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LUNG CANCER AND MESOTHELIOMA

PROFESSOR CHRISTOPHER WHITTY

In all the talks on cancer so far this year there has been strong reasons for optimism; major cancers are being prevented, or treated, with the great majority of people diagnosed with cancers such as breast, prostate or melanoma cancers alive and well a decade later. In this talk we enter a bleaker world. Lung cancer is the commonest cause of cancer deaths in the UK in both men and women. Most people diagnosed with lung cancer today will be dead within a year. The remarkable progress we have seen in treating other cancers has been much slower in lung cancers. The tragedy of this is that great majority of cases occur, wholly avoidably, because a wealthy industry has pushed highly addictive products, that they know will kill their customers, onto them at an early age. Other cases are the by-product of air pollution and (increasingly infrequently) industry.

There are some grounds for optimism. In higher income countries smoking is declining, slowly. There have been substantial improvements in treating some (rarer) types of lung cancer. Earlier diagnosis would be transformative and may well be possible. The field of immunotherapy holds considerable promise to treat at least some cancers. The asbestos epidemic, which drives some lung cancer and almost all mesothelioma, probably peaks this year. But we need to be clear eyed: lung cancer is a terrible curse on humanity, and it mainly exists to make profit. The cumulative lifetime risk around 15% for male smokers, and <2% for non-smokers. And we should never, never blame those who were addicted to nicotine, deliberately, at a young age by a large, wealthy and highly organised industry and then go on to get lung cancer. Most smokers want to stop, and find they cannot, and this is because the products they smoke are designed to be highly addictive.

The evidence that smoking causes lung cancer comes from multiple sources and is overwhelming. The simplest data correlated smoking and cancer rates in the population. Case-control studies from the 1930s onward compared patients suffering from lung cancer (case) with those without (control) and found much higher rates of smoking in the cancer cases. The most convincing evidence was from cohort studies. The British doctors study followed 34,439 male doctors from 1951. Within 4 years lung cancer rates much higher in heavier smokers.

There was good news - stopping works. For men who stopped at ages 60, 50, 40, and 30 the cumulative risks of lung cancer by age 75 were 10%, 6%, 3%, and 2%. It was 16% in current smokers at that stage. For lifelong non-smokers the risk was 0.2% for men and 0.4% for women.

The response of the cigarette industry to this was a highly coordinated attack on science, although their own scientists accepted the findings. The principle aim was to sow doubt, when there was none. Initial attempts were made to undermine data showing active smoking caused health problems. Then, as that gradually failed there was a sustained attempt to undermine data that clearly demonstrated second-hand smoke is harmful. And at every turn they have tried to undermine the evidence for banning smoking in public places...plain packaging...and it goes on.

Targeting of children by the cigarette industry was initially overt, then covert, but it is not an accident children smoke. Cigarette companies make their profit from the most deprived. The unemployed are almost 2x as likely to smoke as those in work. Those with an annual income <£10,000 smoke at 2x rate of those with >£40,000. Smoking prevalence among adults with a serious mental illness is 2.5x greater than the general population. And



increasingly the industry looks to the developing or emerging economies for their profits. Which are huge. The UK High Court accepts that the net economic costs of tobacco use to society is estimated at about £13.7bn p.a. whilst the industry pay approximately £10bn in taxes p.a.

Smoking is not the only preventable risk factor for lung cancer, although it is by far the biggest one. The International Agency for Research on Cancer (IARC) confirmed air pollution has an epidemiological link in 2013. About 1 in 10 lung cancer cases in the UK currently estimated to be caused by exposure to air pollution, mainly particulate matter PM2.5 and possibly PM10. For indoor air pollution the biggest risk is second-hand cigarette smoke. Radon gas is a natural (but small) risk.

Symptoms and signs are unfortunately minimal in early lung cancer, and this is part of the reason for its high mortality as it is usually detected late. They include persistent cough, cough with blood, new shortness of breath, fatigue, weight loss and shoulder or chest pain. Most people with these symptoms do not have cancer, but some do, mainly current or ex-smokers.

Initial investigation is using chest X-ray or CT, usually followed, if there is a suspicious area seen, by bronchoscopy. If a cancer is found it will be described by stage, type and grade. The stage is the size and degree of spread. The grade is the appearance of the cells, the more different from normal cells the higher the grade. Type: there are several types in lung cancer determined by the cell they arise from. The important differentiation for lung cancer is between small cell and non-small-cell lung cancer, as their outlook and treatment are very different.

For early (localised) non-small-cell cancer *surgery* is often the treatment of choice, but for small cell carcinoma it is less effective as it has often spread even if detected when small, so chemotherapy and radiotherapy are more important. In non-small cell cancer *radiotherapy* may have a role if the person is not fit enough for surgery, or after surgery, or with chemotherapy to aid treatment. In small cell cancer radiotherapy is used in early disease with chemotherapy and there may also be prophylactic cranial irradiation (brain). Radiotherapy may also be used to control symptoms (palliative).

Chemotherapy in lung cancer is used in a minority of non-small-cell cancers but a much larger proportion of small-cell cancer. Cytotoxic drugs- which kill cells which are dividing are the basis of this, and many are decades old. Normal cells recover much better than cancer cells after these drugs. They have significant, although in most cases temporary, side effects. Origins include plants, bacteria and mustard gas.

New advances in drugs for lung cancer include:

targeted therapy: drugs which interfere with the functioning of lung cancer cells.

immunotherapy: drugs (or possibly vaccines) which use the immune system to fight lung cancer. Immunotherapy was covered in the first talk in this series.

These newer drugs are currently for quite a restricted range of situations, but likely to expand over the next few years.

Even more important than new drugs, however, is earlier diagnosis, especially of NSCLC (non-small-cell cancers). There is a live debate about screening for lung cancer with CT scans in smokers.

Occupational cancers are a small group, but important because they are preventable. Most manifest through the lung, and the most important is asbestos, which causes both lung cancer and mesothelioma, a cancer of the lung lining. The asbestos-driven mesothelioma epidemic is probably due to peak this year. Like lung cancer mesothelioma is an almost entirely preventable cancer. 94% of the risk is related to exposure to asbestos, almost all occupational. In 1955 Doll showed asbestos link with lung cancer; in 1960s link with mesothelioma clearly demonstrated in South Africa. Its use in industry, homes and schools continued to rise until the 1970s, and it was not banned until the end of the 1990s. It is unfortunately very useful, very versatile, and potentially very dangerous. Mesothelioma mortality rates have increased by 887% since the early 1970s. 59% of patients diagnosed at Stage 1 survived their disease for at least one year, 30% of patients diagnosed at Stage 4. Five-year survival in men ranges



from 13% in 15-49-year-olds to 4% in 80-99-year-olds in England. It is mainly a disease of men from relevant industries (shipbuilding, construction) and is highly geographically concentrated.

Lung cancer is, and will remain for many years, the leading cause of cancer mortality. The great majority due to smoking; it is a profit-driven cancer, using deliberate early addiction. Smoking is falling, and so will lung cancer, but depressingly slowly. A minority is due to air pollution and occupation, also mostly preventable. Earlier diagnosis is essential. Treatment is improving, but from a low base and relatively slowly. Asbestos is the leading occupational cause of cancer- mesothelioma and lung cancer, and we are now at the peak of its toll on those who were occupationally exposed.

Further reading.

Cancer Research UK has very good sites on lung cancer

<https://www.cancerresearchuk.org/about-cancer/lung-cancer>

And mesothelioma. <https://www.cancerresearchuk.org/about-cancer/mesothelioma>

The Roy Castle Lung Cancer Foundation has some additional very useful information <https://www.roycastle.org/>

For clinicians, a recent review of the current filed in the BMJ is here:

<https://www.bmj.com/content/365/bmj.11725>

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