

An Overview of Perfluoroalkyl and Polyfluoroalkyl Substances and Interim Guidance for Clinicians Responding to Patient Exposure Concerns

Interim Guidance

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Introduction

The purpose of this fact sheet is to provide interim guidance to aid physicians and other clinicians with patient consultations on perfluoroalkyl and polyfluoroalkyl substances (PFAS). It highlights what PFAS are, which chemicals fall into this category of substances, identifies health effects associated with exposure to various PFAS, and suggests answers to specific patient questions about potential PFAS exposure.

Background

What are PFAS?

PFAS, sometimes known as PFCs, are synthetic chemicals that do not occur naturally in the environment. There are many different types of PFAS such as perfluorocarboxylic acids (e.g., PFOA, sometimes called C8, and PFNA) and perfluorosulfonates (e.g., PFOS and PFHxS). PFAS may be used to keep food from sticking to cookware, to make sofas and carpets resistant to stains, to make clothes and mattresses more waterproof, and to make some food packaging resistant to grease absorption, as well as use in some firefighting materials. Because PFAS help reduce friction, they are also used in a variety of other industries, including aerospace, automotive, building and construction, and electronics.

Why are PFAS a possible health concern?

According to the U.S. Environmental Protection Agency (EPA), PFAS are considered emerging contaminants. An “emerging contaminant” is a chemical or material that is characterized by a perceived, potential, or real threat to human health or the environment or by a lack of published health standards.

PFAS are extremely persistent in the environment and resistant to typical environmental degradation processes. The pathway for dispersion of these chemicals appears to be long-range atmospheric and oceanic currents transport. Several PFAS and their potential precursors are ubiquitous in a variety of environments. Some long-chain PFAS bioaccumulate in animals and can enter the human food chain.

PFOS and PFOA are two of the most studied PFAS. Exposure to PFOA and PFOS is widespread and global. PFOS and PFOA also persist in the human body and are eliminated slowly. Both PFOS and PFOA can be found in blood, and at much lower levels in urine, breast milk and in umbilical cord blood.

PFOS and PFOA may pose potential adverse effects for human health given their potential toxicity, mobility, and bioaccumulation potential. The likelihood of adverse effects depends on several factors such as amount and concentration of PFAS ingested as well as the time span of exposure.

Routes of Exposure and Health Effects

What are the main sources of exposure to PFAS?

For the general population, ingestion of PFAS is considered the major human exposure pathway. The major types of human exposure sources for PFAS include:

- Drinking contaminated water.
- Ingesting food contaminated with PFAS, such as certain types of fish and shellfish.
- Until recently, eating food packaged in materials containing PFAS (e.g., popcorn bags, fast food containers, and pizza boxes). Using PFAS compounds has been largely phased out of food packaging materials.
- Hand-to-mouth transfer from surfaces treated with PFAS-containing stain protectants, such as carpets, which is thought to be most significant for infants and toddlers.

- Workers in industries or activities that manufacture, manipulate or use products containing PFAS may be exposed to higher levels than the general population.

What are other low level exposure sources?

Individuals can also be exposed by breathing air that contains dust contaminated with PFAS (from soil, carpets, upholstery, clothing, etc.), or from certain fabric sprays containing this substance.

Dermal exposure is a minor exposure pathway. Dermal absorption is slow and does not result in significant absorption.

What are the potential PFAS exposure risks to fetuses and children?

Recent research evaluating possible health effects to fetuses from PFAS exposures have shown that developing fetuses can be exposed to PFAS when umbilical cord blood from their mothers crosses the placenta during pregnancy. It is important to note that different PFAS have varying levels of permeability to the placental barrier.

Newborns can be exposed to PFAS through breast milk. The level of neonatal exposure depends on the duration of breastfeeding. Older children may be exposed to PFAS through food and water, similar to adults. In addition, young children have a higher risk of exposure to PFAS from carpet cleaners and similar products, largely due to time spent lying and crawling on floors in their early years.

How long do PFAS remain in the body?

PFAS with long carbon chains have estimated half-lives ranging from 2-9 years such as:

- PFOA 2 to 4 years
- PFOS 5 to 6 years
- PFHxS 8 to 9 years

What are exposure limits for PFAS in drinking water?

The Environmental Protection Agency (EPA) has published a Lifetime Health Advisory (LTHA) recommending that the concentration of PFOA and PFOS in drinking water, either individually or combined, should not be greater than 70 parts per trillion (0.07 parts per billion). The LTHA concentrations do not represent definitive cut-offs between safe or unsafe conditions, but rather provide a margin of protection for individuals throughout their life from possible adverse health effects. EPA health advisories are non-regulatory recommendations and are not enforceable.

What are PFAS levels in the U.S. population?

Most people in the United States and in other industrialized countries have measurable amounts of PFAS in their blood.

The National Health and Nutrition Examination Survey (NHANES) is a program conducted by the Centers for Disease Control and Prevention (CDC) to assess the health and nutritional status of adults and children in the United States. NHANES (2011–2012) measured the concentration of PFAS in the blood of a representative sample of the U.S. population (12 years of age and older). The average blood levels found were as follows:

- PFOA: 2.1 parts per billion, with 95% of the general population at or below 5.7 parts per billion
- PFOS: 6.3 parts per billion, with 95% of the general population at or below 21.7 parts per billion
- PFHxS: 1.3 parts per billion, with 95% of the general population at or below 5.4 parts per billion

In the last decade, major manufacturers of PFOA and PFOS related products joined EPA in a global stewardship program to phase out production of these agents by 2015. Based on data collected from previous NHANES

cycle years, levels of PFOA and PFOS are generally decreasing in the blood of the general population as a result of this important initiative.

Health Studies

How can PFAS potentially affect human health?

Studies in humans and animals are inconsistent and inconclusive but suggest that certain PFAS may affect a variety of possible endpoints. Confirmatory research is needed.

Below are summaries of studies in animals and humans.

Animal Studies:

Adverse health effects have been demonstrated in animal studies, but these occurred at exposure levels higher than those found in most people. The main health effects observed were: enlargement and changes in the function of the liver, changes in hormone levels (e.g., reduced testosterone synthesis, potential to affect T₄ and TSH levels) and adverse developmental outcomes. Developmental and reproductive effects, including reduced birth weight, decreased gestational length, structural defects, delays in postnatal growth and development, increased neonatal mortality, and pregnancy loss have all been associated with prenatal rodent exposure to PFOS and PFOA.

Human Studies:

C8 Health Project

The C8 Health Project was a large epidemiological study conducted because drinking water in six water districts across two states near Parkersburg, West Virginia were contaminated by release of PFOA (also called C8) from the 1950s until 2002 (when the contamination was discovered). These releases migrated and contaminated the air, parts of the Ohio River, and ground water. The study included 69,030 persons ≥ 18 years of age. The C8 Science Panel analyzed study data and found probable links (as defined by litigation) between elevated PFOA blood levels and high cholesterol (hypercholesteremia), ulcerative colitis, thyroid function, testicular cancer, kidney cancer, preeclampsia, as well as elevated blood pressure during pregnancy. Residents in the area of these releases showed 500 percent higher PFOA-concentrations in blood compared to a representative U.S. population (i.e., NHANES).

Table 1: Overview of C8 and Other Human Studies

Cholesterol	Some epidemiological studies demonstrated statistically significant associations between serum PFOA and PFOS levels and total cholesterol in: - workers exposed to PFAS, and - residents of communities with high levels of PFOA in the drinking water compared to NHANES data that is representative of the U.S. population. Other studies have found no association between PFAS exposures and the total cholesterol levels.
Uric acid	Several studies have evaluated the possible association between serum PFOA and serum PFOS levels and uric acid. Significant associations were found between serum PFOA and uric acid levels at all evaluated exposure levels.
Liver effects	A number of human studies have used liver enzymes as biomarkers of possible liver effects. In occupational studies, no associations between liver enzymes and serum PFOA or PFOS levels were consistently found. A study of highly

	exposed residents demonstrated significant associations but the increase in liver enzymes was small and not considered to be biologically significant.
Cancer	The International Agency for Research on Cancer (IARC) has classified PFOA as possibly carcinogenic and EPA has concluded that both PFOA and PFOS are possibly carcinogenic to humans. Some studies have found increases in prostate, kidney, and testicular cancers in workers exposed to PFAS and people living near a PFOA facility. Findings from other studies report otherwise and most did not control for other potential factors including heavy smoking. Additional research is needed to clarify if there is an association.

Note: Additional studies have identified possible associations between ulcerative colitis, thyroid disease and pregnancy induced hypertension and higher exposure to PFAS.

What health screenings were used in the C8 study?

The C8 Medical Panel suggested health screening to evaluate the C8 study population that included blood tests for cholesterol, uric acid, thyroid hormones and liver function as well as other age or situationally appropriate screenings like blood pressure and urine protein measures. For individual patients exposed to PFAS who are not among the C8 study screening population, there are no official guidelines supporting health screening. However the tests listed above are well established in clinical medicine and may be a consideration to discuss with your patient based on the patient history, concerns and symptoms.

What are potential health effects from prenatal PFAS exposure to fetuses?

Multiple studies have reported an association between elevated maternal blood and cord blood concentrations of PFAS (primarily PFOS and PFOA) and decreased birth weight. Specifically, one meta-analysis suggests that each 1 ng/mL increase in prenatal PFOA levels is associated with up to 18.9 g reductions in birth weight (Johnson, 2014). Studies have also observed decreased birth weight with prenatal exposures to PFOS. The association between maternal PFAS level and decreased birth weight is not statistically significant across all studies. Further, the observed reduction in birth weight does not consistently equate with increased risk of a low birth weight (LBW) infant. Only one study revealed a statistically significant association between LBW risk and PFOS (Stein 2009); no studies have found a statistically significant association between LBW risk and PFOA.

Additional studies are needed to conclusively link the relationships between fetal PFAS exposure and health effects.

Patient Questions and Key Message Answers

As a clinician, you know careful listening and patient engagement is critical for ensuring quality patient care, especially when health concerns are raised. Perhaps the most difficult challenge in speaking with patients about their health concerns is addressing uncertainty. If your patient has concerns about an exposure to PFAS, you may face the challenge of helping your patient cope with the uncertainty of potential health effects from a PFAS exposure.

Based on feedback from clinicians and from individuals who have spoken to their health care provider about their PFAS exposure concerns, a set of patient questions have been identified. To assist you in speaking with your patients about their concerns, key messages and supporting facts needed to answer the anticipated patient questions are provided in the table below for your information and potential use.

Table 2: Patient Questions and Key Message

Questions Patients May Ask	Key Patient Messages	Key Message Supporting Facts
There are high levels of PFAS in my water. What should I do?	If the water you use is above the EPA health advisory level for PFOA and PFOS, you can reduce exposure by using an alternative water source for drinking, food preparation, cooking, brushing teeth or any activity that might result in ingestion of water.	Potential health effects are associated with exposure to PFAS. EPA has established a lifetime health advisory for PFOA and PFOS in drinking water. This advisory states that the concentration of PFOA and PFOS in drinking water, either individually or combined, should not be greater than 70 parts per trillion. There needs to be additional research to establish levels of health risk, but patients may want to reduce exposures below the EPA health advisory level to be on the safe side. A home water filtration system can reduce the contaminant levels in drinking water. Researchers are still clarifying how to best use home filtration for PFAS contamination. Installing a home filtration system or using a pitcher-type filter may reduce PFAS levels. However, these filters may not reduce PFAS enough to meet the EPA Lifetime Health Advisory (LTHA) level. Three factors determine how much PFAS are removed by filtration. These factors are the PFAS contaminant levels, the type of filter, and how well the filter is maintained. Manufacturers of the filtration system may be able to make recommendations to optimize removal of PFAS. This may include more sophisticated media cartridges or increasing the frequency of exchanging filter media. For bottled water questions (how it is treated and if it is safe) contact the CFSAN Information Center at

Questions Patients May Ask	Key Patient Messages	Key Message Supporting Facts
		1-888-SAFEFOOD (1-888-723-3366).
Could my health problems be caused by PFAS exposure? (Based on the health problems the patient has, there are two possible responses to this question.) (a) If the patient's health problem is in the list below, it may potentially be associated with PFAS exposure, based on limited evidence from human studies. The potential health effects include: - Thyroid function (potential to affect T₄ and TSH levels) - High cholesterol - Ulcerative colitis - Testicular cancer - Kidney cancer - Pregnancy-induced hypertension - Elevated liver enzymes - High uric acid (b) If the patient's health problem is not in the bulleted list above, then there is no current evidence that it is related to PFAS exposure. (However, research is ongoing and not all health outcomes have been adequately studied.)	(a) Although the evidence is not conclusive, your health problem could potentially be associated with exposure to PFAS. However, health effects can be caused by many different factors, and there is no way to know if PFAS exposure has caused your health problem or made it worse. (b) Based on what we know at this time, there is no reason to think your health problem is associated with exposure to PFAS.	For supporting facts on the listed health effects in this question (a), see "How can PFAS potentially affect human health." The information on potential illnesses and health effects will be briefly reviewed for each of these illnesses or health effects. This information can be found in this fact sheet on page 3 and 4. If your patient presents with health concerns that might be associated with PFAS exposure, it is appropriate to discuss the patient's concerns and perform a thorough health and exposure history and also a physical exam relative to any symptoms reported.
Are there future health problems that might occur because of PFAS exposure?	We know PFAS can cause health issues but there is no conclusive evidence that predicts PFAS exposure will result in future health problems. We can watch for symptoms related to PFAS associated health problems and investigate any that you notice, especially those that reoccur.	Studies in humans and animals are inconsistent and inconclusive but suggest that certain PFAS can cause possible health effects. Additional research is needed to better understand health risks associated with PFAS exposure.

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Should I get a blood test for PFAS?	If you are concerned and choose to have your blood tested, test results will tell you how much of each PFAS is in your blood but it is unclear what the results mean in terms of possible health effects. The blood test will not provide information to pinpoint a health problem nor will it provide information for treatment. The blood test results will not predict or rule-out the development of future health problems related to a PFAS exposure.	There currently is no established PFAS blood level at which a health effect is known nor is there a level that predicts health problems. Most people in the US will have measureable amounts of PFAS in their blood. There are no health-based screening levels for specific PFAS that clinicians can compare to concentrations measured in blood samples. As a result, interpretation of measured PFAS concentrations in individuals is limited in its use. The patient may be aware of blood and urine test for PFAS being taken at other locations. These tests are used by public health officials to investigate community-wide exposure in order to understand the kinds and amounts of PFAS exposures in a community and how those exposures compare to those in other populations. Serum PFAS measurements are most helpful when they are part of a carefully designed research study.
What do my PFAS blood tests results mean?	The blood test for PFAS can only tell us the levels of specific PFAS in your body at the time you were tested. The blood tests results cannot be interpreted and used in patient care. The blood test results cannot predict or rule-out the development of future problems related to a suspected exposure.	There is currently no established PFAS blood level at which a health effect is known nor is there a level that is clearly associated with past or future health problems. The individual patient's blood concentration of PFAS can only be compared to the average background blood concentration levels for different PFAS that are nationally identified through the representative sampling of the NHANES studies conducted by CDC. A patient's PFAS concentrations can only show the patient if his or her blood levels are within range of the national norms or if the

Questions Patients May Ask	Key Patient Messages	Key Message Supporting Facts
		individual's levels are high or low compared to the national background averages.
An adult patient asks: “Should I be tested for any of the potential health effects associated with PFAS exposure (like cholesterol and uric acid levels, or liver and thyroid function, etc.)?”	Let's look at your health history and past lab results and discuss what steps we may want to consider moving forward. One way we can address cholesterol is through your annual physical. For others PFAS associated conditions, we need to watch for symptoms and investigate any that you notice, especially those that reoccur. If any unusual symptoms occur, we will investigate those and treat as needed. Laboratory tests will not tell us if PFAS are the cause of any of your health symptoms or abnormal lab results, but conducting these routine health screenings and watching for any related symptoms do offer us a way to better understand your current health status.	Health effects associated with PFAS are not specific and can be caused by many other factors. There are no guidelines to support laboratory testing to monitor PFAS health concerns. However, if your patient is concerned about PFAS exposure, discussing routine cholesterol screening can reassure the patient that his or her PFAS exposure concerns are being addressed. Some of the other possible health effects can be screened for based on symptoms.
A parent asks: “Should I have my child tested for any of the potential health effects associated with PFAS exposure (like cholesterol and uric acid levels, or liver, thyroid function, etc.)?”	The American Academy of Pediatrics has endorsed cholesterol testing for children starting at 9 years of age. Following this guidance cholesterol level testing can be done for older children. If cholesterol level measures are outside the normal range, we can discuss options for bringing cholesterol levels within the normal range for your child. For very young children, keeping well child visits is the best plan of action to monitor your child's	According to NHLBI guidelines endorsed by the American Academy of Pediatrics, all children should be screened for cholesterol levels between ages 9 and 11 years, and again between ages 17 and 21 years, even those who are not at an increased risk of high cholesterol and heart disease. Health effects associated with PFAS are not specific and can be caused by many other factors. There are no guidelines to support use of laboratory testing to monitor PFAS health concerns.

Questions Patients May Ask	Key Patient Messages	Key Message Supporting Facts
	health and watch for symptoms of illness. We can discuss any symptoms you notice, especially those that reoccur. If any unusual symptoms occur, we will investigate those and treat as needed. Laboratory tests will not tell us if PFAS are the cause of any of your child's health symptoms and are not recommended. Conducting routine well child visits and watching for any related symptoms do offer us a way to better understand your child's current health status.	However, if your patient presents with health concerns that have been associated with PFAS exposures, discussing recommended cholesterol screening, can reassure the patient's parents that their concerns are being addressed. Some of the other possible health effects can be screened for based on symptoms.
How will exposure to PFAS affect my pregnancy?	Exposure to PFAS before pregnancy has been associated with pregnancy-induced hypertension and pre-eclampsia. We will monitor your blood pressure closely, as we do for all pregnant women; however, there is no need for additional blood pressure measurements as a result of your exposure.	Health effects associated with PFAS are not specific and can be caused by many other factors. Pregnancy induced hypertension occurs in many pregnancies and the specific etiology is often unknown.
Is it safe for me to breastfeed my baby?	Breastfeeding is associated with numerous health benefits for infants and mothers. At this time, it is recommended that you as a nursing mother continue to breastfeed your baby. The science on the health effects of PFAS for mothers and babies is evolving. However, given the scientific understanding at this time, the benefits of breastfeeding your baby outweighs those of not breastfeeding.	Extensive research has documented the broad and compelling advantages of breastfeeding for infants, mothers, families, and society. Some of the many benefits include immunologic advantages, lower obesity rates, and greater cognitive development for the infant as well as a variety of health advantages for the lactating mother. Even though a number of environmental pollutants readily pass to the infant through human milk, the advantages of

Questions Patients May Ask	Key Patient Messages	Key Message Supporting Facts
		breastfeeding continue to greatly outweigh the potential risks in nearly every circumstance.
How will exposure to PFAS affect my child's immunizations? Will I need to get my child vaccinated again?	Although few studies have reported that PFOS and PFOA might slightly lower the immune response to some immunizations, these studies have not suggested a need to re-evaluate the normal immunization schedule. There is no recommendation for repeating any vaccinations.	A study with 656 children has reported that elevated levels of PFOA and PFOS in serum are associated with reduced humoral immune response to some routine childhood immunizations (rubella, tetanus and diphtheria) among children aged five to seven years. Studies have not suggested a need to re-evaluate the normal immunization schedule nor the use of an immunize booster for impacted children.
I have been very anxious about health risks from PFAS exposure. How can I deal with this uncertainty?	It is normal to be anxious about uncertain risks. I am here to listen to your questions and will do my best to provide honest answers. First let's identify ways to reduce ongoing exposures to PFAS so that overtime we can lower your health risks. Let's set up appointment for (X date) and we can discuss any new questions you have and check to see if there are any changes in how you feel. In the meantime, I have more information that may answer questions that you may have later about PFAS.	Listen sympathetically and explore the concerns of the patient Check for serious stress issues such as ongoing depression and treat accordingly. Review resources/references at the end of this fact sheet.

Resources

Below is a list of resources that can be helpful to clinicians. These include the Pediatric Environmental Health Specialty Units (PEHSU). The PEHSU are a national network of experts available to provide consultation and education to clinicians and communities wishing to learn more about PFAS and other hazardous substances. These units are staffed by clinicians with environmental health expertise in pediatrics, reproductive health, occupational and environmental medicine, medical toxicology, and other related areas of medicine.

Resource	Link
ATSDR: PFAS Overview Toxic Substance Portal ToxFAQs	http://www.atsdr.cdc.gov/pfc/index.html http://www.atsdr.cdc.gov/substances/index.asp http://www.atsdr.cdc.gov/toxfaq/tf.asp?id=1116&tid=237
CDC: PFCs	http://www.cdc.gov/biomonitoring/PFCs_FactSheet.html
C8 Science Panel C8 Medical Panel	http://www.c8sciencepanel.org/prob_link.html http://www.c8sciencepanel.org/publications.html http://www.c-8medicalmonitoringprogram.com/ http://www.c-8medicalmonitoringprogram.com/docs/med_panel_education_doc.pdf
EPA: PFAS	https://www.epa.gov/chemical-research/research-perfluorooctanoic-acid-pfoa-and-other-perfluorinated-chemicals-pfcs
IARC	http://www.iarc.fr/
NIEHS: PFAS	https://www.niehs.nih.gov/health/materials/perflourinated_chemicals_508.pdf
NHLBI Lipid Screening in Children & Adolescents	https://www.nhlbi.nih.gov/health-pro/guidelines/current/cardiovascular-health-pediatric-guidelines/full-report-chapter-9
PEHSU	http://www.pehsu.net/
Uncertainty and Stress in the Clinical Setting	Helping Patients and Clinicians Manage Uncertainty During Clinical Care - https://publichealth.wustl.edu/helping-patients-and-clinicians-manage-uncertainty-during-clinical-care/ Navigating the Unknown: Shared Decision-Making in the Face of Uncertainty J Gen Intern Med. 2015 May; 30(5): 675–678. http://tinyurl.com/zrd587f Patient Health Questionnaire to determine if patient is suffering from depression. http://tinyurl.com/gv6h3wk Uncertainty Toolbox: Principles in the Approach to Uncertainty in the Clinical Encounter-J Gen Intern Med. 2015 May; 30(5): 675–678. http://tinyurl.com/gtlf2mk