PFAS: our legacy and our future

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PFAS Exposure

Sunderland et al., J Expos Sci & Epidemiol, 2019
A Multi-System Toxicant

- Thyroid
- Immune
- Liver
- Pancreas
- Kidney
- Cancer
- Reproductive Organs
- Neuro-development

Modified from ATSDR, 2018
PFAS Contamination in the U.S.

More than 1,500 drinking water systems serving up to 110 million Americans may be contaminated.
National Institute of Environmental Health Sciences (NIEHS)

- One of 27 Institutes and Centers at the National Institutes of Health
- Wide variety of programs:
  - Intramural Laboratories
  - Extramural funding programs
  - Disease Prevention
  - Clinical Research Program
  - National Toxicology Program
  - Public Health Focus
PFAS: What is NIEHS Doing?

Office of the Director (OD)
Program coordination, Federal and international collaborations, Informing decision makers

Division of Intramural Research (DIR)
Epidemiology research

Division of Extramural Research & Training (DERT)
Grants program, SRP

Division of the National Toxicology Program (DNTP)
Toxicology research, Systematic review, Hypothesis-driven
DERT PFAS Funding

Fiscal Year

Funding (in millions)

2013 2014 2015 2016 2017 2018
NIEHS PFAS Grants Portfolio

Funded using various NIH grant mechanisms:
- Investigator-initiated basic research
- Time-sensitive awards
- SBIR grants
- NIEHS/EPA Children’s Environmental Health and Disease Prevention Research Centers
- Breast Cancer and the Environment Research Centers
- Superfund Research Centers
- Conference Support
- Environmental influences on Child Health Outcomes (ECHO) Program Awards

44 currently funded research grants

- 73% Epi / Human
- 15% Animal / Basic
- 12% Environmental Systems
NIEHS-Funded Extramural Researchers Study:

**Exposures**
- PFCs
- PFOA
- PFOS
- PFNA
- PFBS
- GenX
- PFHxS
- PFUnDA
- PFDoA
- PFOSA
- Et-PFOSA-AcOH
- Me-PFOSA-AcOH

**Health outcomes**
- Toxicity, underlying molecular mechanisms
- Immune response
- Thyroid dysfunction
- Neurological/behavior
- Birth outcomes
- Cancer
- Metabolic impact
- Cardiovascular disease
- Reproduction and Fertility
- Liver & kidney function
NIEHS Time-Sensitive Research and PFAS
PFAS Assessment of Water and Resident Exposure

- NIEHS-funded researchers launched a cross-sectional and longitudinal study of residents in Fountain, Security, and Widefield, CO (n=220)
  - Total PFASs in untreated well water ranged from 18 – 2300 ppt (ng/L)
- PFASs detected are typical of fire-fighting foam-impacted groundwater

### Chemical in Blood Sample

<table>
<thead>
<tr>
<th>Chemical in Blood Sample</th>
<th>Local Med. (ng/ml)</th>
<th>US Ref. Med. (ng/ml)</th>
<th>% Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFHxS</td>
<td>14.8</td>
<td>1.4</td>
<td>+ 1,000%</td>
</tr>
<tr>
<td>PFOS</td>
<td>9.7</td>
<td>5.2</td>
<td>+ 80%</td>
</tr>
<tr>
<td>PFOA</td>
<td>3.0</td>
<td>2.1</td>
<td>+ 43%</td>
</tr>
<tr>
<td>PFNA</td>
<td>0.4</td>
<td>0.7</td>
<td>- 43%</td>
</tr>
</tbody>
</table>
NIEHS Time-Sensitive Research and PFAS
The GenX Exposure Study

• In early 2017, GenX was detected in the Cape Fear River in North Carolina

• NIEHS-funded researchers launched a community-based study of Lower Cape Fear River area residents served by public utility water
  - **Enrolled:** 345 residents, ages 6+, men and non-pregnant women
  - **Measuring:** GenX in drinking water, blood, urine

Preliminary blood findings
• GenX not detectable in blood 6 months after GenX removed from water supply
• Four new PFAS byproducts identified in the blood of most residents
  • Nafion byproduct2, Hydro-EVE, PFO5DoDA, PFO4DA
• Levels of the new PFAS dropped substantially in 6 months
• Legacy PFAS levels were similar to 1999 US levels, ~ 4 times 2015 levels.
Highlights: Removing PFAS from Drinking Water

• Stephen Boyd, Michigan State University
  – Developing energy efficient nanoreactors capable of breaking C-F bond at low energy irradiation
  – Reported complete defluorination of PFOA and PFOS using hydrated electrons (Tian et al., Sci Rep, 2016)

• Tim Phillips, Texas A&M University
  – Developing reusable sorbents for removing PFAS from solution
  – Reported removal and recovery of 5 target long- and short-chain PFAS (Huang et al., ACS Omega, 2018)

• Gokhan Barin, CycloPure, Inc.
  – Developing novel high-affinity cyclodextrin polymer adsorbents to capture thousands of contaminants, including PFOA and PFOS
Highlights: PFAS Remediation

• Raymond Ball, EnChem Engineering, Inc., R43ES028649
  – Developing an innovative combined in-situ / ex-situ technology to cost-effectively expedite removal of PFAS from soil and groundwater
  – Highly contaminated FTA soils (700 ug/kg Total PFAS) remediated with total PFAS at 97% removal with extracted water down to 70 ppt for 5 of the 6 UCMR PFAS

• Joseph Miller, Lynntech, Inc., R43ES030250
  – Concept: In-situ and ex-situ groundwater purification of contaminants without need for frequent sorbent replenishment and disposal
  – Goal: Less than 70 ppt of PFOA/PFOS in the purified effluent

• David Dumas, Amuratek, Inc., R43ES030678
  – Developing novel custom-designed adsorbents that can be used as passive and easily regenerated sponges. Technology will bind a spectrum of PFAS under a range of environmental conditions
PFAS Levels Associated with Altered Kidney and Thyroid Function

- Repeated measures of serum PFOS associated with increased thyroid stimulating hormone
- Repeated measures of serum PFNA, PFHxS, and PFDeA associated with decreased kidney function
- PFHxS retained high stability between serum measurements over a period greater than 10 years

Blake et al., Environ Pollut, 2018
PFAS Guideline Toxicity Studies

• 28-Day Toxicity Studies: Comparison of Seven PFAS
  – The shorter chained PFASs (perfluorohexanoic acid (PFHxA) and perfluorobutane sulfonic acid (PFBS)) induced similar toxicities as the longer chained analogues,
  – Shorter chained chemicals required higher doses.
  – There were similar effects within the liver and thyroid hormones that occurred for short-chain and long-chain PFAS.

• PFOA Two Year: Comparison of PFOA perinatal and non-perinatal effects
  – Technical Report draft (TR-598) to be reported for peer review soon
2016 NTP Systematic Review Monograph On Immunotoxicity

Translational Toxicology Pipeline

Define Hypotheses & Design a Testing Strategy

Fit for purpose products

Inform Public Health Decisions

Data Mining

In Silico Profiling

Bioactivity Screening

In vitro Studies

Longer-term in vivo Tests

Short-term in vivo Tests

On-going comparisons of PFOA and GenX (HFPO-DA) in mice

REACT PFAS and other on-going screens and targeted tests in vitro

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Informing Decision Making

- **Sept. 26, 2018:** Hearing of the Senate Subcommittee on Federal Spending Oversight and Emergency Management

- **March 28, 2019:** Hearing of the Senate Committee on Environment and Public Works

- **April 25, 2019:** Sen Borrasso (R-WY) Staff Briefing
GenX, (HFPO-DA) Inhibits Efflux Transporters at the Blood-Brain Barrier

Aim: investigate the effect of GenX on three important ABC transporters at the BBB in male and female rats.

Study Design and Methods
1. Ex vivo treated brain capillaries (0.1-1000nM)
2. Dosed in vivo (oral gavage 30-3000 pM/kg)
3. In vitro treated human cells (1-1000nM)

GenX, (HFPO-DA) Inhibits Efflux Transporters at the Blood-Brain Barrier

Birnbaum lab, 2019

National Institutes of Health • U.S. Department of Health and Human Services
Events that have shifted our environmental health paradigm

DDT and Persistent Pesticides  
Sept. 27, 1962

Chernobyl Nuclear Plant  
Pripyat, Ukraine.  
April 26, 1986

Bopal India  
December 2, 1984  
4,000 deaths from Isocyanate.

Libby, Montana  
Vermiculite (Asbestos)  
November, 1999
Will PFAS shift our approach to emerging chemicals?

Parkersburg, WV; Fayetteville, NC; Military Bases...
Key Research Questions

• **Total organic fluorine analysis** – Are we measuring 90% or 10% of PFAS present in a sample?

• **Essentiality** – Where are chemicals really needed and where can we replace with safer alternatives? (Cousins et al. 2019)

• **Assessing alternatives** – Are our substitutes safer?

• **PFAS as a class** – One chemical group or subclasses?
Addressing Hazards to Organo-halogen Flame Retardants as a Class

• The National Academy of Sciences, Engineering, and Medicine (NASEM) recently addressed this question in a report to the Consumer Product Safety Commission (CPSC – 7/24/2019).

• NASEM strongly endorsed the use of subclasses of organohalogens in hazard assessment along with the use of alternative toxicological approaches.

• “….an approach that uses subclasses to assess the chemicals is scientifically justifiable…” [NASEM]
Thank you!

NIEHS Strategic Plan Website
http://www.niehs.nih.gov/strategicplan