



ABSTRACT BOOK

**Modernet meeting Prague 20-21 October
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Abstract

In this book you will find all the abstracts of the oral presentations and posters presented at the Modernet meeting in Prague at 20-21 October 2016 in alphabetical order of the authors.

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REVIEW ON SENTINEL AND ALERT SYSTEMS TO IDENTIFY NEW AND EMERGING WORK-RELATED DISEASES

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Objective: Rapid changes in working conditions give rise to new occupational health risks and work-related diseases. One of the approaches to identify new work-related diseases are early warning systems designed to collect information in order to trigger health interventions and prevention. These systems differ in characteristics, with a lack of ideal model. The aim of this review is to identify sentinel and alert systems suitable for detecting new and emerging work-related diseases, describe their main characteristics, and set up a basic typology of such systems.

Methods: We conducted an extensive scientific literature search combining terms for the following three concepts: 1) surveillance/reporting systems; 2) occupational/work-related diseases; and 3) new or emerging risks. In addition, we performed a grey literature search, including both, grey literature databases as well as relevant EU and research institute websites for additional resources.

Results: A total of 75 surveillance systems covering 26 different countries were identified. We set up a basic typology of these systems dividing them into four main groups: compensation-based systems (n=21), non-compensation related comprehensive systems (n=38), sentinel systems (n=11) and public health surveillance systems aimed at workers and non-workers (n=5). These systems further differed in type of work-related diseases, coverage, data collection, investigation of work-relatedness, follow up of new/emerging risks, link with prevention etc. Finally, a representative selection of 15 good practice examples was made. Out of these, 6 systems will be described in-depth and used for recommendations.

Conclusion: Results of this review provide an international overview of different approaches to identify new and emerging work-related diseases, which is useful for further improvement of their monitoring and prevention.

CHRONIC UPPER AIRWAY INFLAMMATION AND OXIDATIVE STRESS FOLLOWING NANOPARTICLE EXPOSURE IN PHOTOCOPIER OPERATORS

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Background: Several recent studies have linked emissions from printing and photocopying equipment with upper airway inflammation and systemic oxidative stress in healthy humans, lung inflammation in mice, and cytotoxicity and epigenetic effects in human cell lines.

Objective: In this follow-up work to our earlier acute exposure studies with human volunteers we investigate whether chronic exposures to nanoparticles from photocopiers lead to chronic upper airway inflammation and systemic oxidative stress. We further investigate the variability in several inflammatory biomarkers of the upper airways in order to identify optimum sampling strategies for larger scale molecular epidemiological studies with this cohort of workers.

Methods: Detailed quantitative exposure assessment of full time employees in eight copy centers was conducted over a full week. The exposure assessment included daily characterization of real-time nanoparticle number concentration, size distribution, and extensive morphological and physicochemical analysis of size-fractionated aerosols. Nasal lavage (NL) and urine samples were collected on Monday morning (Mo-AM, pre-shift) and evening (Mo-PM, post-shift), as well as at the end of the workweek (Fr-PM, 3 samples /individual/week) from six full time photocopy center employees over three random weeks, and from ten matched controls. Nasal lavage (NL) samples were analyzed for a panel of 14 pro-inflammatory cytokines/chemokines, inflammatory cells, and total protein. Urine samples were analyzed for *8-OH-dG*, an established biomarker of systemic oxidative stress.

Results & conclusion: We document high PM_{<0.1} exposures with complex composition and several engineered nanomaterials (ENM) in toners and PM_{<0.1}. Daily geometric mean PM_{<0.1} concentrations ranged from 3700-34000 particles/cubic-centimeter (pt/cm³) (GSD 1.4-3.3), up to 12 times greater than background, with transient peaks > 1.4 million pt/cm³. PM_{<0.1} contained 6-63% organic carbon, <1% elemental carbon, and 2-8% metals, including iron, zinc, titania, chromium, nickel and manganese, typically in the <0.01-1% range, and in agreement with toner composition. Chronically exposed workers had significantly higher levels of several proinflammatory markers in NL, including total protein, inflammatory cells (2.7 fold), and 5 out of 14 cytokines/chemokines (IL-6, IL-8, TNF α , IL-1 β , at p < 0.0001) and Eotaxin (p < 0.05). Interestingly, one cytokine, G-CSF was significantly down regulated (p < 0.0001) in copier operators. The *8-OH-dG* in urine samples was 4.3 fold higher than in controls. The level of abovementioned five cytokines did not change significantly across days (i.e. Mo-AM, Mo-PM, and Mo-AM, Fr-PM) and between weeks in chronically exposed individuals, indicating that chronically exposed workers are in a state of chronic upper airway inflammation and systemic oxidative stress.

TRACKING NANO-SPECIFIC BIOMARKERS: CHALLENGES AND PERSPECTIVES

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Research of biomarkers reflecting occupational or environmental exposure to certain particles and fibres of concern have already generated a large amount of data supporting the validity of using intermediate end-points to assess changes before clinically apparent disease occurs. To date, several biomarkers can reliably help in assessing exposure and effects of manufactured nanomaterials (NM) and their components. Toxicokinetic considerations, including the dose which can reach target organs and the changes the NM undergo in contact with the biological environment, as well as what consequence the chemical identity has on “nano-specific” toxic effects, represent a challenge in using of biomarkers of exposure for NM and may hamper the applicability of biomonitoring to nano-objects.

Although the nanolevel gives rise to specific concern, it should be recognized that the existence of nano-specific effects is often an arbitrary assumption, whereas there is a gradual change in bio-reactivity associated with specific metrics and mode of actions.

System Toxicology (ST) and “-omic” techniques are recognized means for the identification and application of biomarkers for improved safety assessments. These approaches have mainly been used in effects-oriented nanosafety research for the purpose of hazard identification, but have not been widely applied in biomarkers identification. A very promising field of research for biomarkers development is represented by the study of epigenetic modifications and of modes of intercellular communication, since this could also explain how exposure to NM can result in effects not limited to the portal of entry, but involves a systemic response in non-primary target.

Within the hierarchy of biomarker development, a pragmatic approach is to draw candidate biomarkers from other fields of particle toxicology as well as from metal toxicity studies. Human biomonitoring studies are however mandatory to assess the validity of such biomarkers which can be further studied for assessing their predictive value towards relevant health outcomes thus supporting the implementation of an effective risks management system.

A SURVIVAL ANALYSIS OF VIBRATION-RELATED OCCUPATIONAL DISEASE AND IMPLICATIONS FOR EVALUATING INTERVENTIONS

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Objectives: Regular exposure to hand-arm vibration can lead to hand-arm vibration (HAVS) and carpal tunnel (CTS) syndromes. EU Directive 2002/44/EC, which aims to improve surveillance and reduce exposure to vibration at work, defines exposure limits for hand-arm-vibration. The aim is to investigate whether the staged implementation of the directive since 2005 has been associated with a change in the incidence of HAVS or CTS in European countries. To model the range of potential outcomes of the intervention, we sought to define an exposure-risk relationship based on the best available prospective longitudinal data for exposed workers.

Methods: In a series of studies, which have been subject of previous publications^{1,2}, forestry and stone workers were monitored at intervals of 1 to 5 years, on 1 to 4 occasions. Health status, annual hours of exposure and magnitude of vibration were recorded. In the present study, a novel analytical approach was applied to define a parametric survival function describing the incidence of HAVS as a function of various exposure metrics.

Results: Incidence of the vascular condition vibration-induced white finger was well described by a Weibull distribution with an increasing hazard rate. The resulting parametric equation reveals the role of duration of exposure and the vibration magnitude ($m s^{-2}$) relative to a threshold magnitude.

Conclusion: The exposure-risk relationship, which differs in some respects from the exposure relationship described in current standards (e.g. ISO 5349-1, 2001), has a simple, mechanistically based form that can be easily applied to simulate the consequences of workplace interventions.

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2. Bovenzi M. *Int Arch Occup Environ Health* 2010; 83; 259–272 DOI 10.1007/s00420-009-0461-2

ENVIRONMENTAL EXPOSURE TO ULTRAFINE PARTICLES IN SOUTHERN SARDINIA, ITALY: A PILOT STUDY OF RESIDENTIAL EXPOSURE NEARBY AND INSIDE A MILITARY AIRPORT.

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Abstract

Objective: To assess the environmental UFP's levels in residential areas nearby and inside one military airport in Southern Sardinia.

Methods: Between 2014 and 2015, 12 outdoor air samplings were conducted in three towns nearby a military airport, during the winter and spring seasons. Five outdoor air samplings were also conducted in an urban area, one in a rural area and four outdoor air samplings during flight activities of military aircrafts inside a military airport. The instrument used to detect the UFP concentration (particles/cm³) was an Electrical Low Pressure Impactor (ELPI+™ - Dekati). During each sampling, meteorological, take-offs, landings and passages above the sampling sites data were registered. Collected particles were subsequently chemically analysed by field emission scanning electron microscopy (FESEM) and energy dispersive spectroscopy (EDS).

Results: Median UFP number concentration assessed nearby the airport during winter time (41260-154871 particles/cm³) was higher than during springtime samplings (3223-8851 particles/cm³). Median values assessed during springtime nearby the airport were consistent with measured levels in the rural area. The measurements carried out inside the military airport, during flight activities, showed a correlation between the increasing number of ultrafine particles and flight activities, and between UFP concentration and distance from emitting source. UFP number median values assessed inside the military airport were consistent with the measured levels in the urban area.

Conclusions: Our results show a constant presence of UFP, regardless of the sampling season or the flight activities. Other anthropic sources, such as motor vehicle traffic, wood burning household heating systems, and other domestic activities, may generate UFP exposure in the residential areas, which is significantly higher than those generated by airport activities.

THE USE OF A JOB EXPOSURE MATRIX TO REFINE NATIONAL ESTIMATES OF THE INCIDENCE OF OCCUPATIONAL ASTHMA.

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Objectives: Comparing disease incidence for different causal agents is typically limited by the availability of denominators (i.e. the number of workers exposed). Furthermore, the proportion exposed to each agent is likely to vary between different occupations. This study aimed to use the recently developed Airborne Chemical Exposure Job Exposure Matrix (ACE-JEM), based on the Standard Occupational Classification (SOC2000) coding system, to refine occupational asthma incidence rates attributed to 'asthmagens' (as reported by chest physicians to SWORD).

Methods: The SOC codes associated with case reports of asthma to SWORD (2003-2014) were compared with those SOC codes assigned as exposed (proportion of SOC exposed >5%) and not exposed (<5%) to 'asthmagens' by the ACE-JEM. Incidence rates were compared before and after applying the proportion exposed (within each SOC code) to the population denominators.

Results: Of the 3224 reported asthma cases 2388 (74%) were reported in SOC codes assigned as exposed (>5%) to 'asthmagens' by the ACE-JEM. The 836 (26% of total) 'not exposed' cases encompassed 94 SOC codes, of which 8 had 10 or more cases. Adjusting for the proportion exposed increased the annual, average incidence rate from 12 to 23, per 100,000 and altered the ranking of the SOC codes (high to low incidence rates). However, the top four occupations remained unchanged (vehicle spray painters, bakers, moulders and related occupations, metal making/treatment process operatives).

Conclusions: The application of the ACE-JEM enables more accurate incidence rates both by occupation and by type of exposure to be calculated. Work is ongoing to apply the ACE-JEM to refine SWORD incidence rates for specific exposures. The data may also help inform further iterations of the ACE-JEM.

WORK-RELATED LONG-LATENCY RESPIRATORY DISEASE IN GREAT BRITAIN: 1996 TO 2014

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Objectives: Much of the current burden of long-latency respiratory disease (LLRD) in Great Britain (GB) is attributed to historical asbestos exposure with high risk occupations well documented. However, other agents, for example silica, also contribute and exposures (including asbestos) are still occurring. It is therefore important to continue to monitor the status of LLRD in GB (and elsewhere). The aim of this study was to investigate work-related LLRD incidence in GB (including change over time), as reported by chest physicians to SWORD, including variations by age and gender, occupation and suspected causal agent.

Methods: Case reports of LLRD were extracted from SWORD (1996-2014). Incidence (per 100,000 employed), trends in incidence and incidence rate ratios (IRRs) (by occupation) were estimated using historical denominators (to account for the exposure-disease lag).

Results: Cases were predominantly male (95%) and attributed to asbestos (92% of total cases). Annual average incidence rates (males) per 100,000 employed were; benign pleural disease: 9.8 (9.3, 10.4), mesothelioma: 7.6 (95% CIs 7.1, 8.1), pneumoconiosis: 2.7 (2.4, 3.0), lung cancer: 1.1 (1.0, 1.3) and bronchitis/emphysema: 0.5 (0.3, 0.6). Overall, trends in incidence were flat. Frequently reported industries were construction (39% of cases) and manufacturing (32%). Occupational groups with the highest IRRs were miners/quarrymen and welders (bronchitis/emphysema), construction workers (lung cancer) and shipyard/dockworkers (all other LLRD groups).

Conclusions: LLRD continue to be reported in substantial numbers by chest physicians, many of which are attributed to past exposures to agents such as asbestos and silica but for which there may be ongoing potential for occupational exposures.

SLEEP DISORDERS IN SHIFT-WORKERS AND DRIVERS: AN OCCUPATIONAL AND ENVIRONMENTAL HEALTH CONCERN

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Abstract

Transportation of merchandise and shift-work are two basic features of a global economy. However, while disruption of the natural sleep/wake rhythm in shift-workers and impaired alertness among drivers have become two major occupational health (OH) issues, full awareness on the occupational and environmental relevance of such health issues has yet to come. A substantial fraction of workplace injuries and car crashes is explained by decreased alertness and drowsy driving^{1,2}; besides, fatigue and sleep/wake rhythm disruption also affect social and family life, contributing to work related stress. Lifestyle changes, job strain and stress related to shift-work are also associated with oxidative stress and risk of metabolic syndrome, leading in turn to development of cardiovascular diseases and metabolic disorders. Obstructive sleep apnea syndrome (OSAS), and drowsiness in general, have a strong impact on labor cost as well, as such conditions are reportedly associated with loss of productivity due to impaired work performance². Available monitoring tools include self-administered questionnaires³, simplified protocols for salivary cortisol and melatonin biomonitoring⁴, urinary excretion of 8-hydroxy-2'-deoxyguanosine, a marker of oxidative stress, and calculation of the heart rate corrected QT interval in the electrocardiogram⁵. Large cross sectional surveys might contribute to validate the proposed monitoring tools using polysomnography tests as the gold standard, so to define more precisely risk of occupational injuries, car accidents, household accidents, metabolic syndrome and work-related stress, with proper adjustment for the effect of confounders.

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HEALTH SURVEILLANCE OF WORKERS: A PILOT STUDY ON THE STATUS OF APPLICATION OF THE DIRECTIVE 89/301 CE IN EU

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Objective of the study

Article 14 of the EU Directive 89/391 indicates the necessity of periodical medical surveillance of workers: “Several measures need to be introduced in accordance with national law and/ or practices”, and “each worker, if he wishes, has access to health surveillance at regular intervals.” The directive has been adopted more than 25 years ago. The aim of this study is to verify how this recommendation is implemented in EU countries.

Methods used in the study

A representative of each member state was invited to complete an online questionnaire containing 11 questions on the adoption of the Directive, beneficiaries, providers and financing bodies, as well as on the objectives and results of the medical surveillance.

Results of the study

The answers of 20 countries indicate, as a preliminary result, that the concept of health surveillance is not defined equally in EU. In some countries health surveillance is addressed exclusively at the adverse effects of occupational risks, whilst other countries consider the global health of the workforce, not limited to occupational risks. Employers are mostly obliged to offer health surveillance, and in some countries workers’ participation is obligatory. The provider is usually an Occupational Health Physician, but other options are possible such as family physicians (GPs). Usually, the employer appoints the provider, which could pose independency problems. Finally, the provider can be self-employed, employed by the public health system or a private enterprise.

Conclusions

This study allows us to conclude that the EU Directive is applied in EU, but that harmonization has to be considered seriously. Learning lessons from the implementation in the member states would provide good practices for the way ahead, having in mind that WHO poses full coverage as a main objective for the third millennium.

METHODOLOGICAL DEVELOPMENTS TOWARDS BIOMARKERS OF EXPOSURE AND EFFECTS TO NANOPARTICLES

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Objective

Although it is increasingly widely accepted that nanoparticle exposure and health monitoring for workers is needed, the search and development of biomarkers of exposure and effects is fastidious. For instance, the development of biomarkers of exposure is limited by technical issues and characterization difficulties of NP in biological media. Inductively coupled plasma mass spectrometry coupled to single particle detection (SP-ICPMS) appears as a promising technic to better characterize NP in biological media. Regarding biomarkers of effect, the main issues lie in the non-specificity of available biomarkers and the choice of biological matrices. Exhaled breath presents the advantage of being specific of the inhalation route of exposure, which is of major concern for NP.

Methods and results

The adequacy of SP-ICPMS to characterize NP in biological media was studied on the basis of silver and titanium dioxide NP of different sizes in biological matrices. On standard NP, the concentration and size detection limits were determined, as well as the optimum parameters for proper detection. The influence of ionic concentrations on NP detection and characterization was also assessed.

The collection efficiency of 8-isoprostane in exhaled breath from volunteers was compared using two commercially available devices. A sensitive and specific analytical method was developed for 8-isoprostane detection using high performance liquid chromatography coupled to tandem mass spectrometry.

Conclusions

SP-ICPMS offers the possibility to associate elemental detection coupled to size determination, even in complex matrices such as urine or blood. This is highly promising on the way to biomarker of exposure determination. About exhaled air, the analytical methods need to be highly sensitive since the biomarker levels are very low. The collection efficiency is of main importance to obtain sufficient biological matter and has to be optimized.

INTERNATIONALIZING SIGNAAL: THE ITALIAN VERSION IN PILOT PHASE

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Introduction

Since July 2013, Dutch and Belgian occupational physicians can report suspected new combinations between health problems, exposure and/or the work setting at www.signaal.info. Each report is reviewed by at least two occupational health experts. For unknown and new cases, targeted research on the aetiology is carried out in the scientific literature using a special search string developed for Evidence Based Occupational Medicine. Finally, on the basis of a joint and preferably interdisciplinary consultation, the occupational nature of the reported diseases as well as their newness are deduced. The first evaluation of the system showed that a system like SIGNAAL can provide valuable data on the possible risks of new and emerging occupational diseases also in Italy, by creating a structured tool for reporting and evaluating new associations of health problems and exposures in the workplace. In 2016 we hope to widen the availability and the use of this tool in Italy as well as in other European countries and languages.

Methods

The Dutch online reporting tool with an online form, a public website and an evaluation procedure form were transformed to a multilingual system by translating all necessary parts into Italian, English and French. For each language a separate team of assessors were installed. It offers (occupational) physicians in different countries the possibility to report their suspicions on new occupational health risks for preliminary assessment on both work-relatedness and newness without an obligation to report it to a system linked to workers' compensation.

Results

From May 2016 until October 2016 Italian cases will be registered and assessed within the Italian version of SIGNAAL. The first experiences with the Italian system, that in a pilot phase were tested by Italian Modernet members, will be presented with the objective to assess its feasibility and acceptability. Some examples will be presented to illustrate how possible new occupational health risks can be assessed, but also which obstacles and pitfalls would be encountered.

Conclusion

An online reporting system designed within the occupational health framework can provide valuable data on the possible risks of new and emerging occupational diseases by creating a structured tool for reporting and evaluating new associations of health problems and exposures on the workplace. SIGNAAL is a first step in Occupational Health Vigilance.

IMMUNOLOGICAL AND RESPIRATORY EFFECTS AMONG WORKERS WHO HANDLE ENGINEERED NANOPARTICLES AT WORK

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Objective: Engineered nanoparticles are being increasingly used in industrial processes, but little is known about their potential health effects in workers. The aim of this study was to quantify occupational ENP exposure and to investigate short term changes in markers of inflammation and lung function in workers handling ENPs.

Methods: A prospective panel study of ENP-handling workers in research laboratories was conducted comparing several markers of inflammation in the blood and respiratory tract at baseline to the same markers at the end of a shift and at the end of the working week. Continuous, real-time monitoring of EHP exposure was conducted on participants when handling ENPs. Data were collected at the start of the working week, at the end of the first shift and at the end of the week. Measurements included spirometry, FeNO, CRP and serum cytokines and a range of inflammatory markers, including soluble tumor necrosis factor RII (sTNFR2).

Results: Twenty-seven of the study participants handled ENPs during the week and 57 did not. From Monday morning to Monday afternoon, there was a significantly increased difference in sCD40 for participants who had handled nanoparticles that day compared with those who had not ($p=0.01$). When comparing the change in cytokines from Monday morning to Friday afternoon there was a significantly larger increase for sCD40 for participants who had handled nanoparticles that week compared to those who had not ($p<0.001$), in sTNFR2 ($p=0.002$) and in the CD62P cytokine ($p=0.003$). There were no significant changes in hematological parameters, lung function or airway inflammation related to ENP exposure.

Conclusions: While the number of exposed subjects was small and exposures to ENP low, this study found that increases in three cytokines were significant over the week. These findings suggest that workers handling ENPs in research laboratories are at risk of immunological changes.

PULMONARY INFLAMMATION IN FOUNDRY WORKERS

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Objective: To assess whether cumulative dust exposure in foundry work is associated with airway inflammation measured by the analysis of fractionated exhaled nitric oxide (NO) concentration, or by inflammatory markers in exhaled breath condensate or serum.

Methods: We examined 476 dust-exposed and non-exposed foundry workers, and assessed the individual cumulative exposure to dusts and respirable quartz. Bronchial and alveolar NO production and inflammatory markers in exhaled breath condensate and in serum samples were also analysed.

Results: After adjusting for pack-years of smoking, increased levels of alveolar NO, serum C-reactive protein (CRP), and interleukin-8 were associated with a higher level of cumulative exposure to dust. The referents had higher serum myeloperoxidase levels, bronchial NO output, and 8-isoprostane levels in exhaled breath condensate than in the dust-exposed groups. In Prague, we will present the results of the follow-up study of 116 workers, and also some results of fine and ultrafine particle measurements of ambient air in the foundry.

Conclusion: Dust exposure in foundry work may induce both systemic and alveolar inflammation.

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STRENGTHENING THE OCCUPATIONAL HEALTH EXPERTISE AND SCIENTIFIC PERFORMANCE OF PUBLIC HEALTH INSTITUTION OF TURKEY ESPRIT (H2020 TWINNING PROJECT)

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PHIT (formerly known as “Refik Saydam Hygiene Center” until 2012) has been established as an affiliated body of the Turkish Ministry of Health (MOH) to run primary health care services and to conduct research for protecting public health, controlling and preventing diseases. The general aim of the H2020 TWINNING project [ESPrIT] is to strengthen the scientific standing of “Türkiye Halk Sağlığı Kurumu” - the Public Health Institution of Turkey (PHIT) - in the field of occupational health, with a particular focus on occupational diseases. The project has started in January 2016 and will last for three years. PHIT formed a consortium with the applied research organisation TNO (NL) and the academic institutes VUmc (NL) and UGent (Be).

PHIT has defined research duties towards the Ministry of Health and is obliged to present these research results for further evaluation of national health policies. The current situation regarding occupational diseases in Turkey is in need of vast improvements, supported by rigorous research findings. That is the reason why occupational health and diseases was chosen as the specific research field by PHIT to be strengthened through this twinning project. PHIT and the Ministry of Health in Turkey currently are operating in the blind when it comes to adequate prevention policies to prevent occupational diseases. A large majority of occupational diseases go unreported. Not knowing the size, distribution and nature of the problem, public health officials cannot plan intervention programmes or allocate resources.

In Turkey, the data of the Social Security Institution are the only source for statistics related to Occupational Health and Safety. According to the Social Security Institution statistics 371 occupational diseases have been recorded for compensation in the year of 2013. The number of work related diseases is expected to be between 50.000 and 150.000 cases in Turkey, based on extrapolation of epidemiological data. Showing that a vast majority of cases of occupational diseases are not recognized and that Turkey is no exception to the rule that in many countries the diagnosis and correct handling of work related complaints can be improved.

The starting point and first focus in this project lies on good individual diagnosis and treatment of workers who visit the community- and primary health care centres with (early) health complaints. The project will result in a proposal for a new system for classification of work-related diseases and a (partly implemented) research road map in order to have the policy cycle working in a proper way. The research results of ESPrIT will directly be transferred to the national stakeholders and the (national and international) scientific field, both during and beyond the execution of the project.

CHILDREN'S ENVIRONMENTAL HEALTH: THE PROBLEM AND THE SOLUTION

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Children today are surrounded by a wide array of environmental threats to health. Because of their unique patterns of exposure and great biological sensitivities, children are exquisitely vulnerable to these hazards. Even brief, low-level exposures during critical "windows of vulnerability" in early life can result in acute and chronic disease in childhood and across the life span.

Children in all countries are exposed to environmental health threats, but the nature and severity of these hazards vary greatly. More than 90% of the deaths caused by environmental exposures occur in the world's poorest countries – environmental injustice on a global scale.

In Low-Income Countries, the predominant environmental threats are household air pollution from burning biomass and contaminated drinking water. These are strongly linked to pneumonia, diarrhea and a wide range of parasitic infestations in children.

In wealthier countries, the major threats are ambient air pollution, toxic chemicals and pesticides. These are linked to non-communicable diseases - asthma, birth defects, cancer and neurodevelopmental disorders.

Toxic chemicals are increasingly important health threats, especially in previously poor, now rapidly industrializing countries. A major driver is relocation of chemical manufacturing, recycling, shipbreaking, and other heavy industries to "pollution havens" in poor countries that lack environmental controls and public health infrastructure.

Climate change is another global environmental threat. Its impacts will magnify in the years ahead. Children are the most vulnerable.

Disease of environmental origin in children can be prevented. Prevention requires a combination of research to discover the environmental causes of disease coupled with science-based advocacy. Successful past prevention efforts include removal of lead from paint and gasoline, banning of highly hazardous pesticides and reductions in urban air pollution. Future prevention will require mandatory testing of all chemicals in children's environments, continuing education of health professionals and enhanced programs for chemical tracking and disease prevention.

SKIN EXPOSURE TO NANOPARTICLES

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Due to the increased production and use of nanoparticles (NPs) there are workers and consumers that can be exposed. There is a debate among scientists to define possible effects related to this exposure and there are more open questions.

Skin contamination can happen during different work tasks in direct or indirect way with contaminated surfaces. Decontamination of the skin can be difficult because NPs tend to adhere to the skin and to penetrate quickly in the skin.

In general, it is agreed that NPs can penetrate the stratum corneum reaching viable epidermis using two primary pathways: through sweat glands and hair follicles, which is probably the most efficient way for penetration and permeation of NPs; and through the intercellular route, which is only possible for very small NPs or in damaged skin condition. The intracellular pathway is unlikely to be relevant for NPs, however it might be for released (metal)-ions.

While same kind of NPs can be safe for skin contact (such as titanium dioxide and zinc oxide), others can exert a sensitization effect such as NPs that can release sensitizing metals (i.e. Ni, Pd, Co), as well as a toxic effects for NPs that can release toxic metals such as Cd or As. Due to the high surface/mass ratio NPs can release more metals than bulk materials, increasing the risk of skin or systemic effects after the skin contact with them. For NPs that cannot release toxic/sensitizing metals or chemicals we know that soft NPs as liposomes, can penetrate and permeated the skin because they can squeeze between cells, while for rigid NPs, only very small can penetrate and permeate the intact skin (<4 nm). For NPs 4-20 nm it is possible a skin penetration/permeation, probably through follicles; for NPs 21-45 nm skin absorption can be possible only on impaired skin; for NPs >45 nm skin absorption is unlikely in healthy skin.

In these conditions, the presence of an impaired skin barrier in workers needs to be evaluate, since skin absorption can happen also for bigger NPs. Moreover, considering that NPs can persist on the skin despite decontaminate measures, it is compulsory to avoid skin contamination using personal protective equipment.

More data are needed on real working condition and risk assessment of skin exposure must be performed together with air monitoring for a comprehensive evaluation of workers exposure, particularly in conditions where inhalation exposure is minimized due to use of wet products. Moreover labeling is needed for NPs and products containing sensitizing or toxic metals to advise users to protect them from direct contact with the skin.

ANSES AND OVERVIEW OF ACTIVITIES ON NANOMATERIALS

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Anses (French agency for food, environmental and occupational health and safety)

Despite the advances in scientific knowledge, major uncertainties remain about the effects of nanomaterials on health. Anses, through several reports and opinions produced for ten years, has identified a wide variety of hazard characteristics and noted the great complexity involved in understanding exposure situations for humans, thus making it difficult to conduct specific risk assessments. Given the time it would require, the Agency has recommended the implementation of tools to improve risk management, in particular through a stronger regulatory framework at national and European levels. Then, ANSES produced opinion on the modification of REACH annexes in view of taking nanomaterials into account, has proposed a control banding tool for helping to manage risk at the workplace and recommended limiting the marketing of products containing nanomaterials to applications whose advantages have been clearly demonstrated.

France decided to introduce the mandatory reporting of substances with nanoparticle status, in a pure state or contained in mixtures or certain materials (Grenelle law II Act of 12 July 2010, and decree of February 17th, 2012). The declaration system www.r-nano.fr and the data collected are dealt by Anses. The report must be made for all amounts above 100 grams of nanoparticle substance produced, imported or distributed per year. The main results from the 2014 annual scheme, concerning nanoparticle substances produced, imported and distributed in 2013, are as follows: 14583 declarations submitted, 397 131 tonnes produced or imported in France. Uses frequently declared concern especially agriculture and food, formulation (mixing) of preparations and/or re-packaging (excluding alloys), coatings and paints, thinners, cosmetics, rubber articles... The utilization of the database allows documenting the risk assessment of specific nanomaterials such as titanium dioxide or silica, especially in the framework of REACH regulation. It is also useful to Anses's partners responsible for the measurement and monitoring of occupational exposures.

Finally, Anses supports research to reduce the numerous scientific uncertainties on nanomaterials and develop regulations and standards that provide better protection for humans and the environment.

CREATING A BIBLIOGRAPHIC REFERENCE BASE FOR NEW AND EMERGING OCCUPATIONAL HEALTH RISKS

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Abstract

The identification of new and emerging occupational health risks requires the use of several methods, including the use of spontaneous reporting of cases in a clinical watch system. An online reporting system used in an occupational health setting in the Netherlands and Belgium has proved to be feasible to gather report and assess new combinations of health problems and exposure in the workplace.

In the assessment of new reported cases, one of the main questions is whether the association is likely or not to represent a true signal that needs further examination. Since a signal is by definition something new, the next question arises whether or not the association has previously been described in the literature. A search for reports from other countries as well as a search in both the scientific and grey literature is the following step.

Here we present a new tool to facilitate the search for similar cases and report evidence from the literature. We started building a reference database of case descriptions for new and emerging occupational health risks from different sources to be used within the MODERNET network. We will show how it can be used for consultation, but also how registered users can add new cases or add new information to already existing cases in the database.

The “New and emerging risks database” stores information on health problems, work conditions, exposure, number of workers involved as well as the source of the signal. Finally, the database also provides access to the abstract and some of the literature concerning the case. It can provide corroborating information for assessment of specific cases, but also gives an overview of the appearance as well as assessment of new and emerging work-related health risks over time.

BIOMONITORING OF EXPOSURE AND HEALTH EFFECTS IN NANOMATERIALS WORKERS: UPDATED STATUS OF NANO-EPIDEMIOLOGY

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ABSTRACT

Objectives: Since our publication of “Assessing the first wave of epidemiological studies of nanomaterial workers” on *J Nanopart Res* in October 2015, six more papers were published.

Methods: A total of 13 published papers are reviewed and characterized for their study design, findings, and limitations.

Results: Of the 13 studies, 11 are analytic epidemiological studies, including 10 cross-sectional and 1 longitudinal studies. 2 of 13 studies are descriptive study with description of exposure concentrations or percent of positive detection. Most of these studies involved single nanomaterial exposure, for example, carbon nanotubes (MWCNT), titanium dioxide, iron oxides, carbon black, but 5 studies in Taiwan involved multiple exposures. Generally, biomarkers were used as the dependent variables which were compared between exposed and control groups, except for 1 surveyed work-related symptoms and diseases worsen by work. Exhaled breath condensate (EBC) and sputum were the most frequently used biospecimen (7 studies). All 10 cross-sectional studies and 1 six-month longitudinal panel study showed a positive relationship between nanomaterials exposures and various biomarkers. Positive health effects include: 1). Lung injury markers: elevation of lung fibrosis markers (sputum KL-6 (Krebs Von den Lungen 6)), elevation of lung inflammation markers (sputum IL-1B and IL-6, TNFalpha, FeNO), and reduction of lung function; 2). Cardiovascular markers: elevation of cardiovascular injury markers (fibrinogen, intercellular adhesion molecule (ICAM), and IL 6), and elevation of RR50+/- in HRV; 3). Oxidative damages markers: elevation of EBC nucleic acid, lipid and protein oxidative markers, reduction of antioxidant enzymes.

Conclusions: This review provides some insight into potentially adverse effects that might be related to nanomaterial exposures and provides a foundation for future work. We expect more publications from nanotechnology well-developed countries, e.g. USA, UK, and Germany. We also expect more longitudinal studies with repeated measurements to explore chronic and cumulative effects of nanomaterial exposure. In the future, nanoparticles in the EBC may be served as biomonitoring markers of nanoparticles exposure.

EARLY WARNING SYSTEMS TO DETECT NEW AND EMERGING WORK-RELATED RISKS AND DISEASES IN SPAIN

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Introduction: The European Framework Directive on Safety and Health at Work (Council Directive 89/391 EEC) and the European Strategy have been important landmarks for national policy-makers in EU countries to take action in the improvement of working conditions.

As a consequence, in Spain a new legislative framework on Health and Safety at work has been developed over the last twenty years. Valuable outcomes have resulted from this new situation and perspectives have shifted from compensation to prevention.

Nevertheless, there are still outstanding issues among which is need to develop of “early warning systems” to identify and evaluate new and emerging work related risks (NERCs). In recent years some of these systems have been implemented on a local basis in a limited number of Spanish regions; however, the development of a fully nationwide system is as yet not achieved.

Objective: To provide up-to date information regarding Spanish sentinel and alert systems to identify new and emerging health risks and diseases linked to work.

Methods: Literature review and in-depth description of existing sentinel and alert systems in Spain in a number of regions and at a National level through interviews and qualitative analysis.

Results: Clinical watch systems and databases in use in 10 different Spanish regions (of the 17 in which Spain is politically organized) are described and compared. Differences among them can be observed in methods of gathering information on work-related health effects, work and exposure, etc., but all them are based on epidemiological principles. The exception to the regional fragmentation is the nationwide system of epidemiological health surveillance of workers exposed to asbestos.

Conclusions: This review provides a deep insight into the existing approaches to early identification of new and emerging health problems at work and work-related diseases in Spain. It can provide support to designing policies and prevention measures, including practical advice for specific industries and firms.

OCCUPATIONAL EXPOSURE OF NANO-SCALE OIL MIST/SPRAY IN THE METALWORKING INDUSTRY

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Abstract

Introduction: Occupational safety and health experts' are needed additional information about nanoparticles exposure at the workplaces during different processes (e.g. well known welding processes) for better providing of occupational risk assessment.

Study objective: To investigate the potential occupational exposure of nano-scale oil mist/spray in the metalworking industry.

Study material: Two metalworking pilot companies in Latvia were selected. Oil mist/spray was collected and afterword's analysed using electrical low pressure impactor „ELPI+” which enabled to measure spray concentration (by mass, number and surface area) including particles in size distribution from 6 nm - 10 µm.

Results and conclusions: The employees of metalworking industry were exposed to oil sprays and oil mist in different concentrations. In none of the companies (enrolled in pilot study) the occupational exposure didn't exceed the occupational exposure limit – 5 mg/m³. But it is very important to continue provide research on it in future. Nevertheless, measurements show quite high concentrations (particles' number concentration, pt/ccm) of nano-scale oil mist/spray at metal industries' workplaces during the metal plane and grinding processes (13832 – 21009 pt/ccm). Furthermore there are necessary very serious discussions between occupational hygienists and occupational safety specialists in field of occupational exposure data interpretation (e.g. taking another potential nanoparticle sources in indoor workplaces, etc.). As well as it is required to make additional studies with larger amount of workplaces and bigger number of respondents for better understanding health effect caused by nanoparticles among workers of metalworking industry, too.

THE ITALIAN NETWORK MAREL AND NEW OCCUPATIONAL DISEASES

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Background. Occupational health surveillance is an important issue in many countries since working conditions and occupational exposures are rapidly changing. We aim to create a network of occupational disease consultation centres of Italian university hospitals to which patients are referred for potentially work-related diseases.

Methods. The pilot network, namely MAREL (*MA*lattie e *Rischi* *Emergenti* *sul* *Lavoro*), will include five occupational disease consultation centres of university hospitals located in central-northern Italy. Patients are referred to these consultation centres by their general practitioners, occupational physicians or other specialists for the investigation of the putative occupational origin of the disease. Each centre will collect cases of putative occupational origin through a structured and standardized data collection form. An online database platform will be developed collecting data on: diagnosis; personal habits; occupational history; exposure assessment for potentially associated risk factors; physician's opinion on the possible causal relationship between disease and occupation. The data will be coded according to national and international classifications. To detect emerging disease-exposure associations we intend to apply the proportional reporting ratio used in pharmacosurveillance and adopted by the French occupational disease surveillance system (RNV3P).

Results. The data collection is going to start in 2016. Preliminary data will be available in due course. The detection of new disease-exposure associations is an important public health issue, especially as large numbers of new technologies, products and duty cycles are regularly introduced.

Discussion. The Italian network MAREL will contribute to already existing surveillance systems (i.e. MALPROF) by the detection of new and emerging occupational diseases and risks and will foster the development of preventive measures stimulating research related to this field.

OCCUPATIONAL DISEASE GUIDELINES FOR SIGNALLING AND PREVENTION OF OCCUPATIONAL DISEASES: TWO EXAMPLES FOR LUMBAR HERNIATED DISC DISEASE AND STRESS RELATED DISORDERS

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Objective

The development of evidence informed occupational disease (OD) guidelines to identify and counteract lumbar herniated disc disease (LHDD) and stress related disorders (SRD).

Methods

To support Dutch occupational physicians in signalling and preventing ODs, transparent and evidence-based clinical decision criteria were developed for LHDD and SRD. Systematic reviews and meta-analyses with grading of the evidence were used.

Results

In total 22 (LHDD) and 12 (SRD) studies were included in the systematic reviews. Bending & twisting of the trunk and lifting & bending of the trunk are work-related risk factors for LHDD with relative risks of 2.4 (95%CI: 1.67-3.55) and 3.2 (95%CI: 1.81-5.63), respectively. Effort- reward imbalance, high psychological job demands, little job autonomy, little social support from colleagues and /or managerial, procedural or relational injustice in the organization and high emotional demands are work-related risk factors for SRD, with relative risks varying between 1.3 (95%CI 1.16-1.38) and 2.0 (95%CI 1.81—2.22). An example of a threshold limit for a risk factor of LHDD is daily bending of the trunk more than 20 degrees for at least one hour a day. An example for SRD is a combination of high time pressure and lower autonomy, e.g. after a reorganisation.

Conclusion & discussion

Several disease-specific work-related risk factors for LHDD and SRD have been established confirming the multifactorial aetiology. The clinically assessed threshold limit of the risk factors are the starting point for the selection of effective preventive interventions to reduce these ODs.

MISSING VALUES IN ESTIMATES OF INCIDENCE OCCUPATIONAL DISEASES: LEARNING FROM DATA OF DUTCH CONSTRUCTION WORKERS

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Objective To compare different methods of handling missing data in regression analyses estimating trends in incidence of medically reported occupational diseases (OD) using physician-reported surveillance data. The main problem is whether a missing OD report should be handled as true zero (assessment of no OD and therefore not reported) or as missing OD reports (no assessment and therefore not reported OD), i.e. the accuracy of zero reports.

Methods In a dynamic prospective cohort over a five year period (2010-2014), all OD diagnosed by occupational physicians (OP) participating in construction workers health surveillance (WHS) were reported to the Netherlands Center for Occupational Diseases (NCOD). OD were defined as a disease with a specific clinical diagnosis (ICD classification) that was predominantly caused by work-related factors as assessed by an OP. Annual incidences were determined for the total number of OD and six frequently occurring OD groups. Trends in incidence were estimated using a multilevel negative binomial regression model. In an exploratory sensitivity analysis we compared three scenarios for handling zero cases: 1) including OD reports and corresponding OP, so no zero cases in the regression analyses, 2) imputing zero reports for OP when no OD reported, so true zero report and missing OD analysed both as true zero reports and 3) imputing zero reports only when OP has demonstrated to be active in WHS in specific year, so assuming true zero reports.

Results In the dataset for the construction industry, scenario's 2 and 3 of handling the missing data made relatively small differences to trend estimates. No changes in direction or significance of trends were observed, however, scenario 3 tended to predict smaller change in incidence (i.e. moving the trend towards no change). Scenario 1 led to biggest differences with also changes in directions of trends. In scenario 3, the average annual increase in incidence of all OD was 3% (95%CI: -2% to +9%) to 12,964 per 100,000 workers in 2014. Scenario's 1 and 2 resulted in an annual increase of 8% (95%CI: +3% to +12%) and decrease of 6% (95%CI: -12% to -1%), respectively.

Conclusion & discussion Imputing zero reports only when OP has demonstrated to be active in WHS in a specific year, so assuming true zero reports, was the closest match to the presumed situation where an OP not seeing any cases of OD is unlikely to be reporting in that year. Other models need to be explored to improve the estimates of trends using surveillance with missing data, e.g. a zero inflated negative binomial models.

THE RELATIONSHIP BETWEEN AGE AND THE REPORTED INCIDENCE OF WORK-RELATED ILL-HEALTH

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Objective: Increased life expectancy, a changing population age profile, and hence an increasing dependency ratio, drive a need to keep older workers in employment and encourage those who have left to return to work. Financial incentives are changing so as to encourage later retirement. However, many questions need to be answered such as whether an ageing workforce may have an increased susceptibility to occupational diseases or other work-related ill-health (WRIH). The aim of the study was to investigate the incidence of physician reported WRIH by age categories for the following main groups of disorders: mental, musculoskeletal (MSD), skin (contact dermatitis) and respiratory (asthma).

Methods: Incident case reports of WRIH received from occupational physicians (OPs), general practitioners (GPs), and specialist physicians (dermatologists, chest physicians, rheumatologists and consultant psychiatrists) were extracted from The Health and Occupation Research (THOR) network database and analysed via SPSS.

Results: Incidence rate ratios (IRRs) for mental ill-health showed an increase with age peaking in the 45-54 year category (psychiatrists 2.3, GP 1.3) but falling in the 55-64 and 65 year plus categories. IRRs for MSDs reported by rheumatologists show an increase with age with the highest rate in the 65 year plus category (1.6), but GP IRRs peak at 45-54 years then steadily fall =>55 years. For dermatitis IRRs fall progressively from 1.8 (age 16-24) to 1.0 in those aged =>65. IRRs for sickness absence peak in the 45-54 year category.

Conclusions: Generally these data do not suggest an increased reported incidence of WRIH with increasing age beyond 55 years, apart from MSDs incidence as reported by rheumatologists. However, interpretation has to be cautious on account of confounding by occupational exposure, hours worked, and survivor bias.

EVALUATION OF NANOPARTICLES EXPOSURE AND THEIR RESPIRATORY IMPACT AMONG AIRPORT WORKERS – FOCUS ON EXPOSURE ASSESSMENT USING EXHALED BREATH CONDENSATE

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Objective Aircraft engine exhaust increases the number concentration (PNC) of nanoparticles (NP) in the surrounding environment. Health concerns related to NP raise the question of the exposure and health monitoring of airport workers. A French collaborative study has been set up to address this issue. A part of this study is dedicated to the assessment of NP and metal exposure of airport workers using exhaled breath condensate (EBC) as a non-invasive biological matrix representative of the respiratory tract.

Methods EBC was collected from 458 French airport workers working either on the apron or in the offices. NP exposure was characterized using PNC and size distribution. EBC particles were analyzed using dynamic light scattering (DLS) and scanning electron microscopy coupled to X-ray spectroscopy (SEM-EDS). Multi-elemental analysis was performed for aluminum (Al), cadmium (Cd) and chromium (Cr) EBC contents.

Results Apron workers were exposed to higher PNC than administrative workers ($p < 0.001$). Workers were exposed to very low particles sizes, the apron group being exposed to even smaller NP than the administrative group ($p < 0.001$). The particulate content of EBC was brought out by DLS and confirmed with SEM-EDS, although no difference was found between the two study groups. Cd concentrations were elevated in the apron workers ($p < 0.001$), but they remained very low and close to the detection limit.

Conclusions Our study reported the airways particulate and metal content of airport workers. EBC is a potential useful tool for the non-invasive monitoring of workers exposed to NP in addition to metals. These first results are to be deepened with a second ongoing study that will bring a longitudinal follow-up of the same airport workers.

EARLY WARNING SYSTEMS TO DETECT NEW AND EMERGING RISKS, E.G. CANCER, IN EUROPE

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Early identification of new and emerging risks of chemicals (NERCs) followed by exposure control may prevent workers health risks.

Also at the European level there is much interest in so-called *early warning systems*, but countries use different systems. RIVM made an inventory in 51 European countries for identifying new and emerging risks for workers.

Seven countries developed a signalling tool based on spontaneous reporting, sometimes in cooperation with another country. Using such a tool, physicians can report health effects, e.g. cancer or any other type of work-related disease, when they suspect a hitherto unknown causal relationship between substances or work processes and the reported health effect. Next, a group of experts in occupational disease and exposure will evaluate the possible causal relationship. Ten other countries reported systems which are not specifically designed to identify new and emerging risks of chemicals, but which could be used as such.

Besides signalling tools, several databases are available with information on exposure to hazardous substances and processes, as well as health effects. These databases can be used to identify possible work-related hazards, such as carcinogens. Again, expert groups play a fundamental role in the evaluation.

According to experts in the field, the national centres that investigate work-related health effects of workers play an essential role in the evaluation of a possible causal relationship between exposure and health effect. According to most of the countries in this study, cases should be collected and evaluated preferably at an international level. Many suggestions were given; e.g. using an already existing international network of professionals who evaluate and discuss new and emerging risks for workers (MODERNET) or other international advisory committees.

Once a new and emerging health risk has been established, action has to be taken to control the risk. The study gives an overview of possible actions.

REVISITING THE PHYSICO-CHEMICAL CAUSES OF THE PATHOGENICITY OF SILICA WITH SYNTHETIC QUARTZ CRYSTALS: CRYSTALLINITY VERSUS SURFACE DISORDER.

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Objectives: Exposure to some quartz particles is associated to severe lung diseases, but what imparts pathogenicity to a quartz source over another is still unclear. Crystallinity and various surface features were associated to toxicity. However, the process to obtain quartz dusts for toxicological studies yields dusts with unpredictable and variable surface states and a reliable correlation between surface features and toxic effects has so far been hindered. To clarify the role of crystallinity and surface state in silica pathogenicity, we have here synthesized quartz crystals in respirable size and investigated their toxicity in vitro.

Methods: Two quartz crystals of different size were synthesized and compared with a fractured specimen obtained by grinding the largest synthetic crystals and a mineral quartz (positive control). The physico-chemical features relevant to particle toxicity - particle size distribution, micromorphology, crystallinity, surface charge, cell-free oxidative potential - were evaluated. Membranolysis was assessed on biological (red blood cells) and artificial (liposomes) membranes. Markers of cellular stress were evaluated on RAW 264.7 murine macrophages.

Results: Quartz crystals were obtained by a novel synthetic approach. Independently from size, synthetic quartz crystals with regular intact faces did not elicit cellular toxicity and lysosomal stress on macrophages, and were non-membranolytic. When fractured, synthetic quartz attained particle morphology and size close to the mineral quartz (positive control) and similarly induced cellular toxicity and membranolysis. Fracturing imparted a higher heterogeneity of silanol acidic sites and radical species at the quartz surface.

Conclusions: Our data support the hypothesis that the biological activity of quartz dust is not due to crystallinity per se but to the new faces produced during crystal fragmentation. Besides radical generation, fracturing upsets the expected long-range order of surface functionalities which become able to disrupt membranes and induce cellular toxicity, likely causing the lung inflammatory response to quartz.

ARE NANOTiO₂ SUNSCREENS USEFUL TO PREVENT OXIDATIVE STRESS CAUSED BY UV IRRADIATION?

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Effect of skin exposure on markers of oxidative stress and inflammation tested was in the exhaled breath condensate (EBC), blood and urine as systemic absorption may occur [1,2].

Six subjects, mean age 48.0±8.3 years, 3 males and 3 females, used commercial sunscreen containing TiO₂ nanoparticles for 3.5 days (7 applications for 80% of the body, with and without UV irradiation in the solarium). Total average cream consumption was 131.3±9.9 g/testing period. The same regimen was maintained with the UV application only.

Sample 1 of EBC and urine was collected before the test and sunscreen/ two UV exposures, sample 2 of EBC and urine on the day 4, before the cream skin was thoroughly washed; sample 3 on day 11 (without application of the sunscreen since the day 4), and sample 4 one week later.

Following parameters were analyzed in all samples collected: pH, malondialdehyde (MDA), 4-hydroxy-trans-nonenal (HNE), 4-hydroxy-trans-hexenal (HHE), C6-C12, 8-isoProstaglandin F_{2α} (8-isoprostane), 8-hydroxy-2-deoxyguanosine (8-OHdG), 8-hydroxyguanosine (8-OHG), 5-hydroxymethyl uracil (5-OHMeU), o-tyrosine (o-Tyr), 3-chloro-tyrosine (3-Cl-Tyr), nitrotyrosine (NO-Tyr), and leukotrienes (LT) B₄, C₄, D₄, E₄. Markers were analyzed by LC-ESI-MS/MS. TiO₂ was detected by X-Ray Diffraction method.

Analysis of the sunscreen has confirmed TiO₂ with particles size distribution in the range 60-100 nm, the proportion of rutile and anatase was 80:20. Additionally, traces of Si were found. Ti in all blood, EBC and urine samples was under the limit of detection 1.2 µg/l.

Application of (nano)TiO₂ sunscreen did not change most EBC, blood and urine markers significantly. On the other hand, use of solarium increased majority of markers on the first day in the blood and EBC, but not in urine. Rather surprisingly, the sunscreens did not suppress this effect of the UV radiation.

Conclusions: The oxidation stress effect of (nano)TiO₂ application alone was not found. It appears that the sunscreen may protect against skin burning, but not against systemic deleterious effects of the UVA irradiation due to oxidative stress, such as DNA, lipids and proteins oxidative damage and inflammation.

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WORKERS EXPOSED TO (NANO)TiO₂ HAVE ELEVATED MARKERS OF OXIDATIVE STRESS AND INFLAMMATION IN THE EXHALED BREATH CONDENSATE

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Human health data regarding exposure to nanoparticles are extremely scarce and biomonitoring of exposure is lacking in spite of rodent pathological experimental data. Potential markers of the health-effects of engineered nanoparticles were examined in 34 workers exposed to (nano)TiO₂ pigment and 45 controls in two studies (2012 and 2013). In the exhaled breath condensate (EBC) titanium and markers of oxidation of nucleic acids (8-hydroxy-2-deoxyguanosine, 8-hydroxyguanosine, 5-hydroxymethyl uracil); proteins (o-tyrosine, 3-chlorotyrosine, and 3-nitrotyrosine), lipids (malondialdehyde, 4-hydroxy-trans-hexenale, 4-hydroxy-trans-nonenale, 8-isoProstaglandin F₂α and aldehydes C₆-C₁₂), and inflammation markers leukotrienes (LT) B₄, C₄, E₄, and D₄ were analyzed. Spirometry and fractional exhaled nitric oxide (FeNO) were measured.

In the workshops, the median total mass 2012 and 2013 TiO₂ concentrations were 0.65 and 0.40 mg/m³, respectively. The median number concentrations measured by the scanning mobility particle sizer (SMPS) and aerodynamic particle sizer (APS) were 1.98x10⁴ and 2.32x10⁴ particles/cm³, respectively. About 80% of those particles were smaller than 100 nm in diameter. Titanium in EBC was significantly higher, and all oxidative stress and inflammation markers in EBC were higher in production workers relative to the controls (p<0.01), including the pre-shift EBC samples.

Multiple regression analysis confirmed an association between the production of TiO₂ and the levels of EBC biomarkers studied.

Spirometry and FeNO were not sensitive and/or specific enough to reveal impairments.

Accordingly to experimental findings, these results are consistent with the oxidative stress hypothesis and suggest, at the molecular level, sustained lung injury. Cysteinyl LTs in EBC analysis may signify inflammation and potential fibrotic changes in the lungs. Studied markers may be helpful for monitoring the biological effect of (nano)TiO₂ on workers.

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RANKING OCCUPATIONAL CONTEXTS AND NON-HODGKIN LYMPHOMA

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Abstract

Background: The incidence rate of non-Hodgkin Lymphoma (NHL) was found increasing from the 1970s and started to level off in the last few years. Causes of the increase and associated risk factors remain largely unknown, but there are hypothesis about occupational context.

Objective: To invent from the accumulated knowledge the associations between occupational contexts and the risk of NHL.

Methods: Literature was used to identify the NHL associated occupational contexts. For each context, items were ranked both in terms of scientific interest and of the strength of association with NHL risk.

Results: Three ranked lists of associations between occupational contexts and NHL risk were constructed. We found that NHL was associated with 31 occupational activities, 91 occupational exposures and 35 occupational activity-exposure combinations. Among them, 5 occupational activities, 2 occupational exposures and 3 occupational activity-exposure combinations, involving agricultural or industrial sector and solvents or pesticides products, were highlighted with the highest publications number and the strongest association with NHL risk.

Conclusion: Results reported are very instructive and useful in both providing a ranked inventory of occupational contexts associated with NHL risk and highlighting “hot” occupational activities and exposures.

USE OF FRENCH MEDICO-ADMINISTRATIVE DATABASES FOR HYPOTHESIS GENERATION REGARDING OCCUPATIONAL RISKS IN AGRICULTURE

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Introduction: The French agricultural population is covered by a dedicated social security system named "MSA" (for "Mutualité Sociale Agricole"); this covers health insurance, family allowances, retirement pensions, as well as occupational medicine, and occupational accidents and occupational diseases insurance for salaried and non-salaried workers. Regarding health insurance specifically, 3.3 million individuals are currently covered, including 1.2 million active workers. For its functioning, this systems produces everyday large amount of data regarding contributions from one hand and reimbursements of medical expenses to the other. The issue of Occupational health vigilance for agricultural workers could not be achieved only by the occupational diseases database, as it provides merely only information regarding MSD (more than 90% of the diseases compensated). We decided to consider another paradigm. Individual health issues, regardless of etiology, result in care and health products consumption behaviors. These health expenses are totally or partially reimbursed by the MSA, generating continuous data flows that have as only goal, the reimbursement. These data can be qualified as "big data" due to the following four characteristics: volume, variety, velocity and veracity (the 4V's). Furthermore, for contributions issues, the occupational activity and some information regarding the enterprise are recorded (as location, which might help precise activity subgroups, as for instance within the "arboriculture" group).

Objectives: The objective of this proof of concept project is to link and mine the several MSA databases, in order to look for associations between diseases (or some proxy such as drugs consumption) and occupational activity (which is the proxy available for occupational exposure), in a vigilance purpose, without any prior hypothesis. In other words, the aim is to look extensively for "disease x occupational activity" associations that generate signals over background noise, taking into account as much information as possible regarding known and latent variables that can impact health issues.

Material and methods: The first step concern the analysis of privacy issues (due to re-identification possibilities as we need common individual identifiers for all databases). This is a pre-requisite to be authorized to get the full datasets. Data storage and analyses are conducted on the UGA platform for big-data. The second step is the description of the different MSA databases and their linkage (with R software). Occupational activity x diseases matrices will be built (with R software) in order to apply latent factors mixed model (unsupervised analysis). Observed variables, such as age and gender will obviously also be included in the model. The first study is performed on the chronic illness database (the only database identifying ICD-10 coded diseases, initially for 100% reimbursement issue). With the help of culture x pesticides matrices, some groupings will be proposed for occupational activities. The last step will be to analyze the relevance of signals.

Results & Conclusion: Grants were obtained to start the project, and authorization to get the whole dataset is in progress at the time of abstract writing. Work is for the moment conducted on data samples. Compared to classical epidemiological studies, interests and challenges are to use already existing data, to balance lower-level information regarding exposure to a marked increase of statistical power (the whole French agricultural population), and to conduct non supervised analyses. In 2017, the next step will be to use drugs consumption as a proxy for diseases. This will be done with the help of pharmacists-researchers already working on health insurance datasets. As wider

perspectives, highlighting of statistical signals could lead to specific work (exposure, epidemiological or toxicological studies), and most of all, if relevant, these methods have the potential to be used on continuous data flow for vigilance. A Modernet collaboration on big data could be a research axis for a future EU application.

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EXPOSOME APPROACH ON THE IDEWE DATABASE FOR THE SURVEILLANCE OF WORK-RELATED PROBLEMS

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Surveillance of diseases and associated exposures is a major issue in occupational health, in particular for identifying and preventing new threats for workers health. In Belgium, a database comprised medical data of employees has been collected over several years by the largest Belgian OHS provider Group IDEWE. In France, The French national occupational disease surveillance and prevention network (RNV3P) have constructed a growing database that records every year since 2001 all Occupational Health Problems (OHPs) diagnosed by a network of physician specialists.

In a previous work, Rieutort et al. have developed the observational surveillance (OS) on the RNV3P. This surveillance is characterized by the restructuring of data as a relational network, the exposome, and the specific observational spectrum summing up indicators of the Observational Surveillance. This methodology allows taking into account of the dynamic and the structure of the information, including multi-information as the multi-exposures in the occupational context.

In this collaborative work, we intend to apply this new methodology of Observational Surveillance on the Belgium database in order to 1) confirm the adaptability of the method to another database and another context, and 2) highlight association of occupational activity-occupational exposures from the IDEWE database. In order to do the demonstration, two examples have been chosen: the sore throat symptom, which has been used in the feasibility approach, and the other one, the agricultural activity. In the first one, the objective was to highlight the spectrum of occupational activity potentially related to the sore throat symptom. In the second one, to highlight the spectrum of diseases potentially related to the agricultural activity.

For each example, a classic method will be used to describe the sample (by frequency tables) and the observational surveillance method will be applied and compared to the classic one. An article is currently written about it and analyses are actually running.

WORK ROLE FUNCTIONING AT WORK IN HEALTH CARE

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Objective: To assess the capacity to work for a variety of job tasks demands of health care workers associated to health conditions.

Method: Cross-sectional study among active workers of a main hospital in Barcelona. Information was obtained using the 27-items Role Work Functioning Questionnaire adapted to Spanish (WRFQ-SpaV) and other validated, self-administered questionnaires. Each subscale of the WRFQ were scored separately, divided by the number of items including subscale (answered) and multiplied by 25 to obtain the percentages: 0 % (difficulty all the time) and 100 % without difficulty. A randomly selected sample of 823 workers was calculated, stratified by occupation (6 strata), from a population 3,600 workers and considering a confidence level of 95%, a maximum possible error of 3% and a proportion of 50% subjects obtaining a score higher than the median. A preliminary descriptive analysis is presented.

Results: A total of 544 health care workers have been included up until now (response rate = 66%). Main health conditions reported by participants were cervical (21.3%) and back pain (20.8%), anxiety due to stress (13.0%), allergy (9.5%) and reported high cholesterol (8.5%). No significant differences were observed between the subscales of WRFQ-SpV and sociodemographic and work variables, except the scores of the physical demands. Work performance related to the perceived state of health was high with an average score of 80.

Conclusions: Our results suggest that physical demands are the main difficulties for health professionals of PSMAR, being musculoskeletal diseases the most important health effects, especially in nurses and aides.

Key words: occupational health, health survey, work capacity, health care workers, work functioning; health effects.

OCCUPATIONAL DISEASES CAUSED BY HEXAVALENT CHROMIUM EXPOSURE

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Abstract:

Objectives

Tracing new possible causal relations between hexavalent chromium and cases reported as suspected occupational diseases.

Methods

Two datasources are being investigated for occupational diseases caused by hexavalent chromium. The first datasource consists of notices of objection in the context of a regulation of the Ministry of Defence for Compensation of Occupational Diseases caused by Hexavalent Chromium. The second datasource includes cases of possible Hexavalent Chromium related Occupational Diseases coming from the National Railways Company, referred to the Institute for Clinical Occupational Medicine in the Netherlands (IKA-Ned).

Cases are investigated by a clinical occupational medicine specialist and discussed in a Hexavalent Chromium Team. The Cr6 Team consists of a number occupational medicine specialists, a pneumologist, a dermatologist and an expert in work-related cancer. We especially focus on possible new relationships with hexavalent chromium. In suspected cases of new relationships a literature search is executed and the Cr6 Team is consulted.

Results

Inclusion of cases is still running. Till mid-April 2016 60 cases have been included in the first datasource, whereas 2 cases are included in the second datasource.

Possible new relationships are documented and we try to verify them by literature search and by expert judgement in the Cr6 Team discussions.

Conclusions

Two clusters of suspected hexavalent chromium related diseases provide the opportunity to investigate possible new causal relations.

MYCOBACTERIUM ABSCESSUS – RARE OCCUPATIONAL DISEASE. A CASE REPORT

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Abstract MYCOBACTERIUM ABSCESSUS is a rapidly growing mycobacterium that exists ubiquitously in the environment, for example, in tap water, house dust, soil, ground and domestic and wild animals, and birds. (1) A distinction between M ABSCESSUS and M CHELONAE became apparent only after 1992 with the advent of the polymerase chain reaction method. (2) The clinical manifestations of M ABSCESSUS, which caused a gluteal abscess in a woman with osteoarthritis, were first described in 1953. (3) The most common types of M ABSCESSUS infections are respiratory tract infections (4) and localized skin and soft tissue infections. (5) Here we report a case of M ABSCESSUS respiratory occupational infection.

Case presentation A 57-year-old Slovak man worker at cement producer company in position electrician was admitted to our hospital complaining of exercise dyspnoea and nonproductive cough – only at anamnesis he had previously hemoptysis. He had no family history of TBC diseases. He had a previous history of arterial hypertension, nephrolithiasis, Lyme borreliosis and bilateral coxarthrosis.

Chest X-ray shows micronodular drawing at left lower pulmonary lobe. The cardiopulmonary and abdominal findings were normal.

Laboratory examinations showed that white blood cell count was $6.41 \times 10^9/L$ (normal range $3-10 \times 10^9/L$ - neutrophils 66%, lymphocytes 21%, monocytes 9%, eosinophils 2%, and basophils 0.3%). Elevated serum levels of C-reactive protein (6.45 mg/L, normal range <5 mg/L) and NTproBNP (15.94 pg/mL, normal range 0–5 pg/mL) were shown. No other abnormalities were detected on laboratory testing. (include INTERFERON gamma: Quantiferon TB Gold 0,020 IU/ml – negative, PCR for Mycobacterium TBC complex – negative). M ABSCESSUS, identified by SPUTUM cultivation (BACTEC).

There was initiated a rifampicin, isoniazid, pyrazinamide and ethambutol combination treatment for the patient. This combination therapy was continued for 8 weeks. After that it was ethambutol, claritromycin and ciprofloxacin therapy for 8 months and for 15 months there was provided therapy in combination of ethambutol and ofloxacin.

During his work as electrician he controlled also pumps of sewage treatment plants and in case of mixing the sludge in the sedimentation container.

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