

VIEWPOINT

Clinical Implications of New Drinking Water Regulation for “Forever Chemicals”

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In April 2024, the US Environmental Protection Agency (EPA) announced its new maximum contaminant levels for some perfluoroalkyl and polyfluoroalkyl substances (PFASs), setting safe drinking water levels for these contaminants at near zero.¹ PFASs encompass a class of thousands of synthetic chemical compounds composed of fluorinated carbon chains of varying lengths. PFASs make consumer and industrial products oil- and water-resistant, and many persist in the environment virtually indefinitely and in the human body with multiyear half-lives. The new EPA regulations for specific PFASs reflect what years of epidemiologic and basic science research have shown concerning cancer and other outcomes. This has prompted lay media attention to the dangers of the most commonly studied of these “forever chemicals” as endocrine disruptors and their link to a surprising range of long-term health effects that may share roots in immune, hepatic, cell membrane, and energy metabolism toxicity. The new EPA regulation, far below the previous drinking water health advisory of 70 parts per trillion, and recent media interest will lead many patients to question whether they have been exposed to unsafe PFAS levels. Patients will look to their clinicians for answers regarding their PFAS exposure and risk mitigation, creating a new focus on these chemicals in the clinical realm.

Nearly all of the global population has some detectable PFASs in their bodies, but certain groups are at risk of high PFAS body burden because of occupational exposure (eg, firefighters and some military

personnel) or regular ingestion of contaminated drinking water (ie, by PFAS manufacturing or use operations, including airports, military bases, wastewater treatment plants, farms where biosolids have been spread, and landfills).² Acute toxicity from PFAS exposure is understudied and likely rare, but prolonged exposure to elevated PFAS levels has been identified as a risk factor for immune and cardiometabolic dysfunction, poorer perinatal health, and cancer, with recent meta-analyses highlighting associations with decreased antibody response, dyslipidemia, decreased fetal growth, and kidney cancer. Evolving evidence links PFAS exposure to increased risk of pregnancy-induced hyperten-

sion, testicular cancer, breast cancer, thyroid disease, liver enzyme alterations, and ulcerative colitis.^{2,3} The International Agency for Research on Cancer classifies perfluorooctanoic acid as carcinogenic and perfluorooctanesulfonic acid as possibly carcinogenic to humans.⁴ A National Academies of Sciences, Engineering, and Medicine (NASEM) report called for measurement of PFAS blood levels among patients with occupational or community PFAS exposure.^{2,5} The report outlines risk stratification based on blood levels and clinical guidelines for medical monitoring of individuals with elevated serum PFAS levels.² While the biochemistry and toxicology of PFASs may be overwhelming for clinicians unfamiliar with the subject, testing, risk stratification, and medical monitoring are well within the realm of routine clinical practice across many disciplines. Furthermore, user-friendly information sheets for clinicians are available from the Agency for Toxic Substances and Disease Registry (ATSDR)³ and the federally funded academic consortium PFAS Research, Education, and Action for Community Health (PFAS-REACH).⁶ While NASEM, ATSDR, and PFAS-REACH guidelines differ slightly in their details, all 3 define a portion of the population that has been exposed to elevated PFAS levels, recommend consideration of blood testing, and deem elevated PFAS exposure as a risk for certain long-term health outcomes.

Screening for PFAS exposure can take place as part of routine physical examinations with a few questions about occupational, community, or household exposure. Blood testing can be done through commercial clinical laboratories, direct-to-consumer testing, or online toxicokinetic modeling based on drinking water exposure. Insurance coverage for blood testing is variable, generally shifting the current several-hundred-dollar cost to patients. States such as New Hampshire and Maine have passed or are considering mandates to include coverage of PFAS testing as a part of preventive care for patients at risk of exposure. By taking a brief exposure history and through shared decision-making, clinicians can work with patients to identify those at risk of high exposure who may benefit from testing.

For individuals with PFAS blood levels comparable with those of the majority of the US population, the recommendation is standard preventive care, with emphasis on screening for hyperlipidemia, breast cancer, and hypertensive disorders of pregnancy in accordance with guidelines from national organizations.² For children and adults with elevated PFAS blood levels (estimated by NASEM as the top 9% of the US population) and thus

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higher risk for PFAS-associated diseases, NASEM recommends screening for thyroid disorders and kidney cancer among adults and for hyperlipidemia, testicular cancer, and ulcerative colitis among adults and children. For pregnant patients, obstetric practitioners may consider baseline testing and prevention for hypertensive disorders of pregnancy.² PFAS-REACH also recommends consideration of monitoring liver enzymes and kidney function.⁶ Treatment for conditions that may be associated with PFAS exposure is the same as if these conditions had occurred without PFAS exposure.

The most well-studied PFASs are excreted slowly, with half-lives in the human body ranging from 3 to 8 years depending on the compound. While these “legacy” PFASs have been largely phased out of US manufacturing after EPA advocacy due to their potential health risks, manufacturers now use replacement compounds that generally have shorter half-lives and less well-developed toxicology. These newer PFASs and related byproducts/contaminants can be detected in water at substantial distances from pollution point sources. Animal models suggest that newer PFASs have potentially similar adverse health effects compared with the more well-studied PFASs, but most newer PFASs are not currently measured clinically, as some are excreted before measurement can occur, and others do not have well-developed means of clinical detection.

There are currently no approved treatments for removal of PFASs from the body. Serial phlebotomy and the drug cholestyramine

are well-established entities that have observational and clinical trial-level evidence for hastened excretion of PFASs from the body, but there are no data demonstrating the impact of these active approaches to body burden reduction on the risk of PFAS-associated health outcomes. When patients are motivated by high internal exposures to seek these treatments, a clear discussion of what is and is not known can lead to reasonable and tailored decisions. Other methods for PFAS risk reduction among patients with elevated levels include counseling on removing the source(s) of PFAS contamination (eg, installing a National Sanitation Foundation-approved water filter)⁷ and rechecking the blood to ensure that PFAS levels are decreasing as expected.² Furthermore, emerging PFAS-specific data suggest that excretion may be hastened by a healthy, high-fiber, high-folate diet and regular exercise, which may also mitigate health outcomes related to PFAS exposure.

Clinicians understand risk reduction, and environmental exposure to elevated PFAS levels is a topical issue that falls well within this world but has many unfamiliar details. PFASs are a risk factor for disease akin to other exposures that clinicians routinely discuss, such as lead or secondhand smoke, with the important difference that some PFASs are particularly persistent in the body. As the public becomes more aware of the known and emerging dangers of “forever chemicals,” clinicians can play a valuable role in operationalizing PFAS health concerns in a levelheaded, evidence-based manner that reduces risk and keeps our populations healthy.

ARTICLE INFORMATION

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