# Occupational Exposure to Pentachlorophenol and Other Agents

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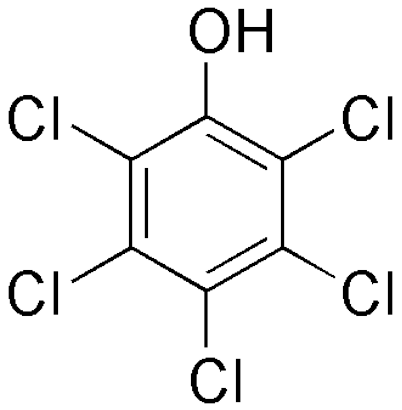
Disclaimer: The findings and conclusions in this report are those of the author and do not necessarily represent the views of the National Institute for Occupational Safety and Health.

# Background

- Pentachlorophenol (PCP), a wood preservative, has been used in the United States since 1936
- PCP has been used to preserve wood structures (cabins and decks). Its current use is restricted to treating telephone poles, rail ties, and wharf pilings

# Background

- All PCP manufactured in the United States was produced by the direct chlorination of phenol in the presence of various catalysts
- PCP is classified by the International Agency for Research on Cancer as a possible human carcinogen (Group 2B)
- PCP manufacturing contaminants include tri- and tetrachlorophenols, furans, and dioxins, but not 2,3,7,8-tetrachlorodibenzodioxin (TCDD)
- Trichlorophenol (TCP) and its derivatives contain TCDD as a contaminant




2,3,4,5,6-pentachlorophenol (CAS 87-86-5)

# PCP Mortality Study

- Four large chemical plants made PCP from 1936 to 2006, employing 2122 workers, the only PCP manufacturing workers in the United States
- About one-third (720) of the cohort also worked in departments using TCP or one of its derivatives that were contaminated with TCDD
- *A priori* hypotheses were that the cohort would have elevated standardized mortality ratios (SMRs):
  - For leukemia and liver, adrenal, thyroid, and parathyroid cancer, as suggested by animal studies
  - For aplastic anemia, soft-tissue sarcoma, and non-Hodgkin lymphoma (NHL), as suggested by human studies

# PCP Plants & Personnel

| Plant Location | PCP Production | Workers in This Study | Processes in PCP Operations |
|---|---|---|---|
| Michigan | 1936-1980 | 788 | production, distillation, finishing, flaking |
| Illinois | 1938-1978 | 939 | production, flaking, prilling, blocking |
| Washington | 1957-1985 | 181 | production, prilling, blocking |
| Kansas | 1958-2006 | 214 | production, flaking |

# PCP Plants Other Exposures

| Plant Location | PCP workers exposed to other chemicals | Other possible carcinogenic exposures in 1975 |
|---|---|---|
| Michigan | 763/788 (97%) | acrylamide, bromochloromethane, catechol, (2,4-dichlorophenoxy)acetic acid, ethylbenzene, ethylene dibromide, ethylene-vinyl acetate copolymer resins, 4,4'-methylenedianiline, o-phenylphenol, sodium salt, potassium bromate, styrene, styrene-butadiene copolymer resins, vinyl bromide monomer. |
| Illinois | 894/939 (95%) | capacitor fluid (Pyranol® series), , p-dichloro-benzene, nitrobenzene, polychlorobiphenyls, transformer fluids (Pyranol) |
| Washing-ton | 103/181 (57%) | formaldehyde |
| Kansas | 151/214 (72%) | carbon tetrachloride, chloroform, tetrachloroethylene |

Only 172 workers in the cohort were exposed only to PCP and to no other chemicals during their employment at these four plants.

# Methods: Exposure assessment

- All departments other than PCP and TCP had been coded as “department 99” when data were collected in the mid 1980s
- For this reason, exposure to feedstock or production chemicals in other operations could not be determined

# Methods: Exposure assessment

- Within the cohort, 236 workers had medical records indicating a diagnosis of chloracne, a skin condition associated with elevated chlorophenol exposure
- A separate analysis was conducted on these workers, since they had definitely had chlorophenol exposure

# Methods: Exposure assessment

- Because of the number of dioxin and furan contaminants, of varying toxicity relative to TCDD, it was not considered feasible to create a job-exposure matrix for this analysis
- Each worker was assigned one day of PCP exposure for each day he or she worked in a PCP production department
- Mortality was compared across quartiles of cumulative PCP exposure

# Methods: Life table analysis

- We compared mortality among workers with mortality in the general population, in age, gender, race, and calendar period strata.
  - For example, we compared the mortality among white male workers who were 30-34 in 1990-1994 with the mortality among all U.S. white males who were 30-34 in 1990-1994
- NIOSH life table analysis system computed person years at risk, expected numbers of deaths and standardized mortality ratios (SMRs) based on U.S mortality rates
- Results are presented as SMRs with 95% confidence intervals (CI)

# Results: PCP Workers as of 2005

| Sex and Race | Total | Alive | Deceased |
|---|---|---|---|
| White males | 1776 | 777 | 999 |
| Males of other races | 277 | 154 | 123 |
| White females | 59 | 17 | 42 |
| Females of other races | 8 | 7 | 1 |
| Other races, sex unknown | 2 | 1 | 1 |
| All | 2122 | 956 | 1166* |

*Various analyses exclude 1-6 deaths missing covariate information

# Results

- From 1940-2005 there were 1165 deaths and an overall SMR of 1.01 [95% confidence limits (CI), 0.95-1.07]
- Overall cancer mortality (326 deaths, SMR 1.17, CI 1.05 -1.30) was in statistically significant excess
- There were excess deaths for NHL (17 deaths, SMR 1.76, CI 1.02-2.82)

# Other Mortality Excesses & Deficits

| Underlying cause of death (UCOD) | Deaths | SMR (CI) |
|---|---|---|
| Trachea, bronchus & lung cancer | 126 | 1.35 (1.13-1.61) |
| Chronic obstructive pulmonary disease (COPD) | 63 | 1.44 (1.10-1.84) |
| Medical complications | 5 | 3.51 (1.14-8.18) |
| Tuberculosis | 1 | 0.17 (0.00-0.93) |
| Hypertension with heart disease | 6 | 0.45 (0.16-0.97) |
| Pneumonia | 19 | 0.64 (0.38-1.00) |
| Symptoms and ill-defined conditions | 4 | 0.32 (0.09-0.82) |
| Transportation accidents | 17 | 0.58 (0.34-0.92) |

# Significant Results by Exposure Group

PCP, no TCP

| UCOD | Deaths | SMR (CI) |
|---|---|---|
| All cancer | 238 | 1.24 (1.09-1.41) |
| Lung cancer | 99 | 1.56 (1.27-1.90) |
| COPD | 53 | 1.78 (1.34-2.33) |

PCP & TCP

| UCOD | Deaths | SMR (CI) |
|---|---|---|
| NHL | 8 | 2.48 (1.07-4.88) |

# Results Among Workers With Chloracne

- Overall mortality and  cancer mortality were not elevated
- No cause of death had a statistically significant excess.  There were one death each from non-Hodgkin lymphoma, multiple myeloma, and leukemia.  One death occurred from connective tissue cancer (soft-tissue sarcoma), none from liver or kidney cancer, and three from pancreatic cancer.

# Significant Results by Sex & Race

| Sex & race | UCOD | Deaths | SMR (CI) |
|---|---|---|---|
| White males | Lung cancer | 113 | 1.40 (1.16-1.69) |
| | NHL | 17 | 1.96 (1.14-3.15) |
| Males of other races | Overall mortality | 123 | 0.78 (0.65-0.94) |
| | Leukemia | 4 | 4.56 (1.24-11.7) |
| | Other heart diseases | 1 | 0.12 (0.00-0.69) |
| | Digestive system diseases | 1 | 0.15 (0.00-0.83) |
| | Accidents | 2 | 0.22 (0.03-0.79) |
| White females | Laryngeal cancer | 1 | 44.8 (1.13-249) |

# Results by Duration of PCP Exposure

| UCOD | <=57 days | 58-<182 days | 182-<650 days | 650+ days |
|---|---|---|---|---|
| **All deaths*** | 284 | 283 | 294 | 299 |
| SMR (95% CI) | 0.96 (0.85-1.07) | 0.94 (0.83-1.06) | 1.03 (0.91-1.15) | 1.10 (0.98-1.23) |
| **All cancers** | 93 | 71 | 78 | 83 |
| SMR (95% CI) | 1.33** (1.07-1.62) | 0.96 (0.75-1.21) | 1.12 (0.88-1.40) | 1.29** (1.03-1.60) |
| **Lung cancer** | 34 | 27 | 34 | 30 |
| SMR (95% CI) | 1.46** (1.01-2.05) | 1.08 (0.71-1.58) | 1.45** (1.00-2.02) | 1.41 (0.95-2.02) |
| **NHL** | 6 | 4 | 4 | 3 |
| SMR (95% CI) | 2.43 (0.89-5.30) | 1.55 (0.42-3.96) | 1.62 (0.44-4.15) | 1.41 (0.29-4.11) |
| **COPD** | 8 | 19 | 21 | 15 |
| SMR (95% CI) | 0.77 (0.33-1.51) | 1.60 (0.96-2.49) | 1.85** (1.15-2.83) | 1.49 (0.83-2.46) |

* N=1160 in this analysis.

# Results by Plant

| UCOD | Illinois (n=939) | Michigan (n=788) | Kansas (n=214) | Washington State (n=181) |
|---|---|---|---|---|
| **All deaths*** | 662 | 411 | 33 | 58 |
| SMR (95% CI) | 1.10** (1.01-1.18) | 0.93 (0.84-1.03) | 0.70** (0.49-0.99) | 0.87 (0.66-1.13) |
| **All cancers** | 191 | 109 | 11 | 15 |
| SMR (95% CI) | 1.29*** (1.12-1.49) | 1.06 (0.87-1.28) | 0.88 (0.44-1.58) | 0.94 (0.52-1.54) |
| **Biliary, liver, gall bladder cancer** | 9 | 8 | 0 | 0 |
| SMR (95% CI) | 1.77 (0.81-3.37) | 2.08 (0.90-4.09) | | |
| **Lung cancer** | 83 | 34 | 5 | 4 |
| SMR (95% CI) | 1.68*** (1.34-2.08) | 1.00 (0.69-1.40) | 1.14 (0.37-2.66) | 0.78 (0.21-1.99) |
| **NHL** | 9 | 8 | 0 | 0 |
| SMR (95% CI) | 1.80 (0.82-3.41) | 2.17 (0.94-4.27) | | |
| **Dis. arteries, veins, pulm. circ.** | 24 | 9 | 0 | 2 |
| SMR (95% CI) | 1.59** (1.02-2.37) | 0.78 (0.36-1.49) | (0.00-3.92) | 1.21 (0.15-4.36) |
| **COPD** | 39 | 15 | 5 | 4 |
| SMR (95% CI) | 1.68*** (1.20-2.30) | 0.89 (0.49-1.46) | 3.19** (1.03-7.43) | 1.85 (0.50-4.74) |

* N=1164 in this analysis

# Discussion—Mortality Study

- Strengths: inclusion of all United States PCP manufacturing workers employed through 1992, comparison with U.S. population by sex, race, age, calendar period

- Limitations: lack of detailed information on other exposures that could affect mortality, previous or subsequent employment, use of duration of employment as a surrogate of exposure, no information on lifestyle choices

# Discussion—Mortality Study

- Why was chloracne not associated with increased mortality?
- Medical records were not comprehensive; some of the 1886 other workers may have had chloracne as well. (This is another limitation of the study.)
- How do we know PCP exposure was associated with mortality?
- We don't. Most workers spent much more time in other departments

# Discussion

- What study design is best for evaluating the health effects of PCP?
- Because of the number of possible exposures, chemical plant workers may not be the most appropriate study group
- Most other workers exposed to PCPs are also exposed to other chemicals

# Other PCP-Exposed Cohorts

- Lumberyard workers applying PCP as a wood preservative
- Telephone pole, railroad, and dock construction and maintenance workers exposed to PCP treated lumber
- Electrical line workers climbing PCP-treated poles
- Hazardous waste workers disposing of treated lumber
- Leather workers

# Other PCP-Exposed Cohorts

| Occupation /industry | Other exposures, limitations |
|---|---|
| Lumberyard workers | Possibly also exposed to creosote, other wood preservatives. Could a study control for other exposures by limiting to those who worked only during eras when only PCP was in use? |
| Railroad and dock construction workers | Possibly also exposed to creosote, other wood preservatives. Could a study control for other exposures by limiting to those who worked only during eras when only PCP was in use? |
| Electrical line workers | Possibly also exposed to creosote, other wood preservatives. Can extent of exposure to freshly treated wood be quantified? |
| Hazardous waste workers | Likely to have been exposed to multiple carcinogens |
| Leather workers | Exposed to dyes, acids, solvents |

# Possible study designs

- A cancer incidence or nested case-control study in the NIOSH cohort would still have the limitation of inability to identify most other chemicals to which workers were exposed, and is therefore not feasible
- If sufficient numbers of lumberyard workers employed only during eras when PCP was the only wood preservative employed could be enrolled, a cancer incidence study would be valuable
- Are there other suitable cohorts exposed only to PCP?

# Conclusions

- In the NIOSH cohort findings include excess cancer overall and particularly excess non-Hodgkin lymphoma, a cancer of a priori interest
- Because of multiple undefined chemical exposures, a cancer incidence study in the NIOSH cohort is not feasible
- A cancer incidence study in a cohort of workers exposed only to PCP could add to the evidence from the Demers et al study of the association of PCP and NHL

# Acknowledgements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- Marilyn Fingerhut, Marie Sweeney, Dave Marlow, and Laurie Piacitelli collaborated on the study protocol

# Any questions?

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