Ontario
Cancer Care Ontario
Action Cancer Ontario

Cancer Risk Factors in Ontario

Complex Mixtures

COMPLEX MIXTURES

Risk factor/exposure	Cancer	The context where high risks were reported	Magnitude of risk*	Strength of evidence[a]
Diesel engine exhaust	Lung	Occupational	1.2–1.8[b-g]	Sufficient
	Bladder	Occupational	…	Limited
Polycyclic aromatic hydrocarbons	Lung	Occupational	1.1–2.3[a,h]	Sufficient
	Skin	Occupational	2.2-4.0[h]	
	Bladder	Occupational	1.4–2.4[a]	
$PM_{2.5}$	Lung	Environmental	1.15–1.37[i,j,k]	N/A

Abbreviations: $PM_{2.5}$ = Particulate matter less than 25 µm in diameter.

Sources: [a]IARC, 2012; [b]Attfield et al., 2012; [c]Silverman et al., 2012; [d]Garshick et al., 2012; [e]Laden et al., 2006; [f]Olsson et al., 2011; [g]Pintos et al., 2012; [h]Partanen & Boffetta, 1994; [i]Chen et al., 2008; [j]Turner et al., 2011; [k]Lepeule et al., 2012

* Relative risk (RR) estimate: exposed vs. unexposed (diesel engine exhaust and polycyclic aromatic hydrocarbons); per 10 µg/m^3 increase in $PM_{2.5}$.
… Magnitude of risk not shown in table if strength of evidence is "probable" or "limited."

DIESEL ENGINE EXHAUST

Background

» Diesel engine exhaust is a complex mixture of gases (e.g., carbon monoxide, nitrogen oxides, benzene, formaldehyde) and diesel particulate matter (DPM), with polycyclic aromatic hydrocarbons and nitroarenes distributed in both gas and particulate phases.[166]

» Occupations with a potential for high exposures to diesel engine exhaust include miners, truck drivers, railroad workers, firefighters, dockworkers and diesel-powered equipment mechanics.[167] For the general population, ambient air is the main exposure source, particularly in areas with heavy diesel vehicle traffic.[168]

» Inhalation is the primary route of both environmental and occupational exposure to diesel engine exhaust.[166]

- The International Agency for Research on Cancer (IARC) recently classified diesel engine exhaust as a human lung carcinogen.[166] Strong evidence comes from three cohort studies of highly exposed occupational groups—miners, truck drivers and railroad workers[169–172]—and two pooled case-control studies that include Canadian data.[173,174]
- Workers generally experience a 20%–80% increased lung cancer risk across different exposure scenarios. Underground miners, who experience some of the highest exposures, have 2- to 3-fold risks of lung cancer.[170] Although the evidence that diesel exhaust causes bladder cancer is inconclusive, a meta-analysis of studies of many exposed occupations estimates 10%–40% increases in risk.[175]
- Dose-response relationships with lung cancer appear most consistently for measures of cumulative exposure.[169,170,173,174] Some studies have demonstrated a strong interaction between diesel exhaust and smoking.[170,174,176]
- Environmental exposure to diesel exhaust also presents risks to the general population; residents of urban areas with heavy diesel pollution are exposed to levels that would cause a 50% increase in lifetime lung cancer risk.[168]

- The biologic mechanism through which diesel engine exhaust induces cancer is genotoxicity.[166] The vast majority (95%) of DPM is composed of particles less than 2.5 µm in diameter,[177] small enough to be inhaled deep into the lungs, where there are no mechanisms to remove debris. Other toxic and independently carcinogenic components of diesel exhaust may also contribute to its carcinogenicity.

POLYCYCLIC AROMATIC HYDROCARBONS

Background

» Polycyclic aromatic hydrocarbons (PAHs) are a group of more than 100 compounds containing carbon and hydrogen atoms in two or more benzene rings.[108] They are formed during incomplete combustion of organic material, such as coal, oil, wood or gas.[152,178]

» PAHs generally exist as complex mixtures, such as coal-tar pitch (the residue formed during the distillation of coal tar) and soot.[179] However, benzo[*a*]pyrene, a simple PAH, is often used as an indicator for PAH exposure.

» PAHs can be found in ambient air pollution, as well as in water, soil and sediments. Major sources of PAH exposure include motor-vehicle exhaust, industrial emissions, forest fires, tobacco smoke and fumes from cooking, furnaces, fireplaces and wood stoves.[152] PAHs are also found in some foods (e.g., charbroiled meats, vegetables and crops grown in contaminated soils).[152]

» Occupational groups highly exposed to PAHs include workers in aluminum production, roadway paving and roofing, coal gasification, coal-tar distillation, coke production and chimney sweeps.[152]

» The primary route of exposure in humans is inhalation, although skin contact in occupational settings and ingestion of PAH-containing foods for the general population are also possible routes.[152,178]

- IARC has classified individual PAHs or PAH-related exposures as carcinogenic, including benzo[a]pyrene, coal tar pitch and soot,[152] based on occupational exposures to PAHs shown to cause cancer of the lung, skin and bladder. Many other specific PAHs have been classified as probable or possible carcinogens.
- Evidence for lung cancer comes from many different PAH-related exposures. There is consistent evidence demonstrating that exposure to coal-tar pitch in roofing and paving or to soot in chimney sweeps causes lung cancer.[152] A 1.2–2.3 times increased risk of lung cancer is seen for road pavers,[152] roofers[180] and chimney sweeps.[152] A large cohort study of chimney sweeps also found evidence of a dose-response relationship with duration of employment after adjusting for smoking.[181] Other occupations with an increased risk of lung cancer include aluminum production, coal gasification and coke production.
- The strongest evidence for skin cancer from PAH exposure comes from occupational exposure to soot in chimney sweeps and coal-tar pitch in roofing and paving, which also has exposure to bitumen.[152] The risk of non-melanoma skin cancer varies across occupational groups; risk is increased 2.2 times for road pavers and highway maintenance workers and 4-fold for roofers.[180]
- The strongest evidence for bladder cancer comes from aluminum production workers, demonstrating a 1.4–2.4 times greater risk among this group[152] and a significant

dose-response relationship with cumulative exposure to benzo[*a*]pyrene.[182,183] Some evidence suggests increased risks of bladder cancer from occupational exposure to soot in chimney sweeps and to coal-tar pitch in roofing and paving, but not enough to support a causal association.[152]

- For most PAH-related exposures, there is strong evidence for genotoxicity as the main biologic mechanism causing cancer; the exception is soot and aluminum production for which the evidence for genotoxicity is weaker.[152]

PARTICULATE MATTER (< 2.5 µm)

Background

» Particulate matter (PM) consists of small solid particles or liquid droplets suspended in air.[184] PM smaller than 2.5 micrometres (µm) in diameter is known as $PM_{2.5}$ and is sometimes referred to as "fine" or "respirable" particulate matter.

» $PM_{2.5}$ consists of a complex mixture of acids (nitrates or sulfates), organic chemicals, elemental and organic carbon, and metals.[184]

» $PM_{2.5}$ is formed from all types of combustion processes, either directly or indirectly from precursor gases, such as nitrogen oxides, sulphur dioxides, volatile organic compounds and ammonia.[184]

» Major $PM_{2.5}$ emission sources in Ontario are fuel combustion from motor vehicles, residential wood burning (fireplaces and wood stoves), and industrial processes.[184] Other sources include forest fires, electric power generation and industrial processes, such as mining and smelting.[184]

» The route of exposure is inhalation; its small particle size makes $PM_{2.5}$ a greater health concern than other sub-groups of particulate matter because it is of capable of penetrating more deeply into the alveolar regions of the lungs, where gas exchange occurs, and there are no effective clearance mechanisms.

- The potential carcinogenicity of $PM_{2.5}$ has not been specifically evaluated by IARC; however, a strong body of evidence suggests that environmental exposure to $PM_{2.5}$ causes a number of adverse health effects, including lung cancer.
- A recent systematic review summarized the risk of lung cancer as increasing linearly in a dose-response fashion by 15%–21% per 10 µg/m^3 increase in ambient $PM_{2.5}$ levels, with some increase in risk observed at all exposure levels.[185] Other studies have found lung cancer risk among non-smokers of 15%–27%[186] and 37%[187] per 10 µg/m^3 increase in ambient $PM_{2.5}$.
- Those living in close proximity to major industrial sources (e.g., smelters, foundries, chemical industries) or heavy road traffic are especially at risk,[188] given their long-term exposure to high ambient levels of particulate air pollution.
- There are several potential biologic mechanisms leading to lung cancer. For instance, local inflammatory responses can cause tissue damage, and particles may enter the bloodstream and have systematic effects. Oxidative stress is another important mechanism that has cytotoxic and genotoxic effects, generating free radicals and damaging DNA.[189]