

Lasting Impacts of PFAS from Childhood Exposures



Sue Fenton, PhD MS

Director, Center for Human Health and the Environment

Professor, Biological Sciences

NC State University

sefenton@ncsu.edu

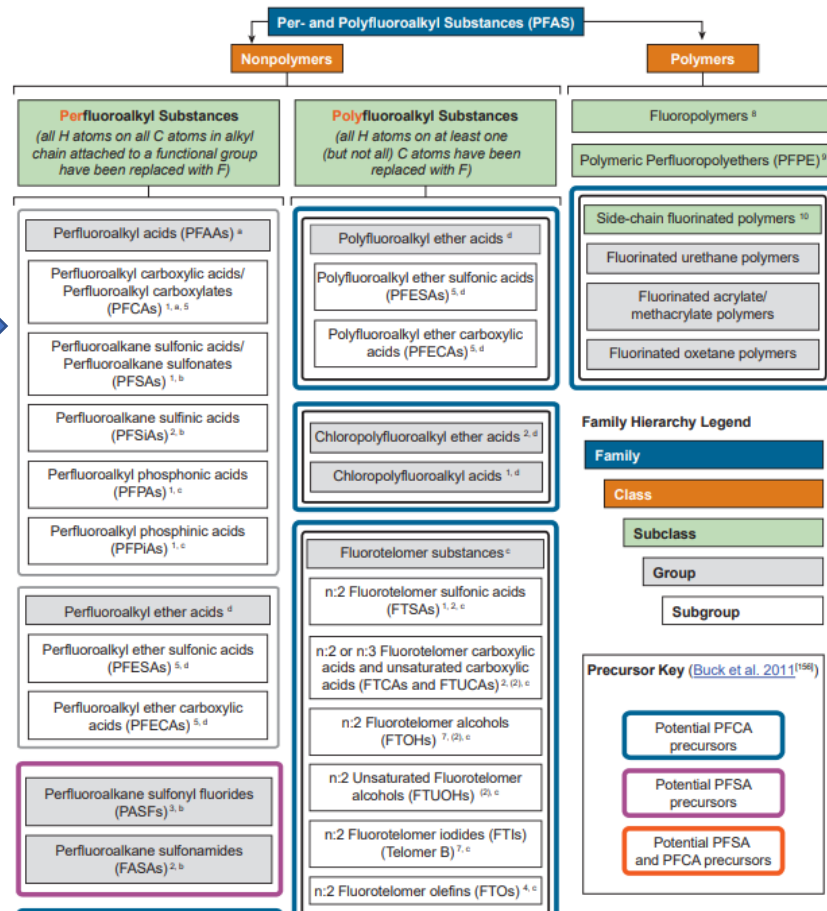


Disclosures

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- I have no financial or personal conflicts of interest to report.

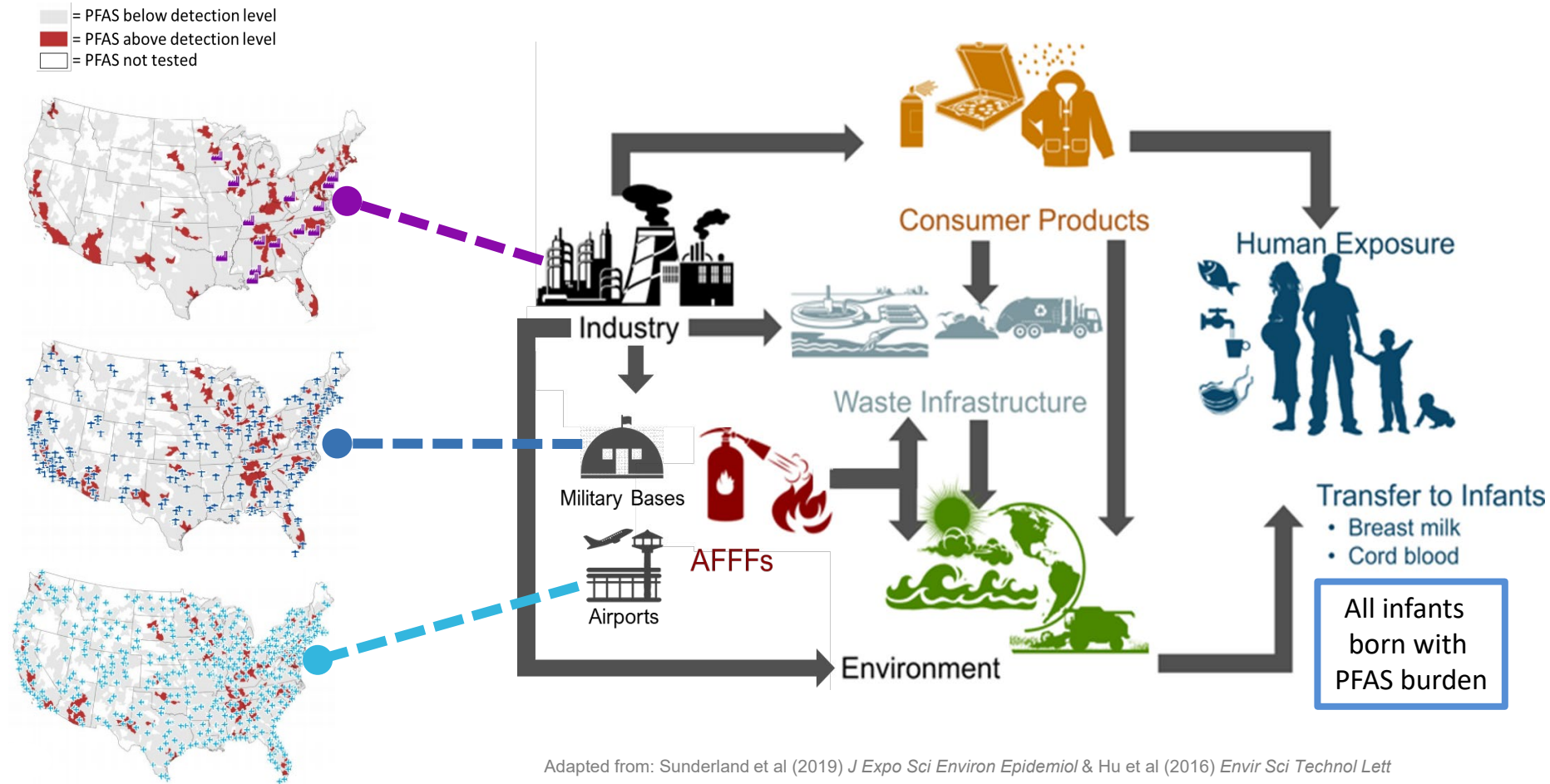
PRESENT PFAS Family Tree

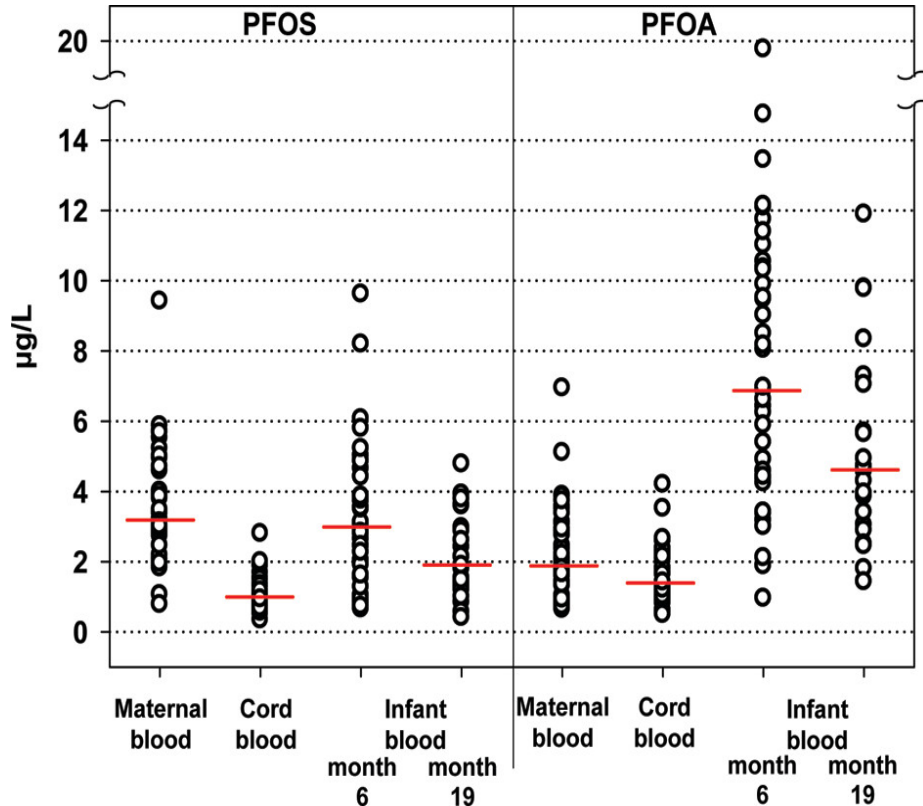
- Thousands of PFAS and PFAS precursors have been identified, depending on the definition
- As legacy PFAS are phased out, replacement species are being developed



Current Drinking Water PFAS Rule

- The U.S. Environmental Protection Agency enforces the strict limit of 4.0 parts per trillion for PFOA and PFOS in drinking water, but has proposed extending compliance deadlines and rescinding rules for four other chemicals (GenX, PFNA, PFHxS and Hazard Index Mixture)
- MCLs determined based on IARC carcinogenicity calls – 4ppt is lowest measurable level, currently
- <https://www.epa.gov/sdwa/and-polyfluoroalkyl-substances-pfas>





PFAS transfer from mother to newborn via blood and milk

- Concentrations of PFOS and PFOA in the blood of mothers at delivery, cord blood, and infants (only values above limits of quantitation (LOQ) are shown; lines represent median values).
- Fromme et al 2010. *Environ. Sci. Technol.* 2010, 44, 18, 7123-7129
- PFOA data in mice (blood and milk)
Fenton et al., *Repro Toxicol* 2009

In utero PFAS exposure sets the stage for a lifetime of increased disease susceptibility

Transplacental and
breastmilk transfer
Hypertensive disorders
of pregnancy
Adverse birth outcomes
Shortened Lactation

Elevated cholesterol/triglycerides
Reduced kidney function
Thyroid hormone disruption

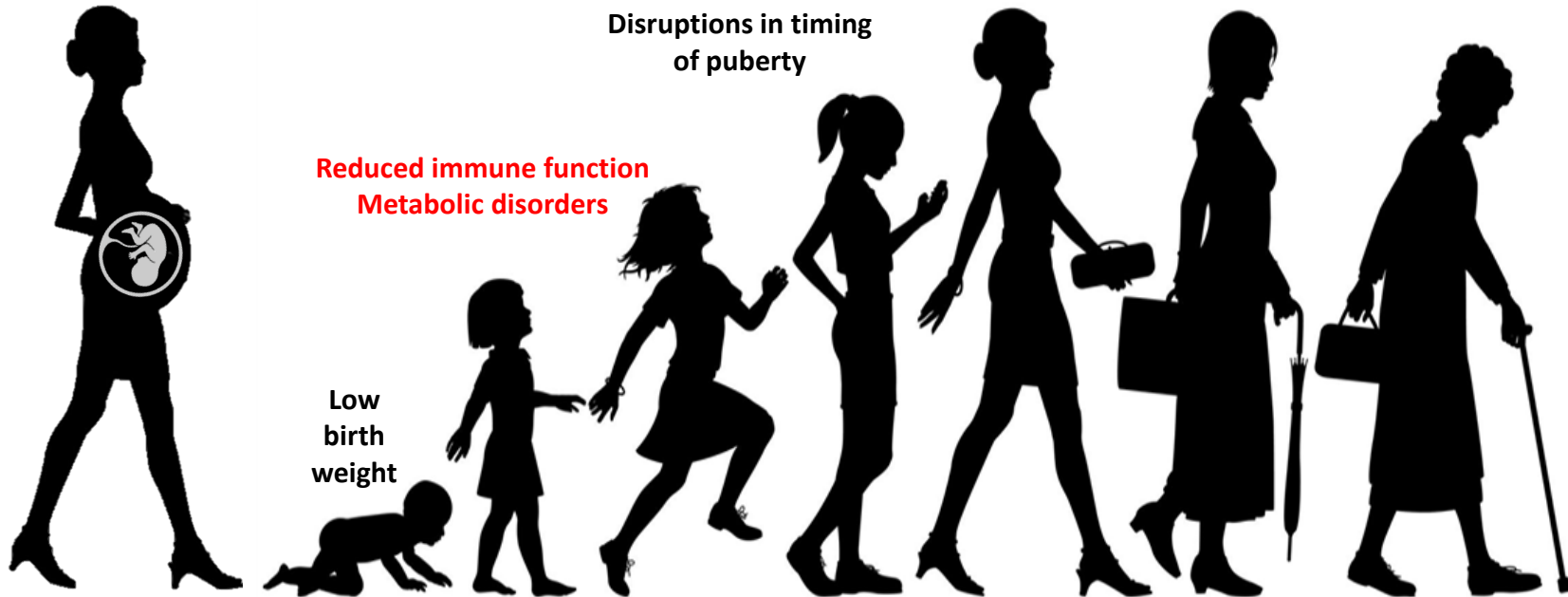
Menstrual Issues
Reduced fertility
Metabolic outcomes

Cancer
Modify Chemotherapy Outcomes

Disruptions in timing
of puberty

Reduced immune function
Metabolic disorders

Low
birth
weight



PFAS and Birth Weight

1880 articles

PFOS

N=829

PFOA

N=570

PFHxS

N=102

PFNA

N=167

PFDA

N=212



Duplicate removal

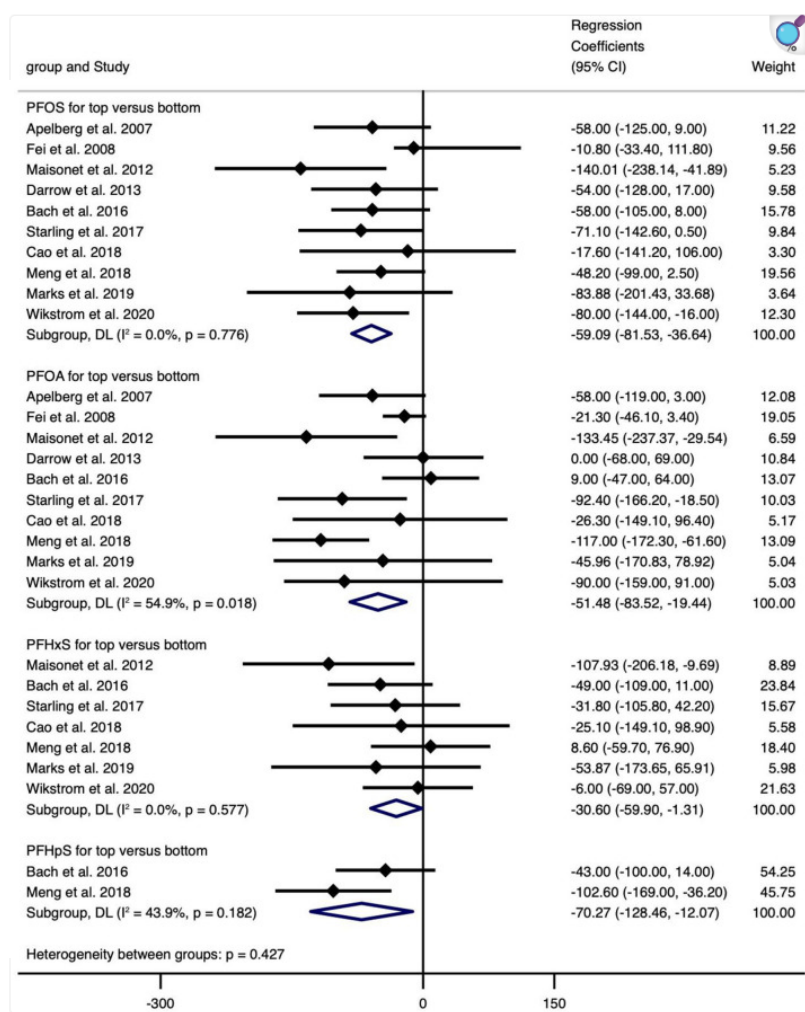
513 articles



Removal of ineligible abstracts
Other adverse outcome than birth weight/size
Systematic reviews, Meta-Analyses, Epi studies
Studies on plants and algae
Algorithm errors

106 articles

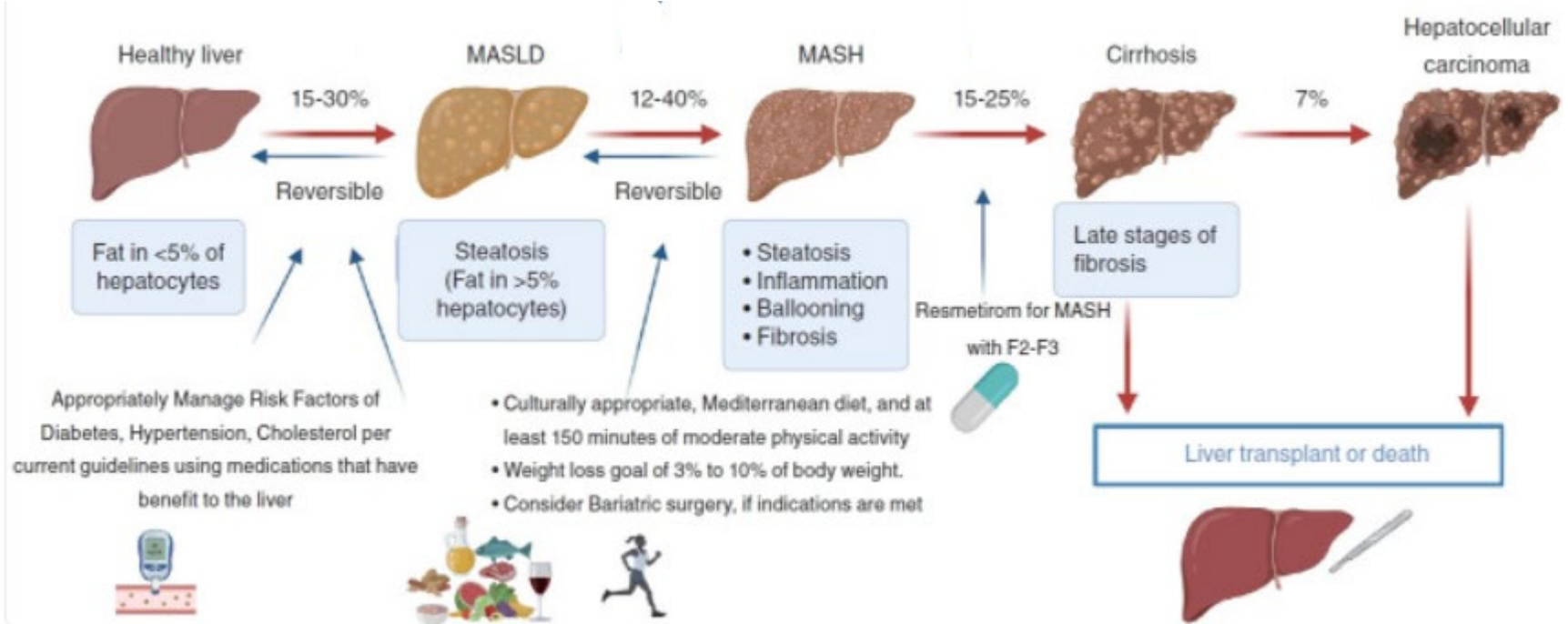
66 *in vivo* animal studies, 55 *in vitro* studies
(15 studies included both animal experiments and
in vitro experiments)



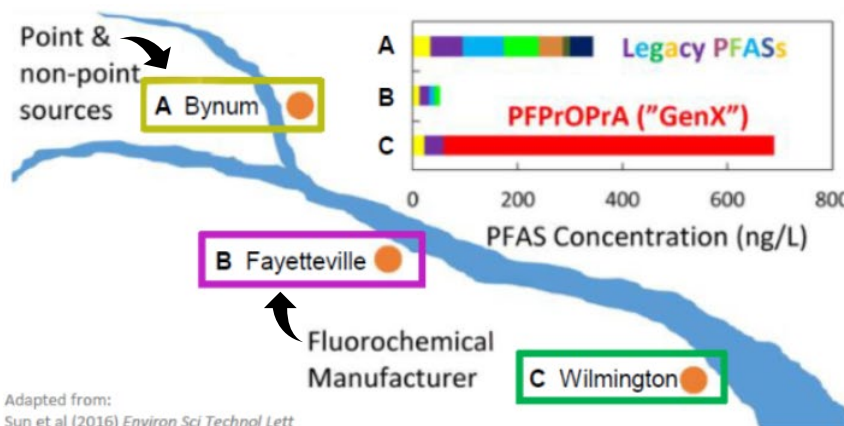
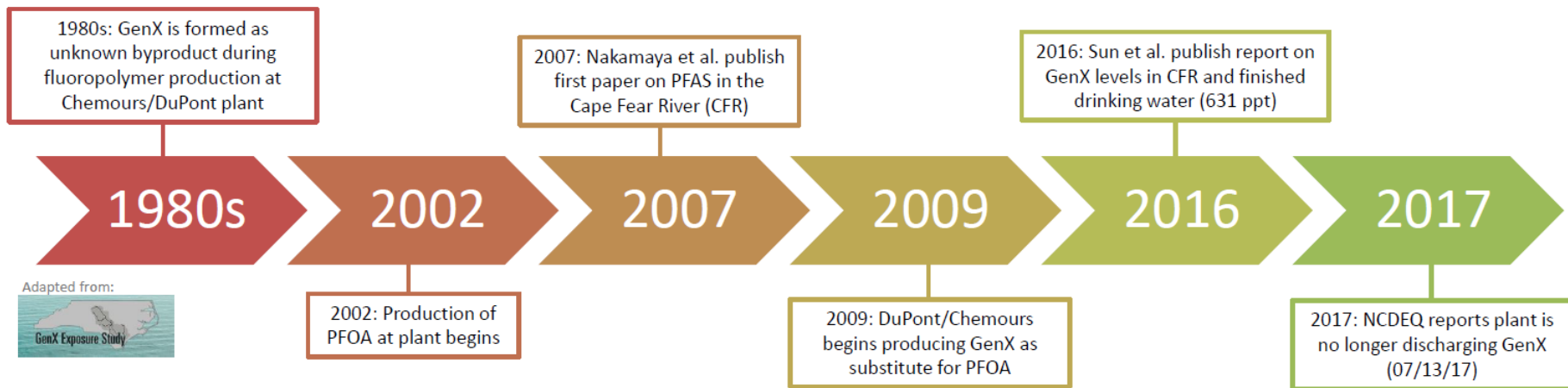
Gundacker et al., 2022 (left); Gui et al., 2022 (right)

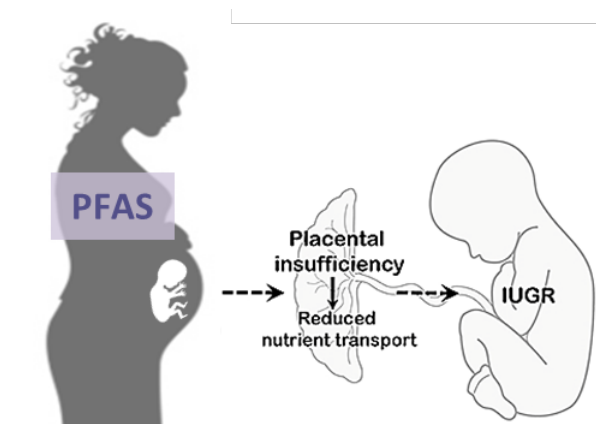
Meta-analysis of the association of PFOS, PFOA, PFHxS and PFHpS with birth weight (g) for top versus bottom categories of exposure.

PFAS, Liver, & Public Health Relevance



- Metabolic dysfunction–associated steatotic liver disease (MASLD) – Fatty buildup with little to no inflammation or liver damage. Globally 38% of adults are diagnosed with MASLD; 7% to 14% of children have MASLD.
- Metabolic-associated steatohepatitis (MASH) – Fatty buildup with inflammation and liver injury that can lead to fibrosis. Numerous reports of PFAS being related to MASLD and MASH.
- PFOS increased risk of adult HCC by 4.5 times (odds ratio 4.5, 95% CI 1.2-16.0). Goodrich et al., 2022; J Hep Report.

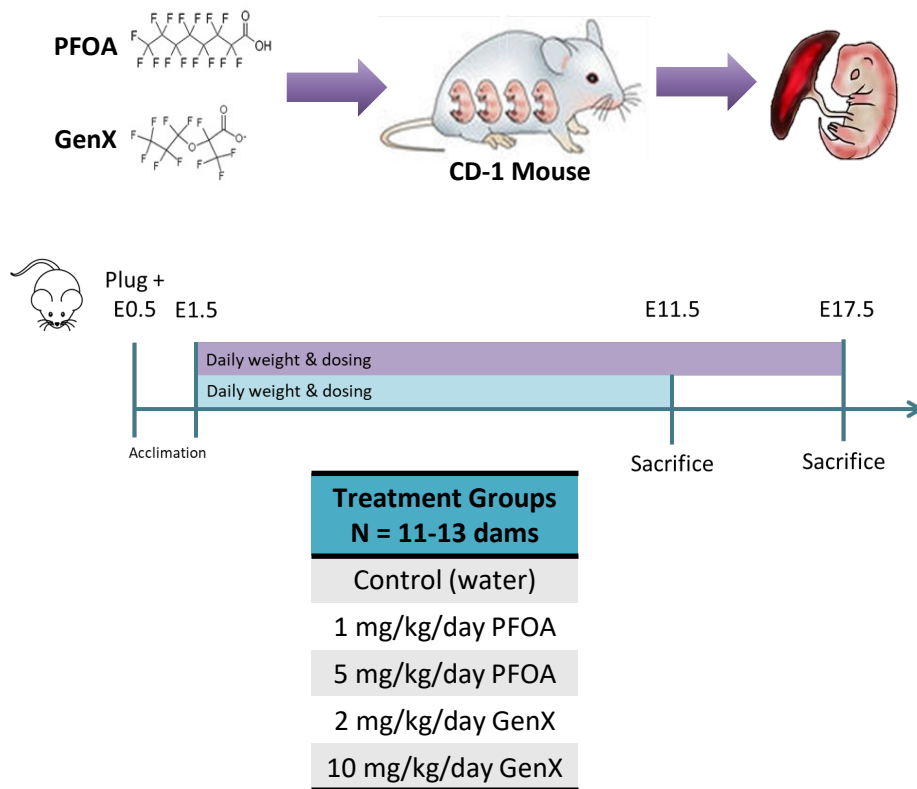




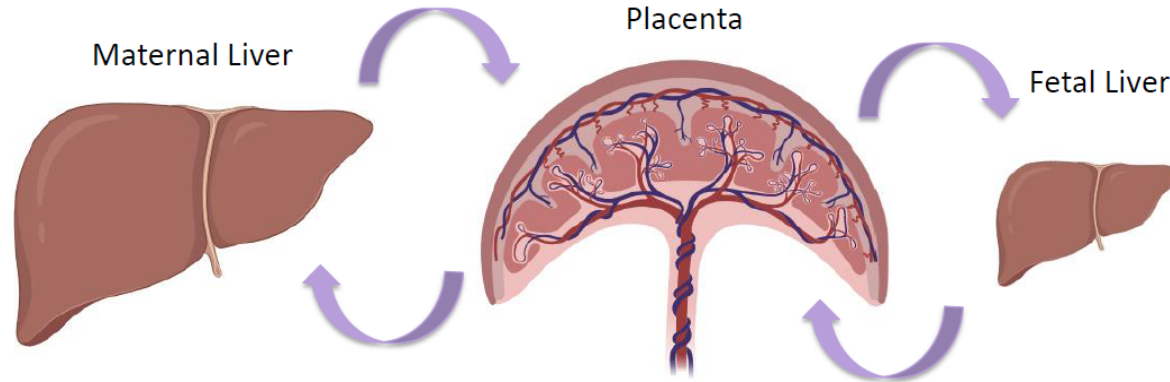
Adapted from: Gaccioli & Lager Front Physiol 2016



- Pre-term birth and SGA
- Gestational diabetes
- Increased gestational weight gain
- Lowered infant birth weight
- Gestational hypertension

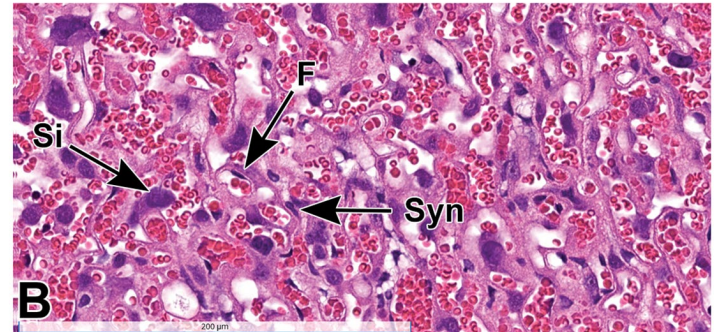
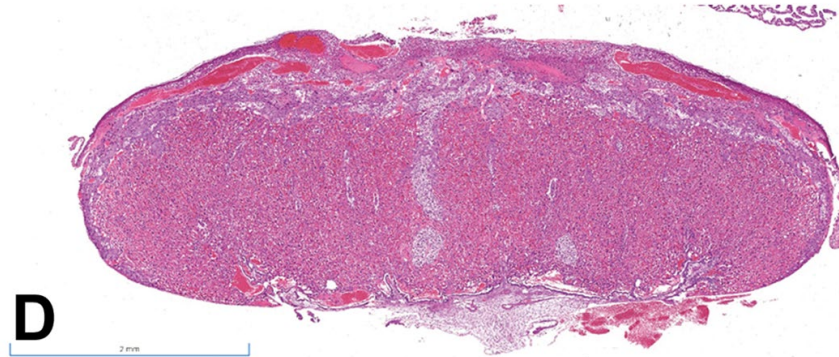
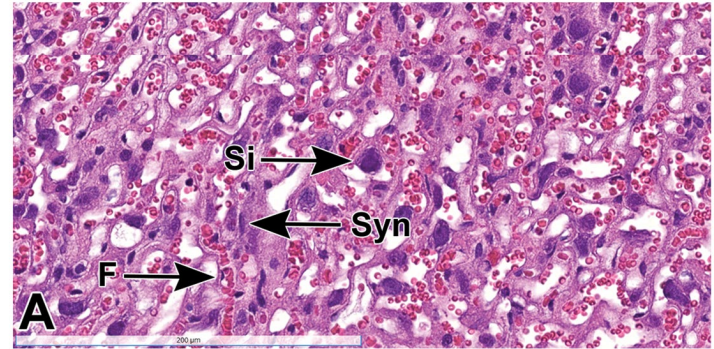
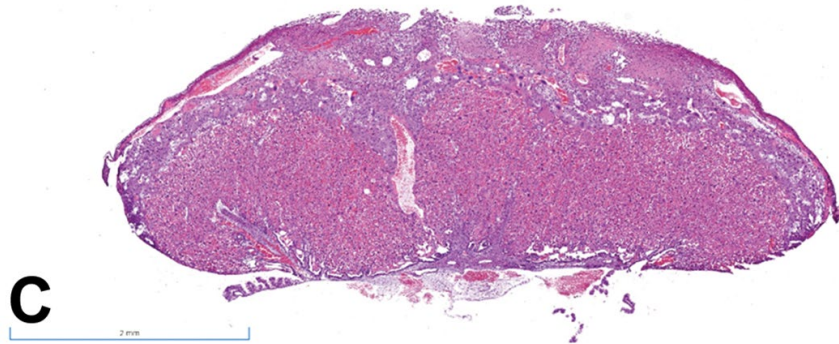


Findings consistent with hypertensive disorder of pregnancy phenotype

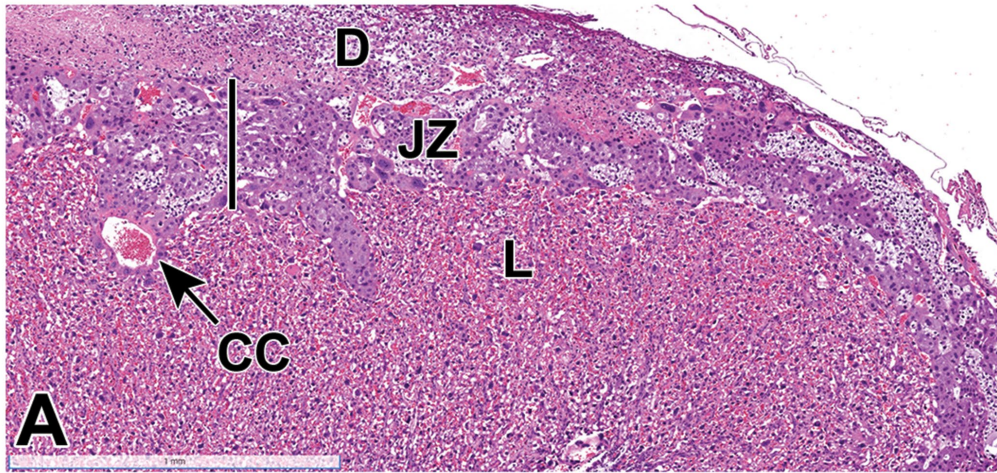


- Excess GWG— clinical feature of HDP
- Disrupted liver enzymes— component of HELLP syndrome
- **Increased maternal & fetal liver size**
- Disrupted fetal-placental growth
- Pathological lesions in the placenta

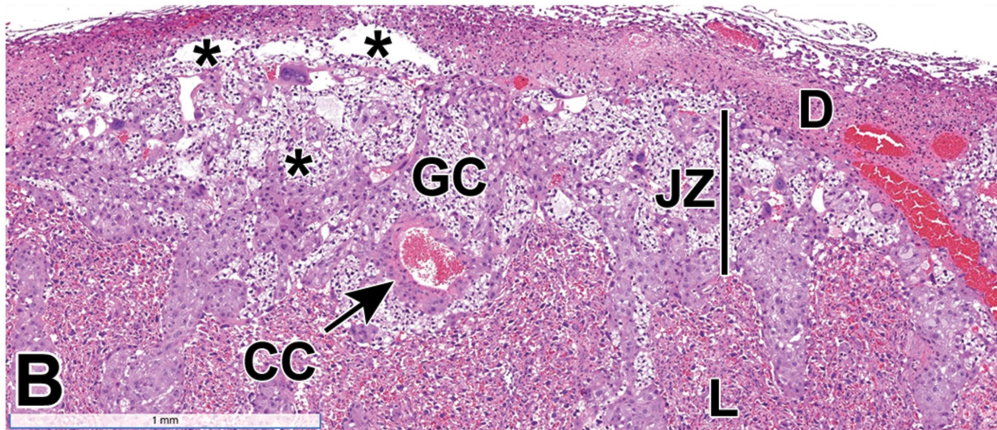
Vehicle control



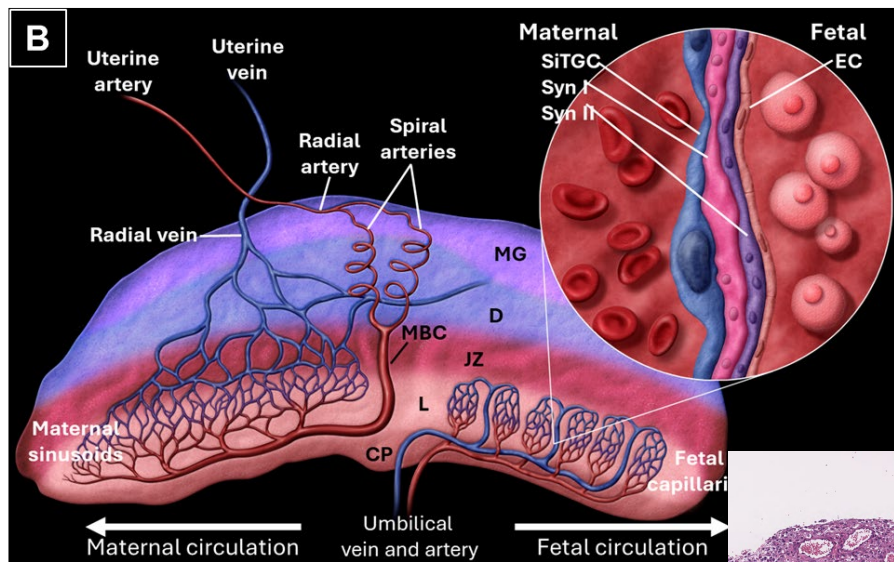
GenX Exposed



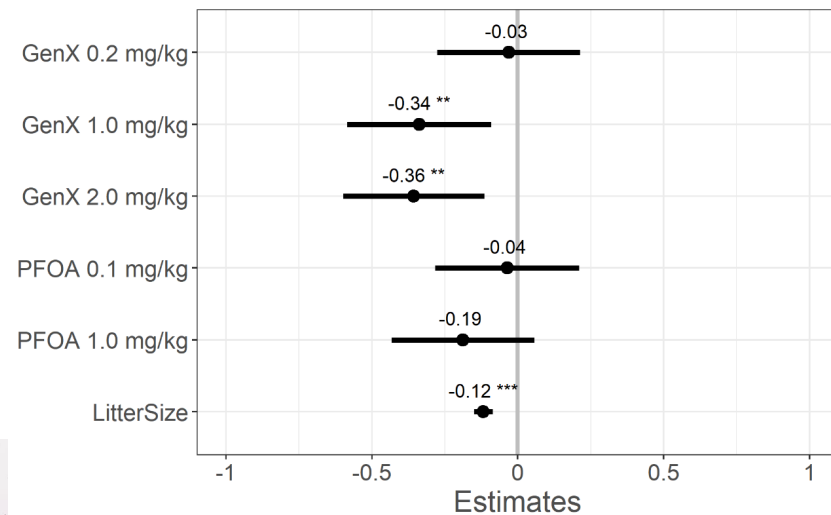
Vehicle control



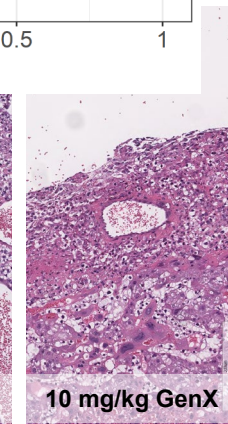
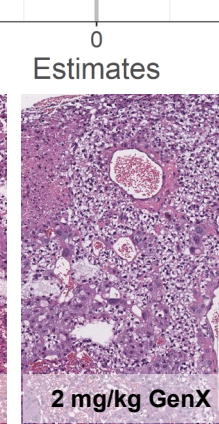
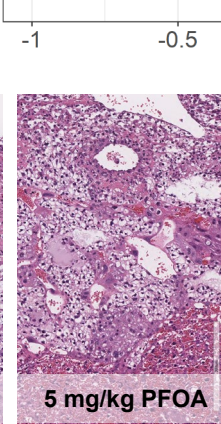
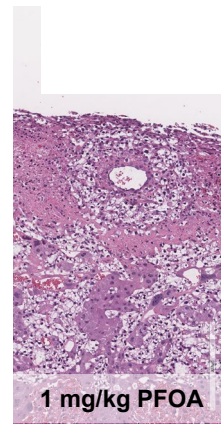
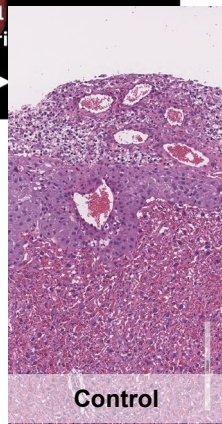
GenX Exposed

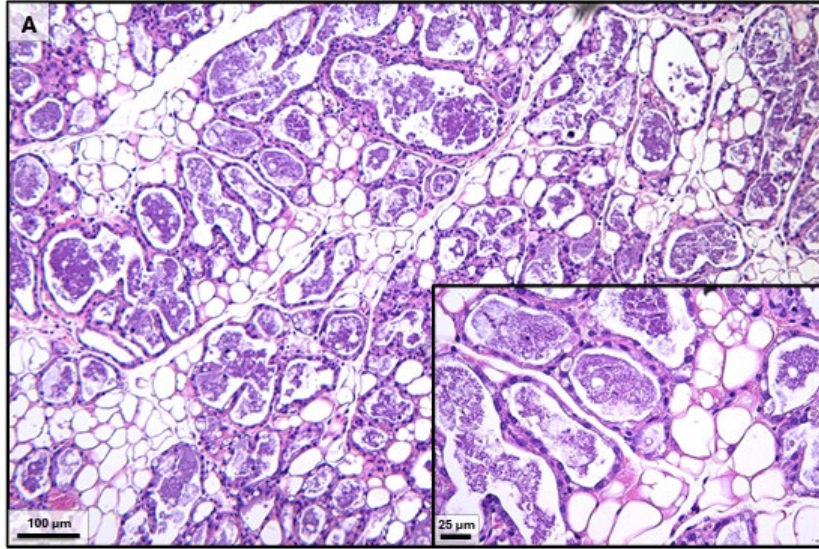


PND 5.5 Body Weight (g)



Foley et al., 2026 Toxicologic Pathology





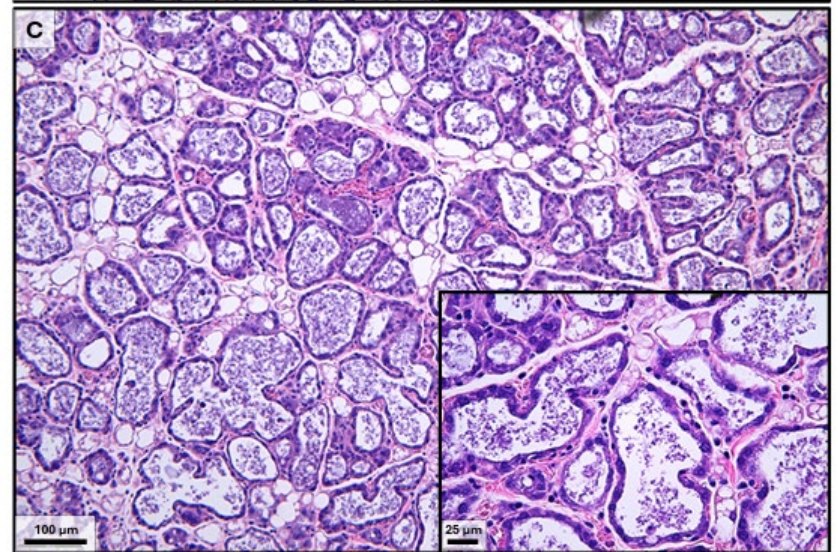
Control Gland at Weaning – Undergoing Involution



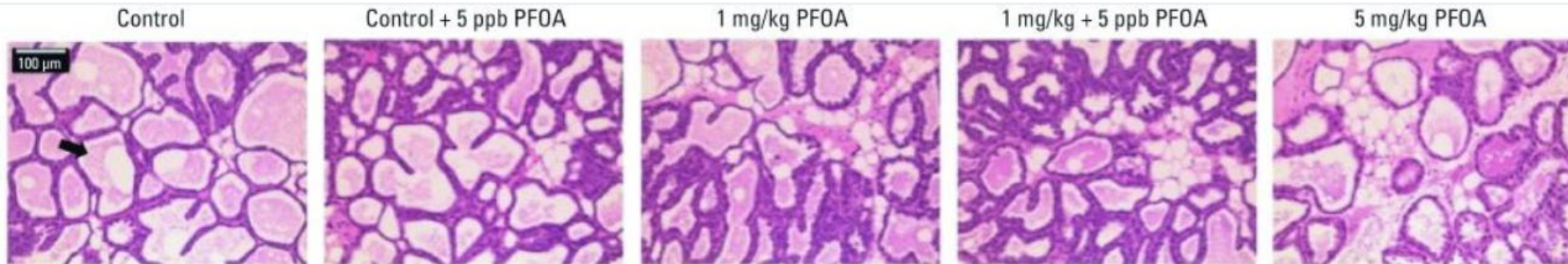
Dr. Alina Hamilton

Hayam Morsy

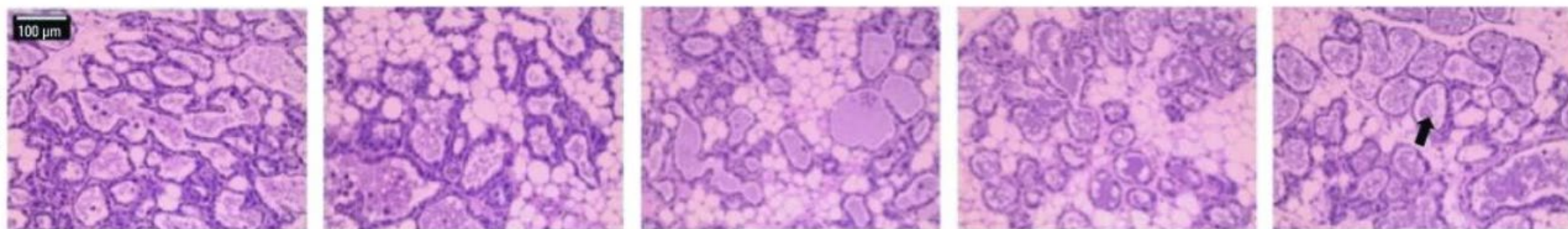
GenX Gland at Weaning – Active Lactation



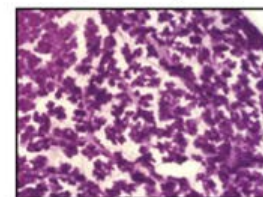
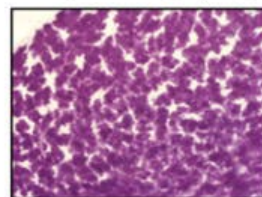
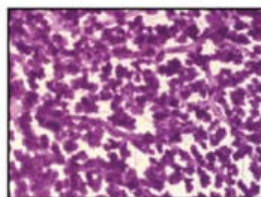
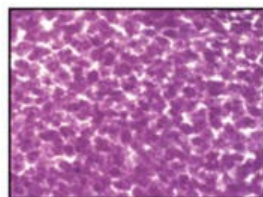
PND10



PND22



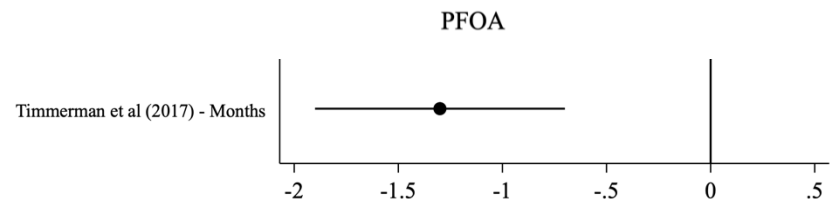
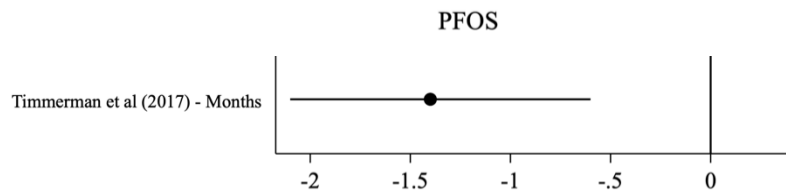
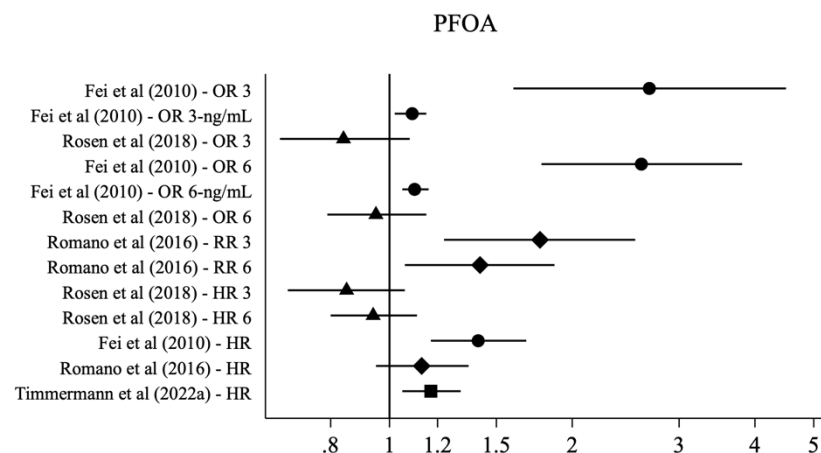
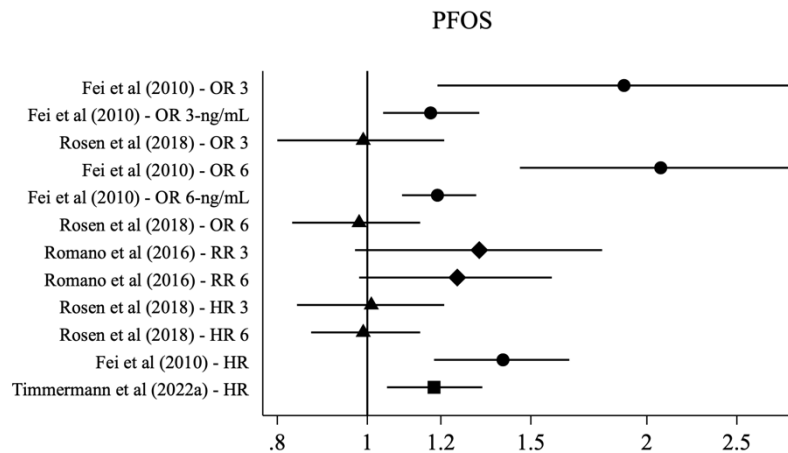
Control

Treated Dam
Nursing Control (5L) PupsControl Dam
Nursing Treated (5U) PupsTreated Dam
Nursing Treated (5U+L) Pups

1. White et al 2007
Reprod Toxicol

2. White et al 2011
Environ Health Perspect

Significant decrease in mouse pup birth weight at 5 mg PFOA/kg BW
(reviewed in Navigation Guide Systematic Review – Koustas et al. 2014 *EHP*)



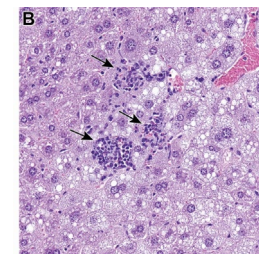
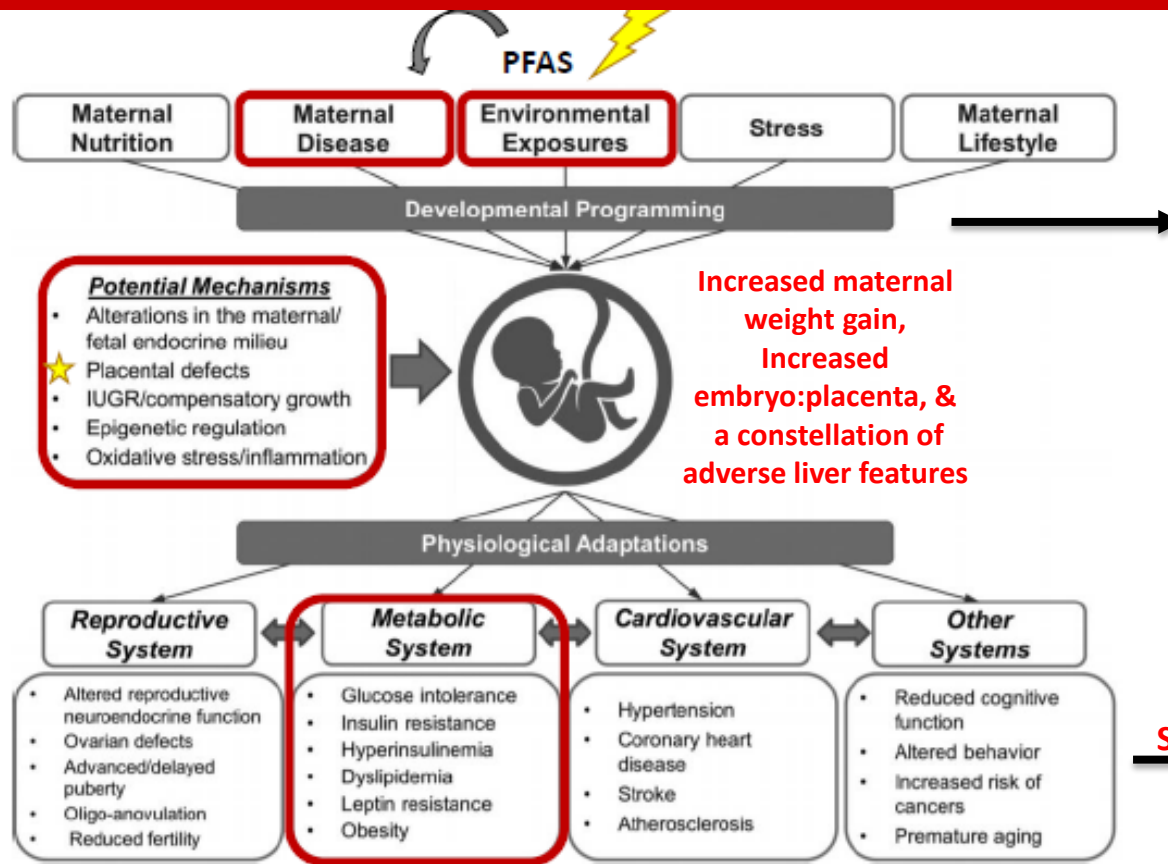
Effect estimates for the association between serum-PFOS/PFOA and breastfeeding

Timmermann et al, Toxics. 2023 PMC10145877

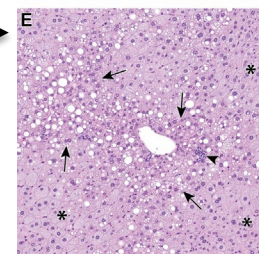
Additional studies since then:

Romano et al, Int J Hyg Environ Health 2024 PMID: 38521049

Rokoff et al, Sci Total Environ 2023 PMID: 37290653



Male
1 mg/kg
GenX



Female
0.2 mg/kg
GenX

Padmanabhan et al. (2016) *Endocrinol*

Rickard et al., Int. J. Mol. Sci. (2022)

Jones et al., JNCI (2025)

Strongest associations at
55-59 years

Childbirth and breastfeeding
decrease PFAS levels

Menopause leads to
increased PFAS levels

Onset of menstruation leads to
decreased PFAS levels

MeFOSAA
PFUnDA
PFOS
PFDA?
PFNA?

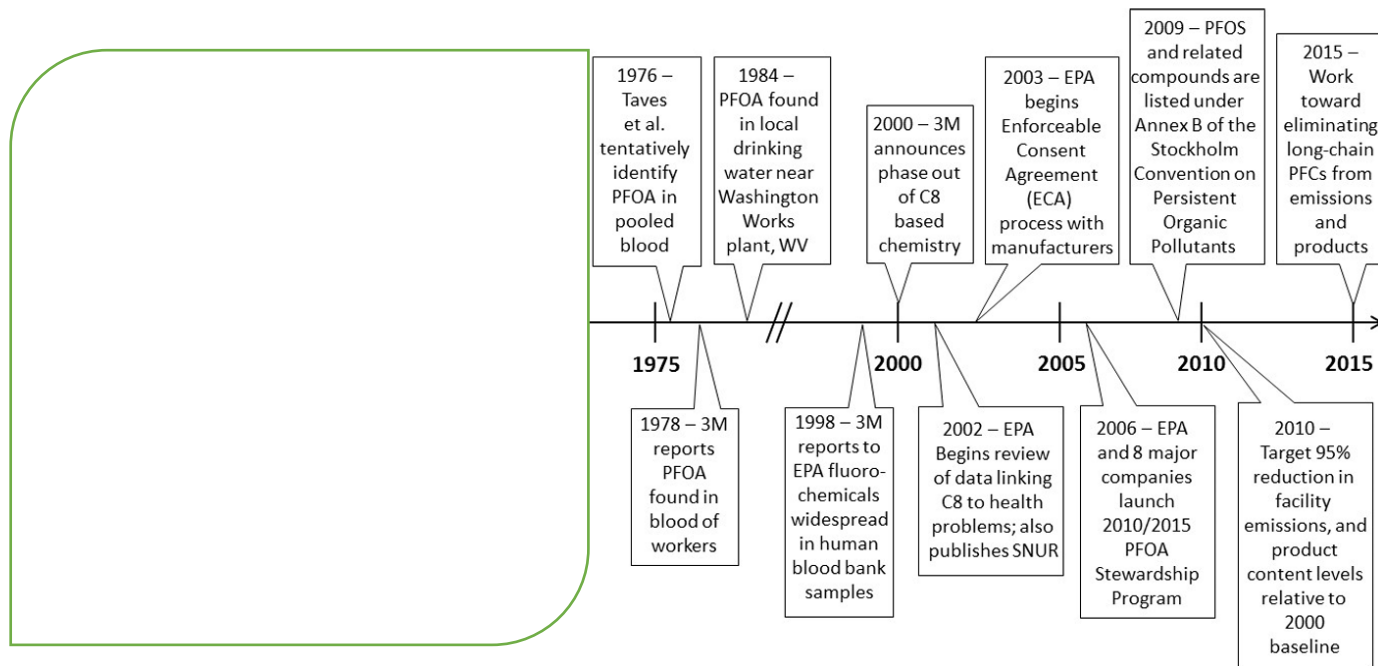
Born with ~50% of
mother's PFAS
burden

Ovarian cancer
mainly affects
post-menopausal
women



From ATSDR's 2021 Toxicological Profile for Perfluoroalkyls

Figure 5-2. Timeline of Important Events in the History of Polyfluorinated Compounds



EPA = U.S. Environmental Protection Agency; PFC = perfluorinated compound; PFOA = perfluorooctanoic acid; PTFE = polytetrafluoroethylene; SNUR = significant new use rule; WV = West Virginia

Source: Reprinted (adapted) with permission from Lindstrom et al. 2011 (Environ Sci Technol 45:7954-7961). Copyright 2011 American Chemical Society.

Potential mechanisms of PFAS-induced carcinogenesis

