

Epidemiology

Fine particles and lung cancer

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Which constituent of particulate matter is causing lung cancer?

Almost five decades have elapsed since the effect of the so-called "urban factor" on lung cancer has been suggested.¹⁻³ Air pollution has always been an attractive explanation for the 10-40% increase in lung cancer mortality observed in urban versus rural areas, but confounding from smoking and other factors has been a great limitation in interpreting geographical comparisons. Several attempts have been made to specifically evaluate the role of air pollution on lung cancer aetiology during the 1960s and 1970s.⁴ In 1976, in a review for the International Agency for Research on Cancer (IARC), Higgins⁵ concluded that the studies available:

"provide support for the view that air pollution is a factor in this disease. But the effect of pollution cannot be large. It is likely to be a small fraction (possibly a tenth) of the effect of cigarette smoking."

When the results of the two large American cohort studies on air pollution, the Six Cities Study⁶ and the American Cancer Society (ACS),⁷ were published, a strong association between particulate matter (PM) concentrations and cardiorespiratory mortality was reported, and even though important individual confounders like smoking and occupational exposure were controlled for, a link with lung cancer was noted. Confirmation of the preliminary suspicions finally arrived, reinforced by the publication of the additional follow up of the ACS cohort in 2002.⁸ In this last report, the mortality of approximately 500 000 adult men and women was followed from 1982 to 1998. The study indicated a significantly increased mortality risk ratio for lung cancer (RR = 1.14, 95% CI 1.04 to 1.23) with each 10 µg/m³ increase of PM_{2.5} (particulate matter with an aerodynamic diameter <2.5 µm). In the American studies, long term exposure was estimated from metropolitan annual average ambient concentrations; contrasts in air pollution exposure were based on inter-city concentration differences, yet no information on exposure to

pollutants was available at the individual level. European data on the link between air pollution and lung cancer came somewhat later, but they had the great advantage of providing information on confounders and exposure to traffic derived pollutants at individual rather than at community levels.^{9,10}

When interpreting the findings regarding the impact of air pollution on the general population, it should not be forgotten that the greatest exposures to vehicular fuels and exhausts occur occupationally. Several studies have indicated that diesel exhaust contributes to the human lung cancer burden.¹¹ Although there are several studies showing that professional drivers in large cities, particularly taxi drivers, experience an increased risk of lung cancer,¹² it is difficult to disentangle the specific role of gasoline versus diesel exhausts.

As in many other instances, results of epidemiological studies raise many questions. One is of paramount importance for public health intervention: Is there a specific air pollutant responsible for the health effect? If a toxic agent is recognised, then regulations can duly follow. Air pollution is a rather complex issue, not only because the air we breathe is a mixture of several gases and PM, but also because the make-up of PM—a variety of airborne solid and liquid particles, including soot, organic material, salts such as sulphates, nitrates, metals (well known carcinogens such as arsenic, chromium, nickel), and biological materials—varies depending on the pollution sources and time period. Consider for example, exhaust from diesel engines, where thousands of different combustion products, including a variety of recognised genotoxins, may adsorb small solid carbon particles, and the organic fraction includes many polycyclic aromatic hydrocarbons (PAH) and PAH derivatives which are powerful mutagens and carcinogens. To complicate the issue, only recently has the biological importance of ultrafine particles (smaller than 100 nm in diameter) come into focus.¹³

Harrison and colleagues, in this issue of the Journal,¹⁴ address the very practical question with an elegant

calculation; whether the lung cancer effect that has been found for exposure to PM in the large cohort studies can be explained on the basis of the ambient concentration of relevant lung carcinogens—arsenic, chromium, nickel, and PAH—or whether there is an overall effect of the PM itself. They combined the WHO unit risk factors with concentrations of cancer causing chemicals found in the atmosphere in typical US cities during the 1960s, and used these to predict annual cancer rates in the ACS study. They found that the cancer rates predicted and observed were rather similar; an indication that known chemical carcinogens are responsible for the lung cancers due to PM_{2.5}. A rather tentative conclusion (in contrast with earlier findings from Rösli and colleagues¹⁵) given that there are several uncertainties regarding this issue that the authors point out.

In the meantime, research into the mechanisms linking PM and lung cancer progresses.¹⁶ In vitro studies suggest that particles impact genotoxicity as well as cell proliferation via their ability to generate reactive oxygen and nitrogen species. This may happen because of the physicochemical characteristics of the particle surface, or due to their ability to stimulate cellular oxidant generation via various mechanisms, including an inflammatory response. However, in vitro studies need confirmation by in vivo experiments.

Is particle matter responsible for causing lung cancer, regardless of its contents? The issue might have several implications for regulatory agencies in the future. For the time being we are left with an unresolved research question. However, international agencies may consider the accumulated evidence on air pollution and lung cancer available so far. Although the relative risks associated with complex, long term exposures are relatively small and difficult to detect, a large fraction of the population is exposed and the overall impact is not negligible.

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ECHO

Filtration technology arrests asthma allergen



Please visit the *Occupational and Environmental Medicine* website [www.occenvmed.com] for a link to the full text of this article.

Measures to abolish the threat of asthma to public health from soybean dust have been so successful that they could underpin future control standards for allergens, according to an evaluation in Barcelona. Success was achieved by combining knowledge and skills across a wide range of sectors and agencies.

The initial alert was an asthma epidemic in June 1996 traced to dust from ships unloading soybeans in the port, near the city. A significant benefit was introducing dry filtration technology in late 1997 to reduce emissions. This took the form of micropore size filter sleeves or special filters in series with PTFE membrane filter cartridges to replace standard filter sleeves in the unloading process. Once new operating licences were granted, in June 1998, the relatively crude control of emissions by limiting unloading brought in in June 1996 was lifted, and the pilot phase ran until December 1998.

Four indicators were used to evaluate effectiveness. Soybean dust emissions, available from 1997, dropped 96-98% between summers 1998 and 1999. Airborne dust load measured at one site in the port fell drastically (mean (median) 1089 (731) RAST U/m³ in June 1996 v 59 (35) U/m³ June-December 1998). No asthma epidemics were recorded in four city hospitals, and sentinel surveillance from the end of 1997 with a panel of high risk asthma sufferers uncovered just one cluster of symptoms, coinciding with unloading in adverse weather.

Similar problems with soybean dust have emerged elsewhere, including outside Spain, but no legislation has been developed to control the public health risk. That may change.

▲ Villalbi JR, et al. *Journal of Epidemiology and Community Health* 2004;**58**:461-465.