

# Occupational Exposure to Pentachlorophenol and Other Agents

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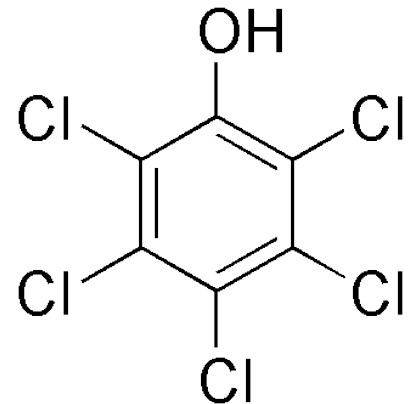
# Background

- 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-dichlorobenzene, nitrobenzene, polychlorobiphenyls, transformer fluids (Pyranol)
Washington	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
<b>All deaths*</b>	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)
<b>All cancers</b>	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)
<b>Lung cancer</b>	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)
<b>NHL</b>	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)
<b>COPD</b>	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)
<b>All deaths*</b>	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)
<b>All cancers</b>	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)
<b>Biliary, liver, gall bladder cancer</b>	9	8	0	0
SMR (95% CI)	1.77 (0.81-3.37)	2.08 (0.90-4.09)		
<b>Lung cancer</b>	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)
<b>NHL</b>	9	8	0	0
SMR (95% CI)	1.80 (0.82-3.41)	2.17 (0.94-4.27)		
<b>Dis. arteries, veins, pulm. circ.</b>	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)
<b>COPD</b>	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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# Any questions?



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