Aerospace Medicine Clinic

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You are the flight surgeon at your Aerospace and Occupational Medicine Clinic when a 50-yr-old male Department of Defense (DoD) civilian flightline fire chief presents for his annual firefighter physical. He has a body mass index of 31 kg · m^{-2}, a blood pressure of 135/91 mmHg, and an otherwise normal physical exam. He has been doing some reading and is concerned about his per- and polyfluoroalkyl substances (PFAS) levels. He has 20+ yr of experience in firefighting and has used aqueous film-forming foam (AFFF) that contains PFAS in training and for control of aviation mishap fires within the past 10 yr. He had his labs drawn prior to this physical and asks what the results of his PFAS testing mean and how they relate to last year's levels drawn before 1 May 2023. His PFAS panel is displayed in **Table I**. His cholesterol panel showed a total cholesterol level of 201 mg · dL^{-1}, high-density lipoprotein (HDL) cholesterol of 47 mg · dL^{-1}, low-density lipoprotein (LDL) cholesterol of 131 mg · dL^{-1}, and triglyceride level of 146 mg · dL^{-1}.

1. What can you tell this fire chief about the basis of PFAS testing for DoD firefighters?
   A. This testing provides information to reliably predict future health outcomes.
   B. This testing provides information to guide treatment.
   C. This testing is part of the medical qualification and surveillance program for firefighters.
   D. This testing represents an assessment to document potential occupational exposure.

ANSWER/DISCUSSION

1. D. PFAS is a group of fluorinated substances characterized by chains with carbon atoms, either fully (per-) or partially (poly-), substituted for fluorine atoms. These carbon-fluorine bonds are extraordinarily stable, leading to long half-lives and the monicker "forever chemicals."[1] The enduring nature and oil- and water-repelling properties of PFAS made them ideal for industry, and widely disseminated production began in the early 1940s. It was not until the first decade of the 21st century that PFAS health and environmental concerns began to reach such a level that the Environmental Protection Agency launched the U.S. perfluorooctanoic acid (PFOA) Stewardship Program, and PFOA and its relatives were placed on the list of globally restricted persistent organic pollutants.

The National Defense Authorization Act for fiscal year 2020 mandated that all DoD installations phase out fluorine-based AFFF by 1 October 2024. The Act additionally required that DoD firefighters be offered PFAS testing at annual physical exams to determine the extent of firefighter PFAS exposure. The exposure of concern for firefighters is AFFF, which has been used by the DoD for suppression of petroleum-based fires since the 1970s.[2] Six PFAS compounds associated with AFFF that were selected for this testing were perfluorobutanesulfonic acid (PFBS), perfluoroheptanoic acid (PFHpA), perfluorohexanesulfonic acid (PFHxS), perfluorononanoic acid (PFNA), perfluorooctanesulfonic acid (PFOS), and PFOA. These six were the only compounds tested through 30 April 2023, but, starting 1 May 2023, the analysis was expanded. Detecting any of these PFAS compounds in the blood can only identify that the individual has been exposed to PFAS. It does not imply that the PFAS has caused or will cause disease or be used to guide treatment. PFAS testing is not a requirement of medical qualification or surveillance for firefighters.

2. True or False. Referencing Table I, the fire chief's current post-1 May 2023 PFAS panel results show his PFAS-related health risk to be decreasing compared to his previous pre-1 May 2023 PFAS panel results.
   A. True. The fire chief's PFAS levels represent less health risk as the levels have gone down.
   B. False. The fire chief's current PFAS levels are not directly comparable to his previous levels.

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Table I. PFAS Panel Showing Patient's Level Compared to Reporting Limit and CDC-NHANES Reference Intervals as Provided with the Result of LC832140—Perfluoroalkyl Substances Expanded, S/P.

PFAS	PRE-1 MAY 2023 LEVEL ($ng \cdot mL^{-1}$)	POST-1 MAY 2023 LEVEL ($ng \cdot mL^{-1}$)	REPORTING LIMIT ($ng \cdot mL^{-1}$)	CDC-NHANES REFERENCE INTERVAL ($ng \cdot mL^{-1}$)*
4,8-dioxa-3H-perfluorononanoate		ND	0.1	<0.1
N-methyl-perfluorooctane sulfonomidoacetic acid (MeFOSAA)		ND	0.1	<0.6
Linear PFOA isomers (n-PFOA)		0.88	0.1	<3.7
Branched PFOA isomers (sb-PFOA)		ND	0.1	<0.2
Sum of n-PFOA and sb-PFOA	1.4	0.88		<3.77
Linear PFOS isomers (n-PFOS)		1.1	0.1	<10.4
Branched PFOS isomers (Sm-PFOS)		3.8	0.1	<4.5
Sum of n-PFOS and Sm-PFOS	6.2	4.9		<14.6
PFBS	ND		0.05	<0.1
PFDA		ND	0.1	<0.6
Perfluorododecanoic acid		ND	0.1	<0.1
PFHpA	ND		0.05	<0.2
Perfluoroheptanesulfoconic acid		0.43	0.1	<1.0
Perfluorohexanoic acid		ND	0.1	<0.1
PFHxS	9.2	8.7	0.1	<3.7
PFNA	0.52	0.37	0.1	<1.4
Perfluoroundecanoic acid (PFUnDA)		ND	0.1	<0.4
NASEM summation value†		17.75		

PFAS = per- and polyfluoroalkyl substances; ND = none detected; PFBS = perfluorobutanesulfonic acid; PFDA = perfluorodecanoic acid; PFHpA = perfluoroheptanoic acid; PFHxS = perfluorohexane sulfonate; PFNA = perfluorononanoic acid.

*95th percentile of the general U.S. population from the Centers for Disease Control and Prevention and National Health and Nutrition Examination Survey (CDC-NHANES) (2017-2018), $N = 1929$.

†The National Academies of Science, Engineering, and Medicine (NASEM) additive sum value for MeFOSAA, PFOA (linear and branched isomers), PFOS (linear and branched isomers), PFDA, PFHxS, PFNA, and PFUnDA.

ANSWER/DISCUSSION

2. B. A revealing analysis of National Health and Nutrition Examination Survey (NHANES) samples determined that more than 98% of the U.S. population had detectable PFAS in their blood.[3] However, due to differences in employed analytical methodologies for the first 3 yr of testing, DoD firefighter levels were not directly comparable to Centers for Disease Control and Prevention (CDC) and NHANES levels.[4] However, on 1 May 2023, NMS Labs began using the CDC method, permitting direct comparison. But, as a result, the PFAS panel analyzed after 1 May 2023 is now not directly comparable to the panel before that date. Another difference between the PFAS panels is that although the post-1 May 2023 panel was expanded, it did drop off PFBS and PFHpA. The DoD Firefighter PFAS Blood Surveillance Report analyzed all 6790 PFAS samples collected during the surveillance period of 1 October 2021 to 30 September 2022. In order of prevalence, the PFAS in this report were PFHxS (found in 99.8%), PFNA (99.5%), PFOS (99.3%), PFOA (94.9%), PFHpA (16.5%), and PFBS (2.5%). The geometric means from this report are 2.36 $ng \cdot mL^{-1}$ for PFHxS, 1.03 $ng \cdot mL^{-1}$ for PFOA, 0.36 $ng \cdot mL^{-1}$ for PFNA, and 2.73 $ng \cdot mL^{-1}$ for PFOS. For PFBS and PFHpA, there were too many samples below the level of detection to provide a valid geometric mean.[4]

Our fire chief's prior PFAS panel had a PFHxS level that is about three times the geometric mean of DoD firefighters and a PFOS level about two times higher, but still within the 95th percentile for all tested PFAS compounds. His current PFAS panel can be compared to the CDC-NHANES reference interval, which shows a PFHxS level of just over twice the 95th percentile of the general U.S. population. This picture is complicated by the lack of exposure data for DoD firefighters. The DoD Firefighter PFAS Blood Surveillance Report includes firefighters who have used AFFF in their careers and those who may not have.[4] Future surveillance reports may include questionnaire data for more detailed analysis. The first large-scale analysis of PFAS epidemiological data was conducted by the C8 Science Panel between 2005 and 2008. The C8 Science Panel established probable links between PFOA and elevated cholesterol, ulcerative colitis, thyroid disease, testicular and kidney cancer, and pregnancy-induced hypertension.[5] Several other studies have continued to find associations between health effects and PFAS compounds, but there has been little statistical significance, and most studies have focused on PFOS and PFOA.[5] The main route of exposure for the community in the C8 Health Study was contaminated drinking water, but subsequent analysis of this population found that PFHxS was statistically significantly higher in firefighters compared to those in other occupations.[6] Thus, firefighters have additional PFAS exposures compared to the general population that further makes direct comparison complicated.

3. With the above caveats, what health issue(s) have been found to be statistically significantly associated in airport firefighters with history of AFFF exposure that may be relevant to this flightline fire chief?
   A. Increased diastolic blood pressure.
   B. Increased total cholesterol.

C. Increased LDL cholesterol.
D. Lowered HDL cholesterol.

ANSWER/DISCUSSION

3. A, B, and C. The prevalence of hypertension in firefighters is significantly higher compared to U.S. adult men. One study that further differentiated between types of firefighters found that just over 10% of suburban firefighters had an elevated diastolic blood pressure, while over one-third of airport firefighters had diastolic hypertension.[7] Another study of AFFF-exposed firefighters demonstrated statistically significant increases in total cholesterol and LDL cholesterol with increasing PFAS quartiles, but there was not a statistically significant association with HDL cholesterol.[8] With detectable levels of PFHxS, PFOA, PFNA, and PFOS, our fire chief has PFAS panel results that would be expected of an airport firefighter. PFOS, PFOA, and PFHxS are consistently found in all participants of firefighter studies regardless of time from AFFF exposure and PFNA in all participants in one study conducted 10 yr after phaseout of AFFF.[9–11] So, these results are likely generalizable to the fire chief.

Metabolic syndrome is an area of current investigation. Although one study of firefighters failed to find a statistically significant association between PFAS and cardiometabolic markers, it used just a small convenience sample that did not represent the same risk from AFFF as airport firefighters.[12] Another positive association in airport firefighters was between doubling of PFOA and elevated thyroid stimulating hormone and urate levels.[8] Yet, there is still limited evidence and no causal associations have been made.[5] It is possible that AFFF exposure contributed to elevated cholesterol and diastolic blood pressure in our fire chief, but there is no way of knowing if the PFAS caused these health issues. The above are still highly multifactorial in etiology (lifestyle, environmental, genetic, etc.), and standard management is still recommended.

Note from Table I that, in addition to the 13 PFAS compounds, the current DoD PFAS panel result includes the National Academies of Science, Engineering, and Medicine (NASEM) summation value. This result represents the additive sum value for N-methylperfluorooctane sulfonomidoacetic acid, PFOA (linear and branched isomers), PFOS (linear and branched isomers), perfluorodecanoic acid, PFHxS, PFNA, and perfluoroundecanoic acid.[9] Drawn from evidence that many PFAS have similar health effects, NASEM recommends analyzing the combined value to assess risk and make screening recommendations. NASEM estimates that a PFAS summation value of 2 $ng \cdot mL^{-1}$ represents the 2nd percentile and 20 $ng \cdot mL^{-1}$ the 91st percentile of the general U.S. population from NHANES data. From this, NASEM recommends that PFAS summation values of $<2\ ng \cdot mL^{-1}$ and 2–20 $ng \cdot mL^{-1}$ represent low and medium risk, respectively, and the usual standard of care should be provided. Those with a value $>20\ ng \cdot mL^{-1}$ have a high risk of adverse health effects and, in addition to the usual care, NASEM recommends screening specifically for thyroid dysfunction, ulcerative colitis, and kidney and testicular cancer. In contrast, the Agency for Toxic Substances and Disease Registry does not recommend PFAS-level-determined screening. Outside of recommended preventive screening, the Agency does not endorse testing to evaluate for potential health effects associated with PFAS exposure in the absence of signs or symptoms of a given condition.[5] Clinicians should use evidence-based recommendations and shared decision making to conduct patient screening, which is most consistent with the DoD intention of PFAS testing to document occupational exposure.

4. What can the fire chief anticipate for his future PFAS panels?
   A. There is absolutely no way to predict what may happen with PFAS levels.
   B. After phaseout of PFAS-containing AFFF, PFAS levels will likely show a meaningful decrease within 5 yr.
   C. After phaseout of PFAS-containing AFFF, PFAS levels will likely remain at pre-phaseout levels.
   D. Even after phaseout of PFAS-containing AFFF, PFAS levels will likely continue to rise.

ANSWER/DISCUSSION

4. B. The half-lives of various PFAS compounds have been measured and aid in predicting how levels may change over time. The half-lives of PFAS compounds in studies of firefighters exposed to AFFF are slightly longer than previous estimates.[1] In firefighters, the half-lives of PFOS and PFOA are around 5 yr and for PFHxS about 7 yr.[8,13] Australia has had a unique opportunity for PFAS research following the nationwide phaseout of PFOS-based AFFF for a shorter chain PFAS AFFF between 2003 and 2005 and finally to a fluorine-free foam in 2019.[11,14] Studies with AFFF-exposed firefighters have demonstrated significant PFAS serum concentrations within 5 yr of the initial phaseout, pointing to AFFF as a major source of PFAS exposure for firefighters.[8] Further, trend analysis of the 2954 individuals in the DoD Firefighter PFAS Blood Surveillance Report who were tested in both fiscal year 2021 and 2022 has already shown a downward trend in PFAS concentrations.[4]

5. In addition to AFFF, what are other potential sources of PFAS exposure for the fire chief?
   A. Ground water.
   B. Textiles.
   C. Non-stick cookware.
   D. Fast-food wrappers.
   E. All of the above.
   F. None of the above.

ANSWER/DISCUSSION

5. E. AFFF is not the sole PFAS exposure for firefighters. The anticipated reduction in PFAS blood levels after phaseout of AFFF is complicated by the ubiquity of PFAS in consumer products. Compounds from the PFAS family can be expected

to be found in almost every home in developed nations. The Organization for Economic Cooperation and Development has identified more than 4700 PFAS. These have been and are used globally in adhesives, building and construction products, ceramics, cleaning products, coatings, paints, inks, cosmetics, dry cleaning, electronics, propellants, packaging, plastics, refrigerants, textiles, and medical supplies.[2] Environmental contamination of soil and ground water in areas around DoD and civilian airports and industry poses another confounder, particularly for PFOS.[15] Firefighting training grounds and accident sites where AFFF has been deployed will pose a long-term risk from PFAS contamination. Getting closer to home, PFAS has also been found to contaminate dust in fire stations, predominantly in apparatus bays and turnout gear lockers.[16] To more fully understand the PFAS levels that firefighters may have received from occupational exposure vs. other exposures will require further study.

After providing the above counseling, the fire chief should continue to be offered PFAS testing per DoD policy to track his potential occupational exposure to PFAS. Although there is limited, weak evidence regarding the possible health effects of PFAS exposure, there is much stronger evidence for current standards of care. His exposure to PFAS is only somewhat modifiable. So, from a clinical standpoint, he should be counselled on or referred to his primary care manager for a discussion of his modifiable risk factors that impact his blood pressure and cholesterol levels. From an occupational standpoint, this fire chief should continue regular duty.

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