



Occupational
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Epidemiologic Studies of Pentachlorophenol Users

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Studies of PCP Users



- Pentachlorophenol and its sodium salt were used extensively in the lumber and wood preservation industry as fungicides
- Epidemiologic evidence on users come from:
 - Cohort studies of workers in the wood industries
 - Case-control conducted in regions where use was relatively high
 - The studies were conducted in the Nordic countries, the NW US, Western Canada, New Zealand, and Australia

BC Sawmill Study: Background



- Penta- and tetrachlorophenol were used as fungicides in the softwood lumber industry 1950-1990
 - Estimated that 100,000 workers were exposed in British Columbia (BC), Canada
- Widespread use in lumber mills was discontinued because of concerns regarding dioxin contamination in the late 1980's

BC Sawmill Study [Demers et al, 2006]

- 14 large softwood sawmills with good records
 - 11 had used pentachlorophenol or tetrachlorophenol
- Enumeration of workers using mill records
 - All workers employed for 1+ years, 1950-1995
 - Info on all jobs abstracted from mill records
- Mortality: 1950-1995
 - 27,464 workers, 4% lost to follow-up
- Cancer Incidence: 1969-1995
 - 25,685 workers, <1% lost to follow-up

Use of Chlorophenols in the Lumber Industry



~95% of Exposure Dermal



Towards a cancer-free workplace

Exposure Assessment



- Historical information collected to establish time periods when technology and work practices were constant
- Panels of 9-20 workers with 5+ years experience in each time period established for each mill
- Reliable estimates (ICC=0.91) [Teschke et al, 1989]
- Validation study of most recent time period using urinary levels ($r=0.72-0.76$) [Hertzman et al, 1988]
- Exposure metrics created for each fungicide

BC Sawmill Workers Cancer Incidence: 1969-1995



| <u>Disease Category</u> | <u>Cancers</u> | <u>SIR (95% CI)</u> |
|-------------------------|----------------|---------------------|
| All Cancers | 2,571 | 1.02 (0.98-1.06) |
| Liver | 21 | 0.79 (0.49-1.21) |
| Sino-nasal | 6 | 1.05 (0.39-2.29) |
| Lung | 519 | 1.05 (0.96-1.15) |
| Kidney | 79 | 1.10 (0.88-1.38) |
| Connective tissue | 13 | 0.84 (0.49-1.44) |
| Non-Hodgkin's lymphoma | 92 | 0.99 (0.81-1.21) |
| Hodgkin's disease | 18 | 0.94 (0.56-1.49) |
| Multiple myeloma | 25 | 0.80 (0.52-1.18) |

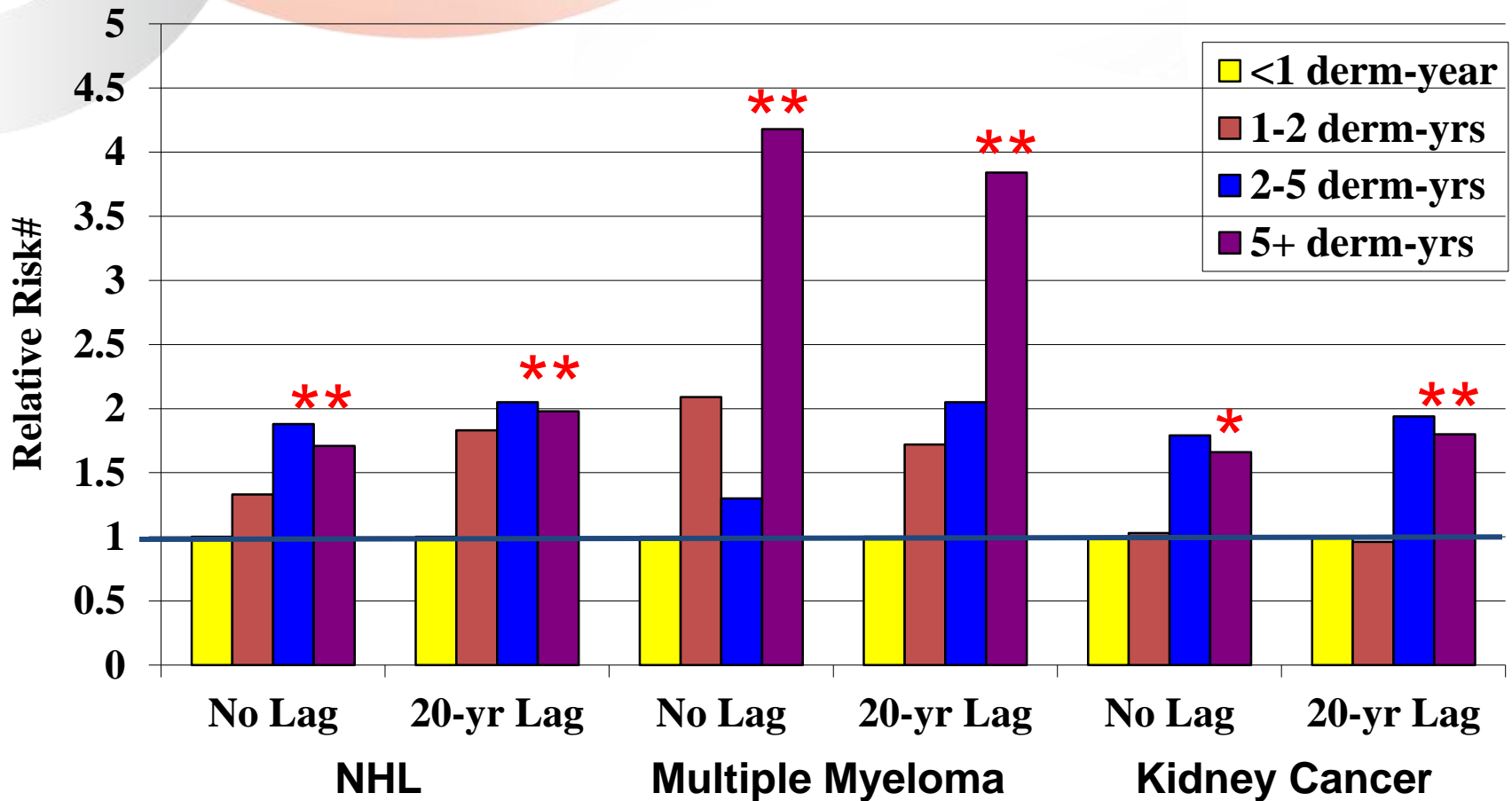
Pentachlorophenol and Cancer in BC Sawmill Workers: Dose-Response Analyses



| Cancer Site* | 1-2 exposure yrs RR (95% CI) | 1-2 exposure yrs RR (95% CI) | 5+ exposure yrs RR (95% CI) |
|----------------|---------------------------------|---------------------------------|--------------------------------|
| Lung (n=519) | 1.11 (0.86-1.45) | 1.07 (0.84-1.36) | 1.12 (0.87-1.44) |
| Liver (n=21) | 4.09 (0.89-18.8) | 8.47 (2.21-32.5) | 1.41 (0.21-9.22) |
| Kidney (n=79) | 1.03 (0.49-2.18) | 1.79 (0.99-3.24) | 1.66 (0.85-3.23) |
| STS (n=23) | 0.64 (0.18-2.20) | 0.18 (0.04-0.85) | 0 observed |
| NHL (n=92) | 1.33 (0.70-2.52) | 1.88 (1.08-3.28) | 1.71 (0.91-3.24) |
| Myeloma (n=25) | 2.09 (0.57-7.61) | 1.30 (0.34-4.98) | 4.18 (1.36-12.9) |

* STS: Soft Tissue Sarcoma, NHL: Non-Hodgkin's Lymphoma

Pentachlorophenol and Cancer in BC Sawmill Workers: Latency Analyses



#Analyses performed using Poisson Regression, adjusted for age, calendar period & race

*Trend: P<0.10

**Trend: p<0.05

Selected Results from Other Cohort Studies



- Robinson et al 1987, mortality among 2,283 men employed 1+ years at four plywood mills in the NW US 1945-1955
 - Sub-cohort, 1+ years of PCP *or formaldehyde* exposure: lymphosarcoma (SMR=2.50, 3 cancers) and Hodgkin's lymphoma (SMR=3.33, 2 cancers)
- Partanen et al 1993, nested case-control study of men in a Finnish wood industry cohort
 - NHL (n=8)/HL (n=4)/leukemia (n=12) and ≥ 1 month chlorophenol exposure, OR=0.91 (0.18-4.51)

Case-Control Studies of PCP, CP, and Non-Hodgkin's Lymphoma



| Study | Population | Exposure* | Results OR (95% CI) |
|--------------------------------------|---|---|--------------------------------|
| Hardell et al 1994, Sweden | Men age 25-85 105 cases, 355 controls | 1+ week continuous or 1 month total exposure to PCP | 8.8 (3.4-24) |
| Hardell et al 1999, Sweden | Men age 25+ 404 cases, 741 controls | Any PCP exposure (>1 year before diagnosis) | 1.2 (0.7-1.8) |
| Garabedian et al, 1999, USA | Men 32-60 995 cases, 1783 controls | High confidence CP - High intensity | 1.1 (0.9-1.4) 1.1 (0.8-1.5) |
| Woods et al 1987, USA | Men age 20-79 576 cases, 694 controls | Any job with possible CP exposure - Wood preservers | 0.9 (0.8-1.2) > 1.5 |
| Pearce et al 1986, New Zealand | Men age <70 83 cases, 168 cancer controls, 228 population controls | Ever exposed to CP - Work as fencing contractor or farmer | 1.3 (0.6-2.7) 2.0 (1.3-3.0) |

* PCP: Pentachlorophenol, CP: Any Chlorophenol

Case-Control Studies of PCP, CP, and Soft Tissue Sarcoma



| Study | Population | Exposure | Results |
|-------------------------------------|--|--|---|
| Hardell et al 1995, Sweden | Meta-analysis, 4 studies men age 25-80 434 cases, 948 controls | 1+ week continuous or 1 month total PCP | 2.8 (1.5-5.4) |
| Hoppin et al, 1998, USA | Men age 30-60 295 cases, 1908 controls | High confidence CP - High intensity | 1.7 (1.1-2.7) 2.1 (1.2-3.7) |
| Woods et al 1987, USA | Men age 20-79 128 cases, 694 controls | Any possible CP Jobs with possible exposure | 1.0 (0.7-1.5) ORs from 0.8-4.8 |
| Smith et al 1984, New Zealand | Men age 20-80 82 cases, 92 controls | 1+ day CP exposure >5 days, 10 yr before diagnosis Jobs with possible exposure | 1.3 (0.5-3.6) 1.6 (0.5-5.2) ORs from 0.7-1.9 |

* PCP: Pentachlorophenol, CP: Any Chlorophenol

Results from Case-Control Studies for Other Cancer Sites

- Case-control studies, primarily in the Nordic countries and the USA, have looked at the risk of other cancers, such as multiple myeloma, colon, nasal, nasopharyngeal, and respiratory cancers, with chlorophenol exposure
- Power often limited
- Results often inconsistent with cohort results
- Too little evidence to evaluate based on PCP users

Challenges for Epidemiologic Studies

- Relatively few studies of Pentachlorophenol users specifically assessed pentachlorophenol exposure
- Many studies lack power
- Need for more studies with strong exposure assessment – difficult for dermal exposure
- Confounding exposures?
- Co-exposures or contaminants?

Cancers* associated with Potential Occupational Confounders & Co-Exposures



| Carcinogen | Sufficient evidence | Limited evidence |
|--------------|----------------------------|-------------------------|
| Dioxins | All cancers combined | Lung, NHL, STS |
| Wood dust | Sino-nasal, nasopharyngeal | |
| Formaldehyde | Nasopharyngeal, leukemia | Sino-nasal |
| Arsenic | Lung, skin, bladder | Kidney, liver, prostate |
| Chromium | Lung | Sino-nasal |

* From IARC Monographs 100c & 100f

Conclusions for PCP Users



- An association with non-Hodgkin's lymphoma in the major cohort with some support from case-control
- Relatively consistent results for soft tissue sarcoma from Swedish case-control studies, mixed results elsewhere
- Some associations observed with other sites, such as multiple myeloma and kidney cancer, but too little data to evaluate based on PCP users

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