ENVIRONMENTAL EXPOSURES. PERSONAL POISONS &RESPONSES, THE ROLE OF NUTRITION

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Faculty Disclosure

Commercial Interest	Nature of Relevant Financial Relationship (Include all those that apply)	
	What was received	**For what role**
• None	• N/A	N/A

Presentation Learning Objectives

After participating in this presentation, learners should be better able to:

- Describe how specific classes of toxins impact the health of certain individuals and susceptible populations differently than others.
- Predict dietary responses to toxic challenges, both beneficial and harmful, based on current knowledge.
- Advocate for science-based changes in toxics policy.

DECLARATIONS

- I HAVE BEEN PRINCIPLE INVESTIGATOR FOR CREATING A PUBLIC WEBSITE (2006-2010) FOR COMMUNICATIONS RELATED TO THE "C8 HEALTH STUDY" WHICH ENROLLED 69,030 PARTICIPANTS EXPOSED TO CONTAMINATED WATER IN THE MID-OHIO VALLEY. THE EXPOSURE WAS PERFLUOROOCTANOIC ACID IN SIX MUNICIPAL WATER SYSTEMS; RESIDENTS OF TWO STATES AFFECTED
- FOLLOWING PROVISION OF PATIENT CARE FOR POSSIBLE TOXIC EXPOSURES, I AM SOMETIMES DEPOSED BY OPPOSING ATTORNEYS. THIS HAS NEVER RELATED TO NUTRITION, HOWEVER. (ANY INCOME HAS GONE TO THE UNIVERSITY OR ITS NOT-PROFIT PRACTICE PLAN)

GOALS

ILLUSTRATE HOW NUTRITION AFFECTS AND INTERACTS WITH EXPOSURE TO ENVIRONMENTAL TOXICANTS

1. ATTENDEES SHOULD GAIN AN UNDERSTANDING OF TOXICITY AND OF DIFFERENCES IN INDIVIDUAL SUSCEPTIBILITY THAT CAN AFFECT:

ABSORBED DOSE, AND TOXICITY OF ABSORBED DOSE

THIS INCLUDES BUT IS NOT LIMITED TO DIFFERENCES IN GENETIC MAKEUP

2. ATTENDEES SHOULD BE ABLE TO MAKE REASONABLE AND HEALTHY RECOMMENDATIONS ABOUT DIET, SUPPLEMENTS (AND OTHER LIFESTYLE BEHAVIORS) THAT ACCOUNT FOR OUR INCREASING (& ALWAYS INSUFFICIENT) KNOWLEDGE OF ENVIRONMENTAL TOXICANTS.

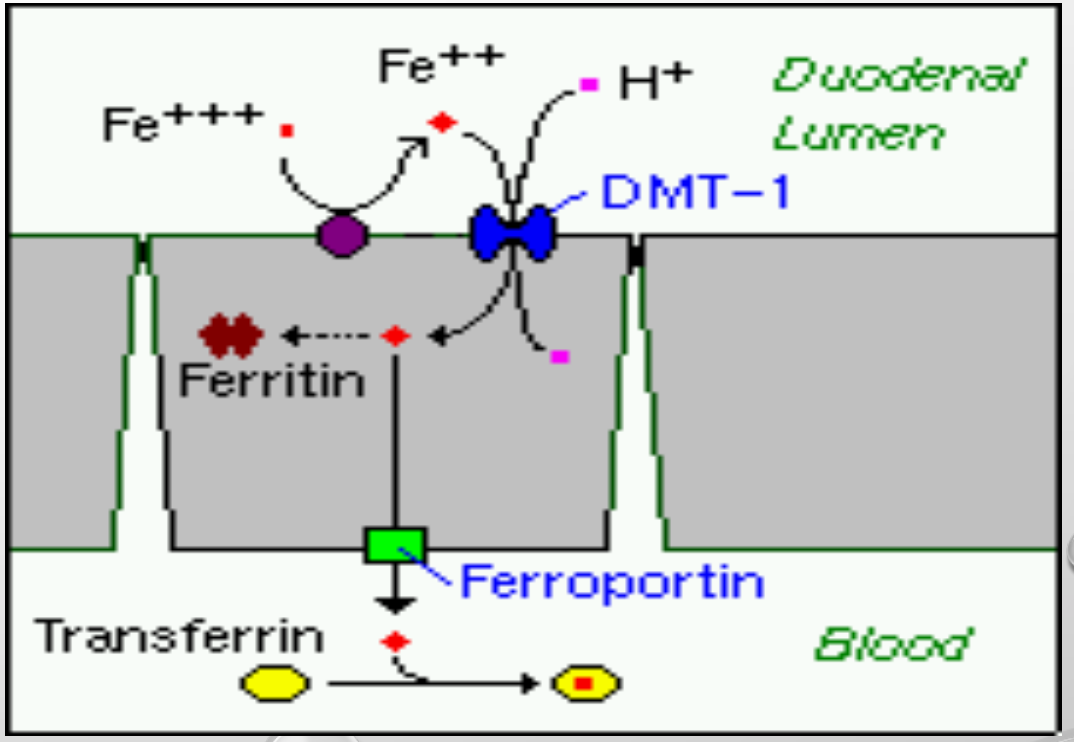
(3. THE PRESENTER WILL DEMONSTRATE LECTURING AS AN AEROBIC SPORT)

THE NUTRITION COMMUNITY: HISTORICALLY ALERT TO INTERACTIONS BETWEEN ENVIRONMENTAL TOXINS AND NUTRITION. THIS IS A SECONDARY PROTECTION

WHY IS GOOD NUTRITION PARTIALLY PROTECTIVE?

FOR LEAD: COMPLEX STORY OF GUT NETABOLISM OF THE +2 VALENCE IN DIFFERENT AGE GROUPS, AND

- THE ROLE OF ANEMIA

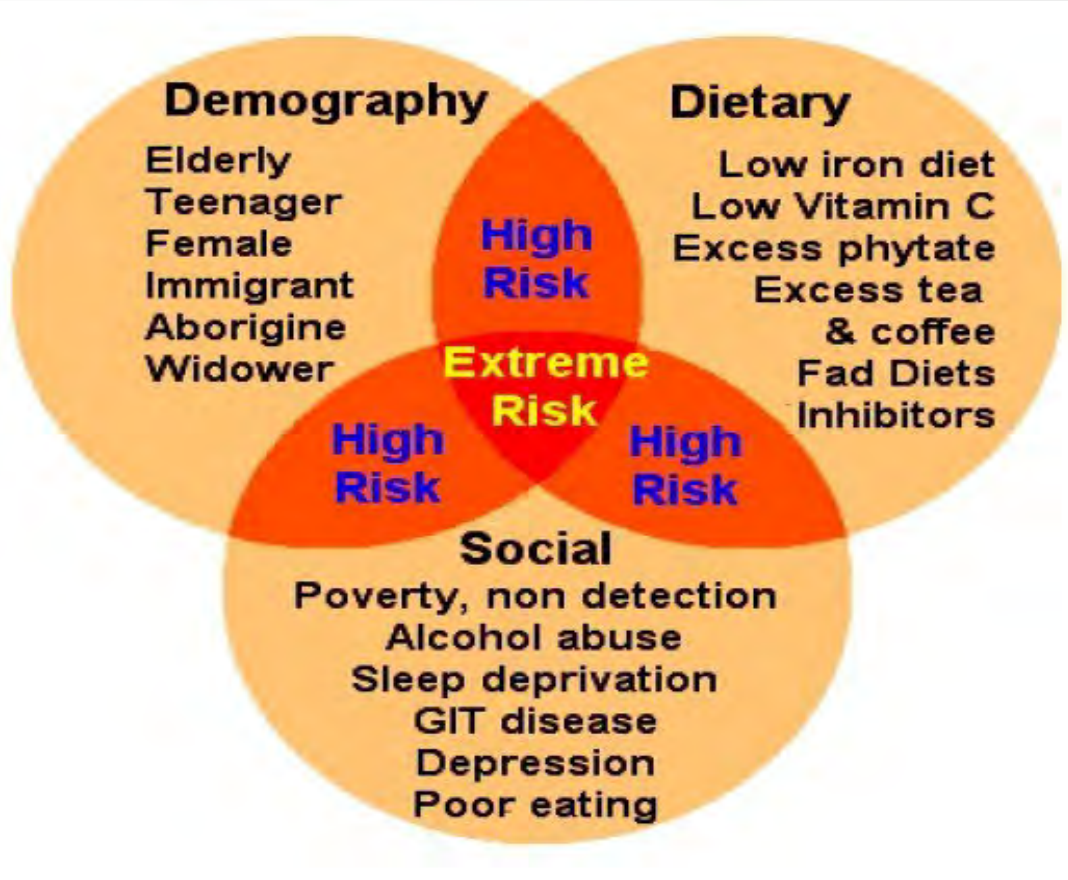


FE - NUTRITIONAL ADVICE: BOTH PROTECTION AND TREATMENT (TO SOME DEGREE)

VELTRI F ET AL DOI 10.1530/EJE-16-0288

ALERT TO SUSCEPTIBLE GROUPS

- INADEQUATE IRON STORES? WELL-KNOWN TO **ABSORB** MORE LEAD. IRON AND VITAMIN C MAY SPEED UP LEAD EXCRETION (A LITTLE)
- WHAT ABOUT TOO MUCH? SCREEN FOR HEMOCHROMATOSIS AT BIRTH? (MISSENSE MUTATION C282Y). AFFECTS ~1:300 CAUCASIANS
- **"NEW STUFF:"** IRON DEFICIENCY IN 1ST TRIMESTER PREGNANCY IS ASSOCIATED WITH THYROID AUTOIMMUNITY (CAVEATS: SMALL STUDY, EARLY DAYS, NO PROOF THAT RX IS PREVENTIVE)



NUTRITIONISTS MANAGE DIET FOR DISEASES WITH GENETIC-ENVIRONMENTAL PATTERNS. EXAMPLE

GENETIC VARIANTS FOR HYPERURICEMIA:

SCL2A9, ABCG2, SCL221A2, GCKR, PDZK1, AND OTHERS

ENVIRONMENTAL CONTRIBUTORS TO URIC ACID:

LEAD (SATURNINE GOUT)

PERFLUOROCARBONS SUCH AS PFOA

ARSENIC (KUO CC, ET AL. ENVIRONMENT I NT, 2015 MARCH)

MODIFY DIET FOR GOUT. NOT INDICATED (NOR CONTRAINDICATED) FOR PROPHYLAXIS

- SUBTRACT: ETOH, PURINE-RICH (MEATS, SOME FISH), HIGH FRUCTOSE, & MEDS SUCH AS THIAZIDES AND LOW DOSE ASPIRIN
- BUT, IF OTHER RISK FACTORS ALIGNED, AND ASA TOLERATED, YOU MIGHT CONSIDER HIGH DOSE ASPIRIN, THAT IS URICOSURIC

NUTRITION COMMUNITY OF PRACTICE: ALSO A ROLE IN COSMETICS AND CONSUMER PRODUCTS??

EXAMPLES: BUTYLATED HYDROXYANISOLE/BUTYLATED HYDROXYTOLUENE, COAL TAR DYES, DIETHANOLAMINE, FORMALDEHYDE-RELEASING PRESERVATIVES, PARABENS, PHTHALATES, 1,4-DIOXANE, POLYCYCLIC AROMATIC HYDROCARBONS, SILOXANES, TALC/ ASBESTOS, AND TRICLOSAN (JUST BANNED), AND POLY/PERFLUORINATED COMPOUNDS

WHY? LOOK HOW COMMON (CHOW E. MAHALINGAIAH M. COSMETICS USE AND AGE AT MENOPAUSE. 2016 DOI.ORG/10/1016.JRERTNSTERT.2016.08.020)

Figure 1.
Path of determination of ingredients most commonly found in beauty products.

WHY DOES THIS HAPPEN? (IMAGES, BREAST CANCER FUND)

Companies can use virtually any raw material in a finished cosmetic product, even those linked to cancer, birth defects or learning difficulties.

EXISTING COSMETIC SAFETY LAW IS >75 YEARS OLD AND PROVIDES LITTLE FDA POWER TO PROTECT CONSUMERS (2016)

metals in face paints

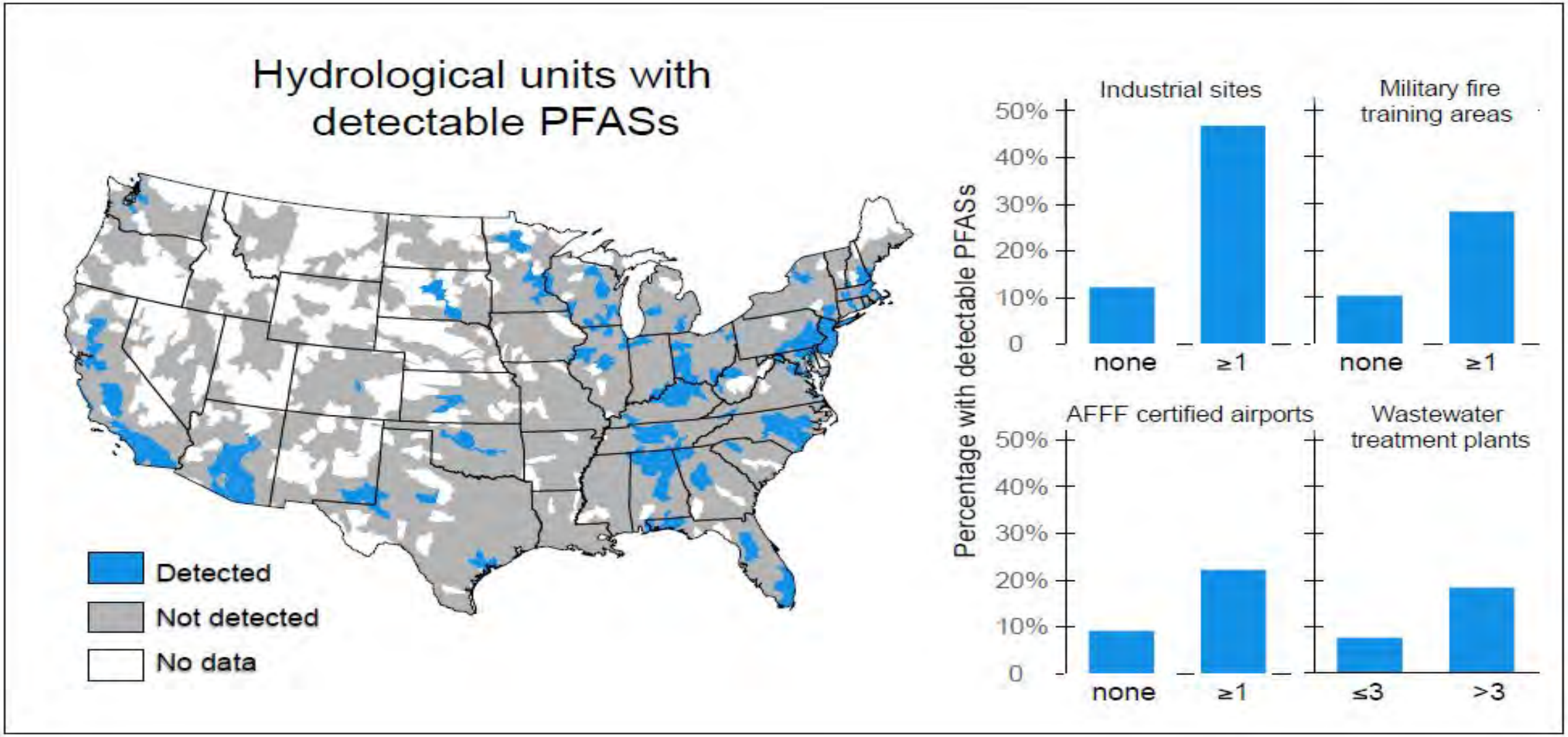
Metal	Number	Percentage	Range of levels detected
Arsenic	4	8%	1.1-1.9 mg/kg
Cadmium	14	29%	.58-14 mg/kg
Chromium	13	27%	1.4-12 mg/kg
Lead	9	4.6%	1.2-3.9 mg/kg
Mercury	0	0	n/a

PER- AND POLY-ALKYL FLUORO CHEMICALS: "POSTER" PRODUCT ILLUSTRATES HOW COMMON

NONSTICK PANS MAY NOT BE THE IMPORTANT SOURCE OF EXPOSURE (IN A WELL-MADE PRODUCT, UNLESS OVERHEATED) (SCHLUMMER M, ET AL. CHEMOSPHERE 2015 DHOI:10.1016/ J.CHEMOSPHERE.2014.11.036)

HOWEVER……..

PERFLUORO & POLY FLUORO-CHEMICALS, COMMON CONTAMINANTS IN HOMES, HOUSEDUST, FOOD, FOOD PACKAGING AND DRINKING WATER (HU ET AL. ENV SCI TECHNOL LTRS, 2016)



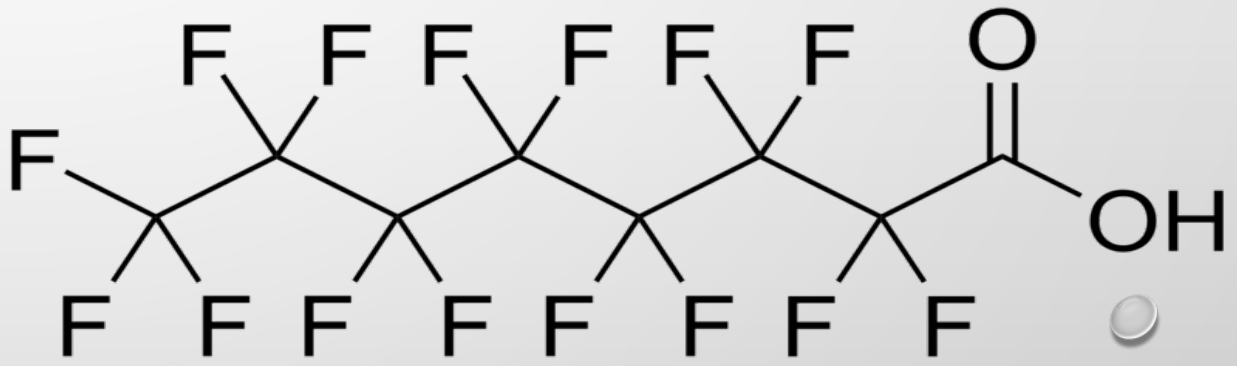
WHY DID EXPOSURE HAPPEN: USEFUL PRODUCTS

IF IT IS PROTECTIVE AND NONSTICK…..

- COSMETICS
- FOOD CONTAINERS (YOUR PETS TOO), SOME BAKING PAPERS, COOKWARE
- CARPET AND TEXTILE TREATMENTS
- WATERPROOF, BREATHABLE CLOTHING
- SURFACE COATINGS (PAINTS, SKI WAXES, GREASE)
- BARRIER INSULATION
- MEDICAL EQUIPMENT
- FIRE SUPPRESSION FOAM
- LITHOGRAPHY, ELECTROPLATING

WHAT MAKES THIS CHEMICAL GROUP A GOOD ILLUSTRATION? (PFOA ILLUSTRATION, WAMC, NE PUBLIC RADIO)

- CONTAMINATES **FOOD**, DRINKING **WATER** (PLUS HOUSE **DUST**)
- IN LIVER, BLOOD, KIDNEYS, TESTICLES, ETC.
- PHYSIOLOGICALLY ACTIVE AT EXTREMELY LOW DOSES (RECENT FEDERAL RECOMMENDATION FOR WATER 70 **PPT** FOR **PFOA.** STATE OF NJ DRAFT: 14 PPT, HARVARD RESEARCH TEAM, 1PPT)
- VERY LONG HALF-LIVES (2.3 - 8+ YEARS FOR THE ≥ 6C-ALKYL AND -SULFONIC ACIDS)



WHAT DOES "PHYSIOLOGICALLY ACTIVE" MEAN?

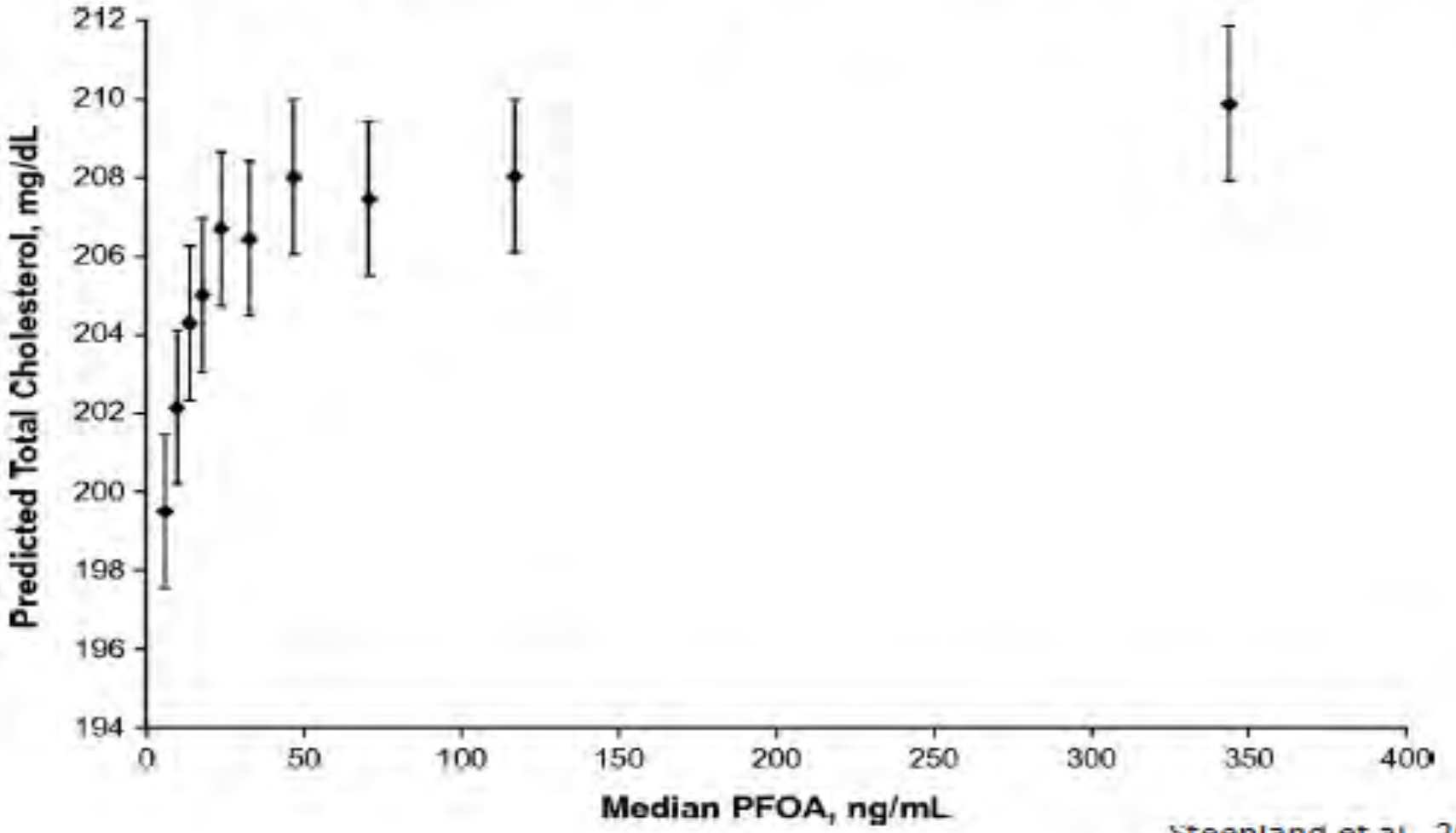
- BIOMARKERS OF CLINICAL IMPORTANCE, INVESTIGATED FOR CONFOUNDING (NONE FOUND TO DATE)
- SERUM CHOLESTEROL
- IMMUNE MARKERS, INCLUDING CRP AND VACCINE RESPONSIVENESS
- "LIVER FUNCTIONS" (ALT, AST)
- THYROID MARKERS, INCLUDING T4 AND PROTEIN BINDING
- TESTOSTERONE

- PENNINGS JLA ET AL, J IMMUNOTOX, 2015

Table 1. Number of genes correlated with PFAS levels and immune parameters.

Parameter	Positive correlation	Negative correlation	Total
PFOS	636	671	1307
PFOA	453	490	943
PFNA	312	289	601
PFHxS	787	225	1012
2 or more PFAS	294	284	578
Common cold episodes	330	250	580
PFAS *AND* common cold			27 (Table 2)
Rubella antibody	522	709	1231
PFAS *AND* rubella			26 (Table 3)

Associations of Health Effects with Low Serum PFOA Levels – Example: ↑ Cholesterol in Communities with Contaminated Drinking Water



Steenland et al., 2009

From: **Perfluorooctanoic Acid, Perfluorooctanesulfonate, and Serum Lipids in Children and AdolescentsResults From the C8 Health Project**

Arch Pediatr Adolesc Med. 2010;164(9):860-869. doi:10.1001/archpediatrics.2010.163

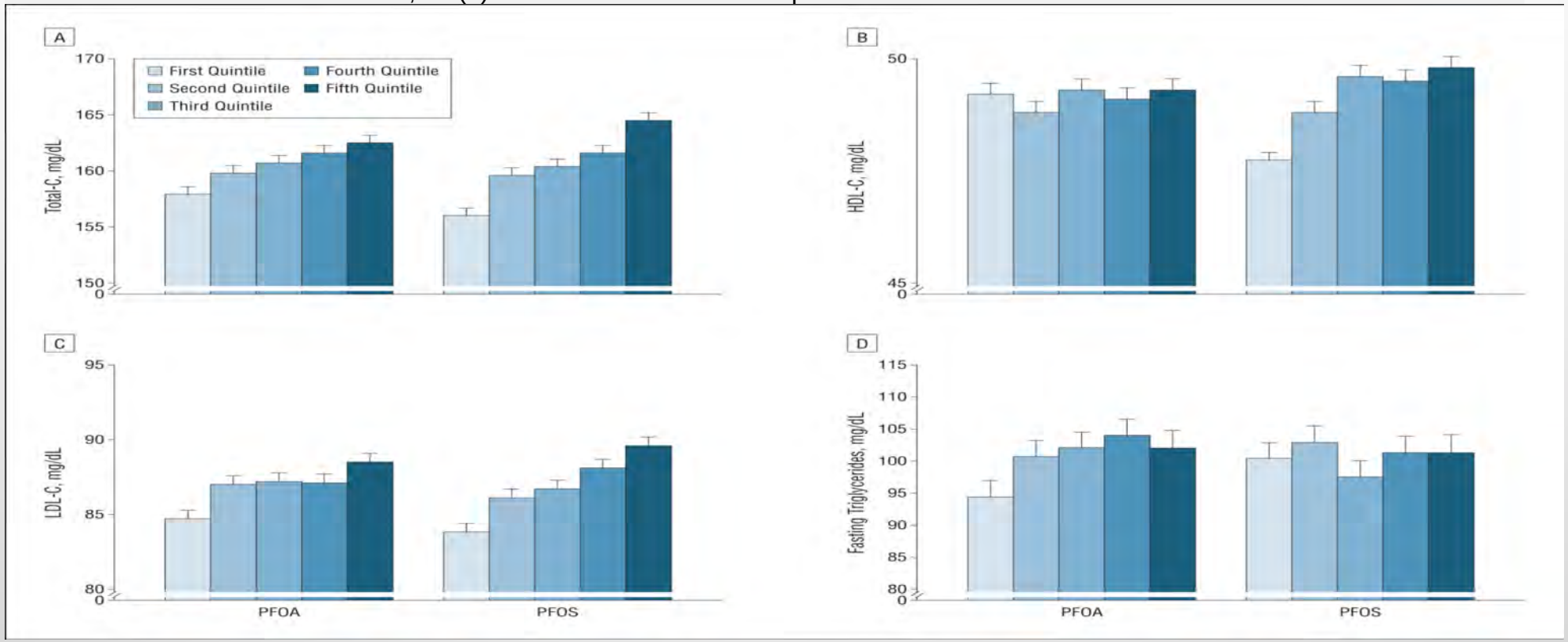
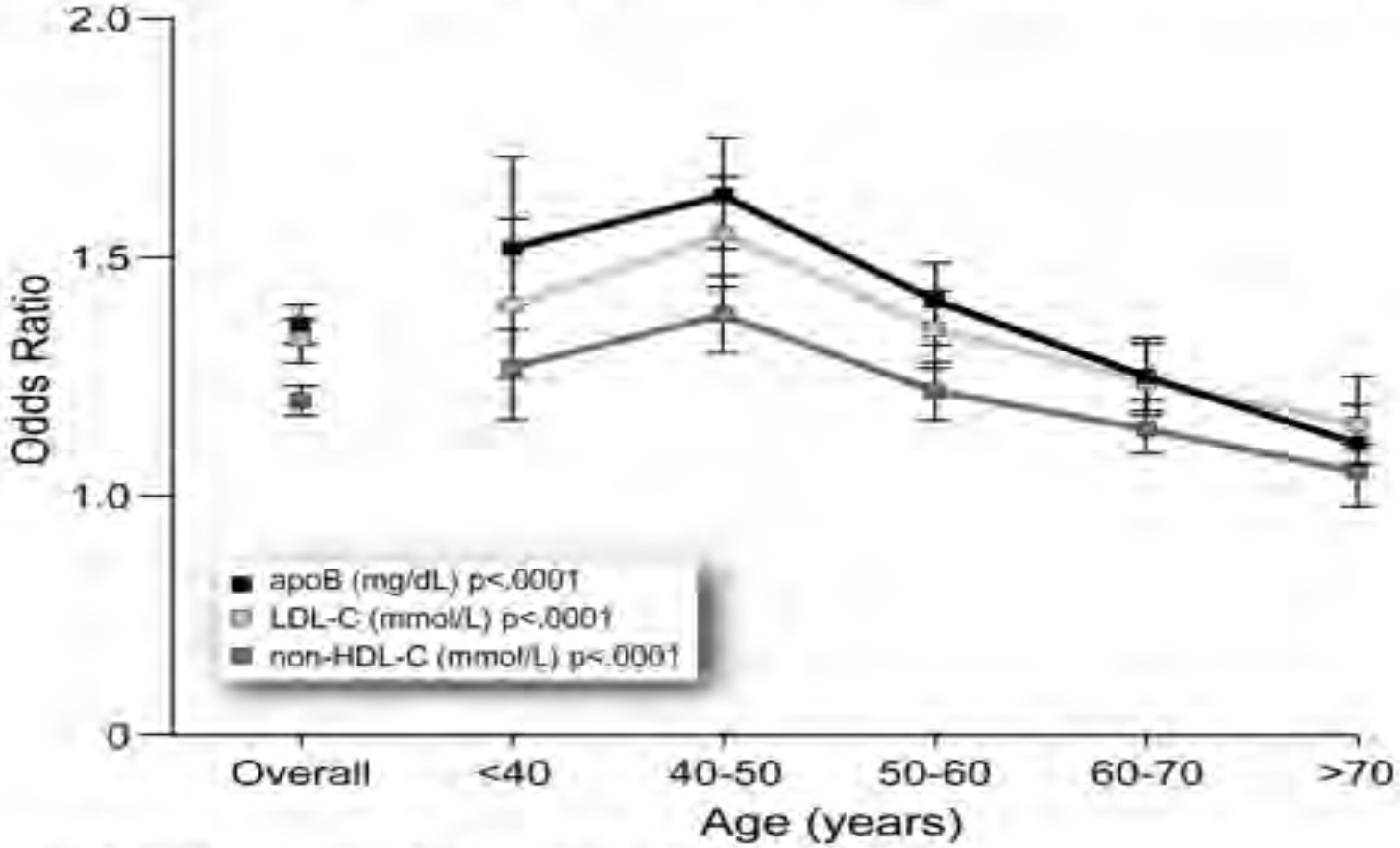


Figure Legend:

Changes in covariable-adjusted estimated marginal means (general linear model analysis) across perfluorooctanoic acid (PFOA) and perfluorooctanesulfonate (PFOS) quintiles. A, Total cholesterol (total-C). B, High-density lipoprotein cholesterol (HDL-C). C, Low-density lipoprotein cholesterol (LDL-C). D, Fasting triglycerides. Lipid values are presented as mean (SE). To convert total-C, HDL-C, and LDL-C to millimoles per liter, multiply by 0.0259; fasting triglycerides to millimoles per liter, multiply by 0.0113.

WHY MIGHT HIGHER LDL EARLIER IN LIFE MATTER ? **(MI)**

Odds ratios for low-density lipoprotein cholesterol (LDL-C), non-high-density lipoprotein cholesterol (non-HDL-C), and apolipoprotein B (apoB) overall and for each decade.



Allan D. Sniderman et al. J Am Heart Assoc 2016;5:e003665

PFAS and Liver Function – Key Findings

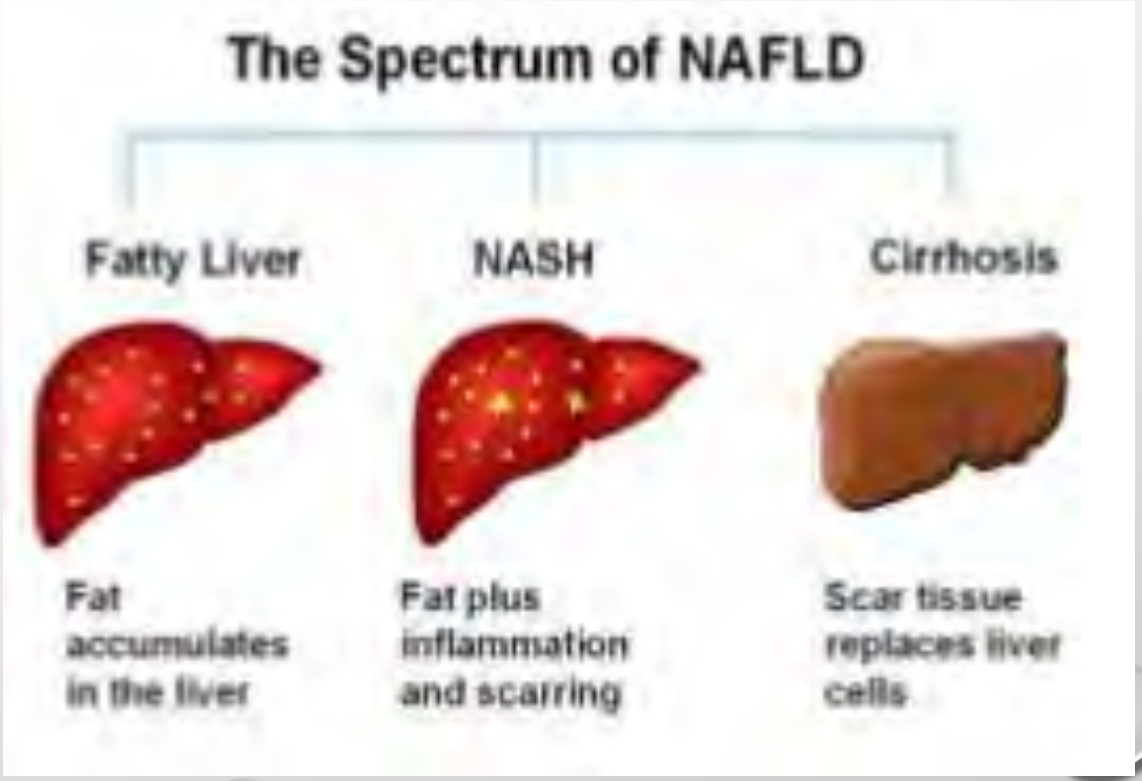
Serum perfluorooctanoate (PFOA) and perfluorooctane sulfonate (PFOS) concentrations and liver function biomarkers in a population with elevated PFOA exposure

- **Methods:**
  - The C8 Health Project collected data on 69,030 persons; of these, a total of 47,092 adults were included in the present analysis. Linear regression models were fitted for natural log (ln)-transformed values of alanine transaminase (ALT), γ-glutamyltransferase (GGT), and direct bilirubin on PFOA, PFOS, and potential confounders.
- **Findings:**
  - These results show a positive association between PFOA and PFOS concentrations and serum ALT level, a marker of hepatocellular damage.
  - ALT enzyme released by the liver when liver cells are damaged

Environ Res. 2015 Jan;136:8-14. doi: 10.1016/j.envres.2014.10.004. Epub 2014 Nov 19.

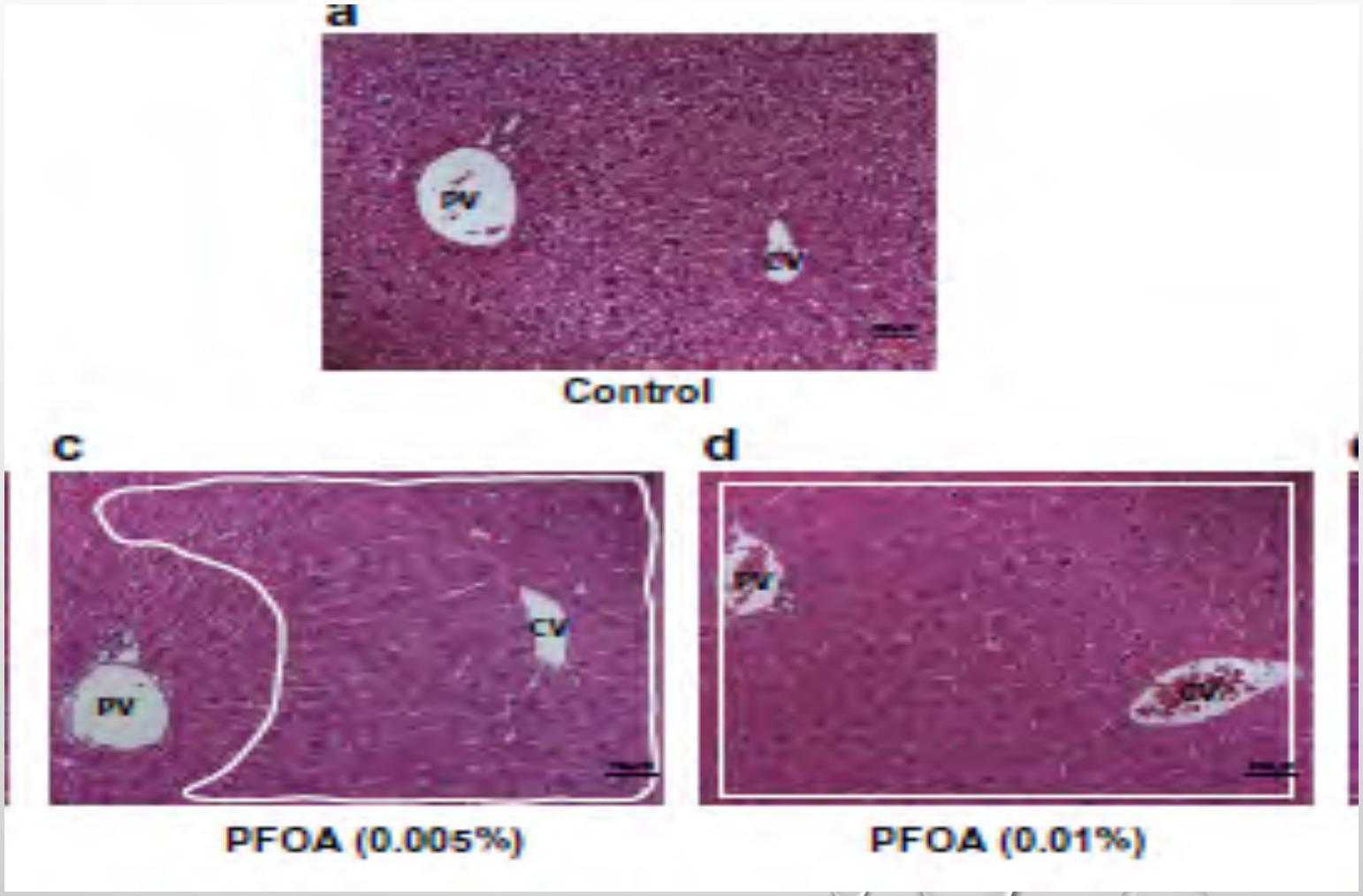
LFTS INSENSITIVE MARKER OF LIKELY CAUSE, NAFLD,

ANIMALS FED A WESTERN DIET AND PFAS EXHIBIT BOTH ELEVATED CHOLESTEROL AND INCREASED LIVER WEIGHT, SIMILAR TO HUMANS WITH NAFLD



REBHOLZ S, ET AL. TOXICOL REPORTS 2016; 3: 46-54

MICE FED PFOA (BOTELHO SC ET AL, CHEMOSPHERE 129;2015:225-31



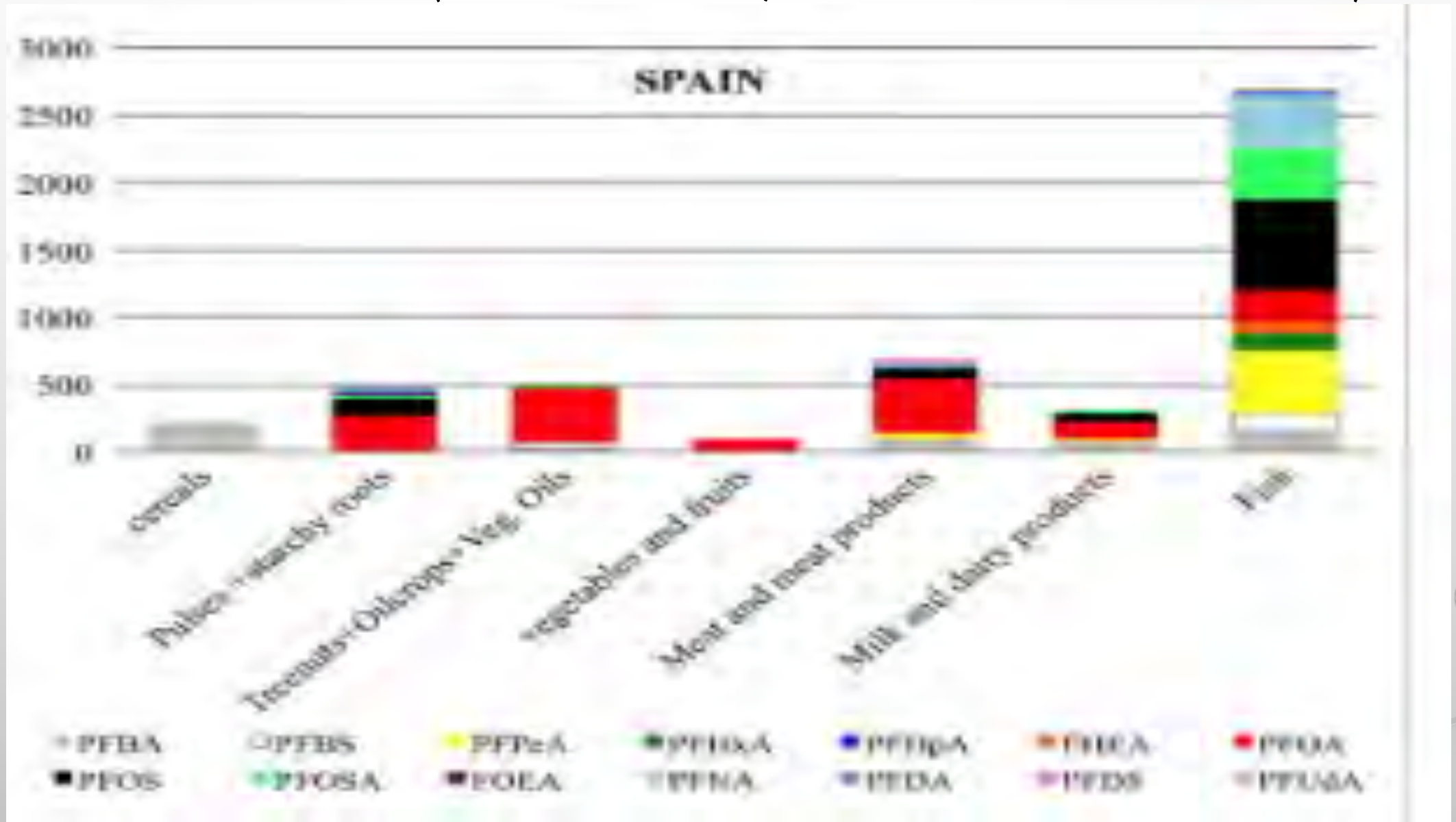
EARLY LIFE EFFECTS

AMNIOTIC FLUID, UMBILICAL CORD BLOOD, AND TO A LESSER DEGREE, BREAST MILK

SERUM LEVELS IN INFANT SIMILAR TO MOM, AND THEN GO UP (START TO FALL AGAIN AT ~6 MONTHS)

ASSOCIATIONS INCLUDE LOWER BIRTH WEIGHT (VERY MODEST ASSOCIATION) LATER OBESITY, LATER ALLERGY. CAUSATION INVESTIGATION ONGOING

DIET IS THE COMMON MAJOR ROUTE OF EXPOSURE, SPECIFICALLY: (IMAGE FROM PEREZ F, ET AL. ENVIRON RES 2014:135: 181-9)



SOURCES: (PARKERSBURG, OHIO RIVER, PFOA OPERATION, IMAGE FROM WASHINGTON POST)

EXPOSURE ROUTES

INHALATION, INGESTION, AND TO SOME DEGREE, DERMAL ABSORPTION

THE DERMAL ABSORPTION CONCEPT IS NOT FOOD CHAIN, BUT IS POTENTIALLY IMPORTANT IN COSMETICS, SHAVING CREAMS, AND ……..

WATER REPELLANT

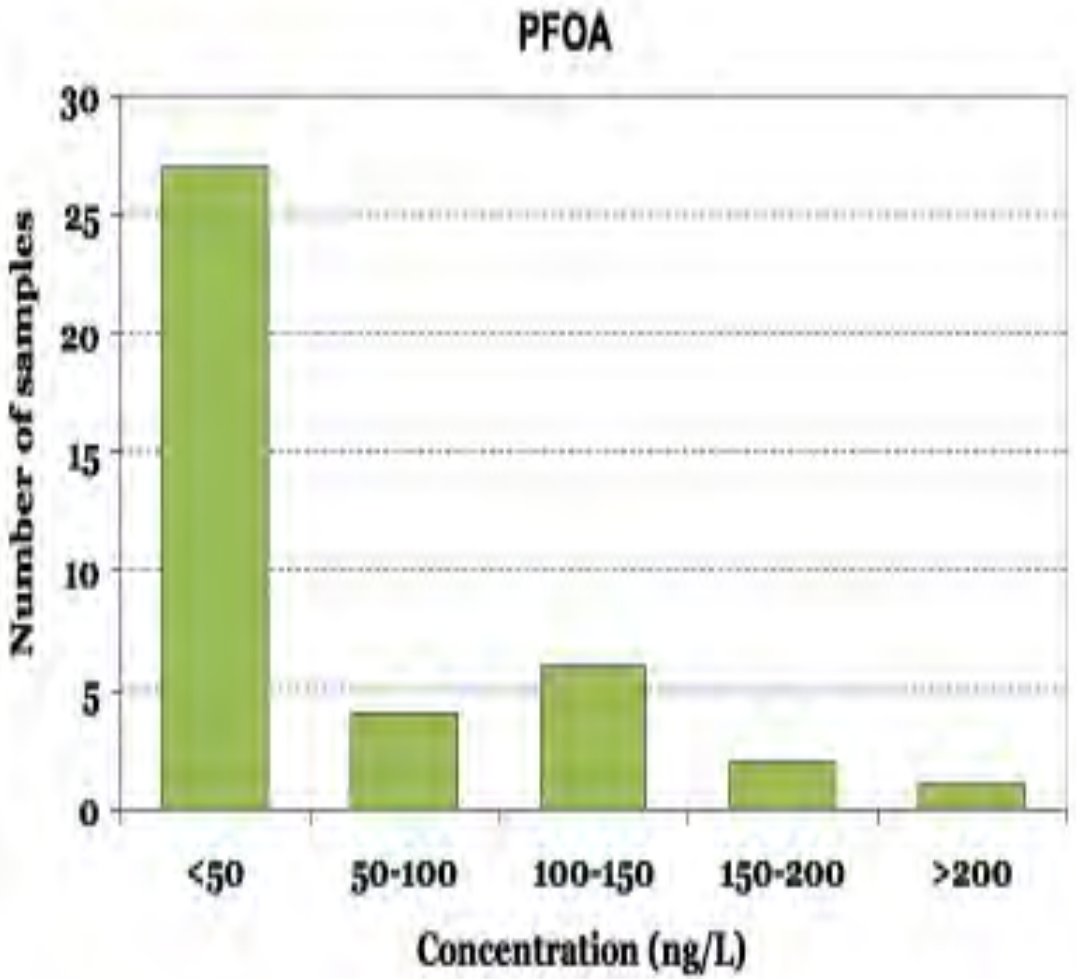
WHAT DO WE KNOW ABOUT DEVELOPING HUMANS (PFOA IN 67 NURSING MOTHERS, SPAIN)

FISH CONSUMPTION ASSOCIATED WITH HIGHER CONCENTRATION IN ADULTS, AND IN COLOSTRUM

FOR DEVELOPING HUMANS, PARITY AND BREAST FEEDING INVERSE-ASSOCIATED WITH MATERNAL SERUM CONCENTRATIONS. THIS IS **NOT** GOOD NEWS.

BREAST FEEDING HAS TRANSFER, BUT, LIKELY < LESS THAN IN UTERO,

IMAGE: GUZMAN ET AL. SCI TOTAL ENVIRON HTTP://DX.DOI.ORG/10.1016/J.SCITOTENV.2015.11.059



HOW ABOUT ANIMAL DATA COMPARED TO HUMAN DATA?

- **DELAYED MAMMARY GLAND DEVELOPMENT APPEARS TO BE THE MOST SENSITIVE TOXICOLOGY OUTCOME IN RODENTS, AND IS CONSISTENT IN MICE.**
- **STRUCTURAL CHANGES PERSIST UNTIL ADULTHOOD**
- **HUMAN STUDIES ALSO ASSOCIATE PFAS WITH SHORTER DURATION OF BREASTFEEDING, HOWEVER, HUMAN OBSERVATIONAL STUDIES NEED A PHYSIOLOGIC CONTEXT (REVERSE CAUSATION POSSIBLE).**

PFAS ARE LOWER IN WOMEN OF CHILDBEARING AGE, AND RISE AGAIN AFTER, AND

RECALL THAT PFAS ARE INVERSELY RELATED TO

- PARITY
- BREASTFEEDING

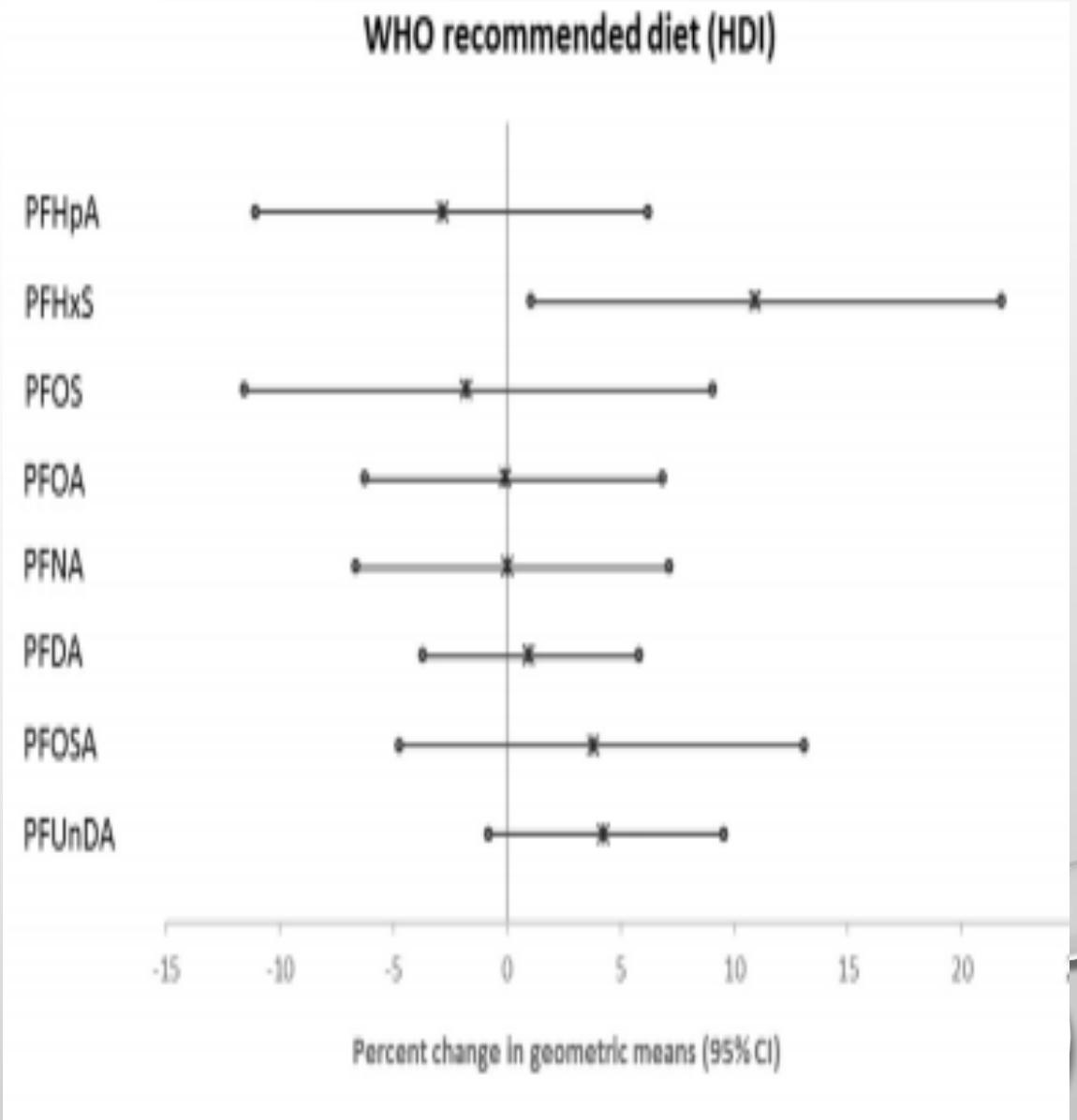
WHAT KINDS OF DIETS AFFECT EXPOSURE (PART 1)

FOOD STUDY CONSIDERED 3 DIET PATTERNS

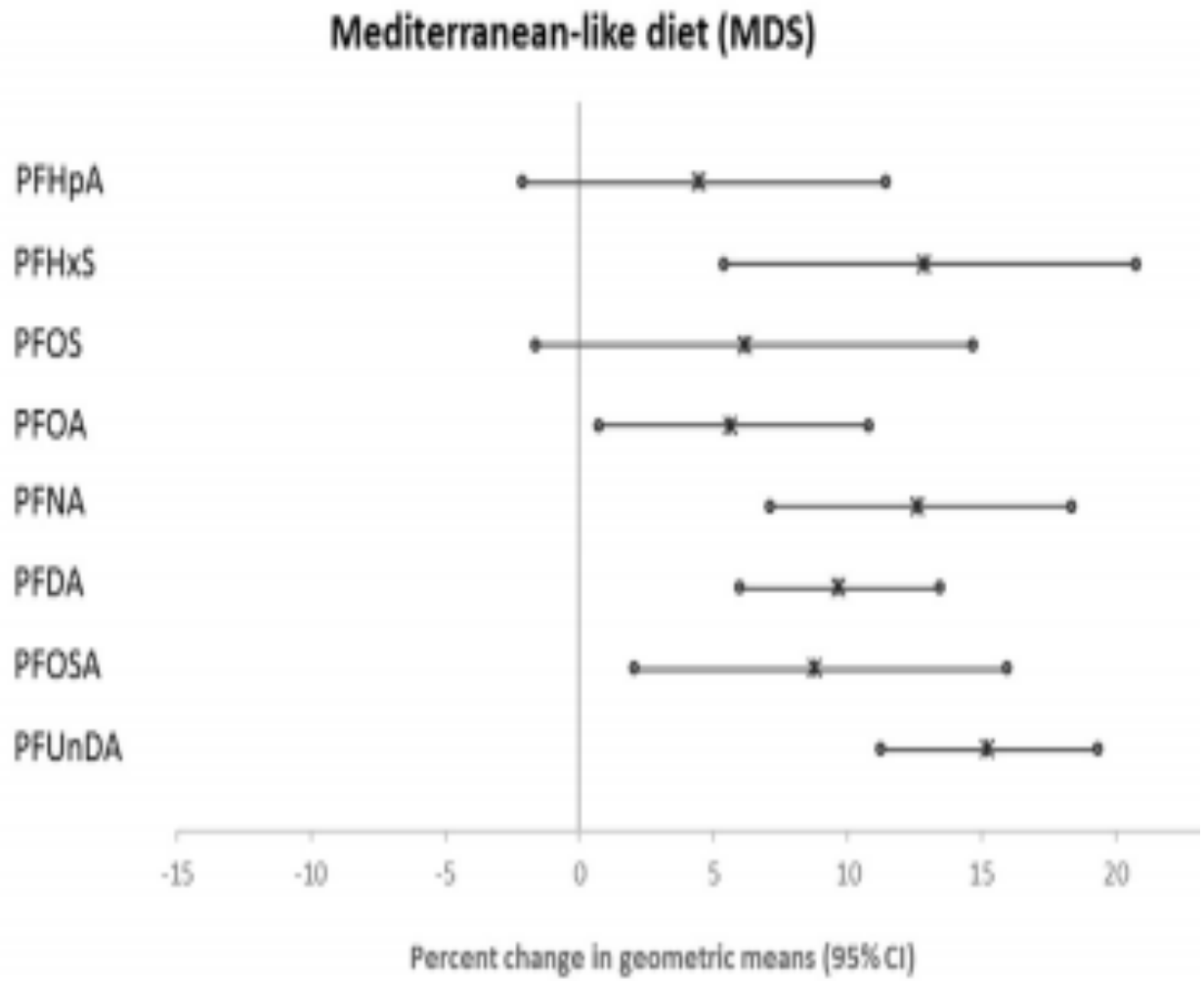
- **WHO**
- **MEDITERRANEAN**-LIKE

  (MORE INTAKE OF OIL AND **FISH** +ETOH)
- **LOW-CARB** HIGH PROTEIN

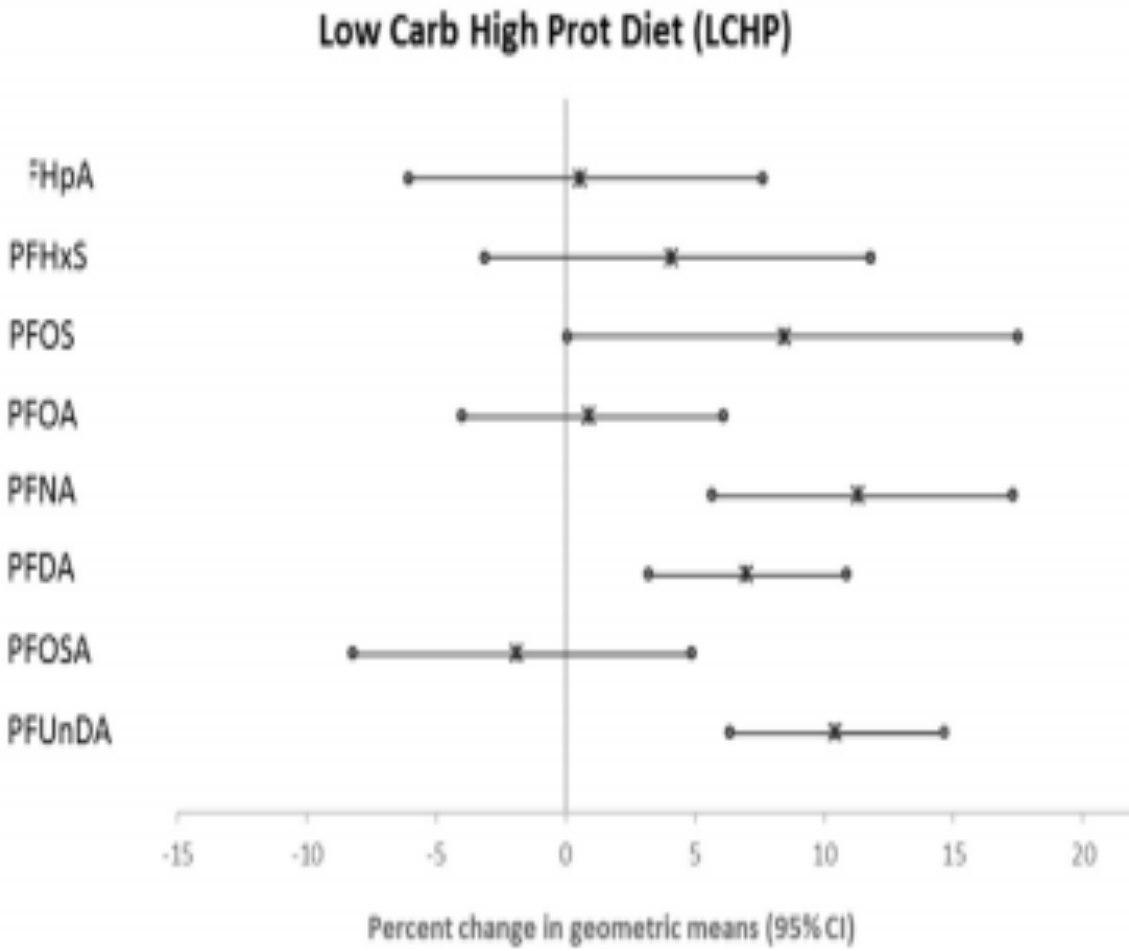
SJOGREN P ET AL. ENVIRON RES 2016 . DOI: 10.1016/J.ENVRES.2016.05.016 STUDY DESIGN CROSS-SECTIONAL IN 855 SWEDISH ADULTS AGE≥70



WHAT KINDS OF DIET (II) (SJOGREN ET AL CONTINUED, FOREST PLOTS SHOW % CHANGE FOR EACH INCREMENT ADHERENCE)



C)



AUTHORS POINT OUT THAT THE LIKELY SOURCE OF PFAS IN MEDITERRANEAN DIET IS FISH…….AND

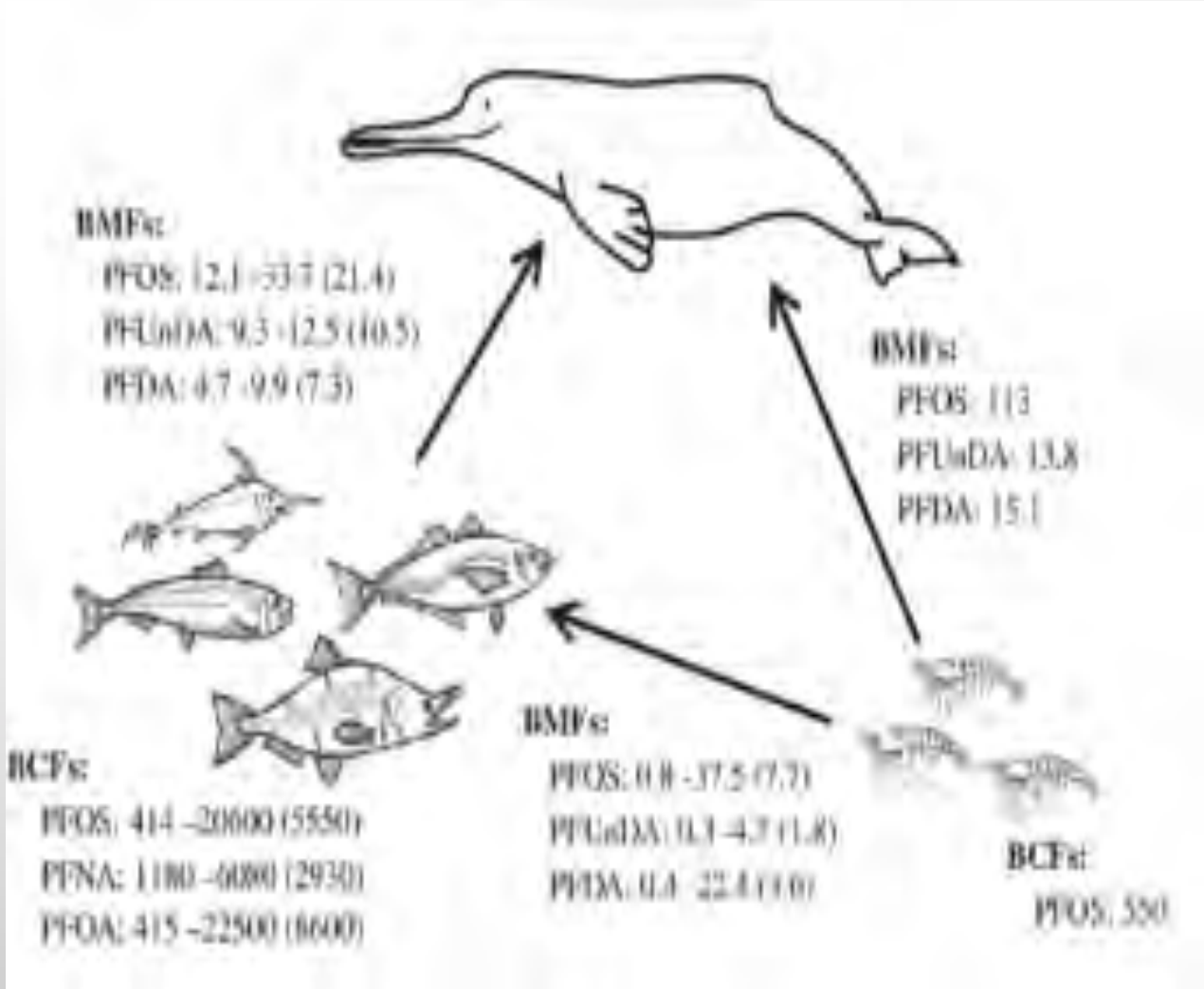
- PFHXS (6-C SULFONIC ACID) INCREASED WITH WHO DIET. (THIS MAY BE AN EXPOSURE FROM REPLACEMENT CHEMICALS)
- AND, THE FINDING ABOUT MEDITERRANEAN DIET IS CONSISTENT WITH FINDINGS CONCERNING METALS, PLASTICS-ASSOCIATED CHEMICALS, AND PERSISTENT ORGANIC POLLUTANTS

1. THE AUTHORS POINT OUT: THE FINDING ABOUT INCREASED EXPOSURE WITH MEDITERRANEAN DIET IS NOT NECESSARILY SUFFICIENT REASON TO OVERLOOK INFERRED HEALTH BENEFITS OF MEDITERRANEAN DIET

2. WE HAVE BEEN DOWN THIS ROAD WITH HG++. FISH WIN! BUT, THERE ARE STILL CHOICES AMONG FISH.

WHY THIS HAPPENS (?WHAT TO DO ABOUT IT?)

- BIOCONCENTRATION AND SOME BIOTRANSFORMATION OF PRECURSOR PRODUCTS *IN VIVO (BUT LITTLE METABOLISM TO SAFER METABOLITES. MORE THE OPPOSITE)*
- *BIOMAGNIFICATION IN FOOD WEB*

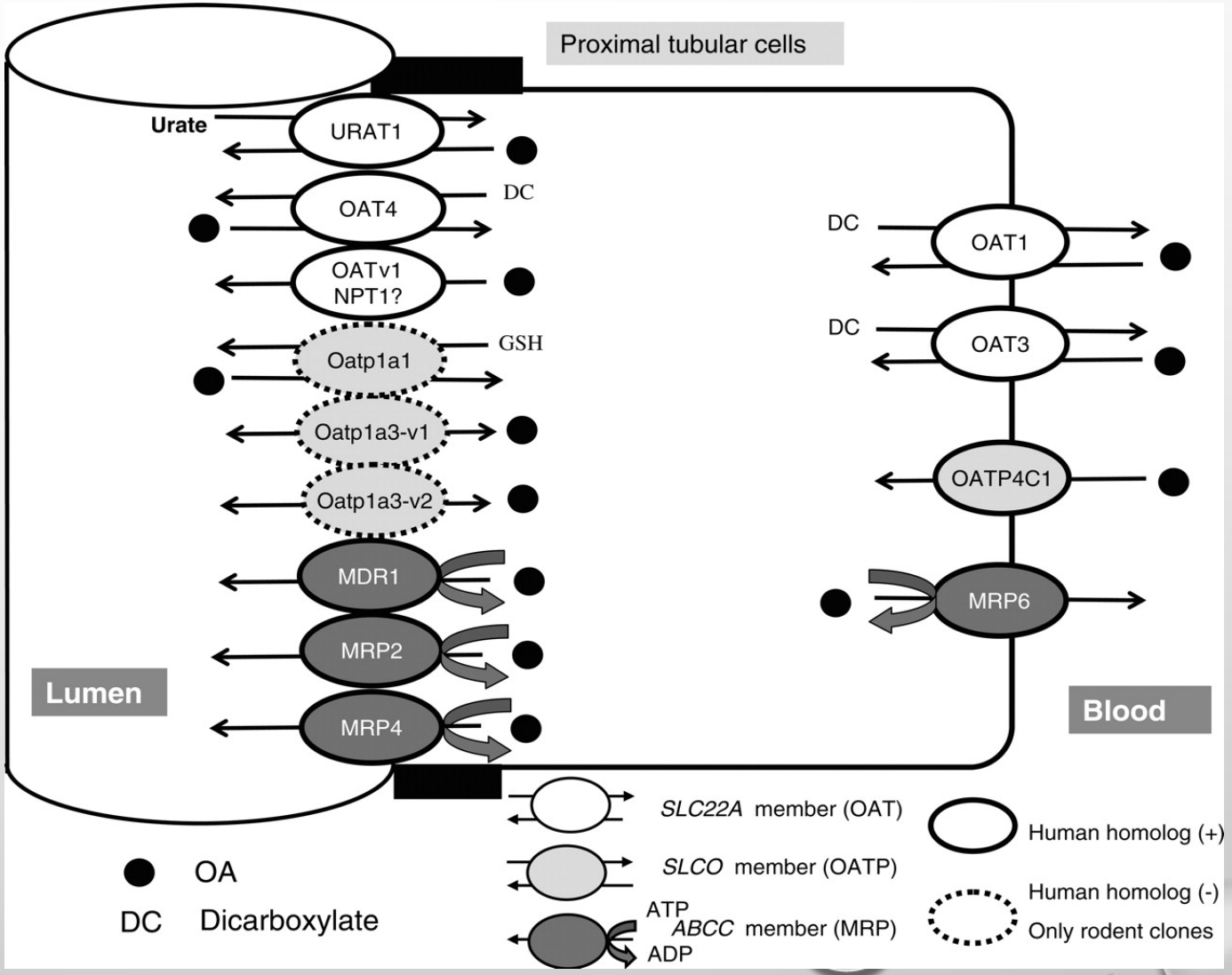


(IMAGE): YEUNG LW ET AL. GANGES FOOD WEB ARTICLE IN CHEMOSPHERE 2009. DOI: 10.1016/J.CHEMOSPHERE.2009.02.055

SOME EXPOSURE NOW INEVITABLE, WE DO HAVE CHOICES. IN ADDITION, WHAT ABOUT EXCRETION??

- HUMAN HALF LIVES ARE MUCH LONGER THAN RODENT HALF LIVES. DIFFERENCES DUE (IN PART) TO INTER-SPECIES DIFFERENCES IN ORGANIC ANION TRANSPORTERS (OAT)

(IMAGE, SEKINE T ET AL. AM J RENAL PHYS 2006; 290: F251-61)



STRESSORS BESIDES CHEMICALS

HEAT-EXPOSED STEEL WORKERS' SWEAT

- LOSSES OF **CA++**, K+, AND VITAMIN C MEASURED
- **SYSTOLIC AND DIASTOLIC BP** ASSOCIATED WITH > LOSSES

TANG YM ET AL. INDUSTR HLTH 2016; 54:214-23

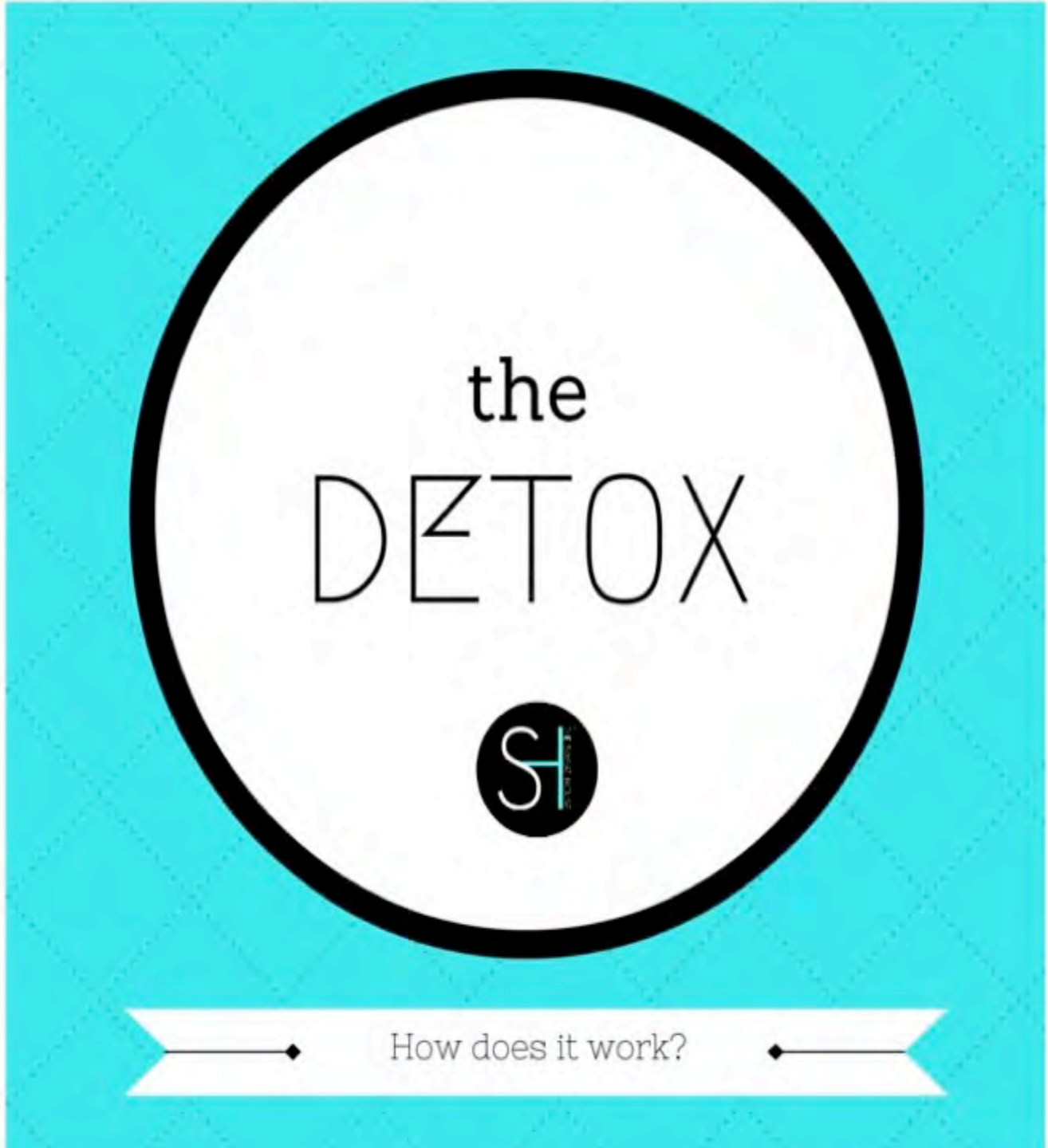
Table 5. Relationships between micronutrient losses in sweat during an eight-hour work shift and BP among heat-exposed steelworkers

Micronutrient losses in sweat	SBP		DBP	
	r	*P*-value	*r*	*P*-value
Vitamin C	0.268	0.003	0.216	0.019
Vitamin B_1	−0.022	0.599	0.096	0.338
Vitamin B_2	−0.053	0.599	−0.052	0.605
Potassium	0.299	0.001	0.233	0.012
Sodium	0.077	0.483	−0.032	0.772
Calcium	0.303	0.005	0.347	0.001
Magnesium	0.030	0.786	0.031	0.776
Iron	0.150	0.170	0.042	0.701
Zinc	0.102	0.359	−0.071	0.521
Copper	0.180	0.099	0.075	0.495
Selenium	0.075	0.592	0.085	0.540

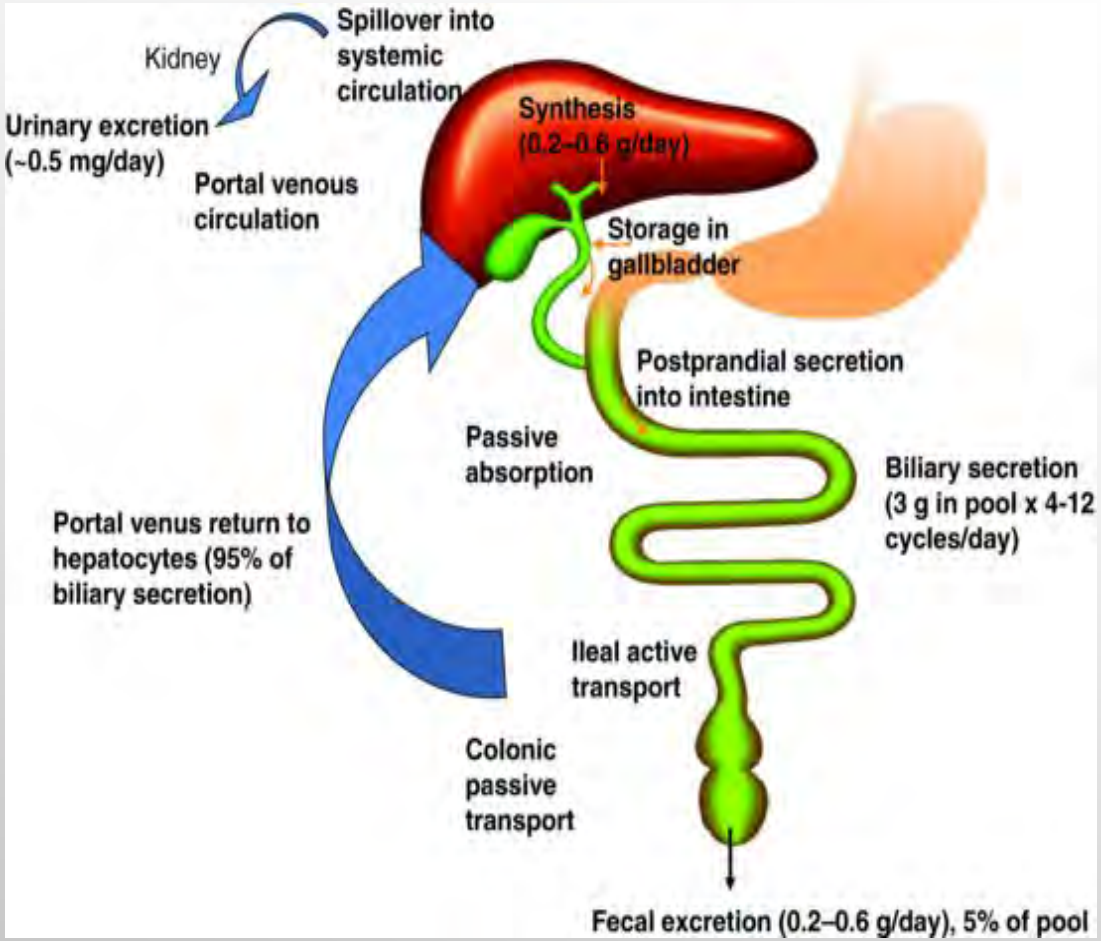
WHY CONSIDER OTHER STRESSORS ?

SWEAT THERAPY IS AN APPROACH TO DECREASING THE BURDEN OF SOME XENOTOXINS., INCLUDING PFAS, PCBS, AND OTHERS (GENUIS SJ, ET AL, ISRN TOXICOL 2013)

ANALYTES SUCH CAN BE MEASURED IN SWEAT. OUTCOME IS NONSPECIFIC, AND WE DO NOT KNOW THAT IT IS "DETOX"



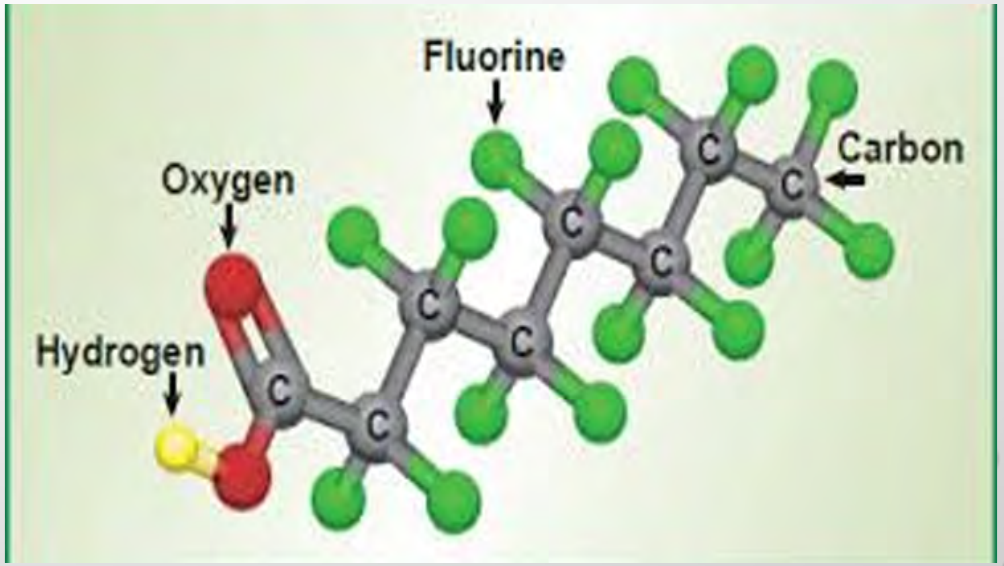
WHAT ELSE? ENTEROHEPATIC CIRCULATION



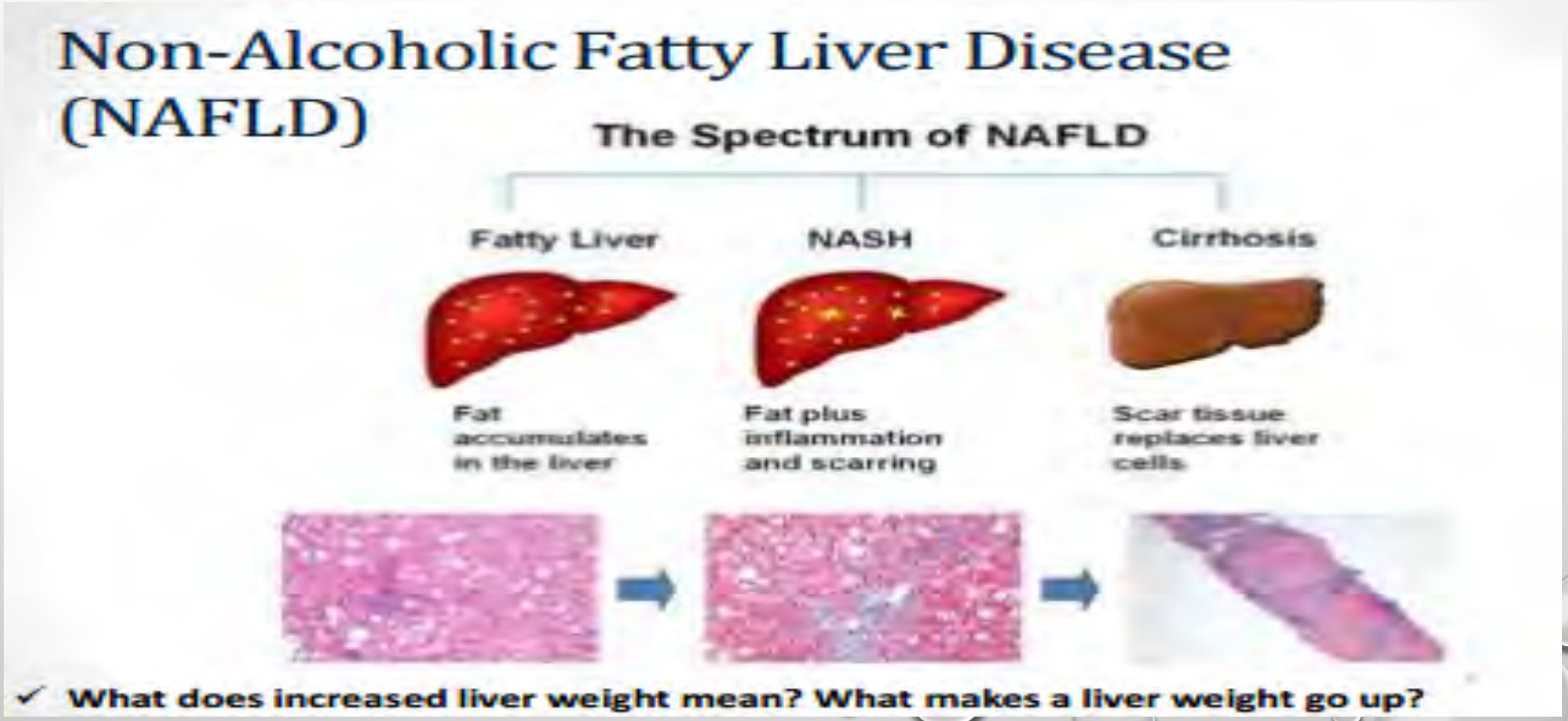
SEVERAL INVESTIGATORS HAVE SHOWN THAT DRUGS WHICH INTERFERE WITH ENTEROHEPATIC CIRCULATION OF BILE ACIDS ALSO <u>DECREASE</u> THE SULFONATED PFAS SUCH AS PFOS AND PFHXS. EXAMPLE: CHOLESTYRAMINE (AN OLD-FASHIONED RESIN-BINDER CHOLESTEROL DRUG).

CAN WE USE THAT DATA TO DECREASE EXPOSURES (AND NOT RISK HARM ??) WE HAVE UNPUBLISHED DATA THAT IT WORKS, BUT NONE ABOUT RISKS/BENEFITS.

AN EASY CLINICAL TRIAL FOR THIS AUDIENCE



WHY MIGHT THIS MATTER? NAFLD IN ANIMAL TOXICITY AND HUMAN STUDIES



HOW ABOUT HUMAN GENETICS?

GILBERT'S SYNDROME

- INHERITED ERROR OF GLUCURONIDATION OF BILIRUBIN
- UNCONJUGATED ("INDIRECT) BILIRUBIN ELEVATED
- IN 5-7% OF HUMANS. USUALLY ASYMPTOMATIC, OFTEN HEALTHY
- AND MAY **LOWER** RISK OF CV DISEASES IN THOSE NOT ILL (POSSIBLY BY ANTI-OXIDATION)

URIDINE-DIPHOSPHOGLUCUORYL-TRANSFERASE 1A1 (UGTIAI)

DIET USUALLY NOT MODIFIED

ALCOHOL AND SOME DRUGS DETOXIFIED BY GLUCURONIDATION CAN BE PROBLEMS

ORGANIC ANION TRANSPORTERS IN LIVER ALSO AFFECTED, SO……..

WHAT WE FOUND (FAN H, ET AL. ENVIRON RES 2014; 135: 70-75)

Table 3
Association between PFC serum concentration (ng/ml) and Gilbert syndrome phenotype (adjusted).

Variables	Cases		Control 1	
	n	Geometric mean (95% CI)	n	Geometric mean (95% CI)
PFPeA (ng/ml)	62	0.63 (0.57–0.69)	2495	0.65 (0.64–0.66)
PFHxA (ng/ml)	**654**	**1.81 (1.72–1.89)**	**27,450**	**1.12 (1.11–1.13)**
PFHS (ng/ml)	1166	3.07 (2.94–3.22)	53,257	2.97 (2.95–2.99)
PFHpA (ng/ml)	384	1.00 (0.94–1.06)	17,333	0.95 (0.94–0.96)
PFOA (ng/ml)	1166	32.70 (30.48–35.07)	53,257	32.79 (32.45–33.12)
PFOS (ng/ml)	1166	19.35 (18.64–20.11)	53,257	19.07 (18.96–19.17)
PFNA (ng/ml)	**1166**	**1.41 (1.37–1.45)**	**53,257**	**1.36 (1.35–1.36)**
PFDA (ng/ml)	**617**	**0.73 (0.72–0.75)**	**24,570**	**0.71 (0.71–0.72)**
PFUnA (ng/ml)	145	0.67 (0.63–0.71)	4951	0.67 (0.66–0.68)
PFDoA (ng/ml)	14	0.60 (0.48–0.74)	403	0.64 (0.62–0.67)

WE HYPOTHESIZED: INTERACTION WITH LONG CHAIN SULFONATES

<u>HOWEVER, WE FOUND</u>

INTERESTING (?IMPORTANT?) DIFFERENCE IN **SHORT CHAIN ALKYLATE, PFHXA**, WHICH IS ONE OF THE "NEWER" GROUP THAT COULD INCREASE

CONCLUSION –

- COINCIDENCE? (ALBEIT WITH PRETTY BIG NUMBERS)?
- OR SOMEONE SMARTER CAN FOLLOW UP ON A GENETIC RISK GROUP

"AT RISK" IS CLEAR (MY BIAS), PREVENTION OF EXPOSURE SEEMS WARRANTED (DITTO), TREATMENTS IN QUESTION.

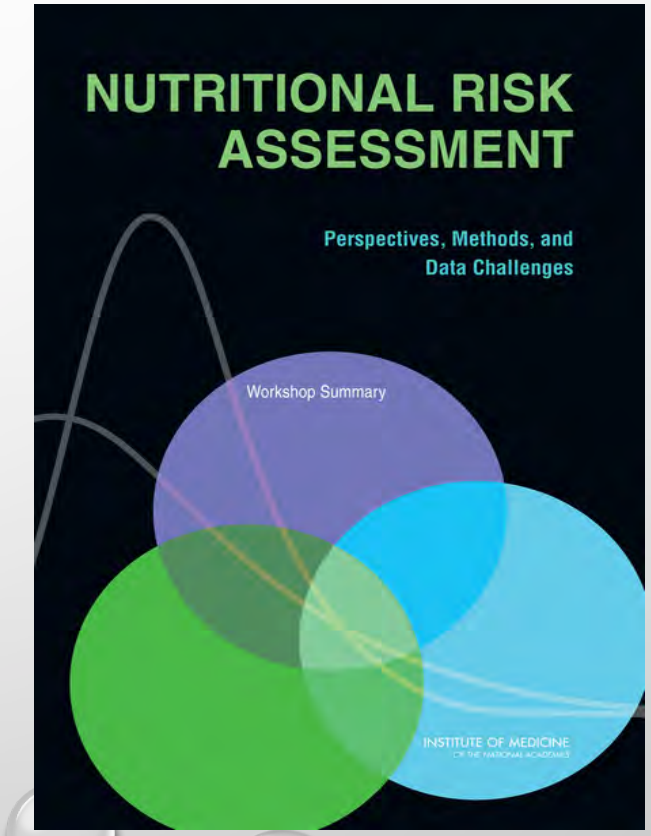
US EPA DEFINES SENSITIVE SUBPOPOPULATIONS AS:

- PREGNANT WOMEN
- LACTATING WOMEN
- BOTTLE FED INFANTS

- THE HALF-LIFE IS YEARS (NOT SOME FRACTION OF 9 MONTHS)
- SENSITIVE END-POINTS ARE TO DEVELOPING HUMANS, OUTCOMES INCLUDE LIPIDS, STEROLS, AND IMMUNE, SO……

IS A NUTRITION RISK ASSESSMENT WARRANTED?

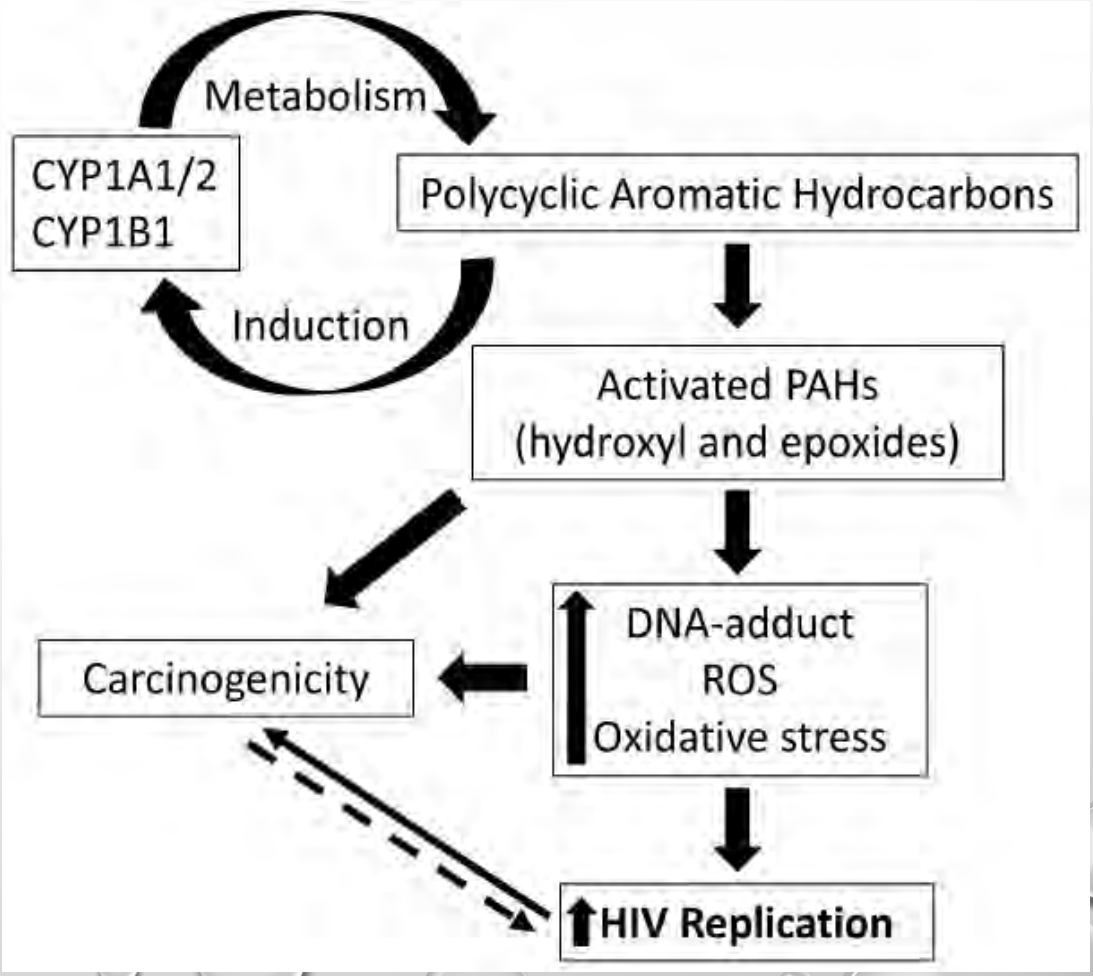
- MY OPINIONS (YES TO BREAST FEEDING, NO TO DECISIONS THAT LEAD TO MORE EXPOSURE, YES TO DIETS THAT MAY ENHANCE EXCRETION, AND YES TO FISH DESPITE THE RISK OF EXPOSURE (FISH IS NOT JUST ONE FOOD).
- THE NAS (SEE IMAGE) SHOULD DEMAND MUCH MORE THAN MY OPINION.



SIMILAR EXAMPLES OF BIOMARKERS OF CONCERN? **PAHS** FROM SMOKING, AIR POLLUTION, DIET

- PAH EXPOSURE LEADS TO UP-REGULATION AND TO MORE ROS, OXIDATIVE STRESS, AND OXIDIZED METABOLITES.
- THESE IN TURN CAN LEAD TO INCREASED RISK IN SUSCEPTIBLE POPULATIONS (EXAMPLE, SMOKERS WITH HIV, INFECTION OR CANCER)

(RAO PS, KUMAR S. FRONTIERS MICROBIOL 2015; HTTP://DX.DOI.ORG/10.3389/FMICB.2015.00550)



1. MONO OH-PAHS ARE COMMON METABOLITES, AND, 2. ASSOCIATED WITH AODM.

NHANES, 3 CYCLES (2001-02, 03-04, 05-06) IN ADULTS AGE 20-65

DESIGN: 8 URINARY OH-PAH WITH: HÞA1C OF >6.5%, OR DIABETES DX, OR INSULIN USE

OUTCOME: SUM OF 8 OH-PAHS (AND SOME SPECIFIC MARKERS SUCH AS 1 OR 2- OH NAPTHOL AND 2- OH PHENANTHRENE ASSOCIATED IN INTER-QUARTILE COMPARISONS (ALSHAARWAY O ET AL OCCUP ENVIRON MED 2014: 71:437-41)

CONCLUSIONS (MINE) :

1. ASSOCIATION IS WORRISOME FOR DIET AND FOR AIR POLLUTION (AND PERHAPS EVEN FOR WATER POLLUTION).
2. SUPPORTED IN OTHER LITERATURE. (ALSO ASSOCIATED WITH LOWER COGNITION)
3. ASSOCIATION IS NOT CAUSATION.
4. SO, WHAT ARE THE POSSIBILITIES, AND WHAT CAN THE NUTRITION COMMUNITY DO ABOUT IT?

WHAT ARE THE POSSIBILITIES?

- NOT A LOT OF STUDIES YET, ASSOCIATION COULD BE

  SPURIOUS.

- OTHER SUPPORTING DATA INCLUDES:
- SUPPORTING DATA IS NOT PROOF (JUST TOO EARLY TO SAY WE KNOW FOR SURE).

DIABETES: CAPPELLETTI R, ET AL. J OCCU MED TOXICOL 2016 DOI: 10.1186/S12995-016-0095-8

OBESITY EPI: RANJIBAR M, ET AL PLOS ONE 2015 DOI: 10.1371/JOURNAL.PONE.0137536

OBESITY TOX: YAN Z, ET AL. PLOS ONE 2014 DOI: 10.1371/JOURNAL.PONE.0110706

WE KNOW ABOUT TOBACCO USE AND DIABETES. HOWEVER, BIOMARKER (COTNINE) NOT AS USEFUL AS EXPOSURE HISTORIES (KEITH RJ ET AL. PLOS ONE. DOI: 10.1371/JOURNAL.PONE.0157592)

CONFOUNDING – REVERSE CAUSATION?

DIABETICS COULD MAKE MORE OH-PAHS, NOT JUST EXCRETE THEM

(SELECTIVELY METABOLIZE TO MORE REACTIVE SPECIES)

- WOULD STILL DEFINE A SUSCEPTIBLE POPULATION, AS SUM OF EXPOSURES NOW GREATER.

RISK FACTOR CONFOUNDING

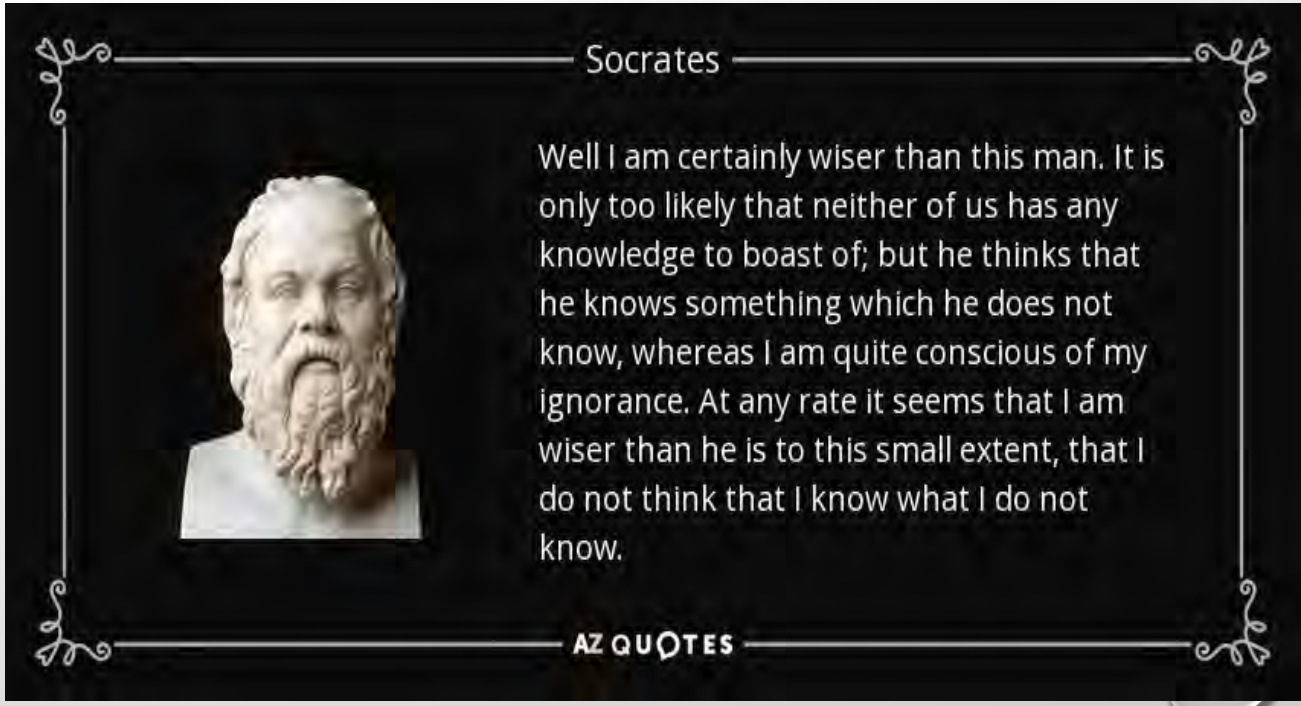
- RISKS OF EXPOSURE TO PAH COULD BE MEDIATED BY FACTORS THAT INCLUDE RISKS OF EXPOSURE TO PAHS, WITHOUT PAHS BEING IN THE PATH TO TOXICITY
- THIS IS A MORE PLAUSIBLE TYPE OF CONFOUNDING .

THIS KIND OF THINKING HAS ALREADY BEEN DISPROVED FOR SEVERAL PAH OUTCOMES OF IMPORTANCE .

SHOULD IT BE THE CASE FOR DIABETES, IT WOULD STILL DEFINE BOTH A USEFUL BIOMARKER AND A LIKELY PATH TO NUTRITION RECOMMENDATIONS, REGARDLESS OF SPECIFIC CAUSATION

GENETICALLY SENSITIVE SUBPOPULATIONS OF SMOKERS?

- GENE POLYMORPHISMS ARE KNOWNS TO BE LINKED TO DIABETES RISK, INCLUDING ADULT ONSET. ASSOCIATIONS ARE GENERALLY MODEST, AND FINDINGS OF MUTATIONS OF INTEREST ARE GENERALLY HETEROGENEOUS
- IT MAY BE PREMATURE TO SAY THAT INHERITED RISK FOR DIABETES EQUALS SUSCEPTIBILITY THAT GOES WITH SPECIFIC TOXINS. IT IS NOT PREMATURE TO BE WORRIED



A CLINICIAN VIEW: REGARDLESS OF MECHANISMS, THE NUTRITION AND ENVIRONMENTAL COMMUNITIES HAVE ALREADY IDENTIFIED CLEAR INTERVENTION(S) THAT **CAN** HELP

Presentation Clinical Actions

After participating in this presentation, clinicians should be better able to:

1. Identify scientifically robust data regarding ingested toxins and application in practice

2. Apply literature in support of clinical interventions which result in positive impacts on health with reasonable cost-benefit profiles.

- In general, preventing/reducing toxic ingestion is preferred, especially for susceptible populations. Nutritional approaches to increasing excretion, and to bioprotection, have some promise