Coal Miners and Lung Cancer

Can mortality studies offer a perspective on the significance of rat inhalation studies for human risk assessment?

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Coal and Lung Cancer

- Is coal an appropriate surrogate to evaluate risk of lung cancer from exposure to poorly soluble particles such as carbon black and titanium dioxide ?

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Coal

- A complex mixture of > than 50 elements and their oxides.
- Mineral content varies with particle size of the dust and the coal seam.
- Airborne respirable dust in underground coal mines has been estimated to be 40–95% coal (Walton *et al.*, 1977; United States National Institute for Occupational Safety and health, 1995);
- Remaining portion consists of a variable mixed dust, introduced into the mine atmosphere through operations other than coal cutting, such as roof bolting or in the distribution of rock dust (a low-silica limestone dust) to prevent explosions.
- **Diesel equipment** underground leads to fine particulates (< 1 μm) in the dust, the composition of which would be fairly typical of diesel exhaust from industrial machines (see IARC, 1989).

* *IARC Monograph, 1997*

Table 2. Carbon content of coals

Coal type	Rank	Composition (%) (dry mineral-matter-free basis)		
		Carbon	Hydrogen	Oxygen
Peat		50–65	5–7	30–40
Lignite	(Low)	65–75	5–6	20–30
Sub-bituminous	↓	75–80	5–6	13–20
Bituminous	(Intermediate)	80–90	4.9–5.7	5–15
Semi-bituminous	↓	90–92	4.5–5.9	4–5
Anthracite	(High)	92–95	2–4	2–4

From Parkes (1994)

Table 5. Elements and trace elements in coal

Constituent	Range (percentage)	Constituent	Range (ppm)
Aluminium	0.43–3.04%	Arsenic	0.5–93 ppm
Calcium	0.05–2.67%	Boron	5–224 ppm
Chlorine	0.01–0.54%	Beryllium	0.2–4 ppm
Iron	0.34–4.32%	Bromine	4–52 ppm
Potassium	0.02–0.43%	Cadmium	0.1–65 ppm
Magnesium	0.01–0.25%	Cobalt	1–43 ppm
Sodium	0–0.2%	Chromium	4–54 ppm
Silicon	0.58–6.09%	Copper	5–61 ppm
Titanium	0.02–0.15%	Fluorine	25–143 ppm
Organic sulfur	0.31–3.09%	Gallium	1.1–7.5 ppm
Pyritic sulfur	0.06–3.78%	Germanium	1–43 ppm
Sulfate sulfur	0.01–1.06%	Mercury	0.02–1.6 ppm
Total sulfur	0.42–6.47%	Manganese	6–181 ppm
Sulfur by X-ray fluorescence	0.54–5.4%	Molybdenum	1–30 ppm
		Nickel	3–80 ppm
		Phosphorus	5–400 ppm
		Lead	4–218 ppm
		Antimony	0.2–8.9 ppm
		Selenium	0.45–7.7 ppm
		Tin	1–51 ppm
		Vanadium	11–78 ppm
		Zinc	6–5350 ppm
		Zirconium	8–133 ppm

Table 6. Compositional data for airborne dusts in British coal mines prior to 1970[a]

Coalfield	Colliery	Mean environmental data[a]			
		Carbon (%)	Non-coal (%)	Quartz (%)	Kaolin and mica[b] (%)
Scottish	SC1	84.1	36	4.3	15.7
	SC2	85.4	42	5.5	12.2
	SC4	82.0	62	5.8	23.0
	SC5	82.6	43	3.0	17.1
Northumberland	NH1	84.0	43	3.0	12.5
Cumberland	C1	86.9	44	6.8	11.5
Durham	D1	86.3	35	3.4	12.6
	D2	89.7	33	5.9	8.6
Yorkshire	Y1	85.3	43	6.2	14.2
	Y2	85.2	51	7.8	17.5
Lancashire	L1	87.8	19	1.2	7.3
North Wales	NW1	84.9	39	6.9	15.1
Nottingham	NT1	81.1	51	5.1	32.8
Warwick	W1	81.8	42	4.2	9.3
South Wales	SWA1	94.0	31	3.2	8.8
(anthracite)	SWA2	92.7	19	0.8	11.4
South Wales	SWS1	91.2	18	2.2	21.1
(steam coal)	SWS3	91.9	20	2.3	8.4
South Wales (bituminous coal)	SWB1	90.6	28	2.8	6.8
Kent	K1	88.6	32	2.0	16.3
All collieries		86.8	36	4.1	14.1

From Jacobsen *et al.* (1971); Walton *et al.* (1977)

Table 7. Quartz percentages in dust for various underground occupations in United States mines, 1985–92

Occupation	Number of samples	Average quartz content (%)[a]
Roof bolter	6 061	6.97
Roof bolter (DA)[b]	3 508	6.77
Continuous-miner operator	10 793	5.54
Continuous-miner helper	1 386	5.48
Shuttle car operator	1 883	4.33
Scoop car operator	721	4.27
Longwall shearer operator	762	4.02
Jacksetter	815	3.98
Coal drill operator	395	3.29
Cutting machine operator	1 067	2.47

From Tomb *et al*. (1995)

Table 9. Mean quartz content in airborne dust generated during coal winning in German mines

Particle size	Number of measurements	Quartz content (% by weight) mean ± SD'
Total dust	165	4.1 ± 3.3
Fine dust < 7 µm	165	4.3 ± 3.0
Fine dust < 5 µm	123	2.9 ± 1.9
Fine dust < 3 µm	159	2.2 ± 1.6

From Leiteritz *et al.* (1971)

Summary

Coal contains significant concentrations of crystalline silica (Type I IARC carcinogen).

Coal mining environment often includes exposure to diesel exhaust particles, another IARC Type I Human carcinogen.

Carbon Black

Carbon Black (CAS No. 1333-86-4)- a manufactured product- is virtually pure elemental carbon (upwards of 98-99%) produced by incomplete combustion of gaseous or liquid hydrocarbons under controlled conditions. Its physical appearance is that of a black, finely divided pellet or powder.

Carbon Black

Powder Form (Particle size < 1 micron)

TiO_2

- Titanium dioxide occurs in nature as the minerals rutile and anatase. It is mainly sourced from ilmenite ore, the most widespread form of titanium dioxide-bearing ore around the world. Rutile is the next most abundant and contains around 98% titanium dioxide in the ore.

Carbon Black, TiO_2 and Coal

There are substantial compositional differences between coal, carbon black and TiO_2.

As a result, considering coal as a poorly soluble particle is not scientifically justified.

Why study coal miners re: PSLTs, rat overload and cancer?

Studies of risk of lung cancer among coal miners may provide perspective on:

- Rat inhalation studies and lung cancer under conditions of lung overload
- Screening for lung cancer among coal workers. If risk of lung cancer exists, should workers be monitored with low dose CT?
- **Caution: Is coal the appropriate surrogate for PSLTs?**

Despite the limitations of using coal as a surrogate for poorly soluble particles like carbon black and TiO_2, let's briefly review the highlights of coal worker mortality studies.

Coal Miners and Lung Cancer

- Risk of lung cancer among coal miners has been investigated in cohort mortality studies conducted over nearly 50 years.
- Over 120,000 coal miners have been evaluated in UK, Germany, Netherlands, USA, Poland, Japan and Australia
- Epidemiological studies provide data regarding the risk of lung cancer in workers exposed to coal dust.

Epidemiological studies of coal-miners and lung cancer mortality (14)

Cohort	Countries	N	Lung Ca. SMR	95% CI
Liddell 1973	UK	3,169	0.63	**n.a.**
Costello et al. 1974	US	3,726	0.67	**0.4-1.0**
Rockette 1977	US	23,232	1.13	**1.0-1.3**
Armstrong et al. 1977	AUS	213	0.25	**0.01-1.4**
Atuhaire et al. 1985	UK	3865	0.78	**0.7-0.9**
Kuempel et al. 1995	US	8,878	0.77	**0.6-1.0**
Swaen et al. 1995	NLD	2941	1.02	**0.9-1.2**
Starzynski et al. 1996	POL	7065	1.07	**0.9-1.2**
Brown et al. 1997	UK	23,630	0.74	**0.50-1.06**
Miyazaki 2001	JP	5,818	< 15 yr: 1.00 >15 yr: 2.08	**0.41-2.43** **1.01-4.27**
Morfeld et al. 2002	DE	4,581	0.79	**0.64-0.96**
Attfield & Kuempel 2008	US	8,899	1.07	**0.95-1.19**
Miller & MacCalman 2010	UK	17,820	0.99	**0.93-1.05**
Graber et al. 2014	US	9,033	1.08	**1.00-1.18**

Examples of studies

Recent US Study- (Graber et al, 2014)

- Lung cancer SMR slightly elevated and of marginal statistical significance- lower limit of the 95% confidence limits was 1.
- (SMR = 1.08, 95% CI: 1.00- 1.18).
- Earlier follow-up of the same cohort of upwards of 9000 coal miners through 2000, showed no association between coal mine dust exposure and lung cancer. (Attfield et al, 2008)

Europe: Synergy Study Taeger et al, 2015

Investigated joint effect of smoking and occupational lung carcinogens in **14 case-control studies** comprising 14,251 lung cancer cases and 17,267 controls.

Exposure assessment based on

- Employment duration
- Time since first employment.
- Job titles maintained for at least a year.

NOTE: Exposure concentrations for coal dust or other lung carcinogens-were not available.

Europe: Synergy Study

For coal miners, employment duration of

- 1-9 years (OR = 1.46; 95% CI: 1.18-1.80) and
- ≥20 years (OR = 1.73; 95% CI: 1.14 – 2.62) implied increased risks of lung cancer.
- Employment duration of 10-19 years suggested **no link with lung cancer** (OR = 0.99; 95% CI: 0.67-1.47).
- **This latter pattern is inconsistent with a dose response relationship** between coal mining exposure and lung cancer, a critical step in evaluating potential causality.

Europe: Synergy Study

- Confounding from carcinogens such as crystalline silica, asbestos, PAH, radon and metals **could not be addressed.**
- Employment duration was used as proxy of cumulative exposure, which is prone to misclassification as to the degree of exposure.
- **Recall bias-major limitation in case-control studies**
- The observed association is unlikely to be directly attributed to coal dust.

Coal worker cohort mortality studies Commentary

"Using a weight of evidence approach, studies of coal-mine workers, who have been exposed to occupationally relevant levels of dust, do not indicate an increase in lung cancer risk.

Classifying all poorly soluble as carcinogenic to humans based on rat inhalation studies in which lung overload leads to chronic inflammation and cancer is not supported by data in humans."

**Morfeld et al. Particle and Fibre Toxicology (2015) 12:3*

Coal Miners and Lung Cancer

- Using a ***weight of evidence*** approach- considered the preferred method when evaluating disparate studies to assess risk- studies of coal-mine workers do not indicate a consistent increase in lung cancer risk.
- **Slight elevations in SMR cannot lead to a reliable conclusion about an increased risk** due to limitations in exposure assessment and control of inherent biases in case-control studies, most notably control of confounding and recall bias.
- In conclusion, the weight of the scientific literature suggests that coal mine dust does not increase lung cancer risk.

IARC and Coal Dust

- Coal dust was tested for carcinogenicity in rats up to 5 hrs per day for 24 months.
- The incidence of tumors was not increased compared to controls.

IARC and Coal

Evaluation

- There is *inadequate evidence* in humans for the carcinogenicity of coal dust. There is *inadequate evidence* in experimental animals for the carcinogenicity of coal dust.

Overall evaluation

- Coal dust cannot be classified as to its carcinogenicity to humans (Group 3).

Conclusions

- Coal mine dust is **not** an appropriate surrogate for assessing whether exposure to poorly soluble particles cause lung cancer.
  - Coal dust is composed of numerous substances, including crystalline silica, an IARC Type I carcinogen.
  - Coal mining activities often occur in the context of exposure to diesel exhaust particles-an IARC Type I carcinogen.
- The preponderance of epidemiological results suggests no increase in lung cancer among coal miners.
- It is of dubious scientific support that coal can be considered a PSLT in light of the major compositional and workplace conditions in coal mining vs CB manufacturing.
- Nonetheless, even if some consider coal a PSLT, the overwhelming evidence of the coal mortality studies- despite a few outliers of low SMRs- suggest no increase in risk of lung cancer.

Questions?/Discussion