

**Health Effects of Preserved Wood:
Relationship Between CCA-Treated Wood
and Incidence of Cancer in the United States**

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CCA: Why the concern?

- ARSENIC
 - Classified by EPA as a carcinogen
 - Associated with other health problems
 - Found as chromium arsenate in CCA
 - Can dislodge onto hands and into soil
 - Particular concern about children and play structures
- Copper and Chromium
 - No evidence that these are carcinogenic

Arsenic

- Natural component of earth's crust
- Contaminant in variety of metal ores
- Extracted in smelting of copper, gold, lead, zinc
- Minute amounts ingested everyday in food and water
- Exists in inorganic and organic (methylated) forms
- Once ingested it is metabolized to organic forms
- Trivalent (+3) and pentavalent (+5) oxidative states are most important for toxicology

Mechanisms of Toxicity

- Arsenate can replace phosphate in biochemical reactions
 - Important for energy production
 - Glucose-6-arsenate instead of phosphate
- Replace phosphate in sodium pump
- Reduce formation of ATP in mitochondria (in vitro and cellular systems)
- Methylated forms bind to variety of proteins

Acute Toxicity of Arsenic

- LD50 in rodent studies ranges between 2-5500 mg AS/kg
- Variance depends on form of arsenic, route of administration, and animal model used
- Symptoms in Humans: Abdominal pain, vomiting, diarrhea, bloody urine, seizures, death

Chronic Toxicity of Arsenic

- Hyper- and hypo-pigmentation and hyperkeratosis (thickening) of the skin
- Peripheral neuropathy
- Altered blood cell production
- Vascular problems (Blackfoot disease)
- Endocrine Disruption?

Arsenic and Cancer

- Inorganic Arsenic classified by EPA as known human carcinogen
- Based on epidemiological evidence in humans demonstrating association
- Mechanism of carcinogenicity is unclear, but it does not cause point mutations
- Associated types: Lung, skin, and urinary tract
- Latency period: mean delay between exposure and cancer is 15-20 years.

Evidence That Arsenic Causes Cancer

STUDY	COUNTRY	COMMENT
CJ Chen, <i>et al.</i> , 1986	Taiwan	Lung, bladder, kidney cancer rates and mortality 30-60 times higher for those with >600µg As/liter in drinking water
C. Hopenhayn-Rich, <i>et al.</i> , 1996	Argentina	Bladder cancer mortality rates as much as 80% higher in areas of country with high water As levels.
T. Tsuda, <i>et al.</i> , 1995	Japan	Lung and bladder cancer rates increased with well water As levels >1000 µg/l
A.H. Smith, <i>et al.</i> 1998	Chile	Bladder cancer relative risk as high as 15.3 for individuals exposed to >50 µg/l for >40 years duration.
C. Steinmaus, <i>et al.</i> , 2003	Western Nevada	Case control study. As levels in smokers of >80 µg/l for >40 years duration associated with bladder CA. No association at lower levels and non-smoke.

Special Issues in Children

- Children are not small adults!
- Behaviors may increase dose (e.g. hand to mouth activity)
- Different capacity to metabolize and excrete chemicals (e.g. pharmacokinetics)
- Cells undergoing rapid growth may be especially vulnerable to chemical exposures
- Limited and conflicting evidence to suggest differences in metabolism from adults

Health Effects of Arsenic on Children

STUDY	ARSENIC EXPOSURE	ASSOCIATED EFFECT	COMMENT
Zaldivar <i>et al.</i> , 1977 (Chile)	Drinking water in N. Chile	More severe “symptoms” of acute toxicity	Very high doses (1000x >CCA)
Bencko <i>et al.</i> , 1977 (USA)	Coal power plant	Hearing deficit	Did not account for other pollutants
Milham, 1977 (USA)	Copper smelter	No hearing deficit	Not blinded
Morse <i>et al.</i> , 1977 (USA)	Copper smelter	Mottled teeth, but no other effects	Fluoride levels unknown
Calderon <i>et al.</i> , 2001 (Mexico)	Copper and zinc smelter	Lower verbal IQ, not total IQ	Confounding by high lead levels

What About CCA?

Difficulties in CCA Risk Assessment

- No animal models
- Limitations in measurement of exposure and ingestion
- Unknowns of intestinal absorption and bioavailability
- Chromium arsenate potentially different than inorganic arsenic
- Lack of known threshold level of arsenic carcinogenesis

CCA and Health Effects

STUDY	COMMENT
Buddy, <i>et al.</i> 1977	Reviewed medical records of 2 groups of carpenters, before (n=232) and after (n=293) introduction of CCA treated wood. No association between exposure and adverse health effects
Flickinger <i>et al.</i> 1982	Studied 109 workers at 2 wood preserving plants. Found no evidence of increased cancer or other health problems.
Gilbert, <i>et al.</i> , 1990	Studied 88 workers at wood preserving plant. No health effects compared with match control group.
Rosenberg, <i>et al.</i> , 1980	Studied 44 workers at wood preserving plant. Increased urine arsenic levels, but no health effects.
Tabershaw study, 1979	63 workers at wood preserving plant. No evidence of health effect.

Cancer Risk Assessment

- United States EPA guidelines
 - Based on probabilities
 - Acceptable range less than or equal to one case in 10^{-6} in exposed individuals
 - In other words, less than or equal to 1 case per 1,000,000
- Risk based on estimated daily exposure (amount and duration)

CCA and Cancer Risk Assessments

STUDY	COMMENT	ESTIMATED LIFETIME RISK
Environmental Working Group (EWG), 2001	Estimate exposure based on wipe tests of wood	1 in 300-500
Gradient Corporation, 2001	Estimate exposure based on available data	1-6 in 1,000,000
Florida Dept. of Environmental Protection, Roberts, 2001	Estimate exposure based on available data	4-200 in 1,000,000 (depending on daily dose of Arsenic from CCA)
Consumer Products Safety Commission, 2003	Estimate exposure based on available data	2-100 in 1,000,000

Why the Difference?

- Major difference is the amount of assumed arsenic exposure by ingestion and dermal route
- Some studies use wipe tests of wood, others use wipe tests of hands
- Differences in assumptions regarding bioavailability of ingested CCA
- Differences in assumptions regarding length of time exposed and amount of CCA ingested

Does Exposure to CCA-Preserved Wood Pose a Cancer Risk?

- CCA treated wood has been used extensively for decks and play structures throughout the United States for over 30 years.
- Millions of children have been exposed
- If exposure to CCA caused cancer, then incidence of arsenic-related cancer should be higher now than 25 years ago.

Methods

- Used cancer incidence data from SEER 9 registry.
- Determined the incidence of all types and subtypes of lung and bronchus cancer and all types of urinary bladder cancer.
- Compared incidence in 20-29 and 30-39 year old population during 1975-1979 (pre-CCA) and 1995-1999 (post-CCA)
- Also determined the annual percentage change in incidence from 1973-1999 using linear regression model

SEER Database

- Surveillance Epidemiology and End Results (SEER 9 registry)(NCI)
- SEER 9 registry includes data from 9 geographic areas in the US since 1973.
- 9 Sites: Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, San Francisco-Oakland, Seattle-Puget Sound, and Utah
- Complete data available from 1973-1999.

SEER Registry Data

*Expressed as incidence per 100,000 persons

TYPE	AGE RANGE	1975-1979*	1995-1999*
Lung and Bronchus	20-29 year old	0.4	0.4
	30-39 year old	4.7	3.3
Urinary Bladder	20-29 year old	0.6	0.5
	30-39 year old	1.7	1.4

SEER Registry Data

*Expressed as incidence per 100,000 persons

TYPE	AGE RANGE	1975-1979*	1995-1999*
Squamous Cell Carcinoma of Lung and Bronchus	20-29 year old	0.0	0.0
	30-39 year old	0.9	0.2
Adenocarcinoma of Lung and Bronchus	20-29 year old	0.1	0.1
	30-39 year old	1.9	1.4

SEER Trend, 1973-1999

*Estimated annual percentage change over time.

†Change is significantly different from zero ($p < .05$)

TYPE	20-29 years of age*	30-39 years of age*
Lung and Bronchus	0.6	-1.7 †
Squamous Cell of Lung and Bronchus	0.0	-6.2 †
Adenocarcinoma of Lung and Bronchus	0.0	-1.4 †
Urinary Bladder	-1.2 †	-1.4 †

Summary Of Data

- Incidence of arsenic-related cancers in adults who could have been exposed to CCA-preserved wood as children was the same or less than it was prior to the widespread use of CCA-preserved wood.
- Incidence of arsenic-related cancers has not changed or has decreased each year since the introduction of CCA-preserved wood to the US market.

What makes CCA different than arsenic in drinking water?

- Primary difference is bioavailability
- Drinking water studies address soluble inorganic arsenic that is readily absorbed
- Preserved wood studies address insoluble chromium-arsenate which is less well absorbed.
- In addition, chromium-arsenate may have different carcinogenic potential

Limitations

- Used only data from SEER9 sites.
- Not a direct measure of exposure to CCA
- Did not account for potential confounding factors (e.g. smoking rates)
- Perhaps CCA is biologically different than arsenic?

Conclusions

- Provide preliminary evidence suggesting that past routine exposure to CCA-preserved wood has not resulted in an increased rate of arsenic-related cancers.
- Our findings are consistent with more conservative estimates of CCA cancer risk.
- More research needed that directly measures exposure and other confounders