CARCINOGEN EXPOSURE IN FIREFIGHTERS

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by
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Abstract

CARCINOGEN EXPOSURE IN FIREFIGHTERS

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PAHs or polycyclic aromatic hydrocarbons are a class of organic pollutants from incomplete combustion reactions that vary in the degree of carcinogenicity. They pose a high risk to organisms and can be absorbed orals, via the respiratory system and dermally. Firefighters are at a small to moderate increased risk to some cancers due to PAH exposure despite wearing personal protective equipment (PPE) and a SCBA respirator.

This literature review focuses on the dermal exposure route. PAH absorption through the skin can be affected by sweat, sebum and temperature and has been proved very challenging to measure. Intradermal microdialysis is a novel approach to dermal absorption that allows for the continuous in vivo sampling of the skin via the interstitial fluid. The semipermeable membrane allows for bidirectional exchange of substances between the MD fiber and the interstitial fluid.

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Chapter 1

Introduction

The National Fire Protection Association (NFPA) estimates 1,115,000 firefighters in the United States dedicated their lives administering aid and suppressing fires in 2018, of which 370,000 (33%) were career and 745,000 (67%) were volunteer firefighters (NFPA, 2018 ed.). Cancer is an increasing concern in the fire service which urgently needs addressed (Baxter, Hoffman, Knipp, Reponen, & Haynes, 2014). Previous research shows a higher cancer incidence in firefighters when compared to the general population in multiple types of cancer including excess myeloma, non-Hodgkin's lymphoma, prostate and testicular cancer (LeMasters et al., 2006).

During fire exposure, firefighters are required to wear National Fire Protection Association (NFPA) personal protective equipment (PPE), including turnout gear and self-contained breathing apparatus (SCBA) (Robert D. Daniels et al., 2015). This includes a fitted respirator comprising a full-face mask, a fireproof hood, boots, gloves, pants and jacket that aid in the protection of the skin and respiratory system from high temperatures and multiple chemical hazards. Previous research has focused on inhalation as a major exposure route, with only limited investigation of dermal absorption during fire suppression. This review aims to address current knowledge of chemical exposure routes in firefighters, focusing on dermal exposure and absorption at the fireground, and highlighting knowledge gaps and future directions for targeting risk mitigation.

Chapter 2

Disease Prevalence

Within the fire service, there is growing concern for disease risk and mortality at all career stages. Firefighters have a higher incidence of a number of different types of cancer when compared to the general population (Pukkala et al., 2014). Carcinogens and other hazardous chemicals have been measured in the breath, on the skin surface and in blood and urine of firefighters following fire suppression during training burns (Fent et al., 2014). There is increasing evidence of a causal relation between firefighters' exposure at the fireground and disease development, particularly cancer and cardiovascular diseases. LeMasters and colleagues used several assessment methods, inlcuding traditional summary risk estimates (SREs), and found that 10 cancers were significantly associated with firefighting (LeMasters et al., 2006). From the highest to the lowest SRE scores, those that were thought to be probable in their relation to firefighting exposure were multiple myeloma (SRE 1.53), non-Hodgkin lymphoma (SRE 1.51) and prostate (SRE 1.28) cancers. The authors reported that there was a probable increase related to firefighting for cancers including testicular cancer (SRE 2.02), skin (1.39), malignant myeloma (1.32), brain (1.32), rectal (1.29), buccal/pharyngeal (1.23), and stomach cancer (1.22), amongst others. Other studies have shown epidemiological data that also support a causal relation between firefighter exposure during their occupational duties and cancer (Robert D. Daniels et al., 2015).

To increase information available on exposure risks and health in firefighters, the National Institute for Occupational Health and Safety (NIOSH) and The National Cancer Institute collected data on nearly 30,000 career firefighters that was published in 2014 (Robert D Daniels et al., 2014). Their findings were interesting, showing that non-malignant diseases were actually lower in the firefighter compared to general population. This may appear surprising, but many firefighting companies have fitness requirements and annual medical checks, which also highlights the active nature of their job and may explain these differences due to their overall health and fitness compared to the population. Importantly, there is some disagreement between studies when looking at disease risk and the firefighting profession, but this study generally agreed with most literature that there is a small to moderate elevation in overall cancer rates and deaths, mostly due to a number of solid cancers (Soteriades, Kim, Christophi, & Kales, 2019).

Specifically, greater risk of urinary, respiratory, and digestive malignancies were reported in firefighters versus the general population. Also, a two-fold higher risk of malignant mesothelioma development and death (Robert D. Daniels et al., 2015), which the authors related to asbestos exposure (Markowitz, Garibaldi, Lilis, & Landrigan, 1991; Pukkala et al., 2014).

Cancer incidence in the fire service is reported to be increasing seen in both younger and more experienced personnel, and direct links to occupational exposure are being increasingly investigated. Unfortunately, some cancers develop very slowing and evidence for occupational links to such cancers has only recently become apparent (Jalilian et al., 2019). The large study conducted by NIOSH did not support greater cancer risk with greater exposure, calculated based on length of employment and potential exposure, but there were limitations to this study and understanding links between exposure through the course of duty and chronic disease is important in trying to improve long term health outcomes (NFPA, 2017). This is further supported by a study conducted by Daniels et al., (Robert D. Daniels et al., 2015) which included more than 19,000 male firefighters and found a causal association between firefighters' work exposure and cancer risk. This study used different quantification of 'exposure' compared to the NIOSH study by using the number of days exposed, 'run totals' and a calculation of 'fire hours' to investigate occupation associated risk (NFPA, 2017). Overall, it was concluded that a causal association exists, particularly in lung cancer and leukemia deaths, with increasing exposure. Further studies are required to support this causal association and increase knowledge of exposure to specific substances that may increase risk in this line of work. This has important implications for development of greater safety procedures and in the potential implementation of medical screening and detection procedures for specific cancers that have a higher incidence in firefighters.

Chapter 3

Environmental Fireground Hazards

3.1 Chemical Hazards

Despite wearing PPE, including turnout gear and self-contained breathing apparatus (SCBA), firefighters are at high risk of exposure to potentially hazardous chemicals due to the nature of their occupation (Stec et al., 2018). Although the duration of exposure during fire suppression and overhaul is often relatively short, the concentrations may be high enough to exceed NIOSH guidelines relating to 'Immediately Dangerous to Life or Health' (IDLH) chemical exposures (Fabian et al., 2014). Smoke from a structure burn contains many hazardous materials which result from a process of incomplete combustion and depend upon the items contained within the structure. Smoke can include toxic gasses, aerosolized particulate matter and many chemicals which can enter the body through multiple routes, including the lungs, skin, and mucous membranes. Notably, the contents and characteristics of smoke can vary considerably depending on its origins, with structural, vehicle and wildfires containing a mixture of hazardous substances, particulate matter, and chemical species, such as polycyclic aromatic hydrocarbons (PAHs), asbestos, formaldehyde, benzene, toluene, and many more. When considering the causal association between occupational exposure and cancer risk, it is important to recognize that many of these organic chemicals (for example PAHs), have been listed by The International Agency for Research on Cancer (IARC) as carcinogenic (group 1), possibly carcinogenic (group 2A) or probably carcinogenic (group 2B) to humans. Firefighters are categorized as 'group 2B' based on the IARC criteria for occupational exposure. PAHs can result from incomplete combustion reactions of organic materials. They can originate from a wide variety of sources including products of burned material. Some PAHs can be carcinogenic, can be toxic and have been known to cause mutations in animals. PAHs are comprised of two or more benzene rings that are bonded in either a linear, cluster or angular arrangement and consist only of carbon and hydrogen atoms (Abdel-Shafy & Mansour, 2016). The common non-carcinogenic PAH anthracene is a liner PAH and smaller in molecular weight. Many of these substances have been sampled in the body fluids of firefighters following fire suppression, despite wearing appropriate PPE. For example, blood and urine samples collected following training burns have shown the presence of PAHs and their metabolites (Fent et al., 2014; Fent et al., 2019; Fent et al., 2020; Stec et al., 2018). Concerns have been raised regarding respiratory rebreathing and skin absorption as potential routes for exposure, but specific exposure routes and their total contribution to overall exposure is currently poorly understood.

3.2 Thermal Hazards and Physiological Strain

A potential, plausible contributing risk factor for both chronic disease risk and systemic carcinogen exposure in active firefighters is the extreme ambient heat exposure experienced during a fire suppression. The thermoregulatory responses, increased toxicity of some substances with higher temperatures (Rider et al., 2014), coupled with high metabolic workloads and additional strain from PPE, results in high cardiac output, and simultaneous elevated demands for muscle and skin blood flow. High sweating rates and potential dehydration exacerbate cardiovascular strain, with potential for progression from hyperthermia to more serious heat illness in some cases (Horn et al., 2018).

In context of carcinogen exposure, thermal and cardiovascular strain may exacerbate risk. This heat strain may potentially increase the rate of dermal absorption and rate at which they enter the interstitial fluid and systemic circulation, which is subsequently discussed later in this review.

Chapter 4

Personal Protective Equipment

Firefighter protective clothing is designed to provide the wearer with protection from burn injury and limit exposure to a variety of different potentially harmful chemicals during fire suppression, including polycyclic aromatic hydrocarbons (PAHs). Firefighters are required to wear certain types of personal protective equipment (PPE), including turnout gear and self-contained breathing apparatus (SCBA). The required PPE includes fire helmets, hoods and face protection, gloves, fire boots and turnout gear. A SCBA is a mask worn that acts in a pressure positive capacity to provide breathable air in environments with oxygen deficiency, smoke, dangerous gases, and other airborne contaminants that may be otherwise dangerous to breathe while allowing the user to expel carbon dioxide.

Despite the precautions taken, multiple studies have shown that volatile substances are present under turnout gear. Fent et al. (Fent et al., 2014) identified PAHs found on the necks of firefighters post structural burn using skin wipes despite the use of PPE and SCBA. Fent and colleagues looked at 15 firefighter's PAH exposure on the forearms, hands, neck, face and scrotum. Dermal wipe samples of the forearms, neck and scrotum were collected pre- and 3 hours post burn. The PAH level found on the neck was measured significantly different compared to the pre burn with a median of 53.8 μg m to post-burn with a median of 62.8 μg m. More recently, Fent and colleagues have observed metabolites of PAH in the urine and VOCs during breath analysis. Concentrations of PAH metabolites were measuring in the urine of 24 firefighters both pre firefighting and 3 hours post-firefighting. Results showed firefighters had a significant increase in PAH concentrations post-burn at 3.1 μg/g. Exhaled breath sampling was taken immediately after firefighting and were found to have increased in all scenarios with the highest increase in the PAH benzene with +18.0% ppbv. In another study, Leitinen et al. (Laitinen, Mäkelä, Mikkola, & Huttu, 2010) found an increased level of PAHs using biomarkers in firefighters post burn. This study looked at agents absorbed during smoke diving simulators using urine analysis. The greatest increase was found in the PAH pyrenol with an increase in 4.3 nmol/L to 9.2 nmol/L when measured 6 hours post exposure.

Chapter 5

Routes of Carcinogen Exposure

Cancer research surrounding firefighters can be broken down into those that have focused thus far on respiratory routes of exposure and dermal routes of exposure. The respiratory route of exposure has gained the most attention in the research community. Research indicates high concentrations of PAHs and other carcinogenic compounds are found in smoke during structural burns and reinforces the need for SCBA, as required by NFPA guidelines.(Baxter et al., 2014) Dermal carcinogen exposure in the firefighter community has gained increased interest in recent years, with PAHs measured on the skin surface of firefighters post burn (Soteriades et al., 2019) and extensive evidence showing the presence of carcinogens in body fluids. Routes of exposure are hard to tease out and remain poorly understood, but the need to gain information on the mechanisms and magnitude of skin penetration, systemic exposure, and ultimately translation to approaches for risk mitigation and PPE improvements are evident.

5.1 Respiratory Route

Respiratory exposure and effects of airway irritants relies on reported symptoms and lung function testing (Brandt-Rauf, Cosman, Fallon, Tarantini, & Idema, 1989). Previous studies have indicated smoke exposure can result in acute respiratory obstruction, acute airway obstruction and reactive airways dysfunction syndrome (RADS) (Miedinger et al., 2007; Ribeiro, de Paula Santos, Bussacos, & Terra-Filho, 2009). Greven and colleagues report a positive association between the number of fires fought in a 12-month period and bronchial hyperresponsiveness that correlates with an elevated asthma risk (Greven et al., 2012). Fire exposure has also been associated with an overall systemic inflammatory response (Chia, Jeyaratnam, Chan, & Lim, 1990; Large, Owens, & Hoffman, 1990). Research today primarily looks at biomarkers in blood to assess respiratory exposure.

Respiratory exposure can be significantly decreased by the use of SCBA. Respiratory protection for firefighters is provided through the positive pressure Self Contained Breathing Apparatus (SCBA). Respirators have allowed for a significant decrease in smoke exposure during fire suppression (Soteriades et al., 2019). The respirator consists of a full facepiece with an assigned protection factor of over 10,000 (OSHA, 2009). Firefights generally wear SCBA when in interior fire responses with high concentrations of combustion products such as PAHs (Jefferey L. Burgess et al., 2020). The development of the respirator has been the most effective development to decrease respiratory exposure to carcinogens. A study done by Burgess and colleagues demonstrated that exposure during overhaul has the potential to cause changes in spirometry measurements and lung permeability (J. L. Burgess et al., 2001).

5.2 Off-gassing

Multiple studies have also looked at the possibility of exposure due to other components such as poor decontamination procedures. Fent at al. (Fent et al., 2017) proposes that firefighter's skin may be exposed due to chemicals permeating and penetrating the skin through or around PPE and SCBA from structural burns as well as from the cross-transfer of contaminants from PPE and other fire equipment onto the skin post burn. Additionally, post burn carcinogenic agents can evaporate from PPE equipment in a phenomenon known as off-gassing and later be inhaled by firefighters (Kirk & Logan, 2015). Off-gassing is the process where VOCs, or volitile organic compounds are emitted from the suites and equipement used during firefighter after firefighting is complete. This poses a risk to firefighters as the SCBA respiratory and PPE are not being worn and these harmful chemicals are easily absorbed into the skin. This research indicates a need for additional PPE, improved decontamination procedures and possible body mapping to identify areas of increased exposure.

5.3 Dermal Carcinogen Exposure

Despite high levels of PPE, exposure to hazardous chemicals including benzene and PAHs still occurs in firefighters. Carcinogenic or potentially carcinogenic substances have been measured from skin surface swabs and in breath samples from firefighters, in addition to metabolites in blood and urine after fire suppression (Fent et al., 2014; Fent et al., 2019; Fent et al., 2020). None of this data directly quantifies the routes of exposure, which remain poorly characterized. Specifically, limited research has been conducted on direct assessment of skin absorption due to methodological challenges, but it is evident that a greater understanding of the extent of exposure is necessary.

The skin is the largest organ of the human body, playing an important role as a selectively permeable barrier that protects us from many hazards in the external environment. The epidermis is the outermost layer of the skin and is semipermeable to water, which aids in inhibiting movement of harmful water-soluble substances through the skin and also in water conservation. Penetration of substances through the skin is highly relevant in fields such as pharmaceutical research and medicine, particularly in relation to specific drugs that require transdermal delivery. Understanding the time course and characteristics of chemical absorption is fundamental, and must consider factors such as solubility, skin pH and thermodynamic responses and subsequent dose delivery. In these circumstances, human absorption testing uses application of a chemical directly to the skin, and blood samples are taken to determine the timing and overall extent of absorption. The source of the substance is known in this situation and therefore determination of absorption via blood samples is applicable. However, when the source and amount of a chemical exposure is unknown, this approach cannot be used to determine these factors (e.g. during firefighting).

Other approaches have used cadaver and animal skin samples to assess absorption, utilized skin stripping of the epidermis with tape, biopsies and, and more recently, intradermal microdialysis (Bitar et al., 2015; Zafar et al., 2017). Several of these techniques, particularly biopsies and cadaver samples, do not replicate true human physiological responses, and the effects of factors such as sweating, high body temperature and skin blood flow are not accounted for. Skin absorption of chemicals and the clearance from the skin into the blood can be altered by several factors that relate to many occupational settings. Firefighters can experience high workloads loads and extreme temperatures during fire suppression, potentially causing hyperthermia or other heat illnesses. In the context of this review, it is important to recognize that normal physiological responses, including increased cardiac output, skin blood flow, and sweating responses, may all act to increase skin absorption (Rider et al., 2014). Prior studies have reported elevated transdermal absorption of drugs when delivered with some form of heating (Hao et al., 2016; Petersen, Rousing, Jensen, Arendt-Nielsen, & Gazerani, 2011), which increases cutaneous vasodilation and alters the permeability characteristics of the skin. As temperatures continue to rise above normal skin values, the lipid matrix of the epidermis becomes more fluid and therefore facilitates more penetration due to this structural change (Petersen et al., 2011). Studies aiming to enhance the delivery of drugs using dermal patches have shown increased delivery of nicotine and testosterone with heated skin patches or other delivery systems (Hao et al., 2016). There is evidence that heating alters absorption of drugs through all layers of the skin, including deep into the dermis, from which clearance occurs into dermal capillaries (Petersen et al., 2011). The outer most layer of the skin, the stratum corneum, selectively permits small molecular weight, lipophilic substances, to move into deeper layers via diffusion gradients from the skin surface (Rider et al., 2014). High skin blood flow during heating or environmental exposure may also contribute to greater quantities of substances entering the circulation, resulting in increased whole-body exposure. Another factor that affects absorption relates to skin thickness, which is thinner in body regions such as the neck, groin region, arms, hands and other extremities. Potential exposure of different body regions to carcinogens can vary, and will depend on clothing or PPE worn. The accumulation at some sites on the skin surface may also be influenced movement of substances due to sweat patterns and dripping, but there is limited information available on this specific topic.

In the context of firefighting, very few studies have attempted to examine skin exposure of PAHs, often indirectly assessing absorption via surface deposition and relating this to biomarkers in fluid samples to assess whole body, systemic exposure. Several researchers have used this approach, including a study by Wingfors et al. who measured 14 PAHs via skin swabs and eight PAH biomarkers in urine samples of volunteer firefighters during a smoke diving exercise (Wingfors, Nyholm, Magnusson, & Wijkmark, 2018). Eight urinary PAH metabolites were meaured in 20 volunteer student firefighters before and after a firefighter training exercise. An 8-fold increase of 0.14 to 1.1 μmol mol-1 creatinine post exposure. PAHs were found to have increased 5-fold. The authors determined that the skin was a considerable contributor to overall exposure even with the use of standard PPE. The authors utilized a correlational analysis, which provides useful information but does not directly determine penetration through the skin. Fent and colleagues (Fent et al., 2014; Fent et al., 2019) have conducted multiple studies that similarly use skin surface deposition of a substance of interest and correlate those values with breath samples and biomarkers in urine samples from firefighters following an exposure. Notably, the authors considered what they termed ‘biological absorption’ in firefighters that had different jobs at a fireground, but this data is still limited to correlations of skin contamination and fluid biomarkers and not quantification of skin absorption itself. Fent and colleagues looked at 15 firefighter’s PAH exposure on the forearms, hands, neck, face and scrotum. Dermal wipe samples of the forearms, neck and scrotum were collected pre- and 3 hours post-burn. The PAH level found on the neck was measured significantly different compared to the pre-burn with a median of 53.8 μg m to post burn with a median of 62.8 μg m. A further study by Fent et al., observed PAH concentrations in the urine of firefighters who responded to controlled residential fires (Fent et al., 2019). PAH concentrations in urine increased from pre-firefighting to 3-hour post firefighting for all job assignments. Results showed that of the 15 firefighters that participated a significant increase in PAH concentrations post-burn was found at 3.1 μg/g (15). Stec and colleagues looked into the occupational exposure and elevated cancer incidence in firefighters by studying the PAH concentration found on the surface of the skin at various locations via skin swabs (Stec et al., 2018). The study looked at 4 firefighters during a training burn; 1 being the instructor with 3 trainees. The study looked at the front of the neck, back of the neck, the hands and jaw of each participant pre-burn and immediately post burn. Results indicated a significantly markedly elevated concentration of PAHs on all four sites, with the highest risk of carcinogenic PAHs on the skin surface of hands and front of the neck (Stec et al., 2018). Overall, there is strong evidence of skin contamination following fore suppression and overhaul, even when PPE is worn correctly and fireground procedures are followed. More information is needed to determine he true extent of absorption in firefighters, with a large knowledge gap still remaining in this field.

Chapter 6

Future Directions

Research has largely used indirect approaches to address skin absorption of substances including carcinogens typically encountered by firefighters in their line of duty. Typically, biological markers in the urine of firefighters are combined with assessing chemicals on the skin post exposure using dermal tape stripping (Strandberg et al., 2018) and dermal swabs (Fent et al., 2014). However, while the presence of PAH metabolites indicates exposure, it does not tell us the specific route and it remains unclear whether it occurred from inhalation or through skin absorption. Approaches such as tape stripping of the outer epidermal layers has provided some evidence of superficial absorption (Strandberg et al., 2018), but greater research is needed to show transdermal absorption and the overall effects on the body. Recent preliminary work by our laboratory and in collaboration with colleagues at NC State University, has shown that PAHs can be dermally absorbed (Sui et al., 2020). This was achieved by applying the non-carcinogenic PAH anthracene to the skin, and recovering the substance from the interstitial fluid using intradermal microdialysis. An analytical approached was developed using Atmospheric Pressure Chemical Ionization-Tandem Mass Spectrometry (APCI-MS/MS) for the detection and quantification of anthracene. Instrument detection limits in addition to the chemical properties of the PAH used in this experiment were considered for the measurement development. Adding an isotopically labeled internal standard allowed for the accurate and precise measurement of the interstitial fluid samples containing anthracene. This approach can be used for other PAHs that firefighters are exposed to and is an important development for future studies.

Measuring skin absorption is very challenging, and common approaches using body fluid measurements are not definitive when the source of exposure is unknown, with limited methods currently available to assess the extent and timeline of absorption. Far more research is needed to develop such methods and help increase our understanding of the exposure of firefighters and other occupational workers to chemical hazards. This has important implications for understanding exposure routes, regional variation, timing of absorption and ultimately informing PPE developments and decontamination procedures in firefighters with the aim of reducing cancer risk.

References

Abdel-Shafy, H. I., & Mansour, M. S. M. (2016). A review on polycyclic aromatic hydrocarbons: Source, environmental impact, effect on human health and remediation. *Egyptian Journal of Petroleum, 25*(1), 107-123. doi:https://doi.org/10.1016/j.ejpe.2015.03.011

Baxter, C. S., Hoffman, J. D., Knipp, M. J., Reponen, T., & Haynes, E. N. (2014). Exposure of firefighters to particulates and polycyclic aromatic hydrocarbons. *J Occup Environ Hyg, 11*(7), D85-91. doi:10.1080/15459624.2014.890286

Bitar, A., Zafar, N., Valour, J. P., Agusti, G., Fessi, H., Humbert, P., . . . Elaissari, A. (2015). Elaboration of sponge-like particles for textile functionalization and skin penetration. *Colloid and Polymer Science, 293*(10), 2967-2977. doi:10.1007/s00396-015-3704-7

Brandt-Rauf, P. W., Cosman, B., Fallon, L. F., Tarantini, T., & Idema, C. (1989). Health hazards of firefighters: acute pulmonary effects after toxic exposures. *Br J Ind Med, 46*(3), 209- 211. doi:10.1136/oem.46.3.209

Burgess, J. L., Hoppe-Jones, C., Griffin, S. C., Zhou, J. J., Gulotta, J. J., Wallentine, D. D., . . . Snyder, S. A. (2020). Evaluation of Interventions to Reduce Firefighter Exposures. J Occup Environ Med, 62(4), 279-288. doi:10.1097/jom.0000000000001815

Burgess, J. L., Nanson, C. J., Bolstad-Johnson, D. M., Gerkin, R., Hysong, T. A., Lantz, R. C., . Witten, M. L. (2001). Adverse respiratory effects following overhaul in firefighters. J Occup Environ Med, 43(5), 467-473. doi:10.1097/00043764-200105000-00007

Chia, K. S., Jeyaratnam, J., Chan, T. B., & Lim, T. K. (1990). Airway responsiveness of firefighters after smoke exposure. Br J Ind Med, 47(8), 524-527. doi:10.1136/oem.47.8.524

Daniels, R. D., Bertke, S., Dahm, M. M., Yiin, J. H., Kubale, T. L., Hales, T. R., . . . Pinkerton, L. E. (2015). Exposure-response relationships for select cancer and non-cancer health outcomes in a cohort of U.S. firefighters from San Francisco, Chicago and Philadelphia (1950-2009). *Occupational and environmental medicine, 72*(10), 699-706. doi:10.1136/oemed-2014-102671

Daniels, R. D., Kubale, T. L., Yiin, J. H., Dahm, M. M., Hales, T. R., Baris, D., . . . Pinkerton, L. E. (2014). Mortality and cancer incidence in a pooled cohort of US firefighters from San Francisco, Chicago and Philadelphia (1950–2009). *Occupational and environmental medicine, 71*(6), 388-397. doi:10.1136/oemed-2013-101662

Fabian, T. Z., Borgerson, J. L., Gandhi, P. D., Baxter, C. S., Ross, C. S., Lockey, J. E., & Dalton, J. M. (2014). Characterization of Firefighter Smoke Exposure. *Fire Technology, 50*(4), 993-1019. doi:10.1007/s10694-011-0212-2

Fent, K. W., Alexander, B., Roberts, J., Robertson, S., Toennis, C., Sammons, D., . . . Horn, G. (2017). Contamination of firefighter personal protective equipment and skin and the effectiveness of decontamination procedures. J Occup Environ Hyg, 14(10), 801-814. doi:10.1080/15459624.2017.1334904

Fent, K. W., Eisenberg, J., Snawder, J., Sammons, D., Pleil, J. D., Stiegel, M. A., . . . Dalton, J. (2014). Systemic exposure to PAHs and benzene in firefighters suppressing controlled structure fires. Ann Occup Hyg, 58(7), 830-845. doi:10.1093/annhyg/meu036

Fent, K. W., Toennis, C., Sammons, D., Robertson, S., Bertke, S., Calafat, A. M., . . . Horn, G. P. (2019). Firefighters' and instructors' absorption of PAHs and benzene during training

Fent, K. W., Toennis, C., Sammons, D., Robertson, S., Bertke, S., Calafat, A. M., . . . Horn, G. P. (2020). Firefighters' absorption of PAHs and VOCs during controlled residential fires by job assignment and fire attack tactic. *Journal of Exposure Science & Environmental Epidemiology, 30*(2), 338-349. doi:10.1038/s41370-019-0145-2

Greven, F. E., Krop, E. J., Spithoven, J. J., Burger, N., Rooyackers, J. M., Kerstjens, H. A., . . Heederik, D. J. (2012). Acute respiratory effects in firefighters. American Journal of Industrial Medicine, 55(1), 54-62.

Hao, J., Ghosh, P., Li, S. K., Newman, B., Kasting, G. B., & Raney, S. G. (2016). Heat effects on drug delivery across human skin. *Expert Opin Drug Deliv, 13*(5), 755-768. doi:10.1517/17425247.2016.1136286

Horn, G. P., Kesler, R. M., Kerber, S., Fent, K. W., Schroeder, T. J., Scott, W. S., . . . Smith, D. L. (2018). Thermal response to firefighting activities in residential structure fires: impact of job assignment and suppression tactic. *Ergonomics, 61*(3), 404-419. doi:10.1080/00140139.2017.1355072

Jalilian, H., Ziaei, M., Weiderpass, E., Rueegg, C. S., Khosravi, Y., & Kjaerheim, K. (2019). Cancer incidence and mortality among firefighters. *International Journal of Cancer, 145*(10), 2639-2646. doi:10.1002/ijc.32199

Kirk, K. M., & Logan, M. B. (2015). Structural Fire Fighting Ensembles: Accumulation and Off gassing of Combustion Products. *Journal of Occupational and Environmental Hygiene, 12*(6), 376-383. doi:10.1080/15459624.2015.1006638

Laitinen, J., Mäkelä, M., Mikkola, J., & Huttu, I. (2010). Fire fighting trainers' exposure to carcinogenic agents in smoke diving simulators. *Toxicol Lett, 192*(1), 61-65. doi:https://doi.org/10.1016/j.toxlet.2009.06.864

Large, A. A., Owens, G. R., & Hoffman, L. A. (1990). The short-term effects of smoke exposure on the pulmonary function of firefighters. *Chest, 97*(4), 806-809.

doi:10.1378/chest.97.4.806

LeMasters, G. K., Genaidy, A. M., Succop, P., Deddens, J., Sobeih, T., Barriera-Viruet, H., . . . Lockey, J. (2006). Cancer risk among firefighters: a review and meta-analysis of 32 studies. *J Occup Environ Med, 48*(11), 1189-1202. doi:10.1097/01.jom.0000246229.68697.90

Markowitz, S. B., Garibaldi, K., Lilis, R., & Landrigan, P. J. (1991). Asbestos exposure and firefighting. *Ann N Y Acad Sci, 643*, 573-577. doi:10.1111/j.1749-6632.1991.tb24507.x

Miedinger, D., Chhajed, P. N., Stolz, D., Gysin, C., Wanzenried, A. B., Schindler, C., . . . Leuppi, J. D. (2007). Respiratory symptoms, atopy and bronchial hyperreactivity in professional firefighters. *Eur Respir J, 30*(3), 538-544. doi:10.1183/09031936.00015307 NFPA. (2017). Fact Sheet: Cancer Risk in Firefighting. In.

NFPA. (2018 ed.). NFPA 1971 standard on protective ensembles for structural fire fighting and proximity fire fighting. Quincy, MA: NFPA. In NFPA (Ed.).

OSHA. (2009). *Assigned Protection Factors for the Revised Respiratory Protection Standard. OSHA 3352-02*.

Petersen, K. K., Rousing, M. L., Jensen, C., Arendt-Nielsen, L., & Gazerani, P. (2011). Effect of local controlled heat on transdermal delivery of nicotine. *International journal of physiology, pathophysiology and pharmacology, 3*(3), 236-242. Retrieved from http://europepmc.org/abstract/MED/21941614

Pukkala, E., Martinsen, J. I., Weiderpass, E., Kjaerheim, K., Lynge, E., Tryggvadottir, L., . . . Demers, P. A. (2014). Cancer incidence among firefighters: 45 years of follow-up in five Nordic countries. *Occupational and environmental medicine, 71*(6), 398-404.

doi:10.1136/oemed-2013-101803

Ribeiro, M., de Paula Santos, U., Bussacos, M. A., & Terra-Filho, M. (2009). Prevalence and risk of asthma symptoms among firefighters in São Paulo, Brazil: A population-based study. *American Journal of Industrial Medicine, 52*(3), 261-269. doi:https://doi.org/10.1002/ajim.20669

Rider, C. V., Boekelheide, K., Catlin, N., Gordon, C. J., Morata, T., Selgrade, M. K., . . . Simmons, J. E. (2014). Cumulative risk: toxicity and interactions of physical and chemical stressors. *Toxicol Sci, 137*(1), 3-11. doi:10.1093/toxsci/kft228

Soteriades, E. S., Kim, J., Christophi, C. A., & Kales, S. N. (2019). Cancer Incidence and Mortality in Firefighters: A State-of-the-Art Review and Meta-́Analysis. Asian Pac J Cancer Prev, 20(11), 3221-3231. doi:10.31557/apjcp.2019.20.11.3221

Stec, A. A., Dickens, K. E., Salden, M., Hewitt, F. E., Watts, D. P., Houldsworth, P. E., & Martin, F. L. (2018). Occupational Exposure to Polycyclic Aromatic Hydrocarbons and Elevated Cancer Incidence in Firefighters. Sci Rep, 8(1), 2476. doi:10.1038/s41598018-20616-6

Strandberg, B., Julander, A., Sjöström, M., Lewné, M., Hatice, K. A., & Bigert, C. (2018). An improved method for determining dermal exposure to polycyclic aromatic hydrocarbons. Chemosphere, 198, 274, 280 doi: http://doi.org/10.1016/j.chemosphere.2018.01.2014

Sui, X., Terán, J. E., Feng, C., Wustrow, K., Smith, C. J., & Vinueza, N. R. (2020). Quantification of anthracene after dermal absorption test via APCI-tandem mass spectrometry. Analytical Methods, 12(22), 2820-2826. doi:10.1039/D0AY00486C

Wingfors, H., Nyholm, J. R., Magnusson, R., & Wijkmark, C. H. (2018). Impact of Fire Suit

Ensembles on Firefighter PAH Exposures as Assessed by Skin Deposition and Urinary Biomarkers. Ann Work Expo Health, 62(2), 221-231. doi:10.1093/annweh/wxx097

Zafar, N., Robin, S., Viennet, C., Humbert, P., Valour, J. P., Agusti, G., . . . Elaissari, A. (2017). Sponge like microparticles for drug delivery and cosmeto-textile use: Formulation and human skin penetration. *Int J Pharm, 532*(1), 623-634. doi:10.1016/j.ijpharm.2017.08.122

Vita

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