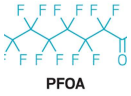
PFAS Exposure and Risk of Cancer

In 2017, the International Agency for Research on Cancer (IARC) classified perfluorooctanoic acid (PFOA), the most well-studied per- and polyfluoroalkyl substance (PFAS), as a possible human carcinogen based in part on limited epidemiologic evidence of associations with cancers of the kidney and testis in heavily exposed subjects. To address the gaps in our understanding of the carcinogenicity of PFAS, DCEG has launched a series of studies aimed at identifying specific cancers associated with PFAS at exposure levels typically found in the general population. These studies are innovative for their direct assessment of exposure to PFOA and other PFAS in banked serum specimens as well as their evaluation of risks at exposure levels comparable to that found in the general population or among military personnel. As such, these investigations have the potential to inform future evaluations of the carcinogenicity of PFOA and to extend our understanding to other PFAS that have not yet been evaluated.

For more information, contact Dr. Debra Silverman, Branch Director of the Occupational and Environmental Epidemiology Branch and chair of the NCI Working Group on PFAS. The Working group initiates, coordinates, and provides guidance to DCEG research with emphasis on overcoming challenges to the research and initiating studies to address gaps in the science.

Kidney Cancer

Serum PFAS Concentrations and Risk of Kidney Cancer



Perfluorooctanoic Acid (PFOA) Associated with Increased Risk of Kidney Cancer

Jonathan Hofmann and collaborators evaluate serum levels of perfluorooctanoic acid (PFOA) in a prospective population-based U.S. cohort.

Higher kidney cancer incidence and mortality have been observed among individuals with high PFOA exposures from employment in a PFAS-producing chemical plant or residence in the surrounding community with contaminated drinking water. However, prospective studies have not assessed the relationship between PFOA and kidney cancer risk at levels of exposure comparable to those seen in the general population, and associations between other PFAS and risk of kidney cancer have not been evaluated. To address these questions, DCEG investigators conducted a nested case-control study investigating the risk of renal cell carcinoma (RCC, the most common form of kidney cancer) in relation to concentrations of PFOA and seven other PFAS measured in banked serum specimens within the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial, a large U.S. population-based cohort. The investigation included 324 RCC cases diagnosed an average of 8.8 years after phlebotomy (range 2-18 years) and 324 individually matched controls. Findings indicated an increased risk associated with increasing PFOA exposure (Shearer et al, *JNCI,* 2020*).* These results add to the weight of evidence that PFOA is a renal carcinogen and demonstrate for the first time that exposures comparable to those observed in the general population are associated with kidney cancer development.

For more information, contact Dr. Jonathan Hofmann.

Testicular Cancer

An Investigation of Serum PFAS Levels and Testicular Cancer Risk Within the Department of Defense Serum Repository

PFAS Linked with Testicular Cancer Risk in U.S. Air Force Servicemen

Dr. Mark Purdue and colleagues report a link between serum PFOS levels and testicular cancer.

Military sites with a history of using firefighting foams have been identified as a major source of PFAS water contamination for several communities. However, the level of exposure to PFAS experienced by military personnel is unclear. Limited evidence suggests that PFOA is associated with increased risk of testicular cancer; however, past epidemiologic studies were limited by the use of indirect exposure estimates and small sample sizes and did not assess exposure to other PFAS. To clarify this relationship, NCI is conducting a case-control study of serum PFAS levels and testicular cancer risk nested within the Department of Defense Serum Repository (DoDSR). PFAS levels will be determined for the earliest and latest (two or more years prior to diagnosis) banked serum samples stored in DoDSR from 800 Air Force servicemen who later developed testicular cancer on active duty and 800 Air Force cancer-free controls.

For more information, contact Dr. Mark Purdue.

Ovarian and Endometrial Cancer

A Nested Case-Control Study of Serum PFAS Concentrations and Ovarian and Endometrial Cancers in the PLCO Cancer Screening Trial

This is the first study to directly assess personal exposure to PFAS through serologic testing in samples collected prior to diagnosis of ovarian and endometrial cancers. Utilizing a nested case-control design in PLCO, the NCI will evaluate serum samples collected after menopause from 318 ovarian cancer cases, 430 endometrial cancer cases, and a shared control group of 589 cancer-free women.

For more information, contact Dr. Rena Jones.

Prostate Cancer

Nested Case-Control Study of Serum PFAS Concentrations and Risk of Prostate Cancer in the PLCO Cancer Screening Trial

Evidence from occupational and community-based studies suggests that elevated levels of PFOA and other perfluorinated chemicals may be associated with increased risk of prostate cancer incidence and mortality. However, evidence is limited and not entirely consistent. Firefighters, who have elevated PFOA levels from occupational exposure to firefighting foam, have an increased prostate cancer risk compared to the general population. DCEG is conducting a nested case-control study within PLCO to evaluate pre-diagnostic serum levels of PFAS and the risk of aggressive prostate cancer (750 cases and 750 cancer-free controls) As many men diagnosed with prostate cancer are unlikely to die from their disease, especially when detected through PSA screening, the focus of this study is risk of aggressive prostate cancer.

For more information, contact Dr. Mark Purdue or Dr. Sonja Berndt.

Non-Hodgkin Lymphoma and Thyroid Cancer

Serum PFAS Levels and Risks of Non-Hodgkin Lymphoma and Thyroid Cancer

The goal of this study is to investigate whether elevated pre-diagnostic serum concentrations of selected PFAS are associated with increased risks of non-Hodgkin lymphoma (NHL) and thyroid cancer. To address these aims, DCEG is conducting a case-control study within PLCO, including incident pathologically confirmed cases of NHL and thyroid cancer (N = 845 and 188, respectively) and a shared control group (N=979).

For more information, contact Dr. Mark Purdue.

Thyroid Cancer and Childhood Leukemia

PFAS in the Finnish Maternity Cohort: Nested Case-Control studies of Childhood Leukemia and Thyroid Cancer in Mothers

DCEG is evaluating PFAS in the Finnish Maternity Cohort (FMC) in two nested case-control studies of: (I) prenatal serum levels and acute lymphoblastic leukemia (ALL) risk in children and (II) pre-diagnostic serum levels and papillary thyroid cancer in mothers. Participants are identified by linking FMC participants to the nationwide Finnish Cancer Registry among mothers with available sera. Cases and controls are sampled from primiparous mothers with no history of cancer at the time of first birth, having a full-term (37-42 week) singleton live birth without Down syndrome. The study includes 400 cases of ALL (children <15 years) and 400 cases of thyroid cancer among the mothers, utilizing frequency matching and a shared control group. This study will contribute to the limited literature describing the association between PFAS and childhood leukemia and thyroid cancer in women.

For more information, contact Dr. Rena Jones or Dr. Mary Ward.

Drinking Water Exposure Assessment in the California Teachers Study (CTS)

The focus of this work is to determine whether a PFAS drinking water exposure assessment is feasible in a California study population and to establish a framework for future studies of PFAS (and other water contaminants). The CTS is a prospective cohort of 133,479 female members of the California State Teachers Retirement System enrolled in 1995; as of 2015, the number of cancers for key sites of interest included NHL=881; thyroid=455; and kidney=318. Drinking water source information was not previously collected, so NCI developed questions relating to drinking water source, treatment, and intake; frequency of bathing/showering; and duration at the residence for a CTS follow-up questionnaire implemented in 2018-2019. Public drinking water utility boundaries have been collated by the California Department of Public Health—these are passively collected data and lack some historical details, but they provide a potential means to assign people to a public drinking water source based on their residence location. Because no historical PFAS measurements in drinking water are available, DCEG has initiated efforts to evaluate whether serum PFAS levels can be predicted by questionnaire- and GIS-based information about CTS participants, their public water supply, and local environmental characteristics/point sources.

For more information, contact Dr. Rena Jones or Dr. Mary Ward.
