**CLINICAL VIGNETTE**

# Freshwater Fish and Kidney Cancer: Potential Environmental Risks

Nazanin Izadpanah Gunn, MD, MHA and David Gunn, MD, MFA

***Case 1***

A 45-year-old healthy male biotechnology worker presented with a "tickle" in throat and occasional mild cough. He recently completed a thorough normal annual history and physical exam with normal laboratory results. He tried empiric therapy for possible seasonal allergies. Four months later he presented with two weeks of headache after changing to a new mattress. A covering physician treated him for a working diagnosis of cervicogenic headache. He returned two weeks later with persistent cough and further evaluation revealed lung and brain metastasis from what was later diagnosed as renal cell carcinoma (RCC).

***Case 2***

A 69-year-old male accountant and avid cross-country bicyclist presented to the Emergency Department via ambulance after a bicycle accident with a motor vehicle with loss of consciousness. Trauma imaging identified an incidental renal mass that was later confirmed to be RCC. Thorough history and physical exam identified only a mood disorder and family history of colon cancer. There were no risk factors for RCC identified.

***Discussion***

Both cases were healthy males without risk factors for RCC. Both ate an entirely healthy Mediterranean diet - including fish, both exercised regularly, were not obese, had no significant medical history and no other risk factors for renal cell carcinoma. Known risk factors for RCC include smoking, obesity, hypertension, chronic kidney disease, kidney stones, diabetes or a family history of RCC or other genetic conditions such as Von Hippel-Lindau syndrome, hereditary papillary renal cell carcinoma, and Birt-Hogg-Dubé syndrome.[1] Interestingly, eating processed meat and occupational exposures including asbestos, benzene, cadmium are also associated with increased risk of RCC.[1]

As we learn more about the multiple risk factors for many types of cancers, one wonders, how much is environmental, the air, water and soil, from which comes our food. In social histories, we take note of typical work or environmental chemical exposures such as asbestos, soot, benzene, arsenic and formaldehyde, aniline dyes or semiconductor work. As we learn more about environmental exposures to specific chemicals known as PFAS (per-and-polyfluoroalkyl substances), as well as what amount and duration of exposure is associated with cancer risk, we can update our screening tools and anticipatory guidance for patients.

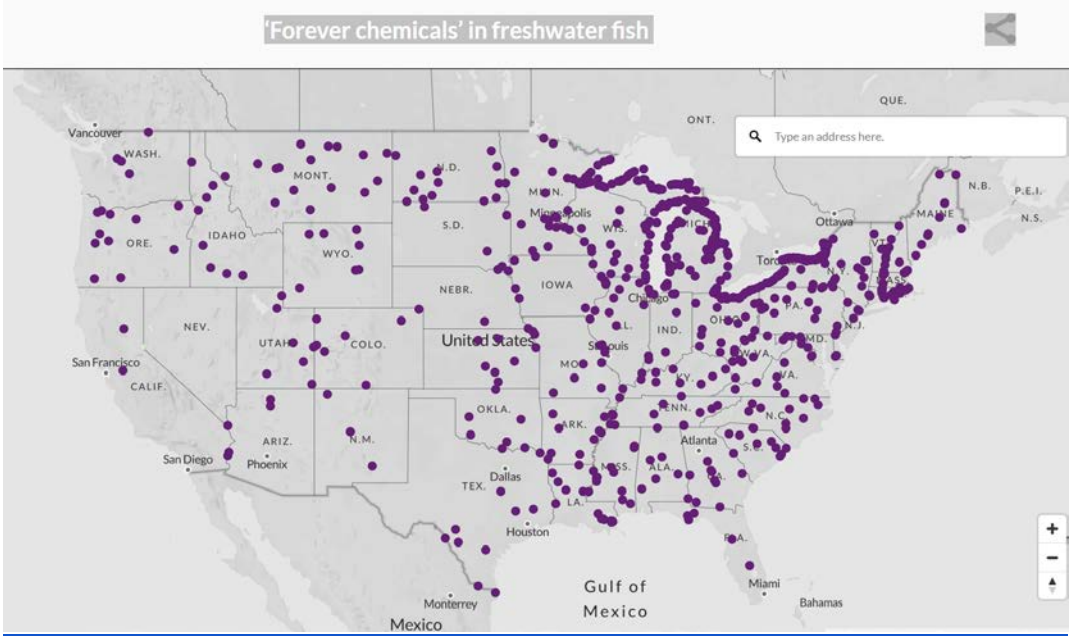
Environmental health risks are not insignificant and may be pervasive. Alcohol increases risk of breast, colon, oral, esophageal and liver cancers. Viral exposure to human papilloma virus (HPV) increases cervical cancer risk. Eating red meat (including pork) increases risk of developing colon cancer. High fructose corn syrup increased risk for metabolic syndrome: high glycemic index foods and diabetes; ultra-high processed foods and breast, endometrial, colon and prostate cancers. Other environmental exposures may be overlooked or as of yet unknown. For now, astute clinicians may consider PFAS exposure through freshwater fish may increase risk of RCC and testicular cancers.[2,3]

PFAS are industrial chemicals that are now found everywhere, including geographic areas not using PFAS.[4] This chemical was first developed by 3M and Dupont in the 1940's.[5] Use has expanded to many industries. Although initially thought to be inert and safe, there was some suggestion of suppression of potentially harmful long-term accumulation. The consequences are now impossible to ignore[4]. This chemical class breaks down at a very slow rate, and are expensive to remove from the environment. Over 5,000 different chemicals in this class are referred to as "forever chemicals." The most common are perfluorooctanoic acid and its salts (PFOA), perfluorooctane sulfonic acid and its salts (PFOS), hexafluoropropylene oxide dimer acid (GenX), perfluorononanoic acid (PFNA), and perfluorohexane sulfonic acid (PFHxS).[6]

3M and DuPont originally developed and produced PFAS in the 1940s, as resistant to heat, water, oil and stains.[2,5] They are found at highest levels in foods, particularly animals that eat other animals, including fish.[2,4] Their harms are thought to be largely due to our ingestion of foods which have accumulated PFAS over time.[2,4,7] They are also found ubiquitously in food packaging, non-stick pans, stain resistant clothes and textiles, lubricants, electronic components and firefighting foams that dissipate into the environment.

What are some PFAS risk mitigating measures? An organization, Environmental Working Group (EWG), has been addressing this area since 1993. Their website presents data from the EPA, and other sources. The map below identifies locations where fish contaminated with PFAS were found.[8]

Their website also includes of other important environmental risks and what individuals can do.




The measurement of PFAS levels in the blood is currently the most commonly used clinical method to determine exposure to these substances.[9] Blood tests provide a snapshot exposure to PFAS at the time the sample was taken and can be used as a baseline measurement for future comparisons.

Labs can be ordered associated with ICD-10 code Z13.88, encounter for screening for disorder due to exposure to contaminants. The test is commonly referred to as "PFAS (Per- and Polyfluoroalkyl Substances) Profile" or "PFAS Chemicals Profile" at LabCorps. At Quest Diagnostics, the test is commonly referred to as "PFAS (Per- and Polyfluoroalkyl Substances) Testing" or "PFAS Panel".

While blood tests are the most commonly used diagnostic tool, they are not always the most reliable indicator of PFAS exposure and provide limited exposure history. Blood tests may be influenced by recent exposure, diet, and other factors affecting the blood levels of PFAS. These tests allow comparing individual to population levels pending improved reference levels.[9]

In conclusion, PFAS are a recently identified risk factor for certain types of cancer, including RCC and testicular cancers. Eating foods in which these chemicals concentrate is one of the leading sources of exposure. Other sources include drinking water, food packaging, clothes and other consumer goods. Similar to women who were exposed to DES, we may need to assess the down-stream effects to individuals who regularly eat freshwater fish. Current research is needed to clarify who is most at risk, and what mitigation, testing and surveillance should be done. The corporations responsible for creating these compounds have created web pages announcing their ambitions to eventually reduce the amount of these chemicals currently discharged into local water supplies.[10,11]

**REFERENCES**


1. **Atkins MB, Bakouny Z, and Choueiri TK**. Epidemiology, pathology and pathogenesis of renal cell carcinoma. Post TW, ed. *UpToDate*. Waltham, MA: UpToDate Inc. http://www.uptodate.com (Accessed on December 29, 2022.)
2. Agency for Toxic Substances and Disease Registry. Potential health effects of PFAS chemicals. [Internet] Available at: https://www.atsdr.cdc.gov/pfas/health-effects/index.html. Accessed 12/29/22.
3. **Nicole W**. PFOA and cancer in a highly exposed community: new findings from the C8 science panel. *Environ Health Perspect.* 2013 Nov-Dec;121(11-12):A340. doi: 10.1289/ehp.121-A340. PMID: 24284021; PMCID: PMC3855507.
4. **Barbo N, Stoiber T, Naidenko OV, Andrews DQ**. Locally caught freshwater fish across the United States are likely a significant source of exposure to PFOS and other perfluorinated compounds. *Environ Res*. 2023 Mar 1;220:115165. doi: 10.1016/j.envres.2022.115165. Epub 2022 Dec 28. PMID: 36584847.
5. Water Finance and Management. A Legal History of PFAS. [Internet] Available at: https://waterfm.com/a-legal-history-of-pfas/. Accessed 2/4/23.
6. United States Environmental Protection Agency. Drinking Water Health Advisories (HAs). [Internet] Available at:

https://www.epa.gov/sdwa/drinking-water-health-advisories-has. Accessed 2/4/23.
7. United States Environmental Protection Agency. [Internet] Available at: https://www.epa.gov/pfas. Accessed 2/4/23.
8. Environmental Working Group. “Forever chemicals” in freshwater fish. [Internet] Available at: https://www.ewg.org/interactive-maps/pfas_in_US_fish/map/. Accessed 2/5/23.
9. Washington State Department of Health. PFAS. [Internet] Available at: https://doh.wa.gov/community-and-environment/contaminants/pfas. Accessed 2/5/23.
10. 3M Corporation PFAS Media Page. [Internet] Available at: https://pfas.3m.com/our-environmental-goals. Accessed 2/5/23.
11. Dupont Corporation PFAS Media Page. [Internet] Available at: https://www.dupont.com/pfas/milestones.html. Accessed 2/5/23.