

Chapter 2

Interactions between chemical exposures and non-chemical exposures in work-related cancers

Andrew Watterson

1. Introduction: mechanisms of action of cancer-causing substances

1.1 Non-chemical carcinogens

Physical agents such as ionizing and non-ionizing radiation and 'heat' and light, biological agents such as viruses, and even 'management systems' (such as shift/night work) can all affect human biology. Some of these agents on their own may be capable of causing work-related cancers.

Ionizing radiation has sufficient energy to remove tightly bound electrons from atoms and so create ions that include gamma rays and some ultra-violet rays. This is the type of radiation people usually think of as 'radiation' and it includes nuclear power and several medical uses of radiation such as X-rays. Non-ionizing radiation has sufficient energy to move atoms in a molecule around or cause them to vibrate, but not enough to remove electrons (EPA 2013). It includes extremely low frequency electrical and magnetic fields, wireless communications, power lines, microwave ovens and mobile phones. There is much controversy with regard to the possible potential carcinogenic effects of such phones. Ionizing radiation, however, has been identified as a human carcinogen for many decades and its precise effects are not always clear at different doses and over different lengths of time.

Several studies of radio frequency radiation mobile phone base stations, antennae for transmitters, smart meters and medical applications as well as various types of radar, mobile and cordless phones, Bluetooth devices and amateur radios have been carried out (IARC 2013:34). There was some limited evidence of human carcinogenicity due to mobile phone radiofrequency radiation but positive associations between mobile phones and two types of cancer: gliomas and acoustic neuromas and so radiofrequency electromagnetic fields are listed as possibly carcinogenic (IARC 2013:419).

Biological agents can occur in workplace settings and several may increase the risk of certain types of cancer in humans. The agents include a range of blood-borne viruses such as hepatitis B and C virus and human immunodeficiency virus which would present threats to health, emergency and lab workers, custodial services, cleaners, plumbers, public sector workers dealing with waste treatment, hairdressers and beauticians and even vehicle recovery and repair workers (HSE 2011). Various zoonotic diseases have also been linked to occupational cancers including lung cancer and to a lesser extent lymphomas and myelomas especially with regard to animal

husbandry and the meat and poultry industries through animal viruses (Johnson *et al.* 2012).

Management systems such as those requiring employees to work a significant number of night shifts are now known to be a cause of work-related breast cancer in women in such sectors as health, emergency services, the military and transport (especially airline cabin crews). The exact mechanisms for the effect have not been established but they appear to relate to long-term exposures to artificial light at night and the effect on organs involved with the endocrine system and its disruption. There may therefore be risks for men as well as women. Denmark compensates women with breast cancer who have worked in the above occupations for more than twenty years and meet other criteria (Watterson 2013).

Very high temperatures can contribute to occupational cancers, with evidence in the mainstream scientific literature that burns from workplace injuries could cause cancer available for well over a quarter of a century (Er-fan *et al.* 1992) and now widely accepted.

1.2 Mechanisms of action of cancer-causing substances and how non-chemical exposure may be relevant

Scientists have researched and identified a number of specific industrial and public sectors, occupations, substances and processes that cause cancer (carcinogens) and mutations (mutagens) in humans and/or lab tests. These often initially involved analysing exposures to one substance and one process rather than the interaction of multiple exposures.

The multi-step stages of cancer causation were unrecognised at the beginning of much research and questions of cancer multi-causality from many different exposures were rarely considered. Methods to investigate them were also often lacking. The complexity of cancer causation was not understood. Debates and sometimes regulatory interest then moved on to identifying substances and processes that might ‘inter-act’, perhaps as promoters (substances that promote but do not cause cancers), or co-cancer-causing substances (co-carcinogens may cause additive or synergistic or combined effects and examples are given below). Then mixtures of chemicals (dealt with elsewhere in this book) and their possible cancer-causing effects were identified as an under-researched and possibly significant factor.

The carcinogens now identified may be used in workplaces but many could be present in the wider environment (our air, food, water and soil) – either naturally or due to human activity – thus creating double jeopardy. Many people have multiple exposures to numerous carcinogenic substances and processes at work and over a working lifetime via different routes, at different levels and in different ways. Trying to establish if there are interactions between chemical and non-chemical carcinogens in the workplace is very complicated and very under-researched at present. Recognition of susceptibility to cancers through a range of factors – including genetics, age, gender and ethnicity –

have emerged as additional factors to consider. Genetics and gender for example have sometimes been wrongly used to exclude or try to exclude workers from endangered workplaces rather than removing or reducing exposure to the carcinogens.

However, the most vulnerable workers may also be those most likely to work with a large range of chemical, biological and physical agents that cause cancer, possibly in the worst-regulated employment sectors where long hours, shifts including night work, poor health and safety management and little or no inspection are the norm. Poverty, poor diet and living conditions as well as other illnesses may also expose such workers to a host of other factors interacting with occupational carcinogens and further increasing their risks of contracting work-related cancers. In 2012, an EU Occupational Health and Safety workshop looked at occupationally-caused and related cancers, identifying 'hidden' groups whose occupational exposure to cancer risks and carcinogenic processes was under-represented in exposure data and intervention strategies (EASHW 2012). Noting an unrecognised work-related cancer burden in lower socio-economic classes, they floated the concept of 'socially discriminating cancers'. Typical exposed groups included migrants, part-time workers, those employed as sub-contracted staff and women and young workers, often working in the service sector. These are some of the groups most likely to be exposed to the interactions briefly discussed in this chapter.

The report of the US President's Panel on environmental cancer published in 2010 specifically noted the poor understanding and definition that existed with regard to the actions and potential interactions of some known carcinogens, especially in the light of emerging technologies, new processes and new substances (Reuben 2010). IARC research also originally dealt only with chemicals but now covers agents that include: "specific chemicals, groups of related chemicals, complex mixtures, occupational or environmental exposures, cultural or behavioural practices, biological organisms and physical agents" (IARC 2012a:8).

2. Biological factors including shift /night work and chemicals

The body itself may produce important chemicals able to keep us healthy or damage our health. Sometimes synthetic chemicals may interfere with the beneficial elements of the process. For example, endocrine disruptors in the workplace or environment may interfere with these biological processes and hence increase, decrease, block - or alter in other ways - our production of hormones. This could potentially lead to breast cancer in women and a small number of men, or prostate cancer in men. These synthetic endocrine disruptors could include various pesticides, agents in plastic or solvents. Other chemicals may interfere with human biology by affecting the immune system – immunotoxic substances. Benzene, formaldehyde and diesel fumes have all been identified as strongly immunotoxic (Veraldi *et al.* 2006). They are also human carcinogens in their own right and widely present in one form or another in many workplaces.

Recent studies on the links between night shift work and breast cancer in women have raised further questions about possible interactions between chemical and non-

chemical workplace exposures. Shift work and artificial light at night appear to affect the human biochemistry of females and males. Management systems requiring such work may thus lead to occupational cancers through impacting a worker's biology. But the risks are potentially even greater in terms of interactions. Some studies have tried to unravel exposures of women cabin crew who may work nights, be exposed to radiation through flying and sometimes spray cabins with suspect cancer-causing pesticides or endocrine disruptors. There are therefore four potential carcinogens here (Colditz *et al.* 2006) and they could theoretically increase the worker's cancer risks. Other recent studies have noted that increased breast cancer risks in anaesthetists could be linked to chemical exposures or night shift work and that interactions between the two could be relevant in breast cancer progression. However, because of the nature of the study, the results were limited (Rabstein *et al.* 2014). Further complications arise when factors such as obesity are considered. Night shift work itself may be an 'obesogen' and access to healthy food at night and physical exercise may be limited and contribute to and be part of the occupational cancer risk (Watterson 2013).

Viral and zoonotic diseases can act as cancer initiators but may also work together with chemical carcinogens. Schistosomiasis (or bilharzia) is a well-known zoonotic disease caused by parasites and linked to bladder cancer. Interactions between tars and viruses in lab tests were revealed as early as 1911. Some kidney cancers, it is suggested, may occur following chemical and viral exposures and Kaposi's sarcoma could result from exposures to viruses, adverse immune effects and exposure to chemicals such as nitrites and alumina-silicates (Haverkos 2004). More recent studies and reviews have also suggested that meat and poultry workers have elevated risks of lung cancer, adjusting for smoking, and that these are linked potentially to exposure to viruses. Such workers can also be exposed to chemical carcinogens like nitrosamines, frying and cooking aerosols and plastic wrapping fumes. The possible impact of these multiple exposures has not been fully studied (Johnson and Choi 2012).

The IARC recently reviewed biological agents, recognising that cancers could result from "the interaction of multiple risk factors including those related to the infectious agent itself, host-related factors including immune status and environmental cofactors such as chemicals, ionizing radiation, immunosuppressive drugs, or another infection". These might reactivate latent oncogenic viruses. They further noted that "the contribution of several of these additional factors to the development of infection-associated cancers is likely to be substantial, but has not yet been elucidated in detail" (IARC 2012: 44).

Finally, there may be indirect factors that could influence exposures to carcinogens. Climate change will lead to the spread in Europe of more zoonotic disease vectors (carriers of disease) that may cause cancer in humans. Biological and physical factors will come together in a different set of interactions that could additionally include the use of cancer-causing agro-chemicals and endocrine disruptors to control the new disease vectors. Working in hot and humid conditions may increase risks of heat stress, dehydration and fatigue including the difficulty of using personal protective equipment in such conditions. This may increase exposures to carcinogens and their uptake. Threats of interactions are thus set to increase.

3. Physical factors and chemicals

Interactions of chemicals, such as those in tars, with physical factors such as sunlight have been recognised in occupations such as roofers in construction work and those working on road surfacing.

Interactions between ionising radiation and chemicals have been studied more closely than other interactions since the 1990s but they still remain relatively under-researched and very difficult to study (see for example Chen and McKone 2001). Most studies have focussed more on chemical exposures and occupational cancer and not interactions between non-ionising radiation and chemicals in nuclear production and uranium-processing plants. IARC's latest monograph on radiation looked at interactions between radon and tobacco smoke but did not look at interactions with other chemicals (IARC 2013:244).

Arc welders and their assistants may be exposed to high levels of ultraviolet radiation when using gas metal and gas tungsten techniques and to medium levels when using shielded metal arc welding equipment. This exposure on its own could lead to work-related skin cancers (Dixon 2007). There could also be other interactions, though proper protective equipment and appropriate types of sun blockers would greatly reduce some of these risks.

4. Psycho-social stress, chemicals and occupational cancer

This field is perhaps the least researched of all. One commentator noted in 2009 that 'there are undoubtedly other interacting factors, such as prenatal and early childhood exposures, nutrition, physical activity, genetics, and psychosocial factors such as stress, which together may ultimately be responsible for the development of cancer in ways we do not yet fully appreciate' (Clapp *et al.* 2009:20). Stress may also be a proxy for other factors that will increase exposures to carcinogens through long hours of work in poor conditions and with poor pay and potential exposure to many and the most hazardous known human carcinogens compounded perhaps by greater exposure in the non-work environment in terms of neighbourhoods and homes. If and how stress may affect the immune system and hence susceptibility to interactions of chemical and non-chemical carcinogens in the workplace has not been fully researched.

5. Conclusions

Major challenges remain with regard to testing methods for chemical/non-chemical interactions and limits, how limits are to be set for these multiple exposures and what the full implications of interactions may be. Asbestos/tobacco interactions have been widely recognised in occupational cancer studies. However, this research has sometimes been used by employers to try and deny worker compensation claims by arguing that tobacco alone explained asbestos worker lung cancers and then that contributory factors such as smoking justified cutting worker compensation. It looks like similar approaches

are or could be adopted by some employers with regard to obesity and lack of physical exercise, citing these as causes of cancers to try to evade responsibility for exposing their employees to known or suspected carcinogens in the course of their work. Trade unions will need to be wary of this ploy.

Much is still either uncertain or unknown about interactions between chemicals and physical and biological factors. Trade unions trying to establish or improve workplace precautionary and prevention occupational cancer policies and practices should thus take into account data gaps and lack of certainty about the multiple causes of cancer.

Until toxicology and epidemiology catch up with this field, the best action employees and their trade unions can take is to focus on the individual workplace chemical, physical and biological carcinogens and related co-carcinogens and promoters that may be used with them. Removing the individual carcinogens or reducing exposure to levels as low as possible through policies such as sunsetting or toxics use reduction will also ensure reductions in known and suspected interactions between all types of substances and processes known or suspected as being carcinogenic. This is an effective use of time and resources for trade unions because it is a win-win approach.

Simple steps to ensure existing regulations are in operation and fully enforced will have a part to play too. In Denmark, following the findings on night shift work and breast cancer in women, labour inspectors began re-checking workplaces where night shift work was done, enforced the Working Time Directive and pressed for the best shift systems and facilities available. Elsewhere in Europe, governments ignored the findings, did not inspect workplaces regularly at night and argued for their own national research on the interactions.

As more research becomes available about interactions between chemical and other carcinogens, specific and more targeted workplace reduction and removal strategies could be developed to take account of the findings, as for instance already done with regard to tars and exposure to sunlight.

References

- Chen W.C. and McKone T.E. (2001) Chronic health risks from aggregate exposures to ionizing radiation and chemicals: scientific basis for an assessment framework, *Risk Analysis*, 21 (1), 25–42.
- Clapp R., Jacobs M. and Loechler E.L. (2009) Environmental and occupational causes of cancer new evidence, 2005-2007, *Reviews on Environmental Health*, 23 (1), 1–37.
- Colditz G.A., Baer H.J. and Tamimi R.M. (2006) Breast cancer, in Schottenfeld D. and Fraumeni J.F. (eds.) *Cancer epidemiology and prevention*, 3rd ed., New York, Oxford University Press, 995–1012.
- Dixon A. (2007) Arc welding and the risk of cancer, *Australian Family Physician*, 36 (4), 255-256.
- EPA (2013) Ionizing and non-ionizing radiation, 17/05/2013, Washington DC, United States Environment Protection Agency.

- Er-fan X. *et al.* (1992) Burn scar carcinoma: case reports and review of the literature, *Annals of the MBC*, 5 (2). http://www.medbc.com/annals/review/vol_5/num_2/text/vol5n2p102.htm
- European Agency for Safety and Health at Work (2012) Workshop 'Carcinogens and work-related cancer': seminar report. <https://osha.europa.eu/en/seminars/workshop-on-carcinogens-and-work-related-cancer>
- Haverkos H.W. (2004) Viruses, chemicals and co-carcinogenesis, *Oncogene*, 23 (38), 6492–6499.
- HSE (2011) Blood-borne viruses in the workplace, London, Health and safety Executive. <http://www.hse.gov.uk/pubns/indg342.pdf>
- IARC (2012) A review of human carcinogens. Part B: biological agents, IARC Monographs on the Evaluation of Carcinogenic Risks to Humans 100B, Lyon, International Agency for Research on Cancer.
- IARC (2012a) A review of human carcinogens. Part D: radiation, IARC Monographs on the Evaluation of Carcinogenic Risks to Humans 100D, Lyon, International Agency for Research on Cancer.
- IARC (2013) Non-ionizing radiation. Part 2: radiofrequency electromagnetic fields, IARC Monographs on the Evaluation of Carcinogenic Risks to Humans 102, Lyon, International Agency for Research on Cancer.
- Johnson E.S. and Choi K.M. (2012) Lung cancer risk in workers in the meat and poultry industries: a review, *Zoonoses and Public Health*, 59 (5), 303-313.
- Rabstein S. *et al.* (2014) Associations between pre-defined occupational job tasks and breast cancer risk, *Occupational and Environmental Medicine*, 71, A84. Doi: 10.1136/oemed-2014-102362.261
- Reuben S.H. (2010) Reducing environmental cancer risk: what we can do now, President's Cancer Panel, 2008-2009 Annual report. <https://deainfo.nci.nih.gov/Advisory/pcp/annualReports/index.htm>
- Veraldi A. *et al.* (2006) Immunotoxic effects of chemicals: a matrix for occupational and environmental epidemiological studies, *American Journal of Industrial Medicine*, 49 (12), 1046-1055
- Watterson A.E. (2014) Competing interests at play? The struggle for occupational cancer prevention in the UK, in Nichols T. and Walters D. (eds.) *Safety or Profit? International studies in governance, change and the work environment*, Amityville, Baywood Publishing, 137-156.

All links were checked on 23.07.2018.