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REVIEW ARTICLE

IMPACT OF CHEMICAL AGENTS THREATS ON INCREASED HEALTH RISK AMONG AIR FORCE MILITARY PERSONNEL

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Abstract: The specific nature of the work of Air Force soldiers involves exposure to defined chemical agents (jet fuel, kerosene, hydrazine, grease and hydraulic oils, exhaust fumes, deicing agents). Long-term exposure to certain chemical agents, such as jet fuel, following occupational exposure can cause damage to the skin, lungs, cardiovascular system, neurodegenerative changes, as well as genetic changes which in result can activate mechanisms promoting uncontrolled cell proliferation leading in turn to carcinogenic changes. Due to the inhalative nature of exposure and the possibility of direct impact on the upper respiratory tract and lungs, petroleum-based mutagenic chemical agents are an important factor in promoting cancer development. These agents can produce changes in the stability of genetic material that increase the likelihood of small cell and non-small cell lung cancer, leukemias, prostate cancer, melanoma of the skin, squamous cell carcinomas of the head and neck, and many other cancers. Effects of jet fuels on DNA methylation level associated with the formation of heritable epigenetic changes have also been observed.

Keywords: jet fuel; carcinogenic effect; military personnel; occupational exposure; military pilots

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OCCUPATIONAL EXPOSURE OF MILITARY AVIATION PERSONNEL

Military personnel are a specific workgroup population that is exposed to hazardous substances in an occupational environment that is radically different from those to which other occupational groups in the civilian population may be exposed. Military personnel are a separate category of individuals who differ from the general population for a variety of reasons, including thorough regular health assessments and the criteria by which they should be qualified to be capable of perform active military duty.

Depending on the type of service, environmental factors will pose a threat to the health, safety and security of soldiers to varying degrees, and can affect combat operations during an armed conflict. Analyses of health impairment caused by chemicals to which military personnel are exposed are extremely relevant.

The most common chemical agents to which Air Force pilots are exposed are primarily propellant components (aviation gasoline, kerosene, lubricating and hydraulic oils), engine fumes (exhaust), combustion dusts, solvents, and deicing agents [31,6].

Airport maintenance workers may be regularly exposed to jet fuel, exhaust fumes, hydraulic fluids and deicing chemicals which can be carcinogenic and neurotoxic [21]. The main environmental pollutants at the airport are nitrogen oxides, carbon dioxide, carbon monoxide, volatile organic compounds, sulfur dioxide, fine and ultrafine particulate matter (PM). The occupational group at greatest risk of exposure is airport ground handlers, particularly technicians who operate and maintain fuel tanks. A similar profile of chemicals will be encountered by mechanics, but chemicals used e.g. in washing engine parts, solvents and greases should be included in this occupational group [31,46].

AVIATION FUELS

All aviation fuels consist mainly of hydrocarbon compounds, namely straight and branched chain alkanes (paraffins), cyclic alkanes (naphthenes), alkenes (olefins) and aromatic hydrocarbons, with additives whose amount depends on the specific application of the fuel. The main components of the fuels used in turbine-powered aircraft are kerosene containing paraffins and cycloparaffins, which have a higher ratio of hydrogen to carbon, i.e. they are more high-energy compounds and burn more cleanly than aromatic hydrocarbons. Aviation fuel additives are most often based on metal compounds, antioxidants, static dissipators, octane enhancers and corrosion and icing inhibitors [1,30,46].

JP-5 and JP-8 are jet propellant (JP) grades developed by the United States Air Force for use in turbine aircraft engines. JP-5 is a general-purpose jet fuel and accounts for about 85% of the jet fuel used by the military. JP-8 is similar to JP-5, but has greater thermal stability and a higher flash point. JP-8 is used in specialized supersonic aircraft. The composition of jet fuels can be very complex. JP-5 is considered a petroleum-type fuel, consisting primarily of alkanes in the C4 to C16 range [37]. JP-8 or Jet fuel A (civilian equivalent of JP-8 fuel) is a blend of aviation kerosene-naphtha with additives; detailed information on the composition of JP-8 is not generally available. The actual chemical composition of these jet fuels exhibits considerable variation, contingent upon the requisite aircraft performance. It has been shown that this type of fuel, and in particular long-term exposure to fuel or its components, can cause changes in gene expression, changes in DNA methylation patterns, and genetic mutations increasing the likelihood of developing many types of cancer, i.e., leukemia, lymphoma, small cell lung cancer, and many others. Apart from the hydrocarbon fuel base, both fuels contain numerous additives improving their parameters, also characterized by harmfulness and carcinogenic potential [3,46].

Aviation fuels for turbine engines differ from Avgas (aviation gasoline), which is a fuel blend with a composition similar to automotive gasoline (i.e., C4-C12 hydrocarbons). To meet the requirements for aviation fuels (i.e., high octane number, high energy, and low freezing point), fuel performance enhancing ingredients such as tetraethyl lead are used. Aviation gasoline has toxic effects mainly on nerve cells, liver, cardiovascular system and bone marrow. Persons showing symptoms of poisoning may experience pulmonary hemorrhages due to damage to blood vessels. Death as a result of substantial exposure occurs due to pulmonary edema or respiratory center paralysis. Prolonged exposure to small doses may cause deposition of active substances in the body causing accelerated development of neurodegenerative diseases, reduced fertility and increased susceptibility to cancer, especially leukemia [46,28].

The last group of fuels are hydrazine fuels, which are common propellants used in rocket and tactical missiles and jet aircraft used by the

Air Force (The Polish Armed Forces do not use hydrazine propelled missiles). F-16 type aircraft use a hydrazine mixture (H-70) as fuel for Emergency Power Unit (EPU) systems. The main symptoms of chronic hydrazine poisoning include headaches, drowsiness or agitation, pale eyelids, exhaustion, stupor, and a tendency to vomit. There are also observed degenerative changes in the liver, kidneys, lungs, spleen, heart muscle, and bone marrow. Furthermore, sensitization changes are also observed in the skin. Hydrazine has strong carcinogenic effects on nervous system, lungs, liver, kidneys, blood system, breast glands, subcutaneous tissue [11].

Exposure factors should additionally include gas emissions from the engine - exhaust fumes and combustion dust. The composition of exhaust gases will vary depending on the type of engine and the type of operation performed by the aircraft, e.g., differences are observed between the emission and composition of exhaust gases from an aircraft taxiing at an airport (low power engine setting) and those emitted during take-off or landing (especially take-off with engine working in afterburning cycle). Exhaust from aviation turbine and diesel engines primarily contains carbon dioxide (CO2) and water, as well as nitrogen oxides (NOx), sulfur oxides (SOx), carbon monoxide (CO), unburned hydrocarbons (UHC), and particulate matter (PM). Of particular importance are the increased emissions near the airport during the landing and take-off cycle (LTO) analyzed up to an altitude of about 1 km above the airport. Epidemiological studies indicate that long-term population exposure to fine particulate matter with an aerodynamic diameter of less than 2.5 μm (PM2.5) is associated with an increased risk of health effects, including premature mortality [11,50,33]. Although associations have been found between other pollutants and premature mortality, there is relatively strong evidence that PM2.5 exposure is closely associated with premature mortality and other negative health outcomes. Premature deaths due to lung cancer and cardiovascular disease from long-term exposure to aviation-related PM2.5 have been observed in adults aged 30 years and older. The potential variability of PM toxicity remains undetermined, aviation-related PM differs in chemical composition, size and permeability compared with polluted urban air PM, which are the reference for epidemiological concentration-response analyses. Using concentration-response functions published by the WHO (World Health Organization), disease statistics, population density data, and GEOS-Chem modeling results, a global number of 9970 premature deaths per year due to emissions from civilian (mainly) and military aircraft was estimated. The annual number of premature deaths in selected countries was: Canada - 67; China - 1890; Ethiopia - 43; France - 380; Germany - 545; India - 1640; Iran - 76; Spain - 189; United Kingdom - 362 and United States - 458. It was estimated that LTO emissions account for 20% of the total number of premature deaths attributed to aviation worldwide, but this is likely a lower bound due to the resolution of the global model under consideration [4,5].

EXPOSURE TO JET FUELS

Occupational exposure to various toxic agents in the aviation environment may occur primarily by inhalation of vapors, absorption through the skin, or accidental ingestion.

Exposure to chemical agents may be a single, short-term exposure associated with the onset of rapid, mostly self-resolving symptoms associated with damage to the skin, lungs, kidneys, hepatoxic effects of fuels, sensory-motor responses disorders. Other type of exposure is repetitive and will be associated with long-term accumulation of substances in the body, and thus causing diseases with long-term development and progression, such as neurodegenerative diseases and some specific types of neoplasms [46].

As environmental studies have shown, that all individuals residing or working in proximity to the airport are exposed to the carcinogenic and genotoxic effects of compounds contained in aviation fuels or their exhaust. This is associated with the long-term deposition of these substances in soil, water and all porous architectural materials.. Larger amounts of harmful hydrocarbon substances are observed if an airport has been in operation for many years, particularly if it was in operation prior to 1994 when more harmful fuel blends were used and different, less constrictive safety standards were in place. Investigations of soil samples taken in the nearest vicinity of the airport showed the phenomenon of accumulation of some chemical substances contained in JP-5, JP-8 and Jet A. Components of the fuels may remain in the soil for over a decade in an unchanged form, posing a serious threat to the environment and health of people staying at the airport and in its vicinity [5,29].

JET FUEL EXPOSURE SYNDROME: NEUROLOGICAL EFFECTS

An early study of jet fuel impact conducted by Knave et al. (1976) showed that some individuals in an occupational group heavily exposed to aviation fuels and belonging to the group of aircraft ground maintenance professionals observe permanent neurological changes. The study included a standardized clinical neurological examination, measurements of conduction velocity in peripheral nerves, and determination of vibration sensation threshold in the upper extremities. All subjects heavily exposed to inhaled jet fuel vapors repeatedly experienced acute effects of exposure, that is, dizziness, respiratory symptoms, heart palpitations, a feeling of tightness in the chest, nausea and headache. A high percentage of symptoms indicative of neurasthenia and psychasthenia and signs or symptoms indicative of polyneuropathy were observed in the exposed group compared with the reference groups [26]. The findings suggested a possible effect of long-term exposure to jet fuel on permanent changes in the nervous system Those results indicated a possible effect of long-term exposure to jet fuel on permanent changes in the nervous system [26].

It has also been observed that even short-term exposure to jet fuels and organic solvents causes transient or permanent changes in the brain, especially in the levels of neurotransmitters and their metabolites. Increases in serum concentrations of 5-hydroxyindoleacetic acid, a metabolite of serotonin, have been observed. Significant decreases in the concentration of dihydroxyphenylacetic acid (DOPAC, the major metabolite of dopamine) in the cerebral cortex, increases in the concentration of dopamine in the hippocampus, and decreases in the concentration of homovanillic acid in the hippocampus were also observed during studies on rats [29,8,20,34,39,15]. Neurological studies have shown a strong and consistent increase in self-reported cognitive problems among individuals exposed to JP-8 fuel through vapors and skin contact, and small but significant exposure-dependent differences in objective tests of cognitive functioning associated with atrophy. These findings are consistent with the development of adverse neuropsychiatric changes associated with occupational exposure to solvents. Further mental health studies showed high concordance between patient-reported mood disorders and objective tests. In the exposed group, diagnoses of depression or anxiety were more frequently reported, antidepressants were more frequently used, and there was an increased risk of a diagnosis of depression or anxiety. The results were statistically significant relative to the comparison groups. People working in high-exposure jobs (exposed in everyday work routine) were more likely to experience psychological distress and social dysfunction compared to the rest of the Australian population. The study found a statistically significant association between exposure during F-111 DSRS (Deseal/Reseal) works and mental health deterioration [8].

Studies of individuals in workplaces that involved the use of solvents showed statistical significance for the development of encephalopathy and accelerated Alzheimer's disease compared to a control group. A history of exposure to one or more solvent groups, specifically benzene and toluene; phenols and alcohols; ketones and other solvents yielded an adjusted odds ratio for the onset of Alzheimer's disease of 2.3 (95 percent confidence interval 1.1-4.7), but this increased to 6.0 (95 percent confidence interval 2.1-17.2) only among men. It is therefore suspected that past exposure to organic solvents may be associated with the onset of Alzheimer's disease or its accelerated development at a younger age. The results show that in healthy individuals, extensive changes in brain structure can be observed in as little as 1 year, with atrophy increasing as exposed individuals age. Some of the observed changes occur in areas associated with the development of Alzheimer's disease, while others occur in areas less characteristic of the disease in its early stages. This suggests that these changes are not primarily due to degenerative processes associated with Alzheimer's disease, although it is likely that preclinical changes associated with Alzheimer's disease overlap with changes due to normal aging in some subjects. It should be noted that exposure in the form of ingestion of small amounts of solvents or jet fuel increases the intensity of observed symptoms compared to inhalation exposure [8,34,39,15].

MECHANISM OF HYDROCARBON-INDUCED CARCINOGENESIS

There are not many studies of carcinogenic effects in humans that explicitly highlight the role of jet fuels in this process. Many of the published studies involve studies on rats and mice. Benzene, as one of the best studied aromatic hydrocarbons, is often used as a model compound rather than aviation fuel, which is a complex substance. Benzene is obtained in the petroleum processing cycle and is a high-energy component of various motor gasolines and solvents, but is also formed,

like polycyclic aromatic hydrocarbons (PAHs), by the incomplete combustion of other high-energy hydrocarbons. It is present in automobile and aircraft exhaust. They are characterized by potent mutagenic, carcinogenic, genotoxic, immunosuppressive, endocrine disrupting properties, and most importantly can alter epigenetic patterning affecting the levels of many genes [4,7].

Polycyclic aromatic hydrocarbons (PAHs) enter the body quickly and easily, with the rate of entry increasing in the presence of oily mixtures and solvents. They are lipophilic compounds, easily pass biological membranes and readily enter all body tissues containing fat, disperse through the body by the lymphatic system and show the ability to accumulate mainly in adipose tissue and to a lesser extent in the liver and kidneys, adrenal glands, ovaries and spleen. PAHs may be expected to be relatively more toxic through inhalation and dermal exposure (owing to focal toxicity at the site of entry) than after oral exposure, because inhalation and dermal exposure bypass the first-pass metabolism in the liver [7,10]. PAHs are rapidly metabolized mostly by oxidation or hydroxylation at first step by a microsomal enzyme system consisting of mixed-function monooxygenases, and the resulting epoxides and phenol-like metabolites are conjugated with glucuronate and sulfate to increase their water solubility and excretion from the body in urine [22,25,32,1].

In the process of microsomal oxidation, PAHs undergo metabolic activation resulting in the formation of highly reactive metabolites that bind to cellular macromolecules such as DNA (deoxyribonucleic acid), proteins, and lipids to form stable adducts, or generate highly toxic reactive oxygen species. The binding of intermediate metabolites of PAHs to DNA and the formation of DNA-PAH adducts may have a promutagenic effect. This can occur when there are an abnormalities in DNA repair mechanisms, mainly failure of the repair system by excision of damaged nitrogenous bases (NER - nucleotide excision repair). High amounts of damage, or faulty replication can result in permanent changes of a mutational nature, which may contribute to the initiation and progression of the neoplastic process. The process of cancer transformation can, among others, occur through activation of protooncogenes or inactivation of suppressor genes [27,24].

PAHs are able to induce, among many others, mutations within the tumor suppressor gene p53, which is the main "guardian of the genome", causing its inactivation. This gene plays a very important regulatory role involving control of the proper course of the cell cycle and stability of chromosomal DNA structure. As a result of damage to the gene encoding the p53 protein, cells with DNA damage are not eliminated by apoptosis mechanisms, and cells containing damage to genetic material may divide and differentiate into cancer cells [23]. Similarly, benzo[alpha]pyrene (B[a]P) can create significant cell stress and induce TP53 expression for cell protection. It was also observed that low doses of B[a]P can downregulate TP53, PTEN, CHD13 or p16 gene by inducing mutations [9,43].

In experimental animals exposed to PAHs, depending on the type of exposure, the formation of neoplastic lesions in lung tissue, mammary gland, lymphomas, skin tumors, liver tumors, papillomas, with associated mutations within the ras gene family, was observed. PAH-induced changes found in the H-ras and K-ras protooncogenes are point mutations (transversions). The ras gene family belonging to the protooncogenes is one of the most frequently activated in pre- and neoplastic lesions in humans and experimental animals. Activated ras genes play a role in disrupting cell proliferation and cell differentiation, which may manifest as promotion of neoplastic lesions [52].

In addition to point mutations, benzene and its derivatives are able to induce genetic changes at the chromosomal level similar to those seen in leukemia cells arising de novo. We observed that exposure to benzene or its metabolites was associated with loss and deletion of the long (q) arm of chromosomes 5 and 7 and translocations involving t(21q), further suggesting that benzene induces leukemias simultaneously through multiple different mechanisms [52,12].

CANCEROGENIC EFFECT OF JET FUELS

Among the more valuable studies for reviewing studies relevant to assessing the carcinogenicity of currently unused fuels, JP-4 and JP-7 were reviewed by the National Research Council (NRC) Subcommittee on Permissible Exposure Levels for Military Fuels. The review included epidemiological studies of exposure to jet fuels and other petroleum-based mixtures, such as gasoline; however, no studies were found for JP-4 and JP-7 [31]. Of the studies discussed in report, a historical prospective cohort study of men in the Swedish Armed Forces [34] and a population-based case study by Siemiatycki et al. (1987) [31,42] appear to be the most relevant to the current assessment of the harmful impact of JP-8. These studies, however, relate primarily to exposure to JP-4 fuels,

which are considered to have higher toxicity than current fuel blends [31,42]. Selden and Ahlborg (1991) reported that total cancer incidence was generally lower than expected in a cohort of 2176 men from the Swedish armed forces, and they observed no association between jet fuel and cancer anywhere. A 1996 report cited the short follow-up period (9-10 years) and selection bias as possible limitations of this study [41]. Siemiatycki et al. (1987) investigated a possible association between exposure to 12 petroleum-based fluids, including jet fuel and kerosene, and cancer in 3726 individuals in Montreal [42]. Screening analyses suggested an association between kerosene exposure and gastric cancer, but this was not confirmed in more detailed analyses. Screening analyses showed that individuals exposed to aviation fuel (e.g., mechanics and aircraft mechanics) (n = 43) had odds ratios (OR) of 2.1 (90% CI, 0.9-5.1) for colon cancer (n = 7), 2.1 (0.6-7.4) for rectal cancer (n = 4), and 2.5 (1.1-5.4) for kidney cancer (n = 7). More in-depth analyses showed an association between jet fuel and kidney cancer with an OR of 3.4 (1.5-7.6) for workers exposed at significant levels (n = 6). A dose-response relationship was found for jet fuel exposure and increased risk of kidney cancer, and the authors rated the strength of evidence for this association as moderate to strong. The model presented suggests which type of cancer aviators are more likely to be at risk for [42,34]. The NRC subcommittee in 2003 published assumption that the data does not represent consistent evidence strong enough to support the conclusion that exposure to military jet fuel is associated with an excess risk of cancer in any location of the human body [17].

A case-control study of men on active duty in the U.S. Air Force found an increased likelihood of brain and testicular cancer among aviators compared with non-aviators [41,17]. A study evaluating prostate cancer incidence in a population of active-duty soldiers in the United States Air Force from 1987 to 2008 found no differences between aviators and non-aviators [19]. A study of male United States Air Force officers on active duty from 1975 to 1989 found that aviators had higher rates of all cancers, particularly testicular cancer and bladder cancer, compared to non-flying officers [19,51].

More recent studies conducted between 2001 and 2004 include a comprehensive, large-scale epidemiological study commissioned by the Australian Department of Defense on the health of all workers involved in fuel tank work in Australia [8]. Studies were conducted on cancer incidence and mortality in aircraft maintenance workers and showed that cancer incidence was higher in the exposed group, with a statistically significant increase in incidence of 40-50% (cancer incidence ratio range 1.45-1.62). Mortality in the exposed group was significantly lower than in both comparison groups (mortality coefficient range 0.33-0.44). The results of the study indicated an increased probability of cancer as a result of participation in activities related to the F-111 DSRS program, related to the cleaning, maintenance and resealing of aviation storage fuel tanks [8,15].

One of the most recent large-scale analyses of cancer rates in fighter pilots and U.S. Air Force officers was conducted in 2020 and found 86 cases of cancer among an analyzed group of 4949 fighter pilots who began active duty between 1986 and 2006 [35,45]. The medical data for this group was analyzed through 2017. The study found that cancer incidence rates for fighter pilots and officers were not significantly different. This lack of difference applied to all malignancies in both men and women, except that 15 different cancer sites were analyzed in men and only melanoma of the skin in women.

Cutaneous melanoma, testicular cancer, colon and rectal cancer, and non-Hodgkin lymphoma were the major cancer types among both male fighter pilots and nonflying officers; for all other cancer locations, fewer than 5 cases were observed for male fighter pilots. Only 2 cancer cases were diagnosed, both melanoma of the skin, occurred in female fighter pilots. Male fighter pilots and nonflying officers had similar rates of all malignancies (RR = 1.04; 95% CI: 0.83-1.31) at each cancer location. Female fighter pilots and matched officers also had similar rates of all malignancies (RR = 0.99; 95% CI: 0.25-4.04). The mean age at diagnosis was 41.6 years for fighter pilots and 41.8 years for officers (p = 0.73). As would be expected in a population composed primarily of young men, incidence rates were the highest for cutaneous melanoma and cancers of the testis, colon, and rectum, which together accounted for 62% of all of the cancers diagnosed [35].

The findings of the latest study are largely consistent with those of commercial and military pilots from around the world. The pilots in these studies had similar overall cancer rates compared to the populations from which they came. In some, the incidence of specific cancers was slightly elevated and included bone cancer, prostate cancer, myeloid leukemia, and melanoma of the skin [36].

However, the presented studies conducted on the airman population should not only be associ-

ated with exposure to fuels and solvents, but also exposure to other cancerogenic factors such as cosmic radiation, ultraviolet radiation, non-ionizing radiation inside the cockpit, and instances of hypergravity that can cause chronic inflammation.

CHANGES IN DNA METHYLATION PATTERNS

Epigenetics deals with off-gene heredity, or the inheritance of changes in gene expression patterns that are independent of the nucleotide sequence in the DNA, but determined by various factors and biochemical modifications that affect the expression of selected genes. Epigenetic modification is defined as any change in the phenotype of a cell that is not the result of changes in the DNA sequence. Epigenetic modifications that control and alter gene transcription involve DNA with methylation tags on CpG islands and changes in chromatin structure and accessibility by chemical modification of histone proteins, which are most commonly methylated, acetylated and phosphorylated [3,13,49].

It is estimated that there are about 29 thousand CpG islands in the human genome, which are located mainly in the promoters of basal cell metabolism genes and tissue-specific genes. The level of methylation is mainly associated with regulation of downregulation or suppression of gene expression. Methylation also influences the degree of chromatin condensation, which regulates the accessibility of DNA to transcription factors. This process has been implicated in the regulation of organismal development, genomic stigma, and cellular adaptation to environmental influences. Improper methylation patterns play a significant role in the development of cancer, neurodegenerative diseases, diabetes, obesity, cardiovascular diseases and many others [13,49,14].

Benzene increases nitric oxide production in the bone marrow, most likely by inducing a transcriptional increase in DNA methyltransferase activity. Furthermore, reactive oxygen species leading to oxidative DNA damage promoted by benzene may decrease the binding affinity of proteins that attach to methyl-CpG, thereby causing epigenetic changes. At the same time, the DNA strand breaks induced by benzene exposure may cause DNA methyltransferases to bind with higher affinity at specific sites also altering the methylation pattern. Although the mechanism of how benzene affects DNA methylation remains unclear, it most likely involves activation of DNA methyltransferases [44,38,40].

Quantitative DNA methylation analysis studies are performed using the pyrosequencing method, which is a highly reproducible and accurate method in measuring even small changes in DNA methylation levels. When changes in methylation levels of LINE-1 (Long Interspersed Nuclear Element-1) elements were analyzed, a stronger correlation with benzene exposure was observed in comparison to changes in AluI repeat elements. Alu elements are a group of repetitive elements that can affect gene expression through CpG residues and transcription factor binding. Altered gene expression and methylation profiles have been found in various tissues and cell lines. LINE-1 is a repetitive DNA retrotransposon that replicates through a copy-paste genetic mechanism. Since LINE-1 represents approximately 17% of the human genome, the extent of LINE-1 methylation is considered a surrogate marker for global DNA methylation analysis. The differential effects of benzene and its metabolites may be explained by the fact that LINE-1 and AluI methylation are controlled by different mechanisms. Alternatively, the lower concentration of CpG sites in AluI elements may result in lower sensitivity for the use of AluI methylation as a global marker of DNA methylation in studies of aromatic compounds such as benzene, PAHs or pyrethroids containing aromatic rings in their chemical structure [8,16,48].

Animal studies have demonstrated the ability of jet fuel (JP-8) exposure to promote epigenetic, transgenerational inheritance of disease susceptibility in subsequent generations. Diseases observed include delayed puberty, kidney failure, obesity, and many other disease pathologies in rats [18].

Studies of specific epimutations may be useful as early-stage biomarkers of jet fuel exposure that may promote disease development in adults or in subsequent generations. The results obtained have relevance to human and animal populations exposed to hydrocarbons such as jet fuel, and their offspring, which may exhibit epigenetic trends of increased susceptibility to certain diseases [2].

CONCLUSIONS

The available data on the impact of JP-5, JP-8, and other similar fuel formulations on human health remains limited. Animal studies have shown that dermal exposure to these mixtures of chemicals can cause skin lesions. Ingestion or prolonged skin exposure can also lead to liver damage, immunotoxic effect, and hearing impair-

ment. Studies have shown that human exposure to jet fuel can impair neuro-behavioral health and cause cardiovascular problems, as well as reduce lung function.

The researchers also found that in healthy individuals, even low levels of benzene in the body can be associated with methylation changes in DNA, the type of which are consistent with abnormal epigenetic patterns found in malignant cancer cells [2,47,48].

Given the long latency period of many cancers, studies should monitor individuals for an extended period after military service. That type of studies should cover as wide a range of cases as possible and take into account socioeconomic differences and the many variables that interfere with comparative analyses between fighter pilots and the control population.

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