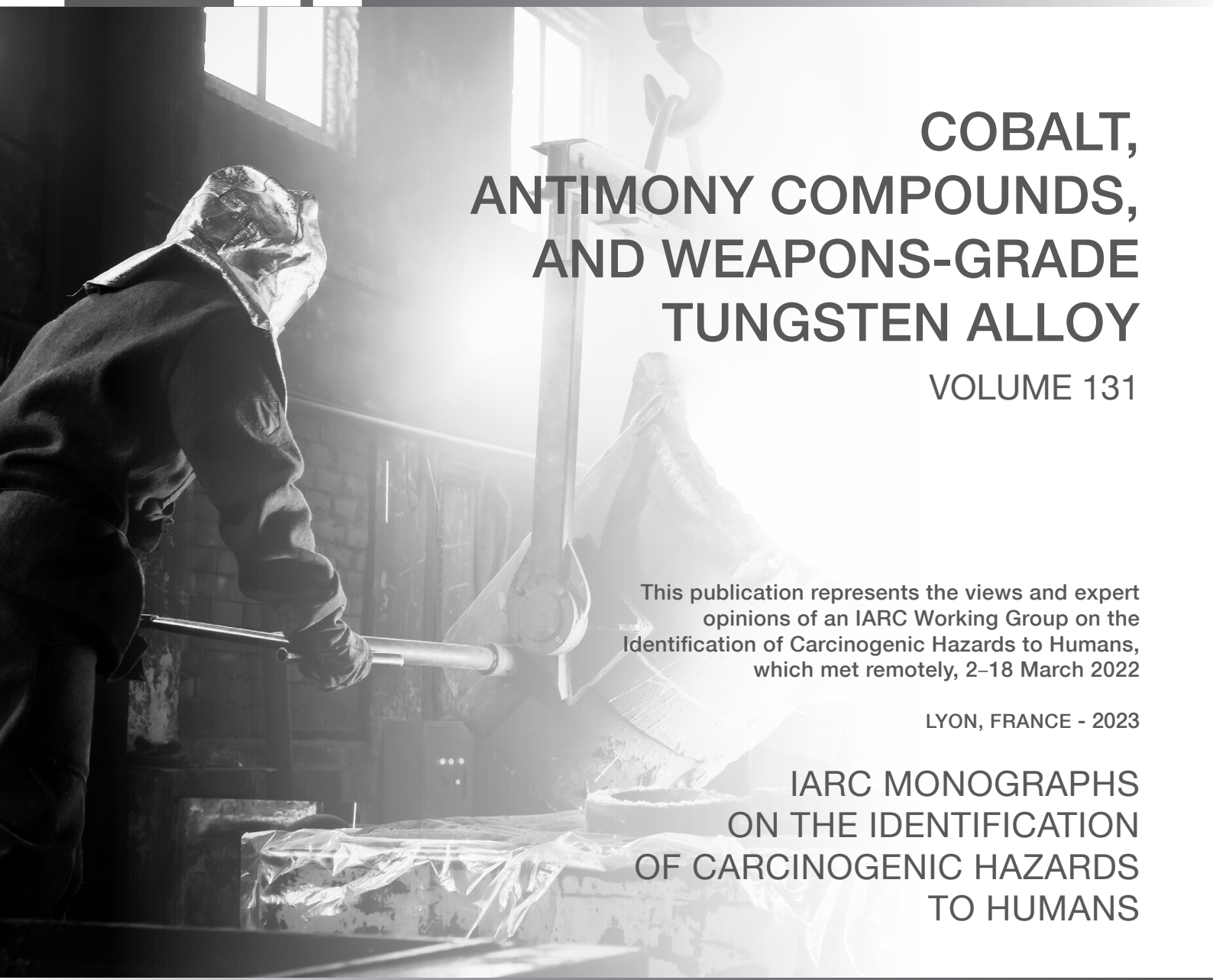
IARC MONOGRAPHS



COBALT, ANTIMONY COMPOUNDS, AND WEAPONS-GRADE TUNGSTEN ALLOY

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International Agency for Research on Cancer

World Health Organization

Table S1.17 Exposure assessment review and critique for mechanistic studies in humans exposed to trivalent and pentavalent antimony

Reference and mechanistic end-point	Agent	What was the study design?	What methods were used for the exposure assessment (including data source, environmental and biological measurements etc.)?	What was the exposure context?	Was exposure assessment qualitative, semiquantitative, or quantitative?	Concerns noted on sampling and collection protocols for metal measurement	What routes of exposure were assessed?	What exposure metrics were derived for use in analyses (e.g. average exposure, exposure duration, cumulative exposure etc.)?	What was the timing of exposure relative to the outcome?	Was there potential for co-exposures to other metals/carcinogens? If yes, were these accounted for in analyses?	Was there potential for differential or non-differential exposure misclassification?
Hantson et al. (1996) Is genotoxic	Meglumine antimoniate(V)	Case study	A daily dose of meglumine antimoniate(V) was given to the patient by intramuscular injection, equivalent to 840 mg/day of Sb	A single patient receiving meglumine antimoniate(V) treatment for 15 days was tested for key characteristic 2 end-points before, during, and at the end of treatment; known dosage of Sb, for which cumulative dose could be calculated	Quantitative	N/A	Intramuscular injection	Comparisons of end-point metrics were made by time point relative to treatment; in addition, exact dose of the compound and its equivalent Sb dose was known, and a total cumulative exposure was reported	Outcomes were measured at 3 time points: before, in the middle (day 7), and at the end of treatment (day 15)	Unlikely as the pharmacological substance was used; impurities were not reported	No
Torrús et al. (1996) Induces chronic inflammation	Meglumine antimoniate(V)	Case study (2 cases)	Known dosage (20 mg/kg per day) and duration of antimonial administration	Treatment with meglumine antimoniate(V)	Quantitative		Intravenous administration	Only that treatment was started, and effects subsequently occurred	Outcome occurred shortly (4 days in case 1 and 8 days in case 2) after treatment starting	The effects were attributed to treatment with antimonials, due to the cessation of other medications and drug use	No
Costa et al. (2018) Induces chronic inflammation	Meglumine antimoniate(V)	Experimental	Known dosage and duration of antimonial administration	Intravenous treatment with meglumine antimoniate(V) 20 mg/kg bw for 20 days	Quantitative		Intravenous administration	Exact doses, duration, and cumulative dose were known for each participant, but end-points were compared at 2 time points: day 0 and day 15 of exposure	Outcomes were measured at 2 time points (day 0 and day 15)	Pharmacological substance was used, but impurities were not reported	No
Wang et al. (2016) Is genotoxic	Not possible to specify	Cross-sectional	Total Sb measured in 2 closely timed spot urine samples with 17 other metals	Total Sb in urine (average of 2 closely scheduled spot samples)	Quantitative, but categorized into quartiles for regression analyses	The average creatinine adjustment method is not theoretically sound; it seems average urinary metal concentrations (from 2 spot samples) were adjusted by average creatinine in the regression; sample specific creatinine levels should have been used to correct individual sample metal concentrations, impact of this is not clear	All routes reflected by urinary biomonitoring	An average urinary concentration from 2 closely scheduled spot samples	Samples used to determine both exposure (urine) and outcome (semen) metrics were provided by participants on the same occasion; t2 spot urine samples were collected between 2 and 11 h apart)	Measurements of 17 other urinary analytes were made, but not all mutually adjusted for in individual models; analysis was adjusted for smoking status and daily cigarette consumption	Short half-life of Sb in urine, 2 closely timed spot samples collected on the same day as semen samples, and lack on information on source of exposure: potential for non-differential misclassification

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Tellez-Plaza et al. (2014) Induces epigenetic alterations	Not possible to specify	Cohort with prospective and cross-sectional analyses	Baseline spot measurements of total Sb in urine expressed as µg/g creatinine	For the analysis, total urinary Sb ≥ 0.27 µg/g creatinine (median)	Quantitative measurements used to generate a binary variable used in regression analyses		All routes reflected by urinary biomonitoring	A single time-point Sb concentration determined in urine, used to generate a binary variable: ≥ 0.27 µg/g creatinine (median)	2 analyses were performed: a cross-sectional analysis of baseline Sb concentrations in relation to baseline outcome measurements; a prospective analysis of baseline Sb concentrations in relation to outcome measurements made ~10 yr later	Only 4 metals/metalloids were reported: Sb, As (including speciation), Cd, and W; smoking; it does not appear that analyses were adjusted for the other elements quantified; analysis was adjusted for smoking status	Lack of information on source of exposure, single spot measurements made at single time point, and short half-life of urinary elements leaves some potential for non-differential misclassification
Domingo-Relloso et al. (2019) Induces oxidative stress	Not possible to specify	Cross-sectional	Total Sb measured in urine samples with 8 other elements expressed as µg/g creatinine	Total Sb in urine	Quantitative measurements used to generate categorical variables used in regression analyses		All routes reflected by urinary biomonitoring	A single time-point Sb concentration determined in urine, used to generate a categorical variable	Cross-sectional	8 other elements and smoking were reported; multi-metal models were further adjusted for Cu, Zn, Sb, Cd, and Cr in urine; the source of exposure to elements was not explored; analyses were also adjusted for smoking status, pack-years, and urine cotinine	Lack of information on source of exposure, single spot measurements made at single time point, and short half-life of urinary Sb leaves some potential for non-differential misclassification
Scinicariello & Buser (2016) Is immunosuppressive	Not possible to specify	Cross-sectional	Total Sb measured in urine samples both corrected and uncorrected for creatinine	Total Sb in urine; for the regression analysis in relation to telomere length, quartile comparisons were made and a dose–response relationship was also investigated	Quantitative measurements used to generate categorical variables used in regression analyses		All routes reflected by urinary biomonitoring	A single time-point Sb concentration determined in urine, used to generate a categorical variable	Collected at the same time (cross-sectional analysis of NHANES data)	The source of exposure to Sb and other elements was not explored (population-based study), making this is difficult to assess; smoking; models were adjusted for smoking status and urinary Pb	Lack of information on source of exposure, single spot measurements made at single time point, and short half-life of urinary Sb leaves some potential for non-differential misclassification
Kim et al. (1999) Is immunosuppressive	Antimony(III) oxide	Cross-sectional: immunological end-points compared between 3 groups: (A) directly exposed to Sb during antimony(III) oxide manufacture, (B) working in the same factory but not exposed, and (C) unexposed hospital controls.	Exposure to Sb was assessed by categorizing the participants as described and supported by significantly elevated creatinine-corrected urinary Sb concentrations in the exposed group; a high prevalence of Sb-attributed dermatological conditions had also been diagnosed among the exposed, and air concentrations of Sb were also detected in the workspaces of this group	Working in the production of antimony(III) oxide and directly exposed to Sb dusts and fumes	Quantitative		Exposure to Sb fumes and dusts described, skin lesions reported, and air Sb concentrations detected: dermal and respiratory exposure	End-points were compared between the groups described, and continuous urinary Sb concentrations were also associated with serum IgG4 levels	The exposures had been occurring for an unspecified duration before end-points being measured; relationship between timings of urine (exposure) and serum (outcome) collections was not specified but implied as a cross-sectional analysis	Co-exposures were not quantified or accounted for	Not suspected

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El Shanawany et al. (2017) Is genotoxic; induces oxidative stress	Antimony(III) oxide	Cross-sectional: DNA damage and oxidative stress were compared between 25 workers occupationally exposed to antimony(III) oxide in polyester production and 25 age-matched unexposed participants	Employment in polyester-manufacturing firm using antimony(III) oxide; elevated Sb exposure relative to unexposed was confirmed by comparative analysis of total urinary Sb	Exposed to antimony(III) oxide for durations ranging 3–36 yr, while working in the polyester polymerization process	Qualitative and quantitative metrics investigated	Urinary Sb concentrations were not corrected for urinary dilution; if large differences in hydration status were present between exposed and unexposed groups, these would have contributed to the differences observed in Sb concentrations	Not specified, but those relevant to the industrial process described: primarily respiratory and dermal	End-points were compared between the groups described, but continuous urinary Sb concentrations were also associated with the quantity of DNA damage among exposed workers; duration of exposure was also investigated among exposed workers	The exposures described had been occurring for between 3 and 36 yr before end-points being measured; relationship between timings of urine (exposure) and blood (outcome) collections was not specified but implied as a cross-sectional analysis	Those with a history of medicinal products containing Sb and exposure to other known genotoxic agents were excluded and smoking was quantified; however, information on other co-exposures in this occupation was lacking; analysis was adjusted for cigarette-years	Not suspected
Bai et al. (2021) Is genotoxic: mosaic loss of chromosome Y	Not specified	Cross-sectional	Measurements of Sb in 20 mL morning spot urine samples collected in October 2010	Sb in urine samples among coke-oven plant workers, employed for > 1 yr, in Wuhan, China who enrolled in October 2010	Quantitative	None noted	All routes	Urinary (μg/mmol creatinine) levels of Sb using a single measure of exposure at single point in time	Preceded	10 urinary metabolites of PAHs, along with BPDE-alb adducts in plasma, and co-exposures to 22 metals were assessed: Al, As, Ba, Cd, Co, Cr, Cu, Fe, Pb, Mn, Mo, Ni, Rb, Se, Sr, Tl, Sb, Ti, U, V, W, and Zn; smoking LASSO regression and BKMR analyses were applied to account for mixtures, smoking pack-years	Differential misclassification: unlikely Non-differential misclassification: likely (use of a single urinary biomarker is subject to substantial intra-individual variability (Wang et al., 2019a)
Cavallo et al. (2002) Is genotoxic: micronucleus formation; sister-chromatid exchange; oxidative DNA-damage marker (comet assay)	Antimony(III) oxide	Cross-sectional	Measurements of antimony(III) oxide from personal air sampling conducted over a work week (Monday to Friday) on workers in the car upholstery industry	Weekly mean levels of antimony(III) oxide (μg/m^3) for 2 groups of workers in the car upholstery industry: 17 workers in the “high” exposure group (A), 6 workers in the “low” exposure group (B)	Quantitative	Sampling duration per work day not specified but earlier paper indicates that sampling was conducted over the entire work shift “in most cases” (Iavicoli et al., 2002) In IARC Groups A and B, 26 and 15 measurements were collected because “more samples per subject could be taken in Group B because of their shift schedules”	Inhalation	Weekly mean antimony(III) oxide levels (μg/m^3) for 2 groups of workers (high-exposure group and low-exposure group)	Preceded	There is potential for co-exposures to other metals or carcinogens, although none were mentioned or evaluated except smoking; analysis was adjusted for smoking status	Differential misclassification: unlikely

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Goi et al. (2003) Alters cell proliferation, cell death, or nutrient supply: plasma levels of lysosomal enzymes *N*-acetyl-β-D-glucosaminidase, β-D-glucuronidase, α- and β-D-galactosidase, α-D-glucosidase, and α-D-mannosidase	Antimony(III) oxide	Cross-sectional	Measurements of Sb in urine samples	Sb exposures among art-glass workers: 16 workers used arsenic(III) oxide and 10 used antimony(III) oxide	Quantitative	No information on methods for collecting urine samples; sparse details on laboratory analyses of metals in urine samples	All routes	Urinary concentrations of Sb (μg/L) using a single measure of exposure at single point in time	Exposures and outcome assessed at the same time	Urinary levels of As (μg/L) were also measured; smoking No assessment for co-exposures in the statistical analyses No difference between smokers and non-smokers was shown	Differential misclassification: unlikely Non-differential misclassification: likely (use of a single urinary biomarker is subject to substantial intra-individual variability)
Guo et al. (2018) Modulates receptor-mediated effects: serum thyroid hormones	Not intended to be specified	Cross-sectional	Measurements of Sb in peripheral whole-blood samples among pregnant women collected at ~25 wk of gestation in 2016	Sb concentrations in whole blood among pregnant women participating in the Hangzhou Birth Cohort Study (HBCS) enrolled in 2016	Quantitative	None	All routes	Tertiles of plasma concentrations (μg/L) of Sb using a single measure of exposure at single point in time	Serum samples for thyroid hormone levels were taken within 1 wk of collection of blood samples for metal measurement	As, Cd, Co, Cr, Se, Mn, Ni, Pb, Sr, and V were also measured and evaluated; smoking Co-exposures were evaluated if single-metal models produced statistically significant results ($P < 0.05$); logistic regression results presented for Mn, Ni, and Sb for free thyroxine (FT4); analysis was adjusted for exposure to second-hand smoke in pregnancy	Differential misclassification: unlikely
Margetaki et al. (2021) Modulates receptor-mediated effects: thyroid hormones	Not intended to be specified	Cross-sectional	Measurements of Sb in maternal spot urine samples	Sb levels in urine at the first prenatal visit (median, 13 wk of gestation) among women enrolled in the Rhea birth cohort in Heraklion, Crete, Greece	Quantitative	None	All routes	Dichotomized (first and second tertiles were collapsed for the reference category) maternal urinary concentrations of Sb (μg/L, adjusted for specific gravity) using a single measure of exposure at single point in time	Exposures and outcomes were assessed at the same time	Cd and Pb were also measured in urine samples Co-exposures were evaluated using BKMR Smoking; all models were adjusted for smoking in early pregnancy	Differential misclassification: unlikely

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Riffo-Campos et al. (2018) Induces epigenetic alterations: subclinical atherosclerosis measures, DNA methylation markers	Not specified	Cross-sectional	Measurements of Sb in spot urine samples collected during 2009–2010	Sb levels in urine collected at baseline (2009–2010) among a cohort of workers (men) at a car assembly plant in Figueruelas (Zaragoza, Spain)	Quantitative	None	All routes	Urinary levels of Sb (μg/g creatinine) using a single measure of exposure at single point in time	Measurement of urinary metal levels before assessment of subclinical atherosclerosis measures In a subsample of participants who provided blood samples, relationships between differentially methylated regions with respect to subclinical atherosclerosis in coronary, carotid, and femoral artery territories, metal concentrations, sociodemographic characteristics, and different cell types were evaluated using a big-data approach (i.e. bump hunter methodology)	Potential for co-exposures to As, Cd, and W; smoking; statistical models were adjusted for active smoking	Differential misclassification: unlikely
Wu & Chen (2017) Is immunosuppressive: serum IgG, IgA, and IgE levels	Antimony(III) oxide (for the workers at the antimony(III) oxide plant) Unable to specify for the other group of workers	Cross-sectional	Measurements of Sb in air samples (area and personal sampling) Measurements of Sb in blood, first-void urine, and hair samples	Airborne Sb levels at work sites and administrative offices at glass-, antimony(III) oxide-, and engineering plastic-manufacturing plants Sb levels in blood, urine, and hair of workers at glass-, antimony(III) oxide- and engineering plastic-manufacturing plants	Quantitative	Unclear how many personal samplers were located and how many area samples were collected	All routes	Average Sb levels in air samples (mg/m^3) at work sites and administrative offices Sb concentrations in blood (μg/L), urine (μg/g creatinine), and hair (μg/g) using a single measure of exposure at single point in time	Exposures and outcomes were assessed at the same time	Potential for exposures to other metals and carcinogens in the workplaces studied; smoking No assessment for co-exposures	Differential misclassification: unlikely
Cooper et al. (1968) Induces chronic inflammation: pneumoconiosis	Sb ore (stibnite) and antimony(III) oxide	Occupational health evaluation	Measurements of Sb in air and in spot urine samples collected	Airborne Sb levels; an Sb plant processing crude ore (antimony(III) sulfide) into antimony(III) oxide Periodic (1 or 2 times/yr) assessment of urinary Sb levels among 28 workers 1962–1966	Quantitative	No information on sampling strategy or sampling and analytical protocols for assessing Sb in air; no information on laboratory methods for analysing Sb in urine	Inhalation	Average Sb levels in air samples (mg/m^3) at different locations in the plant (bagging operations, 10 other locations; 13 other locations) Sb concentrations in urine (μg/L) 1 or 2 times/yr between 1962 and 1966	Preceding: urine samples collected prior to X-ray evaluations of pneumoconiosis; duration of occupational exposure was 1–15 yr. Unable to determine temporal relationship between air measurements of Sb and evaluation of outcome	None mentioned	Differential misclassification: unlikely

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Deng et al. (2019) Induces epigenetic alteration: microRNA expression	Not specified	Cross-sectional	Measurements of Sb in spot urine samples, collected either at the start or end of the work shift	Urinary levels of Sb among 360 coke-oven workers (men) in a steel plant in southern China, classified into exposed (working at the top, side, or bottom of the coke oven; *n* = 122) and unexposed (working in adjunct workplaces or offices; *n* = 238)groups	Quantitative	Urine samples were collected either at the start or the end of the work shift	Inhalation	Sb concentrations in urine (µmol/mmol creatinine)	Exposures and outcomes were assessed at the same time	Smoking; co-exposures to 22 other metals and PAHs evaluated assessed using LASSO penalized regression analysis, adjusted to smoking status and pack-years	Differential misclassification: unlikely
Kirmizi et al. (2020) Induces oxidative stress: oxidative, antioxidative, and pro-inflammatory markers; glucose metabolism parameters	Not intended to be specified	Cross-sectional	Measurements of Sb in fasting blood samples among women with and without PCOS	Women recruited from gynaecology outpatient clinics	Quantitative	Fasting blood samples	All routes	Sb concentrations in blood (ppb) [µg/L]	Exposures and outcomes were assessed at the same time	Co-exposures to 7 other metals (As, Cr, Cd, Pb, Hg, Zn, and Cu) were evaluated	
Alrashed et al. (2021) Is genotoxic; induces oxidative stress	Not possible to specify	Case–control	Blood measurement of total Sb	Blood Sb in a case–control study of women with recurrent pregnancy loss and controls	Quantitative	No practical concerns	All routes	Continuous variable of total blood Sb correlated with end-point metrics	Cross-sectional	Blood As also quantified, but no adjustment performed	Non-differential misclassification: possible
Lobanova et al. (1996) Induces chronic inflammation (bronchitis); immune response	[The Working Group's assessment is antimonite/stibnite ore consisting of antimony(III) oxide, based on a review of mines in the region (Baltukhaev & Solozhenkin, 2009)]	Cross-sectional	Occupational status	Occupational exposure to Sb through mining; 2 "exposed" groups were compared with a control group of gold miners with no known exposure to Sb; implied groups were validated by dust analysis in the exposed	Qualitative	N/A	Primarily inhalation of Sb-containing dust, but also other mining-relevant routes; however, route-specific exposure assessment not undertaken	Qualitative status of employment used to determine groups	70% of examined workers had worked in the mine "up to ten years"	Yes, as dust known to be of complex composition with other elements, including As and sulfur	Unlikely
Potkonjak & Pavlovich (1983) Induces chronic inflammation: pneumoconiosis	Antimony(III) oxide Antimony(V) oxide	Cross-sectional	Occupational status: exposure to dusts containing ≤ 88% antimony(III) oxide and ≤ 7.8% antimony(V) oxide, as previously quantified; years in occupation also briefly examined	Occupational exposure to antimony(III) oxide and antimony(V) oxide dust in a smelting plant	Qualitative	N/A	Routes relevant to dust exposures during smelting	Qualitative employment status in a task involving dust with high Sb content; years in occupation also available and used for comparison	Occupational history in smelting plant between 9 and 31 yr; periodic lung examinations were performed throughout employment	Smelting activities usually involve multiple co-exposures; while antimony(III) oxide and antimony(V) oxide made up the largest portion of dust components (39–88% and 2–8%, respectively), lower concentrations of free silica (0.8–4.7%), ferric oxide (0.9–3.8%), and arsenic(III) oxide (0.2–6.5%) were present	Unlikely

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Al, aluminium; As, arsenic; Ba, barium; BKMR, Bayesian kernel machine regression; BPDE-alb, plasma benzo[*a*]pyrene diol epoxide albumin; bw, body weight; Cd, cadmium; Co, cobalt; Cr, chromium; Cu, copper; Ig, immunoglobulin; LASSO, least absolute shrinkage and selection operator; Mn, manganese; Mo, molybdenum; N/A, not applicable; NHANES, National Health and Nutrition Examination Survey; Ni, nickel; PAH, polycyclic aromatic hydrocarbon; Pb, lead; PCOS, polycystic ovary syndrome; ppb, parts per billion; Rb, rubidium; Sb, antimony; Se, selenium; Sr, strontium; Ti, titanium; Tl, thallium; U, uranium; V, vanadium; W, tungsten; wk, week; yr, year; Zn, zinc.

References

Alrashed M, Tabassum H, Almuhareb N, Almutlaq N, Alamro W, Alanazi ST, et al. (2021). Assessment of DNA damage in relation to heavy metal induced oxidative stress in females with recurrent pregnancy loss (RPL). Saudi J Biol Sci. 28(9):5403–7. https://doi.org/10.1016/j.sjbs.2021.05.068 PMID:34466121

Bai Y, Guan X, Wei W, Feng Y, Meng H, Li G, et al. (2021). Effects of polycyclic aromatic hydrocarbons and multiple metals co-exposure on the mosaic loss of chromosome Y in peripheral blood. J Hazard Mater. 414:125519. https://doi.org/10.1016/j.jhazmat.2021.125519 PMID:33676251

Baltukhaev GI, Solozhenkin PM (2009). Concentration of gold-antimony ores in the Sakha Republic (Yakutia). Russ J Non-Ferr Met. 50(3):199–205. https://doi.org/10.3103/S106782120903002X

Binks K, Doll R, Gillies M, Holroyd C, Jones SR, McGeoghegan D, et al. (2005). Mortality experience of male workers at a UK tin smelter. Occup Med (Lond). 55(3):215–26. https://doi.org/10.1093/occmed/kqi026 PMID:15757978

Cavallo D, Iavicoli I, Setini A, Marinaccio A, Perniconi B, Carelli G, et al. (2002). Genotoxic risk and oxidative DNA damage in workers exposed to antimony trioxide. Environ Mol Mutagen. 40(3):184–9. https://doi.org/10.1002/em.10102 PMID:12355552

CDC (2017). Biomonitoring summary. Antimony. CAS No. 7440-36-0. Atlanta (GA), USA: National Biomonitoring Program, Centers for Disease Control and Prevention, United States Department of Health and Human Services. Available from: https://www.cdc.gov/biomonitoring/Antimony_BiomonitoringSummary.html#, accessed 10 November 2022.

Cooper DA, Pendergrass EP, Vorwald AJ, Mayock RL, Brieger H (1968). Pneumoconiosis among workers in an antimony industry. Am J Roentgenol Radium Ther Nucl Med. 103(3):496–508. https://doi.org/10.2214/ajr.103.3.495 PMID:5659960

Costa RS, Carvalho LP, Campos TM, Magalhães AS, Passos ST, Schriefer A, et al. (2018). Early cutaneous leishmaniasis patients infected with *Leishmania braziliensis* express increased inflammatory responses after antimony therapy. J Infect Dis. 217(5):840–50. https://doi.org/10.1093/infdis/jix627 PMID:29216363

Deng Q, Dai X, Feng W, Huang S, Yuan Y, Xiao Y, et al. (2019). Co-exposure to metals and polycyclic aromatic hydrocarbons, microRNA expression, and early health damage in coke oven workers. Environ Int. 122:369–80. https://doi.org/10.1016/j.envint.2018.11.056 PMID:30503314

Domingo-Relloso A, Grau-Perez M, Galan-Chilet I, Garrido-Martinez MJ, Tormos C, Navas-Acien A, et al. (2019). Urinary metals and metal mixtures and oxidative stress biomarkers in an adult population from Spain: the Hortega Study. Environ Int. 123:171–80. https://doi.org/10.1016/j.envint.2018.11.055 PMID:30529889

Duan W, Xu C, Liu Q, Xu J, Weng Z, Zhang X, et al. (2020). Levels of a mixture of heavy metals in blood and urine and all-cause, cardiovascular disease and cancer mortality: a population-based cohort study. Environ Pollut. 263(Pt A):114630. https://doi.org/10.1016/j.envpol.2020.114630 PMID:33618481

El Shanawany S, Foda N, Hashad DI, Salama N, Sobh Z (2017). The potential DNA toxic changes among workers exposed to antimony trioxide. Environ Sci Pollut Res Int. 24(13):12455–61. https://doi.org/10.1007/s11356-017-8805-z PMID:28361399

García-Pérez J, Fernández de Larrea-Baz N, Lope V, Molina AJ, O'Callaghan-Gordo C, Alonso MH, et al. (2020). Residential proximity to industrial pollution sources and colorectal cancer risk: a multicase-control study (MCC-Spain). Environ Int. 144:106055. https://doi.org/10.1016/j.envint.2020.106055 PMID:32827807

García-Pérez J, Lope V, Fernández de Larrea-Baz N, Molina AJ, Tardón A, Alguacil J, et al. (2021). Risk of gastric cancer in the environs of industrial facilities in the MCC-Spain study. Environ Pollut. 278:116854. https://doi.org/10.1016/j.envpol.2021.116854 PMID:33714062

Goi G, Bairati C, Massaccesi L, Sarnico M, Pagani A, Lombardo A, et al. (2003). Low levels of occupational exposure to arsenic and antimony: effects on lysosomal glycohydrolase levels in plasma of exposed workers and in lymphocyte cultures. Am J Ind Med. 44(4):405–12. https://doi.org/10.1002/ajim.10283 PMID:14502769

Guo J, Lv N, Tang J, Zhang X, Peng L, Du X, et al. (2018). Associations of blood metal exposure with thyroid hormones in Chinese pregnant women: a cross-sectional study. Environ Int. 121(Pt 2):1185–92. https://doi.org/10.1016/j.envint.2018.10.038 PMID:30385064

Guo J, Su L, Zhao X, Xu Z, Chen G (2016). Relationships between urinary antimony levels and both mortalities and prevalence of cancers and heart diseases in general US population, NHANES 1999–2010. Sci Total Environ. 571:452–60. https://doi.org/10.1016/j.scitotenv.2016.07.011 PMID:27396316

Hantson P, Léonard ED, Crutzen-Fayt MC, Léonard A, Vandercam B, Delaere B, et al. (1996). Cytogenetic observations after meglumine antimoniate therapy for visceral leishmaniasis. Pharmacotherapy. 16(5):869–71. PMID:8888081

Iavicoli I, Caroli S, Alimonti A, Petrucci F, Carelli G (2002). Biomonitoring of a worker population exposed to low antimony trioxide levels. J Trace Elem Med Biol. 16(1):33–9. https://doi.org/10.1016/S0946-672X(02)80006-2 PMID:11878750

Jones RD (1994). Survey of antimony workers: mortality 1961-1992. Occup Environ Med. 51(11):772–6. https://doi.org/10.1136/oem.51.11.772 PMID:7849856

Jones SR, Atkin P, Holroyd C, Lutman E, Batlle JV, Wakeford R, et al. (2007). Lung cancer mortality at a UK tin smelter. Occup Med (Lond). 57(4):238–45. https://doi.org/10.1093/occmed/kql153 PMID:17437956

Kim HA, Heo Y, Oh SY, Lee KJ, Lawrence DA (1999). Altered serum cytokine and immunoglobulin levels in the workers exposed to antimony. Hum Exp Toxicol. 18(10):607–13. https://doi.org/10.1191/096032799678839400 PMID:10557011

Kirmizi DA, Baser E, Turksoy VA, Kara M, Yalvac ES, Gocmen AY (2021). Are heavy metal exposure and trace element levels related to metabolic and endocrine problems in polycystic ovary syndrome? Biol Trace Elem Res. 199(1):3570. [Corrected and republished from: Biol Trace Elem Res. 2020;198(1):77–86.] https:// doi.org/10.1007/s12011-020-02473-5 PMID:33219466

Kotsopoulos J, Sukiennicki G, Muszyńska M, Gackowski D, Kąklewski K, Durda K, et al. (2012). Plasma micronutrients, trace elements, and breast cancer in *BRCA1* mutation carriers: an exploratory study. Cancer Causes Control. 23(7):1065–74. https://doi.org/10.1007/s10552-012-9975-0 PMID:22576580

Kresovich JK, Erdal S, Chen HY, Gann PH, Argos M, Rauscher GH (2019). Metallic air pollutants and breast cancer heterogeneity. Environ Res. 177:108639. https://doi.org/10.1016/j.envres.2019.108639 PMID:31419716

Liu M, Song J, Jiang Y, Liu Y, Peng J, Liang H, et al. (2021). A case-control study on the association of mineral elements exposure and thyroid tumor and goiter. Ecotoxicol Environ Saf. 208:111615. https://doi.org/10.1016/j.ecoenv.2020.111615 PMID:33396135

Lobanova EA, Ivanova LA, Pavlova TA, Prosina II (1996). Kliniko-patogeneticheskie osobennosti pri vozdeĭstvii antimonitovykh rud na organizm rabotaiushchikh. Med Tr Prom Ekol. (4):12–5. [Russian] PMID:8768112

Margetaki K, Vafeiadi M, Kampouri M, Roumeliotaki T, Karakosta P, Daraki V, et al. (2021). Associations of exposure to cadmium, antimony, lead and their mixture with gestational thyroid homeostasis. Environ Pollut. 289:117905. https://doi.org/10.1016/j.envpol.2021.117905 PMID:34371266

Mérida-Ortega Á, Rothenberg SJ, Cebrián ME, López-Carrillo L (2022). Breast cancer and urinary metal mixtures in Mexican women. Environ Res. 210:112905. https://doi.org/10.1016/j.envres.2022.112905 PMID:35217012

Niehoff NM, O'Brien KM, Keil AP, Levine KE, Liyanapatirana C, Haines LG, et al. (2021). Metals and breast cancer risk: a prospective study using toenail biomarkers. Am J Epidemiol. 190(11):2360–73. https://doi.org/10.1093/aje/kwab204 PMID:34268559

Potkonjak V, Pavlovich M (1983). Antimoniosis: a particular form of pneumoconiosis. I. Etiology, clinical and X-ray findings. Int Arch Occup Environ Health. 51(3):199–207. https://doi.org/10.1007/BF00377752 PMID:6222000

Riffo-Campos AL, Fuentes-Trillo A, Tang WY, Soriano Z, De Marco G, Rentero-Garrido P, et al. (2018). *In silico* epigenetics of metal exposure and subclinical atherosclerosis in middle aged men: pilot results from the Aragon Workers Health Study. Philos Trans R Soc Lond B Biol Sci. 373(1748):20170084. https://doi.org/10.1098/rstb.2017.0084 PMID:29685964

Schnorr TM, Steenland K, Thun MJ, Rinsky RA (1995). Mortality in a cohort of antimony smelter workers. Am J Ind Med. 27(5):759–70. https://doi.org/10.1002/ajim.4700270510 PMID:7611310

Scinicariello F, Buser MC (2016). Urinary antimony and leukocyte telomere length: an analysis of NHANES 1999–2002. Environ Res. 150:513–8. https://doi.org/10.1016/j.envres.2016.06.044 PMID:27423705

Tellez-Plaza M, Tang WY, Shang Y, Umans JG, Francesconi KA, Goessler W, et al. (2014). Association of global DNA methylation and global DNA hydroxymethylation with metals and other exposures in human blood DNA samples. Environ Health Perspect. 122(9):946–54. https://doi.org/10.1289/ehp.1306674 PMID:24769358

Torrús D, Massa B, Boix V, Portilla J, Pérez-Mateo M (1996). Meglumine antimoniate-induced pancreatitis. Am J Gastroenterol. 91(4):820–1. PMID:8677970

Wang Y-X, Pan A, Feng W, Liu C, Huang L-L, Ai S-H, et al. (2019a). Variability and exposure classification of urinary levels of non-essential metals aluminum, antimony, barium, thallium, tungsten and uranium in healthy adult men. J Expo Sci Environ Epidemiol. 29(3):424–34. https://doi.org/10.1038/s41370-017-0002-0 PMID:29269756

Wang YX, Sun Y, Huang Z, Wang P, Feng W, Li J, et al. (2016). Associations of urinary metal levels with serum hormones, spermatozoa apoptosis and sperm DNA damage in a Chinese population. Environ Int. 94:177–88. https://doi.org/10.1016/j.envint.2016.05.022 PMID:27258659

White AJ, O'Brien KM, Niehoff NM, Carroll R, Sandler DP (2019). Metallic air pollutants and breast cancer risk in a nationwide cohort study. Epidemiology. 30(1):20–8. https://doi.org/10.1097/EDE.0000000000000917 PMID:30198937

Wingren G, Axelson O (1987). Mortality in the Swedish glassworks industry. Scand J Work Environ Health. 13(5):412–6. https://doi.org/10.5271/sjweh.2019 PMID:3433043

Wingren G, Axelson O (1993). Epidemiologic studies of occupational cancer as related to complex mixtures of trace elements in the art glass industry. Scand J Work Environ Health. 19(Suppl 1):95–100. PMID:8159983

Wu CC, Chen YC (2017). Assessment of industrial antimony exposure and immunologic function for workers in Taiwan. Int J Environ Res Public Health. 14(7):689. https://doi.org/10.3390/ijerph14070689 PMID:28672853