CHE call on PFASs
1 May 2018

A brief discussion of some recent epidemiologic studies of PFAS
Dr. Tom Webster
Dept of Environmental Health
BU School of Public Health
Some things to note about PFAS

• large & complicated class of compounds
• moving target (changing regulations & production -> shorter chain or altered structures)
• occur as mixtures
• structurally related to fatty acids—one of the reasons researchers are interested in metabolic effects (e.g., obesity, diabetes, cholesterol, etc.)
Human serum levels

- widely found in human serum
- North America ~ Europe
- men > women
- **time trends of 4 PFAS currently measured in US serum by CDC (NHANES)**

- **PFAS in whole blood can differ from serum**
- **unidentified organofluorine compounds in human blood**

Quantifiable PFAS accounted for 31-100% of total extractable organic fluorine, with a trend towards more unidentified compounds (German & Chinese samples) (Yeung & Mabury 2016)
Exposure

- exposure usually measured using samples of serum or plasma
- levels in blood reflect exposure to those compounds & precursors
- for most people, exposure is estimated to be predominantly via diet followed by indoor exposure with water small (e.g., Gebbink et al 2015). Needs follow-up
- for some populations, water is a dominant source of exposure
Explosion of human epidemiologic research published since we gave the last CHE call Dec 2016

~ 40 published PFAS epidemiology papers since then!
  • metabolic effects (obesity, lipids, diabetes related, etc.),
  • birth outcomes
  • neurodevelopmental
  • immune system
  • other (thyroid hormones, reproductive, etc.)

I will briefly discuss today some of these new studies, particularly PFAS & Project Viva. I am not providing a full literature review, e.g., evaluating these new studies in comparison to previous literature.
Some important things to know about environmental epidemiology

• Epidemiology and animal toxicology are complementary—they tell us different facets of the story
• Hard & expensive!
• A good epidemiology paper discusses strengths & weaknesses of the study (nothing is perfect).
• The proper design of studies and methods to mitigate potential weaknesses is a major part of the work
• Environmental epidemiologists rarely if ever rely on a single study. Evidence can be inconsistent. It typically takes a substantial body of studies to come to scientific conclusions (which should not preclude policy!)
Some important things to know about environmental epidemiology

- **cross-sectional study**: measure exposure and outcome at the same time
- **follow-up study**: measure exposure at beginning and follow-up to determine who develops the outcome
What we’re trying to determine

PFAS exposure → health outcome

does PFAS cause this outcome in people at these doses?

A few of the things to worry about (among many!)

PFAS exposure → health outcome

Is the outcome changing the blood level of PFAS? (reverse causation) (cross-sectional studies)

PFAS exposure ← health outcome

Is something else related to PFAS exposure & outcome affecting the observed association? (confounding)

* e.g., SES, behavioral, physiology…
PFAS and Project Viva

• about 1000 mother-child pairs from Boston area (numbers depend on particular study)
• recruited during pregnancy 1999-2002, ~ peak serum levels for most PFAS typically measured in USA
• PFAS measured in mother’s plasma from early in pregnancy and in children ~8 yrs old
• primary focus on PFOS, PFOA, PFNA, PFHxS (depending on study)
• follow over time: examining birth outcomes and child health
• large, well designed study
PFAS and Project Viva: Results

Preterm and birth weight (Sagiv et al 2018)
- prenatal PFAS: increased risk of preterm birth
- also decreased birth weight (after adjusting for gestational age)
- NOT confounded by maternal physiology (e.g., kidney function)

Thyroid hormone disruption (Preston et al 2018)
- prenatal PFAS: decreased free T4 (a main thyroid hormone) in moms (cross-sectional)
- also decreased T4 in male infants

Obesity-related outcomes in children (Mora et al 2017)
- prenatal PFAS: small increases in girls, not boys (e.g, BMI, waist circumference, skinfold thickness, DXA)
- outcomes not related to childhood PFAS levels
PFAS and Project Viva: Results

Metabolic function in children (Fleisch et al 2017)
• studied markers related to insulin resistance (e.g., HOMA-IR), etc.
• no evidence for adverse effect with PFAS
• indeed children with higher PFAS had lower (better) HOMA-IR in girls, no effect in boys (cross-sectional)
• some toxicology data suggest mechanisms that may work in opposite directions; possibility of reverse causation

Blood lipid/cholesterol levels in children (Mora et al 2018)
• prenatal PFAS: improved blood lipid profile in girls, no effect in boys (e.g., “good” and “bad” cholesterol)
• childhood PFAS: increased “good” and “bad” cholesterol; possibility of reverse causation
PFAS and Project Viva: Results

Neurodevelopmental outcomes (Harris et al 2018)
• published only last week!
• cognitive testing in early childhood (median age 3.2) & mid-childhood (median age 7.7)
• some evidence for decreased visual motor ability
• other results in the study were inconsistent, sometimes associated with better cognitive outcomes
PFAS and the Diabetes Prevention Program Trial

- study of prevention of type 2 diabetes among high-risk people: lifestyle or drug intervention or placebo (PFAS study added later)
- PFAS measured in plasma of 957 people at baseline (1996-1999)
- follow-up 2 - 5 yr

PFAS & diabetes (Cardenas et al 2018)
- at baseline, small associations between PFAS & markers of insulin resistance etc. (cross-sectional)
- no strong evidence of association between PFAS & diabetes incidence (some evidence for branched PFOA) or prospective changes in glycemia indicators

Stay tuned: something interesting currently in review
Conclusions

Of the outcomes I discussed today, I think birth weight is the best established by the existing literature (e.g., this study and others on birth weight)

If real, some interesting differences in effects on boys and girls

Lots more, high quality epidemiology under way. We will know more reasonably soon

Environmental epidemiologists rarely if ever rely on a single study. Evidence is often inconsistent. It typically takes a substantial body of studies to come to scientific conclusions (which should not preclude policy!). I did not present a full literature review today.

Thanks to NIEHS for funding this kind of research
References

Project Viva

DPP