

PFAS: An Overview of the Science and Guidance for Clinicians

Revised 11/20/2019

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Introduction

This document provides an overview of what is known about per- and polyfluoroalkyl substances (PFAS) and identifies health effects associated with PFAS exposure. The following information will help clinicians respond to patient concerns about PFAS exposure. The document is divided into four sections: 1) PFAS basics, 2) PFAS health studies, 3) questions patients may ask clinicians about PFAS, and 4) where to find additional PFAS resources and references. Understanding potential health issues associated with PFAS exposure is an ongoing collaborative effort of federal, state, tribal, and local governments. New research PFAS is growing quickly; to learn the latest about CDC/ATSDR work on PFAS, visit https://www.atsdr.cdc.gov/pfas/related_activities.html.

PFAS Basics

What are PFAS?

PFAS are a family of synthetic chemicals characterized by a fully or partially fluorinated carbon chain, some with a hydrophilic tail. These compounds do not occur naturally in the environment. There are thousands of different PFAS; some are characterized as long-chain compounds, and some are characterized as short chain compounds. For example, there are:

- Perfluorocarboxylic acids, which includes perfluorooctanoic acid (PFOA) and perfluorononanoic acid (PFNA), and
- Perfluorosulfonic acids, which include perfluorooctane sulfonic acid (PFOS) and perfluorohexane sulfonic acid (PFHxS)

PFAS are widely dispersed and ubiquitous in the environment globally. The long-chain compounds are known to be extremely persistent and resistant to typical environmental degradation processes.

How are PFAS used?

PFAS have the ability to reduce friction, so they are used in a variety of industries including aerospace, automotive, building and construction, and electronics. They are used for fire suppression because they can quickly douse fuel fires. They are also used to keep food from sticking to cookware, make food packaging resistant to grease absorption, make sofas and carpets resistant to stains, and make clothes and mattresses waterproof.

Who are at increased risk of exposure to PFAS?

Workers in industries that manufacture, manipulate, or use products containing PFAS are at higher risk for PFAS exposure. Where manufacture or use has contaminated local drinking water sources, PFAS exposure is likely higher than in the general population.

What is the main source of exposure to PFAS?

Ingestion:

- For the general population, ingestion of PFAS is the primary exposure pathway. Major ingestion sources for PFAS include:
- Eating foods like fish and shellfish grown or raised with PFAS contaminated water or soil.
Note: For local fish advisories, please refer to the EPA fish advisory website (<https://fishadvisoryonline.epa.gov/General.aspx>) or to your local or state health department.
- Eating food packaged in materials containing PFAS (e.g., popcorn bags, fast food containers, pizza boxes).
Note: Some long-chain PFAS such as PFOS and PFOA were phased out of food packaging by the FDA in 2016. New shorter chain PFAS may have replaced those phased out in food packaging.
- Drinking contaminated water.

For infants and toddlers PFAS sources include:

- Formula mixed with PFAS contaminated water.
- Breastmilk from women who have current or past exposure to PFAS.
Note: The level of exposure depends on the duration of breastfeeding and the level of PFAS in the mother. Several studies suggest that some PFAS can cross the placental barrier and is excreted through lactation. Even with these PFAS transfers, these studies have not shown a causal relationship with a specific health effect in infants or children. Despite potential PFAS exposure from breastmilk, breastfeeding has important benefits for the infant, including immunologic advantages. Further, breastfeeding is good for the health of both infants and mothers. Some of the many benefits for infants include a reduced risk of ear and respiratory infections, asthma, obesity, and sudden infant death syndrome (SIDS). Breastfeeding can also help lower a mother's risk of high blood pressure, type 2 diabetes, and ovarian and breast cancer. More information on breastfeeding is available at <https://www.cdc.gov/breastfeeding/about-breastfeeding/why-it-matters.html>.
- Hand-to-mouth behaviors place infants and young children at increased risk of exposure to a variety of pollutants due to the time they spend crawling and playing on the floor. If surfaces were treated with PFAS-containing stain protectants, toddlers may be exposed through these behaviors.

69 **What are other routes of exposure?**

70 *Inhalation:* Breathing PFAS-contaminated dust in the air (e.g. dust can be contaminated by particles and fibers from carpets, upholstery, clothing,
71 other PFAS treated products like certain fabric sprays, and from soil).

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73 Most PFAS are not volatile so showering does not pose a significant inhalational risk, but people may ingest contaminated water while bathing.

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75 *Dermal:* Absorption of PFAS through the skin is limited and is of minimal concern as an exposure route.

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77 *Transplacental:* Some PFAS have been shown to cross the placenta and enter umbilical cord blood. Different PFAS have varying levels of permeability
78 to the placental barrier. Some studies have shown that PFOA has more transplacental transfer efficiency than PFOS.

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81 **What are exposure limits for PFAS in drinking water?**

82 EPA has established a Health Advisory level for PFOA and PFOS in drinking water at 70 parts per trillion (ppt) (0.07µg/L), individually or combined.¹
83 The Health Advisory does not represent a definitive cut-off between safe or unsafe conditions, but rather provides a margin of protection for
84 individuals throughout their life from possible adverse health effects. Some states have established their own PFAS drinking water guidelines. In
85 some cases, these state guidelines are lower than the EPA Health Advisory ([https://www.epa.gov/ground-water-and-drinking-water/drinking-](https://www.epa.gov/ground-water-and-drinking-water/drinking-water-health-advisories-pfoa-and-pfos)
86 [water-health-advisories-pfoa-and-pfos](https://www.epa.gov/ground-water-and-drinking-water/drinking-water-health-advisories-pfoa-and-pfos)).

87 **Note:** EPA health advisories are non-regulatory recommendations that are not enforceable and are intended to provide technical information to
88 state agencies and other public health officials on health effects, analytical methodologies, and treatment technologies associated with drinking
89 water contamination.

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91 **How long do PFAS remain in the body?**

92 Some PFAS remain in the body for a long time. However, biological half-life varies by chemical species. The half-life of chemical is the amount of time it
93 takes for 50% of the substance to be metabolized and/or eliminated from the body. A few examples are:^{2,3,4,5,6}

PFBA: 72 to 81 hours	PFOA: 2.1 to 10.1 years	PFOS: 3.3 to 27 years	PFHxS: 4.7 to 35 years
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95 **Note:** PFAS compounds like pentafluorobenzoic acid (PFBA) with shorter carbon chains may have a shorter half-life.

1 ¹ <https://www.epa.gov/ground-water-and-drinking-water/drinking-water-health-advisories-pfoa-and-pfos>.

2 ² Harada K, Inoue K, Morikawa A, et al. 2005a. Renal clearance of perfluorooctane sulfonate and perfluorooctanoate in humans and their species-specific excretion. Environ Res 99:253-261.

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4 ³ Li Y, Fletcher T, Mucs D, et al. 2018. Half-lives of PFOS, PFHxS and PFOA after end of exposure to contaminated drinking water. Occup Environ Med 75(1):46-51. 10.1136/oemed-2017-104651.

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6 ⁴ Olsen GW, Burris JM, Ehresman DJ, et al. 2007a. Half-life of serum elimination of perfluorooctanesulfonate, perfluorohexanesulfonate, and perfluorooctanoate in retired fluorochemical production workers. Environ Health Perspect 115:1298-1305.

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8 ⁵ Worley RR, Moore SM, Tierney BC, et al. 2017a. Per- and polyfluoroalkyl substances in human serum and urine samples from a residentially exposed community. Environ Int 106:135-143. 10.1016/j.envint.2017.06.007.

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10 ⁶ Zhang Y, Beesoon S, Zhu L, et al. 2013. Biomonitoring of perfluoroalkyl acids in human urine and estimates of biological half-life. Environ Sci Technol 47(18):10619-10627. 10.1021/es401905e.

96 **Note:** Because some PFAS are persistent in the human body, blood PFOS and PFOA levels can be a surrogate for total PFAS body burden and
97 provide a better indication of the PFAS dose to a target organ than an externally measured dose like PFAS water concentration.
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99 **What are PFAS levels in the U.S. population?**

100 Most people in the United States and in other industrialized countries have measurable amounts of protein-bound and free PFAS in their blood.
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102 The National Health and Nutrition Examination Survey (NHANES) is survey of the health and nutritional status of U.S. adults and children that has
103 been conducted by the National Center for Health Statistics⁷. Since 1999, NHANES has measured the concentrations of PFAS in the blood of a
104 representative sample of the U.S. population (12 years of age and older). The average blood levels found in 2015-16 were as follows:⁸

- 105 • PFOA: 1.56 parts per billion, with 95% of the general population at or below 4.17 parts per billion
- 106 • PFOS: 4.72 parts per billion, with 95% of the general population at or below 18.3 parts per billion
- 107 • PFHxS: 1.18 parts per billion, with 95% of the general population at or below 4.90 parts per billion

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109 In 2006, EPA enlisted major manufacturers of PFOA- and PFOS-related products to join in a global stewardship program to phase out production and
110 reduce facility emissions of these agents by 2015. This facilitated significant reductions in PFOA and PFOS by all participating companies as
111 measured by EPA PFOA Stewardship Program goals between 1999 and 2016. According to 1999–2000 NHANES data, blood levels of PFOA and PFOS
112 in the general population were 5.2 and 30.4 parts per billion, respectively. NHANES data in 2015-2016 for the general population found that PFOA
113 was 1.56 parts per billion and PFOS 4.72 parts per billion, indicating decreases of PFOA and PFOS by 70% and 84% respectively⁸.
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115 **PFAS and Human Health**

116 **How can PFAS potentially affect human health?**

117 PFAS exposure is associated with an increased risk of some adverse effects for human health. Risk differ among PFAS based on their potential
118 toxicity, mobility, and bioaccumulation. The risk of adverse effects depends on several factors, including the exposure dose, the frequency of
119 exposure, the route and duration of exposure, and the time of exposure during the lifecycle (e.g., fetal development, early childhood). PFOS and PFOA
120 are two of the most studied PFAS. PFOS and PFOA bind to tissue proteins, accumulate in the blood, and at much lower levels in the liver, kidneys, and
121 brain. Most PFAS are not metabolized by the body. PFOS and PFOA are slowly eliminated through menstruation, breastmilk and feces but are
122 primarily excreted in urine. Some, but not all, studies in humans and animals suggest that certain PFAS may affect a variety of health endpoints.
123 Additional research to investigate many of these health endpoints is underway. Below is a summary of current findings from animal and human
124 studies.
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127 *Animal Studies*

128 Animal studies have demonstrated increased risk of adverse health effects following PFAS exposure, but these effects occurred at exposure levels
129 higher than most people experience. The main health effects observed were:

12 ⁷ <https://www.cdc.gov/nchs/nhanes/index.htm>

13 ⁸ Center for Disease Control and Prevention (CDC). Fourth National Report on Human Exposure to Environmental Chemicals, Updated Tables, Volume One. January 2019. U.S
14 Department of Health and Human Services [update 2017 April 14; accessed 2019 October 16]. Available from: <https://www.cdc.gov/exposurereport/index.html>

- Enlargement and changes in the function of the liver
- Changes in hormone levels
- Suppression of adaptive immunity
- Adverse developmental and reproductive outcomes

The postnatal effects most often observed in rodents exposed to PFAS are increased risk of mortality in the first hours or week after birth, effects on weight that may persist beyond weaning, delayed eye opening, delayed puberty, abnormal mammary gland development, reduced offspring body weight, pup mortality, and reduced ossification. Additionally, liver hypertrophy was identified in adult rats.

The comparison of the toxicity of PFAS across species is difficult because of the differences in half-lives, mechanisms of toxicity, and measured exposure levels in epidemiological and experimental studies.

Human Studies

Human studies have found associations between exposure to PFAS and adverse health effects in many organ systems. The C8 Health Study^{9,10} an early epidemiological study of 69,030 persons ≥ 18 years of age, found evidence suggestive of associations (though not statistically significant) between exposure to PFOA and six diseases:

- high cholesterol (hypercholesterolemia),
- ulcerative colitis,¹¹
- thyroid toxicity,¹²
- testicular cancer,¹³
- kidney cancer,¹⁴ and
- preeclampsia, and elevated blood pressure during pregnancy.¹⁵

At the time of the study, C8 Health Study participants had five-times higher PFOA-concentrations in blood compared to a representative U.S. population (i.e., NHANES 1999-2000)¹⁶. Epidemiological studies performed since the C8 Health Study have continued to evaluate the health effects listed above, as well as others (e.g., liver, kidney, endocrine, immune, pulmonary, reproductive, and neurobehavioral). Although causal relationships have not been established, some studies find positive associations between PFAS exposure and adverse health effects (see Table 1). These studies

⁹ The C8 Health Study was a series of exposure and health studies in the Mid-Ohio Valley communities, which had been potentially affected by the releases of PFOA (or C8) emitted since the 1950s from the Washington Works plant in Parkersburg, West Virginia. C8 signifies that the study looked at selected long chain PFAS.

¹⁰ <http://www.c8sciencepanel.org/index.html>.

¹¹ C8 Medical Panel Guidance. http://www.c-8medicalmonitoringprogram.com/docs/med_panel_education_doc.pdf

¹² <https://ehp.niehs.nih.gov/doi/10.1289/ehp.1206449>.

¹³ <https://ehp.niehs.nih.gov/doi/10.1289/ehp.1104370>.

¹⁴ <https://ehp.niehs.nih.gov/doi/10.1289/ehp.1205829>.

¹⁵ <https://ehp.niehs.nih.gov/doi/10.1289/ehp.1205829>.

¹⁶ <https://academic.oup.com/aje/article/170/7/837/92302/>; <https://insights.ovid.com/crossref?an=00001648-201205000-00007>.

¹⁷ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2799461/>

are limited by the lack of exposure monitoring data associated with epidemiological studies and the limited analysis of other routes of exposure. Further, most studies have focused on the potential health effects related to PFOA and/or PFOS, while fewer studies have evaluated the potential health effects for other PFAS. The overall health effects are summarized below in Table 1.

Table 1: Overview of Human Studies

Cholesterol	Several epidemiological studies report statistically significant associations between serum PFOA and PFOS concentrations and total cholesterol in: 1) workers exposed to PFAS, and 2) residents of communities with high levels of PFOA in their drinking water. However, the associations between cholesterol levels and PFAS exposure are not consistent among human studies and no causal relationship has been established.
Uric acid	Several epidemiological studies report positive associations between serum PFOA and PFOS concentrations and serum uric acid concentrations in residential community and occupational populations, but reverse causality may be applicable, and no causal relationship has been established.
Liver Effects	Several epidemiological studies report a positive association between serum PFOA concentration and liver enzymes (AST, ALT, GGT, ALP) and an inverse association between serum PFOA and bilirubin level in occupational and residential community populations. However, the associations between liver enzymes and PFAS exposure are not consistent among human studies and no causal relationship has been established.
Kidney Effects	Several epidemiological studies on occupational, general, and community populations report an association between exposure to PFAS and reduced kidney function, cellular and histological derangements in proximal tubules of the nephron, and dysregulated metabolic pathways. Variations in these effects are reported based on the specific PFAS and/or the age, sex, ethnicity, and medical history of the individual. However, there is a lack of strong evidence to definitively establish a causal relationship.
Endocrine Disruptors	Several epidemiological studies on occupational, general, and community populations report prenatal exposure to PFAS, in particular PFOS and PFOA, is associated with increased body fat, increased risk of cardio-metabolic disorders, and obesity during childhood and adulthood. However, these associations are not consistent among human studies and no causal relationship has been established.
Thyroid Effects	General population and occupational studies report an association between serum PFOA and increased risk of thyroid disease. There may also be an association between serum PFOS and thyroid disease. Other studies report an association between serum PFOA and PFOS and thyroid stimulating hormone (TSH), triiodothyronine (T3), or thyroxine (T4) levels. However, these associations are not consistent among human studies and no causal relationship has been established.
Immune Effects	The National Toxicology Program (NTP) conducted a systematic review of the human, animal, and in vitro data examining immunotoxic effects of PFOA and PFOS. They concluded that both PFOA and PFOS are “presumed to be immune hazards to humans.” Evidence was considered strong that both compounds were associated with decreased antibody response to vaccines, while there was weaker evidence for PFOA-induced impairment of infectious disease resistance, and increased hypersensitivity-related outcomes. The NTP is undertaking additional systematic reviews to evaluate immunotoxicity of six other related PFAS.
Ulcerative Colitis	Limited epidemiological studies have investigated the relationship between ulcerative colitis and PFAS. Few studies report a positive association with PFOA and UC. However, this is not consistent in the literature, but reverse causality may be applicable, and no causal relationship has been established.
Asthma	Few general population and occupational studies have investigated a relationship with asthma. Some of these studies report a positive association between several serum PFAS and asthma. However, these associations are not consistent among children in varying age ranges and no causal relationship has been established. Population studies have not found an association between PFAS exposure and atopic eczema, allergic rhinitis, food allergy, and pollen allergy.
Neuro-behavioral	Few studies address neurobehavioral changes in children (e.g., ADHD, autism, hyperactivity) and PFAS exposure. Variations of neurobehavioral changes are reported based on the specific PFAS, child age and sex. However, these associations are not consistent among human studies and no

	causal relationship has been established. Learning problems and PFAS exposure have also been studied in children but there is weak evidence to support health endpoints. ATSDR and partners are conducting further investigations into neurobehavioral and learning health effects.
Reproductive Health	A few epidemiological studies report an association between PFAS exposure in women and lower fertility and fecundity. However, the associations are not consistent among human studies, especially in relation to parity, and no causal relationship has been established. In men, a few studies have shown a weak association between PFAS exposure and semen quality or levels of productive hormones, however, no causal relationship has been established for these findings.
Preeclampsia	Few epidemiological studies have investigated the relationship between preeclampsia and PFAS. Early general population studies ⁹⁻¹⁷ reported a possible association between serum PFOA exposure and preeclampsia. ¹³ However, these associations are not consistent among all pregnant women and no causal relationship has been established.
Birth Weight	Several epidemiological studies report a possible association between elevated maternal blood and fetal cord blood PFAS concentrations (primarily PFOS and PFOA) and decreased birth weight. However, the association between the maternal PFAS level and decreased birth weight did not consistently show statistical significance. Further, the observed reduction in birth weight does not consistently equate with increased risk of a low birth weight (LBW) infant.
Cancer	The International Agency for Research on Cancer (IARC) has classified PFOA as possibly carcinogenic to humans (Group 2B), and EPA has concluded that evidence suggests carcinogenic potential for both PFOA and PFOS in humans. Some studies report increases in prostate, kidney, and testicular cancers in workers exposed to PFAS and people living near a PFOA facility. Other studies have not found increases in cancer. However, these associations are not consistent among human studies and no causal relationship has been established.

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How may clinicians approach patient care for PFAS exposed individuals?

Epidemiological and toxicological research on PFAS as a risk factor to human health is ongoing. The correlation of PFAS as human health risks are building a body of evidence. However, the evidence does not establish a causal relationship between PFAS exposure and disease.

The C8 Medical Panel suggested certain health screenings for the C8 study population, including blood tests for cholesterol, uric acid, thyroid hormones and liver function.¹⁸

Care of a patient exposed to PFAS may be considered based on the patient's overall risk factors, exposure, family history, patient signs and symptoms of illness, and physical examination. Standard medical care for the given condition should be applied based on these factors.

For asymptomatic individuals exposed to PFAS, insufficient evidence exists at this time to support deviations from established standards of medical care. Clinicians should approach additional screening or testing with caution if there is a potential to cause harm. The clinician should use clinical judgement to care for individual patients.

For patients with signs or symptoms of disease, clinicians can treat these patients using the same established standards of care they would use for a patient who did not have PFAS exposure.

¹⁷ Wikström S, Lindh CH, Shu H, Bornehag CG. Early pregnancy serum levels of perfluoroalkyl substances and risk of preeclampsia in Swedish women. *Sci Rep.* 2019 Jun 24;9(1):9179. doi: 10.1038/s41598-019-45483-7. PMID: 31235847; PMCID: PMC6591359.

¹⁸ C8 Medical Panel Guidance. http://www.c-8medicalmonitoringprogram.com/docs/med_panel_education_doc.pdf

For patients with elevated PFAS serum or urine levels or who have concerns about PFAS exposure, important components of the patient visit include identifying and reducing exposure sources and promoting standard age appropriate preventive care measures for general health and wellness (i.e., *Bright Futures*¹⁹ and *Clinical Preventive Services Guidelines*²⁰).

Patient Questions about PFAS

If your patient has concerns about PFAS exposure careful listening, authentic engagement, and practical advice are especially important for quality patient care.

We used feedback from clinicians and patients about PFAS exposure concerns to develop the following set of patient questions. We have also provided key messages and supporting facts to help you answer patient questions about PFAS.

There are high levels of PFAS in my water. What should I do?

Message for Patients	Supporting Facts
<p>If the PFAS detected in your drinking water are above the EPA’s health advisory level or your state’s regulatory limit or if you are concerned, you may consider reducing your exposure by installing filtration or by using an alternative water source for drinking, food preparation, cooking, brushing your teeth, or any other activity that might result in ingestion of water.</p>	<p>Potential adverse health risks are associated with exposure to PFAS.</p> <p>The Environmental Protection Agency (EPA) has established a health advisory level for PFOA and PFOS in drinking water at 70 parts per trillion (0.07µg/L), individually or combined.</p> <p>Some states have established their own drinking water guidance values, some of which are lower than the EPA health advisory. For state-specific guidance values, please contact your local or state health department.</p> <p>Installing a home filtration system or using a pitcher-type filter, if monitored, maintained, and used properly, can reduce PFAS levels. However, these filters may not reduce PFAS below guidance levels. Three factors determine how much PFAS are removed by filtration: 1) the PFAS contaminant levels, 2) the type of filter, and 3) how well the filter is maintained.</p> <p>Manufacturers of the filtration systems 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. Granular activated carbon</p>

¹⁹ Bright Futures: Guidelines for Health Supervision of Infants, Children and Adolescents, 4th Edition [eBook] Editors: Joseph F. Hagan, Jr, MD, FAAP, Judith S. Shaw, EdD, MPH, RN, FAAP; and Paula M. Duncan, MD, FAAP. <https://shop.aap.org/bright-futures-guidelines-for-health-supervision-of-infants-children-and-adolescents-4th-edition-1/>

²⁰ Published Recommendations. U.S. Preventive Services Task Force. <https://www.uspreventiveservicestaskforce.org/BrowseRec/Index>

Message for Patients	Supporting Facts
	<p>(GAC) filters are one type that may be used for water filtration. GAC requires proper maintenance and periodic testing for PFAS compounds.</p> <p>Ultimately, public water system level, treatment and remediation decisions are guided by the EPA. Patients can be referred to the EPA website for further details: https://www.epa.gov/sciencematters/reducing-pfas-drinking-water-treatment-technologies).</p>

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Could my health problems be caused by PFAS exposure?

Message for Patients	Supporting Facts
<p>a. The types of health problems that may be associated with PFAS are also caused by a variety of factors (lifestyle, environmental, social, genetic). It is possible that PFAS contributed to your health problems but there is no way to know if PFAS exposure has caused your illness or made it worse.</p> <p>b. Based on what we know at this time, there is no reason to think your health problem is associated with exposure to PFAS. Researchers continue to evaluate the potential health risks from PFAS exposure so more may be known in the future.</p>	<p>Information on potential health risks associated with PFAS exposure are briefly discussed in Table 1 of this document.</p> <p>Based on the health problems the patient has, there are two possible responses to this question.</p> <ul style="list-style-type: none"> a. If the patient has a health problem discussed in this document, patient message “a.” is offered for uses in answering the question. b. If the patient’s health problem is not covered in this document as a potential health risk, then there is currently little or no evidence that the health problem is related to PFAS exposure. The patient message offered for unrelated health problems is message “b.”. <p>If your patient presents with health concerns that may or may not be associated with PFAS exposure, it is appropriate to discuss the patient’s concerns and perform a thorough health and exposure history, a physical exam, and appropriate laboratory evaluation if indicated by the reported signs and symptoms and potential differential diagnosis.</p>

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Will I have future health problems because of PFAS exposure?

Message for Patients	Supporting Facts
<p>Exposure to PFAS substances has been associated with health risks, but there is no way to predict whether PFAS exposure risks will result in a future illness. We can watch for symptoms related to PFAS associated health risks and investigate, if necessary.</p> <p>If any signs or symptoms of illness do occur, we will not know if those are related to PFAS. We will however be able to provide the</p>	<p>Studies in humans and animals suggest that certain PFAS may be associated with certain health risks. However, it is not possible to determine whether a specific adverse health endpoint is the direct result of a PFAS exposure in a specific patient.</p>

Message for Patients	Supporting Facts
care you needed based on your signs and symptoms.	

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Should I get a blood test for PFAS?

Message for Patients	Supporting Facts
<p>The blood test will not provide information to predict a health problem, nor will it provide information for treatment. Test results will only tell you the levels of PFAS in your blood.</p> <p>PFAS blood test results will not indicate whether a current illness can be attributed to past or current PFAS exposure. Neither will it predict or rule out the development of future health problems related to a known or suspected PFAS exposure.</p>	<p>There is no established PFAS blood level at which a health risk is expected, nor is there a level that predicts health problems. Most people in the United States will have measurable amounts of PFAS in their blood because of wide-spread use of consumer products containing PFAS.</p> <p>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.</p> <p>The patient may be aware of blood and urine test for PFAS being taken in some study 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.</p> <p>However, serum PFAS level tests are commercially available, if the clinician decides to test the patient.</p>

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What do my PFAS blood tests results mean?

Message for Patients	Supporting Facts
<p>Most people in this country have PFAS in their blood. The blood test for PFAS only tell us the levels of specific PFAS in your body at the time you were tested.</p> <p>PFAS blood test results will not indicate whether a current illness can be attributed to current or past PFAS exposure. Neither will it predict or rule out the development of future health problems related to a known or suspected PFAS exposure.</p> <p>If you know or suspect you have been exposed to elevated levels of PFAS, the best action to take is to minimize ongoing PFAS exposure you may have from contaminated drinking water or other possible sources in your diet or home.</p>	<p>There is no established PFAS blood level at which a health risk is expected, nor is there a level that is clearly associated with past, current, or future health problems.</p> <p>The individual patient's blood concentration of PFAS can be compared to PFAS concentrations measured in the general US population as part of NHANES, or to PFAS levels identified through population studies in other PFAS-impacted communities.</p> <p>A patient's PFAS concentrations can only show if their blood levels are within or out of the ranges reported for PFAS in national or local population studies.</p>

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An adult patient asks: “Should I be tested for any of the potential health effects associated with PFAS exposure?”

Message for Patients	Supporting Facts
<p>Maintaining a healthy lifestyle that limits overall health risks is our first step for keeping you healthy. We will need to do all of the clinical preventive services that are recommended for a person your age.</p> <p>Clinical preventive services like checking for elevated cholesterol have been established for the general population. We will conduct these recommended health screenings. This will help us evaluate your current health status.</p> <p>Some of the testing for PFAS-related health concerns have risks and are not generally performed on patients showing no signs or symptoms of illness. We need to base your care on your overall risk factors, family health and environmental exposure histories, and any signs and symptoms of illness you may have. If any unusual symptoms occur, we will investigate those and treat as needed.</p>	<p>Health risks associated with PFAS are not specific to PFAS exposures. These health risks are also influenced by many other environmental, social, or genetic factors.</p> <p>Care of a patient exposed to PFAS may be determined based on the patient’s overall risk factors, family health and environmental exposure histories, patient signs and symptoms, and physical examination. The clinician should use appropriate clinical judgement to determine the uses of diagnostic tests and screenings associated with PFAS health risks.</p> <p>Any reoccurring symptoms can be investigated at the clinician’s discretion and treated based on established standards of care.</p>

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A parent asks: “Should I have my child tested for any of the potential health effects associated with PFAS exposure?”

Message for Patients	Supporting Facts
<p>Maintaining a healthy lifestyle that limits overall health risks for your child is our first step. There are recommended preventive services and screenings for children at every phase of development. These preventive services are known as <i>Bright Futures</i>. We can follow that guidance to help keep your child healthy.</p> <p>Some of the testing for PFAS-related health concerns have risks and are not generally performed on patients showing no signs or symptoms of illness.</p> <p>Following the Bright futures recommendation and conducting routine well-child visits will help us understand your child’s health status.</p> <p>We will base your child’s care on overall risk factors, family health</p>	<p>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, regardless of PFAS exposure.</p> <p>Health risks associated with PFAS are not specific to PFAS exposures. These health risks are also influenced by many other environmental, social, or genetic factors.</p> <p>Care of a patient exposed to PFAS may be determined based on the patient’s overall health risks, family and environmental exposure histories, patient signs and symptoms, and physical examination. The clinician should use clinical judgement to determine the appropriate uses of diagnostic tests and screenings associated with PFAS health risks.</p> <p>However, if your patient presents with health concerns that are associated with</p>

Message for Patients	Supporting Facts
and environmental exposure histories, and any signs and symptoms of illness that arise. If any unusual symptoms occur, we will investigate those and treat as needed.	PFAS exposures, discussing recommended screening may reassure the patient's parents that their concerns are being addressed.

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How will exposure to PFAS affect my pregnancy?

Message for Patients	Supporting Facts
<p>Some studies suggest that exposure to PFAS before pregnancy may be associated with pregnancy-induced hypertension and pre-eclampsia.</p> <p>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.</p>	<p>Health effects associated with PFAS are not specific and can be caused by many other factors.</p> <p>Pregnancy-induced hypertension occurs in many pregnancies, and the specific etiology is often unknown.</p>

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Is it safe for me to breastfeed my baby?

Message for Patients	Supporting Facts
<p>Breastfeeding is associated with numerous health benefits for infants and mothers. It is recommended that you as a nursing mother continue to breastfeed your baby. Taking steps to eliminate ongoing exposure from PFAS contaminated drinking water and other sources of PFAS contamination is appropriate, like selecting a safe drinking water source for you and your baby.</p> <p>The science on the health risks of PFAS for mothers and babies is evolving. However, given the scientific understanding at this time, the benefits of breastfeeding your baby outweigh those of not breastfeeding. More information on breastfeeding is available at https://www.cdc.gov/breastfeeding/about-breastfeeding/why-it-matters.html.</p>	<p>Extensive research has documented the broad and compelling advantages of breastfeeding for infants, mothers, families, and society.</p> <p>The AAP recommends exclusive breastfeeding for about 6 months, with continuation of breastfeeding for 1 year or longer as mutually desired by mother and infant.</p> <p>Some of the many benefits for infants include a reduced risk of ear and respiratory infections, asthma, obesity, and sudden infant death syndrome (SIDS) as well as immunologic advantages. Breastfeeding can also help lower a mother's risk of high blood pressure, type 2 diabetes, and ovarian and breast cancer.</p> <p>Even though a number of environmental pollutants readily pass to the infant through human milk, the advantages of breastfeeding continue to outweigh the potential risks.</p>

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How will exposure to PFAS affect my child's immunizations?

Message for patients	Supporting Facts
Although a few studies have reported that PFOS and PFOA might slightly lower the immune response to some immunizations, these	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

Message for patients	Supporting Facts
studies have not suggested a need to re-evaluate the normal immunization schedule.	routine childhood immunizations (rubella, tetanus, and diphtheria) among children aged 5 to 7 years. However, they did not show an association with increased rates of vaccine-preventable diseases.

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214 **Will I need to get my child vaccinated again?**

Message for patients	Supporting Facts
At this time, there is no recommendation for repeating any vaccinations.	<p>Studies have not suggested a need to re-evaluate the current immunization schedule nor use of immunize boosters for impacted children.</p> <p>Studies of PFAS exposure and immune response have not shown an association with PFAS exposure and an increased rate of vaccine-preventable diseases.</p>

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216 **I have been very worried about health risks from PFAS exposure. How can I deal with this uncertainty?**

Message for patients	Supporting Facts
<p>It's normal to worry about uncertain risks.</p> <p>I am here to listen to your concerns and will do my best to provide helpful advice.</p> <p>First, let's talk about ways to reduce ongoing exposures to PFAS.</p> <p>Second, I'd like to perform an exposure history to document your PFAS exposures in your medical record. Let's discuss PFAS-related health concerns and any changes in how you feel at your annual checkups. Please schedule your next appointment before you leave today.</p> <p>Third, when there is uncertainty about the long-term health effects of a chemical exposure we have to wait and see. This can feel nerve-racking. That said, there are steps we can take to manage stress and keep you healthy. Are you interested in talking about ways you can manage stress?</p>	<p>Listen empathetically. Acknowledge and explore the patient's concerns.</p> <p>Take an exposure history. Offer ways to reduce ongoing significant sources of current exposure to PFAS.</p> <p>Discuss PFAS concerns with patient at regular checkups.</p> <p>When a patient presents with stress or worry about PFAS exposure, review the ATSDR "Coping with stress" fact sheet with them. Prepare by reviewing ATSDR's tips for using that fact sheet.</p> <p>Check for mental health issues such as chronic or posttraumatic stress, anxiety, and depression and treat and refer accordingly.</p> <p>Review the resources section at the end of this document.</p>

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Resources and References

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.

1. **ATSDR**

PFAS Overview: <http://www.atsdr.cdc.gov/pfas/index.html>

Toxic Substance Portal (Tox FAQs): <http://www.atsdr.cdc.gov/toxfaqs/tf.asp?id=1116&tid=237>

PFAS related activities across the country: https://www.atsdr.cdc.gov/pfas/related_activities.html

Taking an Exposure History: <https://www.atsdr.cdc.gov/csem/csem.asp?csem=33&po=0>

Coping with the stress that environmental contamination can cause: <https://www.atsdr.cdc.gov/docs/factsheet/ATSDR-Stress-Fact-Sheet.pdf>

Tips on using the “Coping with stress” fact sheet: https://www.atsdr.cdc.gov/docs/factsheet/Stress_Tips_Fact_Sheet-508.pdf

2. **CDC**

PFAS Biomonitoring: https://www.cdc.gov/biomonitoring/PFAS_FactSheet.html

Breastfeeding: <https://www.cdc.gov/breastfeeding/about-breastfeeding/why-it-matters.html>

3. **C8 Panel**

C8 Science Panel: http://www.c8sciencepanel.org/prob_link.html

C8 Medical Panel: http://www.c8medicalmonitoringprogram.com/docs/med_panel_education_doc.pdf

C8 Medical Panel: http://www.c-8medicalmonitoringprogram.com/docs/med_panel_education_doc.pdf

4. **EPA**

PFAS: <https://www.epa.gov/pfas>

PFAS: <https://www.epa.gov/chemical-research/research-perfluorooctanoic-acid-pfoa-and-other-perfluorinated-chemicals-pfcs>

PFAS in water: <https://www.epa.gov/ground-water-and-drinking-water/drinking-water-health-advisories-pfoa-and-pfos>

5. **NIEHS**

PFAS: <https://www.niehs.nih.gov/health/topics/agents/pfc/index.cfm>

6. **NHLBI Lipid Screening in Children & Adolescents**

Cholesterol: <https://www.nhlbi.nih.gov/health-pro/guidelines/current/cardiovascular-health-pediatric-guidelines/full-report-chapter-9>

7. **PEHSU Pediatric Environmental Health: <http://www.pehsu.net/>**

8. **Uncertainty Recourses**

Uncertainty and Stress in the Clinical Setting. Helping Patient and Clinician Manage Uncertainty During Clinical Care:

<https://publichealth.wustl.edu/helping-patients-and-clinicians-manage-uncertainty-during-clinical-care/>

257 Navigating the Unknown: Shared Decision-Making in the Face of Uncertainty. J Gen Intern Med. 2015 May;30 (5): 675-678:
258 <http://tinyurl.com/zrd587f>
259 Uncertainty Toolbox: Principle in the Approach to Uncertainty in the Clinic Encounter. J Gen Intern Med. 2015 May; 30 (5): 675-678.
260 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4395589/>

References

- Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological profile for Perfluoroalkyls. (Draft for Public Comment). 2018. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service [updated 2019 April 8; accessed 2019 May 1]. Available from: <https://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=1117&tid=237>
- Averina M, Brox J, Huber S, Furberg AS, Sørensen M. Serum perfluoroalkyl substances (PFAS) and risk of asthma and various allergies in adolescents. The Tromsø study Fit Futures in Northern Norway. *Environ Res.* 2019 Feb;169:114-121.
- Ballesteros V, Costa O, Iniguez C, Fletcher T, Ballester F, Lopez-Espinosa MJ. Exposure to perfluoroalkyl substances and thyroid function in pregnant women and children: a systematic review of epidemiologic studies. *Environment international.* 2017 Feb 1;99:15-28.
- Braun JM. Early-life exposure to EDCs: role in childhood obesity and neurodevelopment. *Nature Reviews Endocrinology.* 2017 Mar;13(3):161.
- Center for Disease Control and Prevention (CDC). Fourth National Report on Human Exposure to Environmental Chemicals, Updated Tables, Volume One. January 2019. U.S Department of Health and Human Services [update 2017 April 14; accessed 2019 April 28]. Available from: <https://www.cdc.gov/exposurereport/index.html>
- Conway BN, Badders AN, Costacou T, Arthur JM, Innes KE. Perfluoroalkyl substances and kidney function in chronic kidney disease, anemia, and diabetes. *Diabetes, metabolic syndrome and obesity: targets and therapy.* 2018;11:707
- Domazet SL, Grøntved A, Timmermann AG, Nielsen F, Jensen TK. Longitudinal associations of exposure to perfluoro alkylated substances in childhood and adolescence and indicators of adiposity and glucose metabolism 6 and 12 years later: the European Youth Heart Study. *Diabetes Care.* 2016 Oct 1;39(10):1745-51.
- Frisbee SJ, Brooks Jr AP, Maher A, Flensburg P, Arnold S, Fletcher T, Steenland K, Shankar A, Knox SS, Pollard C, Halverson JA. The C8 health project: design, methods, and participants. *Environmental health perspectives.* 2009 Jul 13;117(12):1873-82.
- Jensen AA, Leffers H. Emerging endocrine disruptors: perfluoroalkylated substances. *International journal of andrology.* 2008 Apr;31(2):161-9.
- Kielsen K, Shamim Z, Ryder LP, Nielsen F, Grandjean P, Budtz-Jørgensen E, Heilmann C. Antibody response to booster vaccination with tetanus and diphtheria in adults exposed to perfluorinated alkylates. *J Immunotoxicol.* 2016;13(2):270-3.
- Kim S, Choi K, Ji K, Seo J, Kho Y, Park J, Kim S, Park S, Hwang I, Jeon J, Yang H. Trans-placental transfer of thirteen perfluorinated compounds and relations with fetal thyroid hormones. *Environmental science & technology.* 2011 Aug 12;45(17):7465-72.
- Landrigan PJ, Sonawane B, Mattison D, McCally M, Garg A. Chemical contaminants in breast milk and their impacts on children's health: an overview. *Environmental health perspectives.* 2002 Jun;110(6):A313-5.
- Lee YJ, Kim MK, Bae J, Yang JH. Concentrations of perfluoroalkyl compounds in maternal and umbilical cord sera and birth outcomes in Korea. *Chemosphere.* 2013 Feb 1;90(5):1603-9.
- National Toxicology Program. Monograph on Immunotoxicity Associated with Exposures to PFOA and PFOS. Sept. 2016. Research Triangle Park, NC [updated 2019 January 17; accessed 2019 May 19]. Available from: <https://ntp.niehs.nih.gov/pubhealth/hat/noms/pfoa/index.html>.
- National Institute of Environmental Health Sciences. Perfluoroalkyl and Polyfluoroalkyl Substances. March 2019. Research Triangle Park, NC [updated 2019 March; accessed 2019 July 29]. Available from: https://www.niehs.nih.gov/health/materials/perfluoroalkyl_and_polyfluoroalkyl_substances_508.pdf.
- Centers for Disease Control and Prevention (CDC). National Center for Health Statistics (NCHS). National Health and Nutrition Examination Survey Data. Hyattsville, MD: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 2014. https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/SSPFAS_H.htm. []

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- Romano ME, Xu Y, Calafat AM, Yolton K, Chen A, Webster GM, Eliot MN, Howard CR, Lanphear BP, Braun JM. Maternal serum perfluoroalkyl substances during pregnancy and duration of breastfeeding. *Environmental research*. 2016 Aug 1;149:239-46.
 - Stanifer JW, Stapleton HM, Souma T, Wittmer A, Zhao X, Boulware LE. Perfluorinated Chemicals as Emerging Environmental Threats to Kidney Health: A Scoping Review. *Clinical Journal of the American Society of Nephrology*. 2018 Oct 8;13(10):1479-92.
 - Timmermann CA, Budtz-Jørgensen E, Petersen MS, Weihe P, Steuerwald U, Nielsen F, Jensen TK, Grandjean P. Shorter duration of breastfeeding at elevated exposures to perfluoroalkyl substances. *Reproductive Toxicology*. 2017 Mar 1;68:164-70.
 - Wang J, Zeng XW, Bloom MS, Qian Z, Hinyard LJ, Belue R, Lin S, Wang SQ, Tian YP, Yang M, Chu C. Renal function and isomers of perfluorooctanoate (PFOA) and perfluorooctanesulfonate (PFOS): Isomers of C8 Health Project in China. *Chemosphere*. 2019 Mar 1;218:1042-9.
 - Woods MM, Lanphear BP, Braun JM, McCandless LC. Gestational exposure to endocrine disrupting chemicals in relation to infant birth weight: a Bayesian analysis of the HOME Study. *Environmental Health*. 2017 Dec;16(1):115.