year relative survival rates by race and stage at diagnosis, United States, 2008-2014

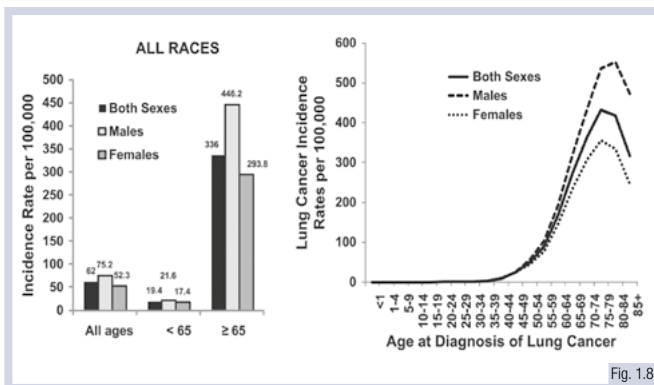


Fig. 1.8

Lung cancer in both sexes is predominantly diagnosed in the elderly population (median age at diagnosis is 71 years).

Compared with men, women are less likely to have a smoking history, are generally younger at the time of diagnosis, and have a better survival expectancy at any stage, independent of the therapeutic approach.

Lung adenocarcinoma is the most common histological subtype among women.

Adenocarcinoma accounts for 38.5% of all lung cancer cases, while squamous cell carcinoma and large cell carcinoma account for 20.0% and 2.9%, respectively.

Over the past decades, adenocarcinoma incidence has progressively increased, and it has now replaced squamous cell carcinoma as the most prevalent non-small cell lung cancer histotype.

Lung adenocarcinoma is also the most represented histotype among never-smokers.

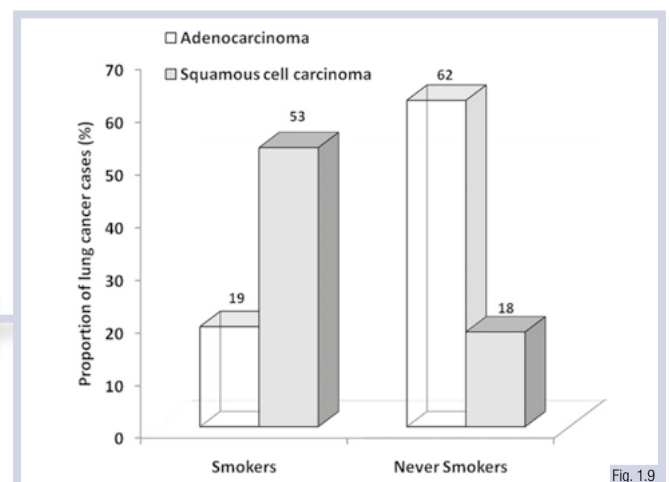


Fig. 1.9

REVISION QUESTIONS

1. What is the proportion of patients with lung cancer diagnosed at early stage of disease?
2. Is there a correlation between a clinical characteristic (such as female gender or smoking attitude) and one specific histotype?
3. Is the subtype histology prevalence the same compared with 30 years ago?

Pathogenesis of lung cancer

The major function of the lungs is respiratory exchange. Inhaled air and potentially dangerous substances are conducted to the alveoli through a network of bronchi and bronchioles.

The putative stem cells of the bronchus are basal cells, which are believed to give rise to the differentiation of ciliated, mucous and neuroendocrine cells.

Lung cancer may arise from all these differentiated and undifferentiated cells, from either the central (small cell lung cancer and squamous cell carcinoma) or the peripheral (adenocarcinoma) airway compartment.

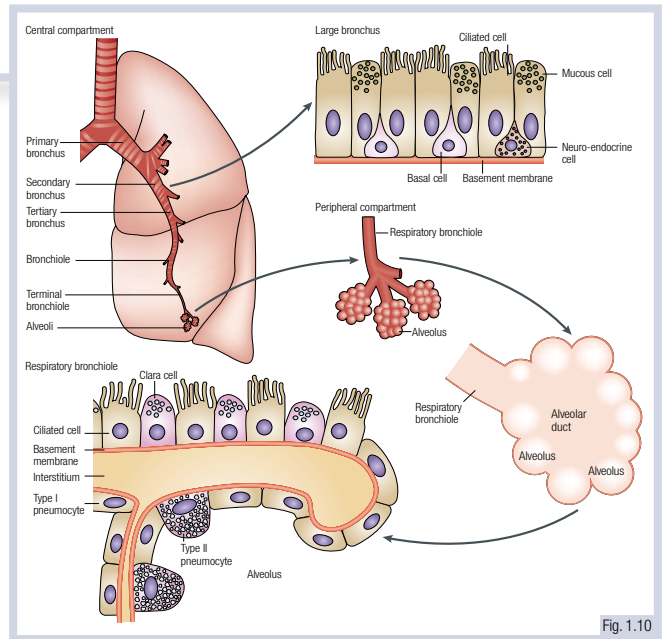


Fig. 1.10

The interaction between inhaled carcinogens and the epithelium of upper and lower airways leads to the formation of DNA adducts: pieces of DNA covalently bound to a cancer-causing chemical.

Repair processes may remove the DNA adducts and restore normal DNA, or alternatively cells with damaged DNA may undergo apoptosis.

If DNA adducts persist or are misrepaired, they result in a mutation and can cause genomic alterations. These are key events in lung cancer pathogenesis, especially if they occur in critical oncogenes and tumour suppressor genes.

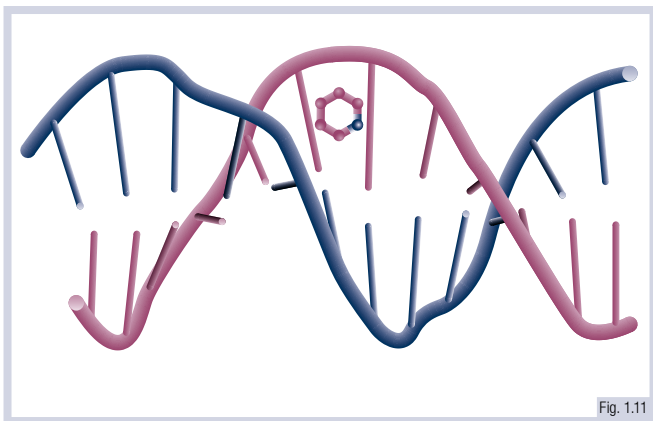


Fig. 1.11

Lung cancer pathogenesis is also affected by a genetic component: it relates to the host susceptibility to lung cancer, with or without exposure to carcinogens.

Studies on familial aggregation have supported the hypothesis that a multifactorial hereditary component is possible, even if a clear mechanism of familial transmission is still not described.

The addition of smoking to this genetic inheritance is associated with a three-fold increased lung cancer risk.

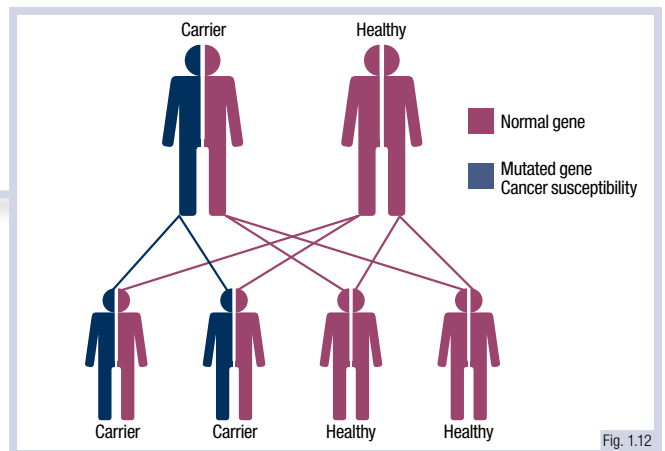


Fig. 1.12

REVISION QUESTIONS

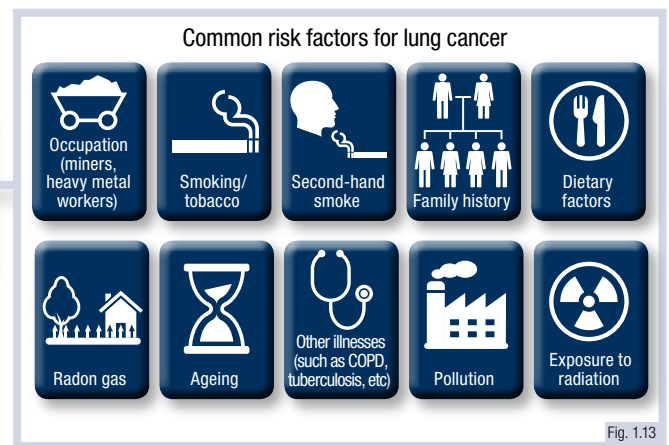
1. Is there a unique and specific component of airway epithelium from which lung cancer can arise?
2. What are the consequences of the action of inhaled carcinogens on the airways' epithelium?
3. Does the hereditary component have a role in lung cancer pathogenesis?

Risk factors

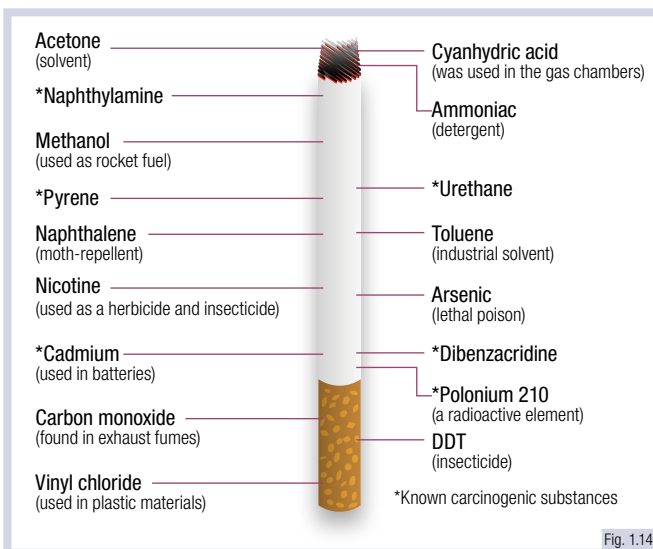
Smoking is considered the principal risk factor in lung cancer patients, causing more than 80% of all cases.

Non-smoking-related risk factors include occupational exposure to asbestos, chromium, arsenic, cadmium, silica and nickel, as well as second-hand smoke, outdoor air pollutants, previous lung diseases, radon exposure and dietary factors.

The main **modifiable risk factors** for cancer pathogenesis are smoking habit, alcohol consumption, overweight and obesity, and the correct intake of meat, fruit and vegetables in the diet.



COPD, Chronic obstructive pulmonary disease



The International Agency for Research on Cancer (IARC) has identified at least 50 carcinogens in tobacco smoke, targeting both central and peripheral airways.

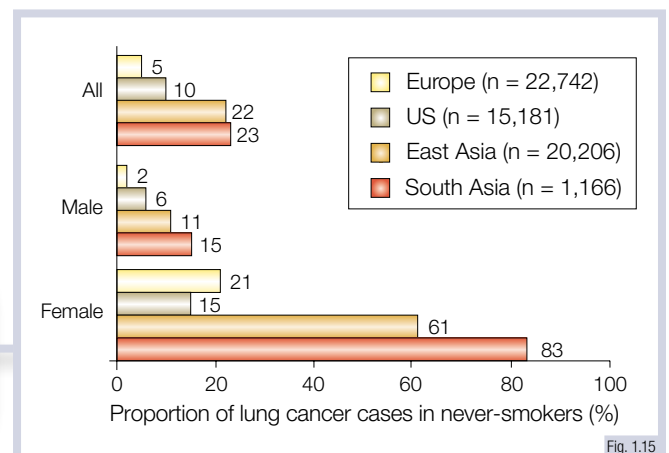
The most **potent carcinogens** in cigarette smoke are the **polycyclic aromatic hydrocarbons (PAHs)** and the **aromatic amines, N-nitrosamines**. It also contains benzene, vinyl chloride, arsenic, chromium, radon, and its decay products, bismuth and polonium.

In the absence of such risk factors, the genetic susceptibility to lung cancer remains the only other parameter predisposing to the onset of the disease.

An estimated **10%–25% of lung cancers worldwide occur in never-smokers**, defined as individuals who have smoked less than 100 cigarettes in their lifetime.

Cancers arising in **never-smokers** predominantly target the distal airways, favouring adenocarcinoma histology and female gender. One of the most relevant risk factors is environmental tobacco smoke exposure.

Lung cancer prevalence in never-smokers is **higher in Asian countries**, especially in women, probably due to the inhalation of cooking oil vapours and particles emitted by domestic use of coal for cooking and heating.



REVISION QUESTIONS

1. What is the definition of 'never-smokers'?
2. Is there a different distribution of lung cancer in never-smokers across the world?
3. Which are the most potent carcinogens of cigarette smoke?

Summary: Epidemiology, pathogenesis, and risk factors

- Lung cancer is the leading cause of cancer-related death worldwide in both genders
- USA incidence rates in both genders increased until the 1990s and began to decline later, similar to the trend in mortality
- In Europe, lung cancer-related deaths in women are secondary only to breast cancer and, in contrast to the USA scenario, the mortality rate continues to increase
- Worldwide, every year, as many people die from lung cancer as from the other 'big killers' (prostate, breast, and colon cancer) combined
- Only 15% of all lung cancer cases are diagnosed at an early stage, while the majority present with distant metastases at diagnosis and a 5-year survival rate of about 5%
- Median age at diagnosis is 71 years and adenocarcinoma is now the most prevalent histotype
- Lung cancer may arise from all the differentiated and undifferentiated cells of the upper and lower airways. The formation of DNA adducts as a consequence of the inhalation of carcinogens plays a central role in lung cancer pathogenesis
- Lung cancer pathogenesis is also affected by a genetic multifactorial susceptibility, which may be further influenced by exposure to certain carcinogens
- Smoking is the principal risk factor for lung cancer, causing more than 80% of all cases
- Non-smoking-related risk factors include occupational exposure to carcinogens, second-hand smoke, pollution, dietary factors, radon exposure and genetic susceptibility

Further Reading

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