Occupational Medicine 2018;**68:**80–82
doi:10.1093/occmed/kqx188

EDITORIAL

New and emerging risks of chemical carcinogens: detection and prevention

Cancer is a major cause of death worldwide and there are many efforts to tackle it. Occupational cancer is a cancer caused fully or partially by exposure to a cancer-causing agent at work. It has been estimated that 8% of all cancers are caused by exposures to carcinogens in the workplace. Using the cancer incidence numbers in the EU-27, this means that there are about 122 000 new cancer cases in the EU each year caused by occupational exposure [1]. This number is very likely to be an underestimate because of the long latency of cancer, and difficulties in establishing a causal relationship between occupational exposure and cancer. On the other hand, millions of EU workers are currently exposed to thousands of (process generated) substances and mixtures for which a detailed risk assessment of their carcinogenic properties is not available [2,3]. Occupational cancer can be prevented by limiting exposure to zero. Since limiting exposure will reduce the number of cases in the long run, it is worth focusing on this by timely understanding the risks and developing measures to control them. In the European Environment Agency report *Late Lessons From Early Warnings* [4], a selection of occupational, public health and environmental emerging risks were evaluated. One of their main conclusions was that there is a lack of institutional and other mechanisms to respond to early warning signals. The report shows that by ignoring early warnings by businesses, and manufacturing doubt about the science supporting such warnings, costs are transferred to society. Reducing the delay between early warnings and actions is one of their main recommendations.

In May 2016, a conference *Preventing Work Related Cancer: Conference on Carcinogens* was organized as part of the Dutch EU presidency [5]. The audience consisted of researchers, policy makers, industry and workers representatives. Currently, most regulations are primarily based on risk assessments starting with the identification of the carcinogenic properties and subsequently reducing exposure to carcinogens. However, for most agents currently used in the workplace, essential information in this regard is lacking or incomplete. Consequently, work-related cancers still occur and need to be detected as early as possible to both treat and prevent new cases.

It is understandable that risk assessment and risk containment have a strong position when it comes to preventing cancer and other diseases. This approach is proactive and is called the 'exposure first' method (N. Palmen, personal communication). To make a proper risk assessment, one needs all information on both the hazardous properties of a substance and the exposure to the substance. This was also recognized by the participants of the conference as they indicated that more data on exposure, toxicology and risk assessment methods are needed. In the ideal situation of full data availability, deductive reasoning can be used to link a reported health effect to occupational exposure taking into account the (historical) chemical exposure of the patient.

However, in practice, toxic effects of substances are never fully assessed and often tested only *in vitro* or, when indicated, through *in vivo* experiments with animals. In these experiments, the agents are administered orally, which may not be a proper model for workers since they are mainly exposed via inhalation and skin. Animals are not humans and consequently may react differently compared with man, for example due to a different metabolism. Furthermore, derivation of occupational exposure levels by scientific panels (e.g. Scientific Committee on Occupational Exposure Limits) is complex, difficult and time-consuming. Next, this scientific process needs to be translated into preventive measures and legal requirements by regulators, which can be very slow, mostly due to the lack of (human) data. As a consequence, only a small percentage of occupational agents have undergone the complete process thoroughly.

Thus, in spite of the regulations, unexpected adverse effects of new and emerging risks on worker's health are reported regularly [6]. This also applies to carcinogens like asbestos, benzene, vinyl chloride and radium, which once were new and emerging risks of chemical carcinogens (NERCCs) too. New risks are created continuously due to the changing world of work. So, in our view, the 'exposure first' method, which is based on deductive reasoning, has its limitations and an additional method is needed to identify potential NERCCs as soon as possible, to prevent further damage to worker's health. Complementary to the deductive reasoning of the 'exposure first' method, the 'disease first' method implements an inductive way of reasoning. This inductive way of reasoning starts from observations of cancer cases and tries to identify the causal factors. The 'disease first' method acts as a form of 'early warning systems (EWS)' comparable with the methods applied in pharmacovigilance, which aims to detect and evaluate adverse health effects of drugs after introduction on the market (post-marketing surveillance). It is only after the drugs are on

the market, that some of the adverse effects might come to light. This is true especially if there is a long latency effect, which is the case for most carcinogens.

EWS are generally based on two approaches to detect adverse health effects: spontaneous reporting of cases by physicians and/or workers and research in existing databases. EWS comprise clinical watch systems, which aim for ongoing and rapid identification of health events (cases and their corresponding occupational risks) for the purpose of follow-up and for developing statistical trends. Clinical watch systems are dependent on vigilant health professionals who collect information on exposure or biomarkers of exposure and health effect or biomarkers of early health effects. Health professionals need to be aware that chemical risks can still occur despite all regulations being in place. After reporting a possible early warning by a health professional, the signal has to be evaluated by subject matter experts, i.e. physicians, toxicologists, epidemiologists, industrial hygienists. The evaluation comprises a literature search for a possible causal relationship, and/or strengthening and validating the signal by looking into (inter)national databases. The possible NERCCs may be a consequence of an unknown hazard of a substance, a known hazard of a substance used in a different way leading to a different exposure (e.g. other route of exposure, exposure scenario), or a known exposure in a new work situation. Despite the fact that several EWS are available in Europe [7,8], there is a lack of integration and collaboration between the systems and countries. Since we probably deal with rare events with a long latency, it is important to have a wide and international surveillance system, or a combination of existing initiatives, and interdisciplinary and international research and debate. In addition, expert collaboration is important to use limited resources in the most effective way.

Consequently, in order to make EWS effective it is in the authors' opinion that awareness regarding the existence of NERCCs among all stakeholders should be raised. Obviously, occupational health specialists (occupational physicians, medical specialists, industrial hygienists, etc.) need to be vigilant to the occurrence of any possible work-related health effects and should systematically check whether workers with cancer were exposed to substances in the past and keep track of their exposure history. Therefore, education of physicians on work-related health effects should be improved to reach this goal, which was also stated by Rushton [9]. Furthermore, workers must have access to occupational health clinics to evaluate health effects, exposure and the association between them. These should be funded to perform the necessary studies.

It is important to realize that the 'disease first' method is not a method for primary prevention, since health effects are reported. The aim of the 'disease first' method is to reduce the impact of a disease that has already occurred (secondary prevention). It partially fills knowledge gaps, provides input for the basic assumptions used in deductive reasoning and it has the intention to prevent a new cancer case in an early phase.

There is an urgent need for (inter)national expert groups and an institutionalized expert group at EU level for the evaluation of new and emerging risks, including cancer. Expert groups should bring further the identification and evaluation of causality of possible NERCCs according to the 'disease first' method. International collaboration is very important since most expert groups are active at a national level and at that level cases are rare. Bringing signals together will make it easier to strengthen and validate them and turn them into actions, like preventive measures or regulations. An international expert group already exists in the voluntary MODERNET network, consisting of experts in the field. MODERNET is the acronym of Monitoring trends in Occupational Diseases and tracing new and Emerging Risks in a NETwork.

In the authors' opinion, occupational cancer is preventable, but it needs more than looking at exposure to the current most important carcinogens. We need vigilant professionals and workers, and as soon as an NERCC has been identified, the signal should be picked up, strengthened and validated by researchers. Subsequently policy makers should translate the findings into policy. Strong collaboration between all stakeholders is imperative to prevent delay between early warnings and actions to tackle all the new risks, which may come our way.

Nicole G. M. Palmen
National Institute for Public Health and the Environment, Bilthoven, The Netherlands
e-mail: nicole.palmen@rivm.nl

Annet F. Lenderink
Netherlands Center for Occupational Diseases, Coronel Institute on Occupational Health, AMC, University of Amsterdam, Amsterdam, The Netherlands

Lode Godderis
KU Leuven, Centre for Environment and Health, Leuven, Belgium
IDEWE, External Service for Prevention and Protection at Work, Heverlee, Belgium

References

1. Jongeneel W, Eysink P, Theodori D *et al. Work-Related Cancer in the European Union: Size, Impact and Options for Further Prevention*. National Institute for Public Health and the Environment, RIVM Report 2016-0010. 2016. http://rivm.nl/en/Documents_and_publications/Scientific/Reports/2016/mei/Work_related_cancer_in_the_European_Union_Size_

impact_and_options_for_further_prevention (November 2017, date last accessed).
2. Cherrie J, Hutchings S, Gorman Ng M *et al.* Prioritising action on occupational carcinogens in Europe: a socio-economic and health impact assessment. *Br J Cancer* 2017;**117:**274–281.
3. Terwoert J, Goedhart E, Theodori D *et al. Bedrijfsgrenswaarden stoffen; Functioneren regeling in de praktijk, naleving en effectiviteit, situatie in andere Europese landen* [summary in English]. RIVM-TNO Report TNO2013 R10319. 2013. http://publications.tno.nl/publication/101019/g4qDBg/TNO-2013-R10319.pdf (November 2017, date last accessed).
4. European Environment Agency. *Late Lessons From Early Warnings: Science, Precaution, Innovation* [summary]. EEA Report No 1/2013. 2013. https://www.eea.europa.eu/publications/late-lessons-2 (November 2017, data last accessed).
5. Dutch Ministry of Social Affairs and Employment. *Preventing Work Related Cancer: Conference on Carcinogens*. 2016. http://www.magazine-on-the-spot.nl/pwrc/ (November 2017, date last accessed).
6. Palmen N, Salverda-Nijhof J, van Kesteren P *et al.* Detecting Emerging Risks for Workers and Follow-up Actions. National Institute for Public Health and the Environment. RIVM Report 601353004/2013. 2013. http://www.apbmt.be/websites/53/uploads/file/Nieuws/2014/601353004%20MK%20bev-definitief%20rapport.pdf (November 2017, date last accessed).
7. Palmen N. Early Warning Systems to Detect New and Emerging Risks in Europe. National Institute for Public Health and the Environment. RIVM Letter Report 2016-0022. 2016. https://www.ifv.nl/kennisplein/Documents/20160501-RIVM-Early-warning-systems-to-detect-new-and-emerging-risks-in-europe.pdf (November 2017, date last accessed).
8. Bakusic J, Lenderink A, Lambreghts C *et al. Methodologies to Identify Work-Related Diseases: Review of Sentinel and Alert Approaches*. European Agency for Safety and Health at Work. 2017. https://osha.europa.eu/sites/default/files/publications/documents/Alert_%20centinel_systems.pdf (November 2017, date last accessed).
9. Rushton L. Occupational cancer: recent developments in research and legislation. *Occup Med (Lond)* 2017;**67:**248–250.