

Impaired endothelium-dependent vasodilatation among workers with IGT may decrease heat dissipation by conduction, convection, radiation, and sweat evaporation and may pose a risk to develop HRI.

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OCCUPATIONAL HEAT ILLNESS IN OUTDOOR WORKERS BEFORE AND AFTER THE IMPLEMENTATION OF A HEAT STRESS AWARENESS PROGRAM

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Introduction Heat Stress is an occupational hazard expected to increase in severity and breadth with climate change. Workers exposed to heat and hot environments can have increased injuries, exacerbation of disease, reduced productivity, and heat illness resulting in death. Strategies to respond are mitigation policies and preparedness. The National Institute of Occupational Safety and Health's (NIOSH) Revised Criteria for a Recommended Standard, Occupational Exposure to Heat and Hot Environments outlines training for and medical surveillance and research of worker populations exposed.

Methods Heat illness and worker's compensation costs before and after the implementation of a Heat Stress Awareness Program (HSAP) were evaluated retrospectively in a cohort of outdoor municipal workers from 2010–2016. The HSAP brought training and medical surveillance to at risk workers as outlined in NIOSH's Criteria for a Recommended Standard Occupational Exposure to Heat and Hot Environments.

Results 526 outdoor workers met inclusion criteria. Prior to implementation of the HSAP the occupational heat illness rate was 3%, this decreased to 1% the first three years of the program and less than 1% the last two years. Workers with heat illness were more likely to be extremely obese ($p < 0.0003$) and more likely to have two or more heat illness risk factors. Total worker's compensation costs decreased approximately 50% per illness or less than prior to HSAP.

Discussion Training, determining fitness for duty and regular medical monitoring prior to work in a hot environment may decrease frequency of occupational heat illness and occupational medical care costs in exposed workers. This study supports NIOSH's Occupational Exposure to Heat and Hot Environments' promulgation into U.S. law which can provide protection to vulnerable U.S. workers and may provide valuable guidance to the unknown numbers that will be added to the climate-vulnerable population as the global temperature continues to rise.

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TRANSITION OF GOVERNMENTAL GUIDELINES TO PREVENT HEAT STROKE AT WORK IN JAPAN

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Introduction In Japan, the prevention of fatal heat strokes at work has become more important along with the global warming.

Methods This research introduces the transition of methods to prevent heat stroke at workplaces in Japan within the latest 20 years.

Results The number of fatal heat stroke at work in Japan had been less than 20 until 1993; however, it exceeded 20 in 1994 and in 1995, consecutively because of the heat wave attack during summer. Therefore, in 1996, the guideline on prevention of heat stroke at work was formulated and published by the Labour Standard Bureau, Ministry of Health, Labour and Welfare. It advocated fundamental methods for the prevention of heat stroke such as working environment management, work management, health management and occupational health education at workplaces exposed to heat stress. Besides, the government started to announce the number of compensated cases of heat strokes every year. In 2005, another guideline was issued advocating the measurement of WBGT at the workplaces and the utilisation of the value for appropriate countermeasures. In 2009, the first guideline was totally revised by adding many new contents: the utilisation of WBGT, the promotion of heat acclimation, the method of desirable water and salt intake, the consideration for vulnerable persons with underlying diseases and the management of daily physical conditions. In addition, due to the impact of the Great East Japan Earthquake in 2011, nuclear power generation in Japan was temporarily suspended, and the need for the development of measures against heat stroke that did not use electric power as much as possible had increased, from the viewpoint of energy saving. Therefore, sports drinks and oral rehydration, salt candy, cool best to cool the body, clothing of quick-drying/cool feeling materials, etc. have started to be sold and widely spread.

Discussion Although the motivation for the prevention of heat strokes have spread rapidly during the last 20 years, according to the guidelines formulated by the government, the number of mortality often exceeds 20, including 47 in the historically worst year of 2010. While easy and inexpensive devices to prevent heat stroke such as nutritional supplements and special wears have become widespread, it is important to verify its effectiveness in an objective manner and to standardise the definition of devices able to cool down the body heat.

Toxicology of Metals

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METHYLTRANSFERASE GENE EXPRESSION AS POSSIBLE MEDIATOR OF THE EFFECTS OF ARSENIC EXPOSURE: AN EPIGENETIC STUDY IN FOUNDRY WORKERS

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Introduction Arsenic is an environmental carcinogen that undergoes methylation while metabolised. Subsequent intracellular methyl groups depletion can decrease global DNA methylation, facilitating carcinogenesis. On the other hand, hypermethylation in promoter regions of tumour suppressor genes related to arsenic exposure has been observed *in-vivo*. The effects of arsenic on enzymes regulating gene-specific methylation (DNA-methyltransferases) have not been fully

investigated. We analysed methyltransferase gene expression in workers exposed to high levels of metal-rich particles, and its relationship with the DNA methylation of nine inflammatory and tumour suppressor genes.

Methods We recruited 63 healthy male foundry workers. Individual exposure to arsenic and other metals was estimated based on metal components in PM10 collected in each work area (by coupled-plasma mass spectrometer) and on time spent in different areas by each worker. Methyltransferase gene expression was measured by real-time PCR in blood leucocytes DNA. Gene-specific DNA methylation was measured through bisulfite PCR-pyrosequencing. Multivariable linear regression models adjusted for age, BMI, smoking and drug consumption, were applied to assess the association between exposure and methyltransferase expression and, in turn, between methyltransferase expression and gene-specific methylation. Geometric mean ratios (GMR) were used to express results of log-transformed variables.

Results Enhanced methyltransferase (DNMT3B) gene expression was associated with increased exposure to arsenic (GMR=1.52, 95% CI: 1.06 to 2.20) and to other contaminants (Cu, Mo, Sn, Sb). DNMT3B expression was in turn associated with hypermethylation of the RASSF1A tumour suppressor gene ($\beta=0.54$, 95% CI: +0.15 to +0.94) and with hypomethylation of the Et-1 and IL-6 genes.

Discussion Our preliminary data suggest the possible role of methyltransferase gene overexpression in the pathway linking metal exposure to oncogene regulation. In particular, we found an increased DNMT3B expression in arsenic-exposed workers, that resulted also in hypermethylation (down-regulation) of RASSF1A. Interestingly, RASSF1A is a tumour suppressor gene involved in the development of cancers related to As exposure (bladder, lung).

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PKC θ -MEDIATED Ca^{2+} /NF-AT SIGNALLING PATHWAY MAY BE INVOLVED IN T-CELL IMMUNOSUPPRESSION OF COAL-BURNING ARSENIC-POISONED POPULATION

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Introduction Arsenic poisoning is a worldwide endemic disease that affects thousands of people. Growing evidence from animal, cell, and human studies indicates that arsenic has deleterious effects on immune systems, but its specific mechanism needs to be further explored.

Methods This is a population-based study that observed the changes in the proliferation of human T cells, IL-2, and INF- γ mRNA expression of coal-burning arsenic-poisoned population and control population. In addition, the intracellular calcium index, expression of PKC θ and phosphorylated PKC θ , and the DNA binding activity of NF-AT in PBMCs were analysed.

Results In the exposure group, and the mild, moderate, and severe arsenic poisoning groups, the stimulation indexes of the T cells, the mRNA expression of IL-2 and INF- γ significantly reduce in comparison to the control group. A correlation

analysis shows a clear correlation between PKC θ /NF-AT signalling, (Intracellular calcium index, PKC θ , p-PKC θ and the activity of the NF-AT binding DNA) T cell proliferation, and inflammatory factors (IL-2 and INF- γ).

Conclusion Coal-burning arsenic can cause T cell immunosuppression in the population, and participates in the occurrence and development of arsenic poisoning. In addition, the PKC θ -mediated Ca^{2+} /NF-AT signalling pathway may be involved in the T-cell immunosuppression of the coal-burning arsenic poisoned population. The study provides important research data towards a mechanistic understanding of endemic arsenic poisoning. The next step should be to verify the results of this research *in vitro* and with a larger cohort.

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THE ASSOCIATION BETWEEN PARKINSONISM AND QUALITY OF LIFE IN SOUTH AFRICAN MANGANESE MINE WORKERS

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Introduction Manganese is an essential micronutrient but excessive levels are harmful, and have been associated with parkinsonism. We sought to confirm the association between parkinsonism and quality of life (QoL), previously described in manganese-exposed welders, in a cohort of manganese mine workers, thereby also testing the usefulness of a tool originally designed for use in clinical settings.

Methods The study population comprised 418 manganese mine workers in South Africa. Parkinsonism was defined as a Unified Parkinson Disease Rating Scale motor score (UPDRS3) >15. The 39-item Parkinson Disease Questionnaire (PDQ-39) was used to assess miners' health status and/or QoL – our primary outcome. For this analysis, violation of the constant variance assumption led to a 'square root' transformation of the outcome variable. We used Mann-Whitney and Pearson's Chi-Square (or Fishers exact) tests to compare participants' parkinsonism status regarding baseline continuous and categorical characteristics. Multiple linear regression modelling was used to quantify associations.

Results The mean age of participants was 41.5 years; 97.6% were male. The prevalence of parkinsonism was 29.4%. QoL sub-scores and total scaled PDQ-39 score means were higher in mine workers with parkinsonism, relative to the rest of the cohort. Age ($\beta=-0.48$, $p=0.031$) and parkinsonism ($\beta=0.63$, $p=0.004$) were strong predictors of QoL. QoL was negatively associated with age; and parkinsonism predicted poorer QoL and/or health status.

Conclusion We found a strong association between parkinsonism and QoL abnormalities in manganese mine workers, confirming previous reports in manganese-exposed welders. The PDQ-39 proved to be a robust tool for assessing QoL in these workers.