Assessing PAHs in the Real World

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PAH are Ubiquitous

- Astronomers: ~20% of the carbon ***in the universe*** is in the form of PAHs
  - NASA's web site: "Polycyclic aromatic hydrocarbons… are among the building blocks of life… are pervasive in galaxies like our own Milky Way, and play a significant role in star and planet formation."
- On Earth, there is no exposure to any one PAH, but the real world is full of PAH-containing mixtures
  - Of which there are uncounted thousands
  - PAH-containing mixtures also contain a variety of heterocyclic PAH compounds and non-PAH compounds
  - Industrial and natural processes produce and use complex mixtures which contain PAHs and hundreds of related and unrelated compounds.
    - In regulatory-speak, Class 2 chemicals: "**U**nknown or **V**ariable composition, **C**omplex reaction products or **B**iological materials" (UVCBs)

The PAH Literature is Vast

- PAH-containing mixtures are arguably the most studied materials in the environment
  - and there are human exposure data including occupational, clinical and ambient data
- One deliberately isolated PAH - benzo(a)pyrene -is arguably the most studied substance in toxicology
  - but there are no human exposure data to individual PAHs with 3 or more rings

Everyone is Exposed

"The majority of exposure (>95%), to high molecular weight PAHs in nonsmokers, is through the diet in a variety of foods including breads and cereal grains, vegetables, and smoke-cured or barbequed meats." Madeen et al. *Chem. Res. Toxicol.*, 2015, 28 (1), pp 126–134
DOI: 10.1021/tx5003996

Summary of Estimated Daily Intakes of Benzo(a)pyrene Toxic Equivalents (BaP-TE)

Source of Exposure	Average Daily Intake (ug/day)
Ambient air and indoor air	0.006 to 0.02
Diet	0.2 to 0.6
Smoking	0.2 to 1
Second hand smoke	0.005 to 0.26
Coal tar pharmaceuticals	33
Coal tar shampoo	0.017

The Regulation and Science of PAHs

- Some Regulations and Regulatory Tools Need Updating
  - Human Health Risk Assessment Methods
  - Hazard Assessment
- Ecological Assessments Should be More Focused on Risk

Assessment Methods: Human Health Toxicity Values Need to be Updated

- "Relative Potency Factor" (RPF) approach
  - Additive toxicity
  - Add B(a)P equivalency factors of EPA-16 Priority Pollutant PAHs or an expanded PAH list [EPA 2010 proposal, California list, etc.]
  - Use of expanded list may exacerbate overestimation of risk
  - 1993 EPA Guidance is provisional, not promulgated
- EPA's Science Advisory Board
  - RPF approach is scientifically problematic
  - Antagonism, bioavailability/bioaccessibility important mediators of PAH risk
  - Recommended conducting toxicity testing on a variety of PAH-containing mixtures with a view to replacing RPFs
  - Currently promulgated IRIS assessment for B(a)P is out-of-date

Assessment Methods: Hazard Characterization of Mixtures Should be Re-evaluated

- National Academy Recommendation: EPA/IRIS assessment of chemicals adopt methods developed for use in pharmaceutical approvals
  - Systematic Review & Risk of Bias analysis of existing studies, meta-analysis
  - NTP & EPA have been developing guidance
- 5 recent Systematic Reviews (including risk of bias evaluations) including dozens of studies of occupational exposures in PAH-using industries
  - Industries: iron & steel foundries, aluminum plants, cokeries, carbon electrode manufacturing, asphalt pavers & roofers, creosote, tar distilleries
- Little to no association between occupation entailing high PAH exposure and cancer risk
  - Endpoints considered: cancers of the skin, larynx, lung, respiratory tract, bladder, kidney, Hodgkin lymphoma, non- Hodgkin lymphoma, leukemia, multiple myeloma

One Recent Systematic Review

Table 2 Overall standardized mortality ratios (SMRs) and pooled relative risks (RRs) with 95 % confidence intervals (CIs) for selected cancer sites for workers exposed to polycyclic aromatic hydrocarbons in various industries and occupations

Industry, cancer site	No. of cohorts	Obs/Exp	SMR	Pooled RR[a] (95 % CI)	*p* value for heterogeneity
Aluminum production					
Larynx	7	71/63.4	1.12	1.15 (0.91–1.45)	0.700
Lung	10	1,314/1,154.7	1.14	1.07 (0.93–1.23)	<0.0001
Respiratory tract[b]	11	1,349/1,183.9	1.14	1.08 (0.95–1.23)	<0.0001
Bladder	10	279/202.2	1.38	1.28 (0.98–1.68)	0.002
Kidney	8	131/126.4	1.04	1.06 (0.89–1.25)	0.728
Iron and steel foundry					
Larynx	5	59/41.2	1.43	1.48 (1.14–1.91)	0.537
Lung	13	2,903/2,762.4	1.05	1.31 (1.07–1.61)	<0.0001
Respiratory tract[b]	14	2,932/2,784.7	1.05	1.31 (1.08–1.59)	<0.0001
Bladder	9	151/127.7	1.18	1.38 (1.00–1.91)	0.001
Kidney	6	68/69.4	0.98	1.03 (0.78–1.35)	0.304
Asphalt workers					
Larynx	2	45/42.7	1.05	1.89 (0.45–7.95)	0.013
Lung	3	827/735.7	1.12	1.59 (0.68–3.76)	<0.0001
Bladder	2	109/107.1	1.02	1.03 (0.82–1.30)	0.305
Carbon black production					
Lung	3	249/201.1	1.24	1.52 (0.91–2.52)	<0.0001
Respiratory tract[b]	4	283/243.6	1.16	1.30 (0.84–2.01)	<0.0001
Bladder	3	15/14.8	1.02	1.10 (0.61–2.00)	0.288

Obs/Exp observed/expected number of cancer cases/deaths

[a] Calculated as a weighted average of the SMRs through random-effects models

[b] Including lung and other respiratory cancers not specified

"It cannot be ruled out whether such excesses are due, at least in part, to possible bias or residual confounding."

Rota et al., Arch. Toxicol,. 2014, 88(8), DOI: 10.1007/s00204-014-1296-5

5 Recent Systematic Reviews of Occupational Exposure Literature ….

Patient undergoing coal tar application as part of Goeckerman treatment.

Photo courtesy of the University of Michigan Health System

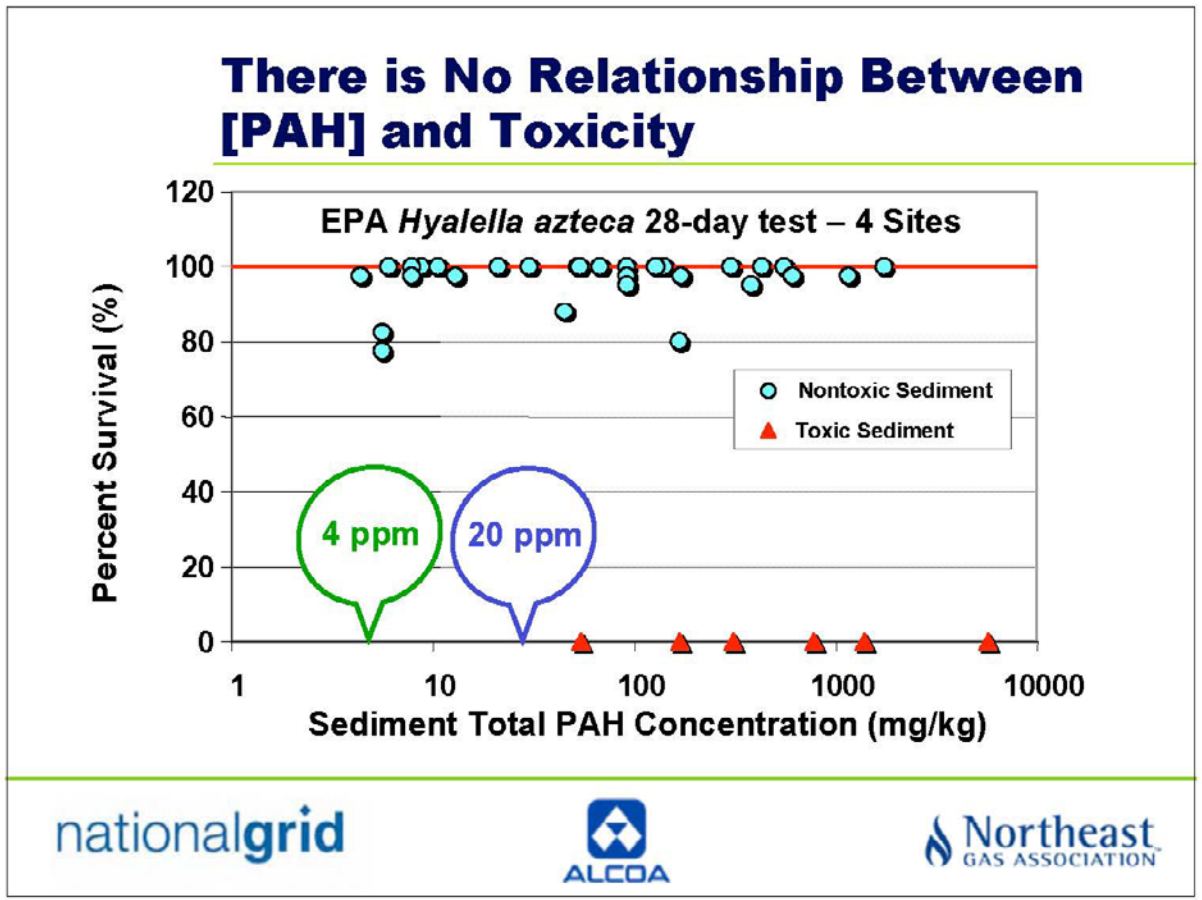
… Does not include data from clinical literature

Assessment Methods: Ecological Risk

- Often, comparisons are made using “consensus standards”
  - Is that meaningful?
- In Superfund site evaluations, EPA found that sediment toxicity rarely correlates with sediment PAH concentrations
  - Development of Equilibrium Partitioning Benchmarks
  - PAH concentrations in sediment pore water is often a better predictor of bioaccessible PAHs
- Bioavailability found to vary with PAH sources

“…*PAH source materials have a dominating influence on partitioning, highlighting the importance of using native field soils in bioavailability and risk assessments.”* Xia et al., ES&T, 2016, DOI: 10.1021/acs.est.5b06164

Sediment PAH Concentration vs. *H. Azteca* Survival



Nuehauser et al. (2006) Land Contam. Reclam. 14(2):261-266

Another example – Anacostia River sediment:
Geiger, S. (2009) ESTCP Project ER-200709 available at https://www.serdp-estcp.org/

Creosote treated piling in Sooke Basin

Anemones, which are related to jellyfish, became increasingly abundant on the piling in deeper water (left). Food is collected on the tentacles of these animals using stinging cells called nematocysts, which are triggered by contact with prey. These tiny spears are tipped with poison that quickly subdues copepods, amphipods and other living organisms. In Puget Sound, mussels are generally found high in the intertidal, or on piling in the Pacific Northwest because the bottom is home to a host of species of starfish who are voracious predators on these and other bivalves. The Sooke Basin creosote treated pilings were no exception and armies of starfish, like the ochre stars (*Pisaster ochraceus*) seen at right were frequently found grazing on the barnacles and mussels that had settled on the piling.

The piling became home to a community of animals that any aquarium would be proud of.

Assessing PAHs in the Real World

- It’s not as easy as adding up B(a)P-equivalencies or comparing to consensus standards
- Must work towards understanding….
  - Source(s) of the PAHs
  - Sinks…
    - What is the behavior of PAH-containing particles once away from their sources, in soil, sediment, air?
  - Bioavailability (& Bioaccessibility)
  - A Mixture approach to toxicity

We will hear progress on all these fronts in the platform presentations & posters (18) today

Questions?