Exposure to polycyclic aromatic hydrocarbons (PAHs) and breast cancer incidence: Evaluating the sate of the science

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Abstract

Exposure to PAHs can occur in certain work places and from tobacco smoke, specific foods, or contaminated air. Linkage between female breast cancer (BC) and specific exposure sources of PAHs has been reported in some studies, and some PAHs exhibit estrogenicity. To investigate the potential associations, we conducted a state of the science review of epidemiological studies of PAH exposure and BC.

Based on analytical epidemiology studies of BC incidence or mortality found in PubMed, Scopus and Web of Science, we mapped evidence, evaluated study quality issues, and summarized findings by exposure assessment type. Five prospective and 12 case-control studies reported BC risk estimates specific for PAH exposure. PAH exposure was assessed from a specific source or from all sources. The former included occupation-based exposure (N=3), air pollution (N=2), and food (N=6). The latter included PAH-DNA adducts in breast tissue (N=2) or blood (N=1), PAH-albumin adducts in blood (N=1), and PAH metabolites in urine (N=2).

All occupational exposure and air pollution studies reported positive associations, in overall or subset analyses, with stronger associations for higher PAH exposure intensity, exposure from a specific occupational source, or during a specific exposure window. Most studies assessed exposure over long periods of time, although they suffer from imprecise assessments and potential confounding from co-exposure to other carcinogens. All four studies of PAH adducts, reflecting combined recent exposure (months) and susceptibility, were associated with an increased risk of BC. One adduct study was a nested case control within a prospective cohort, and the other three were case-controls studies, which may be subject to reverse causality. Studies using urinary biomarkers, which assess very recent exposure, and food intake, which are prone to measurement error, reported inconsistent findings.

Most studies across this wide variety of exposure scenarios reported elevated risks of BC in overall and/or in subgroup analyses. However, interpretation of the findings is complicated considering accuracy and specificity of exposure assessment methods, relevant exposure windows, and potential confounding. Studies capturing lifetime exposure, integrating multiple sources, and examining source apportionment will elucidate this evidence base.

Background and Objectives

- Environmental causes of breast cancer remains a research gap.
- PAHs are ubiquitous in the environment.
- People are exposed to mixtures of PAHs from certain occupations, foods, tobacco smoke, and contaminated air.
- Some PAH exhibit estrogenic activity and associations with specific PAH sources have been reported.
- State of the science review of epidemiology studies was conducted reporting effect estimates for PAHs and breast cancer (BC).

Approach

- We searched PubMed, Web of Science, and Scopus for analytical epidemiology studies reporting effect estimates for PAHs and BC incidence and mortality.
- We mapped and characterized the studies by type of exposure assessment (**Table 1**):
  - (1) biomarkers integrating exposure from multiple sources, and
  - (2) PAH exposure from specific sources.
- We created forest plots of effect estimates of each study for
  - (1) ever vs. never exposed (**Figure 1**) and
  - (2) high exposure vs. low (e.g., level, duration) (**Figure 2**).

Table 1: Characterization of PAH and breast cancer studies by exposure source

	Study Design	Exposure	Findings/patterns	Comments
Multiple Exposure Sources				
Adducts: DNA or protein (albumin)	3 case-control 1 nested case-control	Assessment: measurement Window: Recent, months PAH: Proxy PAH	⇧ risk: all 4 studies Effect modifiers: menopausal status	Measure exposure & susceptibility Reverse causality
Urinary metabolites	1 nested case cohort 1 case-control	Assessment: measurement Window: recent, hours/days PAH: Proxy PAH	Cohort: Null Case-control: 1OH levels, but not other urinary metabolites, significantly higher in case than controls (no OR and not plotted)	Case-control: reverse causality Cohort: bias toward the null
Specific Exposure Sources				
Occupational	3 case-control	Assessment: JEM Window: Years PAH: Mixtures	⇧risk: all 3 studies (including subgroup analysis) Higher risk for higher, longer exposure Effect modifiers: earlier age of exposure, family history of BC, receptor and menopausal status	Co-exposures to workplace carcinogens
Traffic related air pollution	2 case-control	Assessment: Models Window: long-term, years PAH: Proxy PAH	⇧risk: all 3 studies Effect modifiers, earlier age of exposure, menopausal status, receptor status, diet	Co-exposure to other environmental contaminants
Total food intake	2 case-control	Assessment: Dietary questionnaire of total diet + linkage with PAH tables/databases Window: Years PAH: Proxy PAH	⇧ Risk in one study, null in the other.	Very high concern for measurement error and very high potential for confounding by other dietary components
Meat intake	1 case-control 3 cohort	Assessment: Dietary questionnaire or meat intake and cooking preferences + linkage with PAH tables/databases Window: Years PAH: Proxy PAH	Null in all studies, except in receptor positive	Very high concern for measurement error and a very high potential for confounding by other dietary components. Meat not the largest source of PAHs in the diet

Figure 1 – Ever vs. never exposed to PAHs

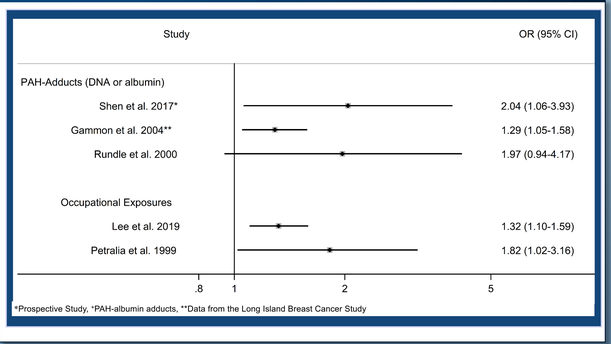
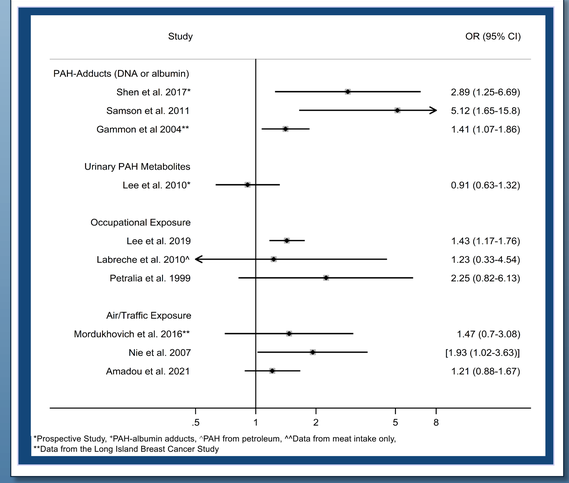


Figure 2 – High vs. low exposure to PAHs



Discussion

- Most studies (except occupational studies) measured a specific PAH, which served as a proxy for exposures to PAH mixtures.
- Stronger associations seen with higher exposure intensity (e.g., higher levels of exposure in the environment or occupation), specific occupational source, or duration of exposure (e.g., exposure began earlier in life).
- Largely null findings were seen for PAHs in the dietary studies. These studies have a very high risk of exposure misclassification. It is unclear if these studies should be included in a future hazard evaluation.

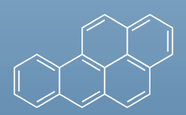
Next Steps and Conclusions

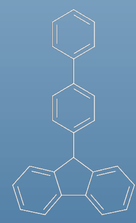
This state of the science report found that –

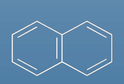
- An adequate database of studies is available to evaluate BC and exposure specific for PAHs.
- Timing, duration, and window of exposure (earlier age) may impact risk.
- Studies integrating multiple sources of exposure and using improved exposure assessment methods at different time periods (especially earlier ages) are needed.

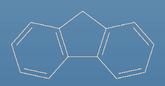
Next Steps –

- Conduct a hazard assessment of PAH exposure and Breast Cancer. The review would include:
  - Evaluation of risk of bias and study sensitivity.
  - Evaluation of effect modifiers.









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