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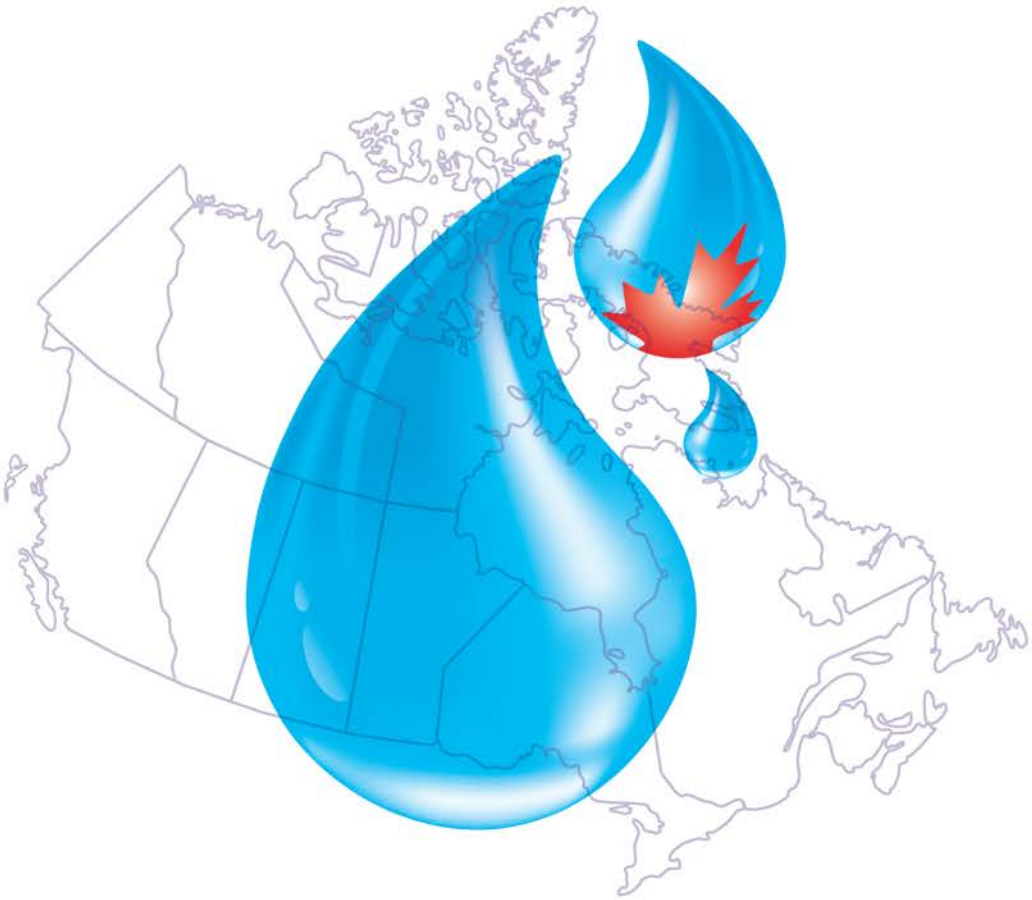
Guidelines for Canadian Drinking Water Quality

Guideline Technical Document

Antimony



Canada

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Antimony

Guideline

The maximum acceptable concentration (MAC) for antimony in drinking water is 0.006 mg/L (6 µg/L).

Identity, Use and Sources in the Environment

Elemental antimony (Sb) is a silvery white, brittle solid that, along with arsenic and bismuth, belongs to group VA of the periodic table. It is classified as both a metal and a metalloid. Its principal oxidation states are +3 and +5.

Antimony is present in the Earth's crust at a concentration of about 0.2–0.5 mg/kg. It is seldom found in the environment as a pure element, but it is often found as trivalent and pentavalent sulphides and chlorides. A major source of antimony in Canada is its recovery as a by-product from lead smelting operations in British Columbia and New Brunswick. Antimony is also recycled in lead bullion recovered during the recycling of lead-acid batteries in Toronto and Montreal.[1] Canadian production of antimony was 652 000 kg in 1997, with a total estimated value of approximately $2 million.[2]

Antimony, as a pure metal, is used for the production of semiconductors, infrared detectors and diodes. Alloys of antimony are used in the manufacture of batteries, cable sheathing, printing type, plumbing solder and antifriction materials; non-metal antimony products are used in flame retardant materials, paint pigments, ceramic enamels, plastics, glass and pottery, ammunition primers and fireworks.[3] Potassium antimony tartrate is widely used in the pharmaceutical industry.

Antimony may enter the aquatic environment by way of natural weathering of rocks, runoff from soils, effluents from mining and manufacturing operations, and industrial and municipal leachate discharges.[4,5] Household piping and possibly non-leaded solders are sources of antimony in tap water, as soft water may leach antimony from the pipes. The potential for antimony to leach from copper pipes with solder joints made from 95% tin/5% antimony into high-purity, tap and well water samples has been investigated.[6] The high-purity water had a pH of 6.8; the pH, alkalinity and chloride values of the tap water were 7.8, 30 mg/L (as $CaCO_3$) and 4 mg/L, respectively, whereas the corresponding values for the well water were 8.1, 155 mg/L and 19 mg/L. There was no detectable leaching (detection limit 1.2 µg/L) of antimony into the high-purity water or the well water; however, leaching occurred into tap water, but only after 7 days of contact. After 7, 28 and 90 days' contact time, the amount of antimony leached into tap water resulted in final concentrations of 2.0, 3.7 and 7.3 µg/L, respectively. It is noted that no tests were conducted with acidic (below pH 6) waters.

Antimony is released into the air as stack dust from industrial sources, such as coal-fired power plants, inorganic chemical plants and metal smelters.[7]

Antimony is not degradable *per se*. The two main factors that influence the behaviour of antimony are its solubility and complexation. Antimony compounds range in solubility from insoluble to fully soluble. Most inorganic antimony compounds are insoluble, whereas compounds that become attached to organic ligands are soluble.[8] Some antimony salts, such as the trichloride, sulphate, potassium tartrate and pentachloride, are soluble in water, whereas the oxides tend to precipitate.[9] Sorption may also be a key environmental process, but the available information is incomplete. Antimony does not bioaccumulate.

The fate of antimony in the aquatic environment is determined by several factors, including pH, oxidation–reduction potential, sorptive interactions and biologically mediated methylation. In the aquatic environment, antimony can be present as an ion or a soluble complex. Most of the dissolved antimony (in the +5 oxidation state)[10] that might be discharged to natural water would soon precipitate as antimony trioxide or antimony pentoxide and be removed by sedimentation.[9]

Exposure

Canadians can be exposed to antimony via water, air, food and urban dust. The concentrations of antimony detected in Canadian surface water range from 0.001 to 9.1 mg/L.[11] Concentrations are typically less than

10 µg/L and are often closer to 1 µg/L.[12] In a recent survey of water supplies in Newfoundland,[13] samples were taken from both homes and raw water sources (surface water and groundwater); antimony was found at concentrations below 5 µg/L, regardless of the source or type of water. The levels of antimony in community drinking water supplies in New Brunswick were generally less than 5 µg/L; however, in one well water sample, antimony was reported at 17 µg/L.[14] In a survey of municipal water supplies of 88 cities in the United States, the levels of antimony found in tap water were on average less than 0.2 µg/L.[15] In an analysis of 3834 drinking water samples collected from randomly selected households in 35 geographic areas of the United States, antimony was found in 16.5% of the samples, at concentrations ranging from 0.6 to 4.0 µg/L, with a mean value of 1.87 µg/L.[16] The average intake of antimony from drinking water has been estimated to be less than 8 µg/d.[17]

Antimony concentrations are higher in urban air than in non-urban air, presumably due to fossil fuel combustion, automobile emissions and incineration in urban areas. The mean, median and maximum concentrations of antimony in aerosols at three sites in Quebec, Ontario and Nova Scotia were 0.04–0.10, 0.11–0.23 and 0.37–2.17 ng/m^3, respectively.[18] Twenty-four-hour samples collected at 10 locations in Washington, DC, yielded average antimony concentrations ranging from 1.1 to 3.0 ng/m^3.[19]

Concentrations of antimony in meat, freshwater fish, poultry, cereals, fruit and vegetables appear to range from about 1 to 10 ng/g wet weight; significantly higher levels have been measured in marine organisms.[7] The daily intake of antimony from food has not been estimated for Canadians. A study was conducted in 1967 to measure the concentrations of antimony in the diets of children (aged 9 to 12) in 28 U.S. cities. Concentrations of antimony (measured by atomic absorption spectrophotometry) ranged from 0.209 to 0.500 mg/kg of food (weighted average 0.361 mg/kg), resulting in daily dietary intakes between 0.25 and 1.28 mg.[20] These values are thought to be too high because of the analytical method used.[21] Iyengar *et al*.[22] estimated the intake of antimony from food for 25- to 30-year-old males in the United States by analysing 201 foods (by instrumental neutron activation analysis) from the U.S. Food and Drug Administration's Total Diet Study. Antimony was found at a mean concentration of 0.0093 ± 0.0014 µg/g dry weight (mixed-diet composite); assuming an adult male consumes approximately 3075 g wet weight or 498 g dry weight (16.2% of wet weight), the authors suggested a total antimony intake of approximately 4.6 µg/d from food.

The information on levels of antimony in Canadian drinking water, air and food was insufficient to allow the determination of national intakes by these three routes of exposure. U.S. exposure levels and intakes are probably a reasonable approximation of Canadian exposure levels and intakes because of the similar environment and food habits in North America. Assuming a contribution of 4.6 µg from food (as calculated above),[20] 0.04 µg from air (calculated using the maximum measured Canadian concentration of 2.17 ng/m^3 and a daily air intake of 20 m^3)[18] and 2.8 µg from water (calculated from the mean value of 1.87 µg/L and an average daily water consumption of 1.5 L),[16] an adult would receive 7.44 µg of antimony per day; approximately 38% of this total intake would come from drinking water.

Analytical Methods and Treatment Technology

Antimony may be analysed in water using an atomic absorption spectrophotometer equipped with a graphite furnace.[6] The detection limit given by the laboratory was 1.2 µg/L (based on three times the standard deviation of the blank). The practical quantitation level, based on a minimum of five times the detection limit, is 6 µg/L. Although more sensitive methods are available for the analysis of antimony in water,[23] lower detection limits are not currently readily achievable by many mon-itoring laboratories.

Little information is available on the removal of antimony from source water during water treatment. However, as antimony is chemically similar to arsenic, the methods used for the removal of arsenic (which can be removed to <5 µg/L from groundwater containing natural arsenic levels as high as 1.0 mg/L using activated alumina columns)[24,25] could possibly be used for antimony removal.[26] Coagulation with alum or ferric salts, particularly in the presence of turbidity, may have potential for conventional treatment. Lime softening can very effectively remove antimony from hard waters. The removal will be dependent on the pH and antimony valence. In bench-scale tests, a water-insoluble starch xanthate, which acts as an ion exchange material, has been reported to be effective in removing antimony from wastewater (from 5 mg/L to roughly 0.01 mg/L).[8]

Because antimony may also be introduced to drinking water after the water leaves the treatment plant as a result of leaching from materials in the distribution system or household plumbing, corrosion control is a more effective method of preventing high concentrations of antimony at the point of consumption. Adjustment of the pH from less than 7 to 8 or 9 and moderate increases in alkalinity will reduce the corrosiveness of the water and minimize leaching. Corrosion inhibitors may also be added to the water.[6]

Health Effects

Pharmacokinetics

Absorption

The respiratory tract is the principal route by which antimony enters the body in occupational exposure. Precise information regarding respiratory absorption is lacking,[21] although it is known to be correlated with particle size.[27] Absorption of antimony from the gastrointestinal tract is thought to occur slowly and in small amounts.[28] The extent of gut absorption depends on solubility and chemical form. After their administration (as 1-mL solutions of ^{124}Sb tartrate) by gavage to eight Syrian hamsters, only 1.6 and 2% of the initial body burdens of trivalent and pentavalent antimony, respectively, were present on day 4, 61% and 64% of which were found in the gastrointestinal tract.[29] The median value of 1.6% includes two hamsters that received the largest amount of trivalent antimony, which retained 15% and 9% of the initial body burden on day 4.

About 15% of a single oral dose of soluble isotopic antimony potassium tartrate (4.4 mg/kg bw, or 7 µg of antimony) was absorbed in the gastrointestinal tract of white rats; absorption was determined following recovery of antimony in urine, faeces and tissues.[30] Cows administered a single oral dose of ^{124}Sb trichlorides (21 mg Sb/kg bw) absorbed less than 5% in their gastrointestinal tract.[31] No estimate of gastrointestinal absorption in humans has been reported.

Distribution

The distribution of antimony within the body and its excretion are a function of both the route of administration and the valence state of antimony. After inhalation, tissue distribution studies show that the trivalent form accumulates more rapidly than the pentavalent form in the liver, whereas pentavalent antimony is found preferentially in the skeleton. In the blood, the trivalent form is lodged primarily in red blood cells, whereas the pentavalent form is carried by plasma.[29] Following ingestion in animals, liver, kidney, bone, lung, spleen and thyroid are the major sites of accumulation outside the gastrointestinal tract.[10] In humans, the therapeutic use of trivalent antimony against parasites leads to higher accumulation in the liver, the thyroid and the heart.[32]

Antimony was found in placental tissues, milk, amniotic fluid and the umbilical cord of pregnant or nursing women who had worked in smelters.[33] In mice, antimony appears to cross the placental barrier more readily after intraperitoneal injection than when given in the diet. The newborn mouse is also able to take up antimony from its mother's milk when the mother is fed a contaminated diet during pregnancy and after delivery.[34] Antimony concentrations in breast milk were measured in 21 Italian women (>130 samples) during a 2- to 3-month period starting 15 days after childbirth. Concentrations ranged from less than 0.05 to 12.9 ng/g, with a mean of 3.0 ± 0.4 ng/g.[35]

Excretion

Excretion rates and routes differ depending on animal species, routes of administration and the valence of antimony. In general, trivalent antimony is excreted primarily in faeces, whereas pentavalent organic antimony is excreted primarily in urine.[36] In a study performed to investigate the metabolism of antimony,[31] three cows (in a lactating phase) were given antimony (as $^{124}SbCl_3$) orally at 2.84, 2.72 and 2.00 mCi, respectively (corresponding to an average dose of 21.1 mg Sb/kg bw). The excretion of antimony in faeces accounted for 82% of the dose, whereas milk and urine accounted for 0.008 and 1.1%, respectively. The spleen, liver, bone and skin contained the highest tissue concentrations. In a parallel study performed by the same authors, one cow received an intravenous injection of $^{124}SbCl_3$ (0.234 mCi), which corresponded to a dose of 1.5 mg Sb/kg bw. Faecal excretion accounted for 2.4% of the administered dose, whereas 0.08% and 51% of the total dose were excreted in milk and urine, respectively.

In humans, urine accounts for 1.2–3.6 µg of daily antimony excretion. Approximately 0.3–0.9 µg/d is excreted in faeces, and less than 1 µg/d is excreted by other routes.[8]

Effects in Humans

Acute and Subchronic Toxicity

Antimony poisoning has resulted from accidental occupational inhalation, ingestion of food contaminated by storage containers and therapeutic treatment with tartar emetic (potassium antimony tartrate).[37] Antimony compounds have been used for a long time as therapeutic agents for parasitic diseases such as schistosomiasis, leishmaniasis, trypanosomiasis and ulcerative granuloma. Side effects of antimony therapy (the average dose is up to 1 g/d for 10 days) include myocarditis, hepatitis and nephritis.[4]

Acute intoxication is characterized by abdominal pain, vomiting, diarrhoea, dehydration, muscular pain, shock, haemoglobinuria, anuria and uraemia.[37] In addition, severe myocardial symptoms and convulsions have been observed with acute doses of antimonials, and some deaths were attributed to liver necrosis. In humans, the lowest lethal dose by ingestion was 0.75 mg potassium antimony tartrate/kg bw.[38] Antimony levels of about 30 mg/L in a contaminated drink caused nausea, vomiting and diarrhoea in 150 children.[39]

Dermal contact with antimony can cause eczema and dermatitis, resulting in papular, vesicular and

pustular eruptions.[37] Symptoms of gastrointestinal disturbance and mild jaundice appear 2–3 weeks after a course of injections of antimony compounds.[40]

Chronic Toxicity and Carcinogenicity

Chronic exposure to lower doses of antimony compounds is primarily associated with myocardial effects. Heart complications, altered electrocardiogram (ECG) patterns and sudden deaths were observed in eight out of 125 workers who were occupationally exposed to antimony trisulphide at concentrations ranging from 0.58 to 5.5 mg/m^3 (average 3.0 mg/m^3) for 8–24 months.[41] Seven out of 111 (6.3%) surviving workers were found to have ulcers, compared with 59 out of 3912 (1.5%) control group workers.

In a recent mortality study, the lung cancer death rates of 1014 men (91.5% of Spanish ancestry) employed between 1937 and 1971 in an antimony smelter in Texas were compared with ethnic-specific lung cancer death rates in Texas. Mortality from lung cancer among antimony workers was elevated (standardized mortality ratio [SMR] 1.39; 90% confidence interval [CI] 1.01–1.88), and a significant positive trend in mortality with increasing duration of employment was observed. A significant increase in mortality from cancers of the liver, biliary tract and gall-bladder (SMR 3.17; 95% CI 1.27–6.52) was observed in the smelter workers compared with white males.[42] In a study of men employed in a British antimony smelter between 1961 and 1992, a significant increase in deaths from lung cancer was found in the census population of men working at the smelter before 1961, but not in the prospective cohort recruited after that date. It was not possible to attribute the increased risk of lung cancer to any particular agent, as the antimony workers were exposed to a variety of agents in addition to antimony and its oxides, including arsenic, sulphur dioxide and polycyclic aromatic hydrocarbons. No relationship was found between length of time worked and mortality from lung cancer.[43]

Reproductive Toxicity

A higher incidence of menstrual disorders and spontaneous late abortions (77.5% and 12.5%, respectively) was reported in female smelter workers who were exposed to metallic dust and antimony trioxide and pentoxide compared with a control group (56% and 4.1%, respectively).[33] The weight of the babies born to these exposed women was slightly less at three months of age and was significantly less at one year of age. Antimony was also found in breast milk (3.3 ± 2 mg/L), placental tissue (3.2–12.6 mg/100 mg) and amniotic fluids (6.2 ± 2.8 mg/100 mg).

Effects in Laboratory Animals and *In Vitro* Test Systems

Acute and Subchronic Toxicity

The acute oral LD_{50} value for potassium antimony tartrate in mice is 600 mg Sb/kg bw.[44] Minimum LD_{50}s for antimony of 100 and 150 mg/kg bw have been reported in rats and in guinea-pigs, respectively, after intraperitoneal injection; death was attributed to myocardial failure. In contrast, the minimum LD_{50}s for potassium antimony tartrate were 11 and 15 mg Sb/kg bw after intraperitoneal injection. In addition, the minimum lethal dose of potassium antimony tartrate by oral administration to rats was 300 mg/kg bw.[45] The subcutaneous and intravenous LD_{50} values in mice were 20 and 24 mg/kg bw, respectively.[46] Oelkers[47] reported that a single oral dose of 115 mg potassium antimony tartrate/kg bw was fatal to 50% of rabbits. A single oral dose of potassium antimony tartrate administered to rats at 300 mg Sb/kg bw resulted in death, attributed to myocardial failure.[45] However, no rats died following a single exposure to 188–16 714 mg Sb/kg bw or lower as inorganic antimony or to a dose of 7000 mg antimony as metallic antimony.

An increase in non-protein nitrogen in the blood and urine was reported in rabbits orally fed a dose of 15 mg potassium antimony tartrate/kg bw in a subchronic study.[48] Jaundice was noticed during the last two days of exposure, and the livers of some of the animals showed fatty degeneration and parenchymal necrosis. Following administration of 25 subcutaneous doses of antimony trifluoride (15 mg/kg bw) in rats over a one-month period, the rats developed oedema, fatty infiltration and cloudy swelling in the liver; in the kidney, swelling of epithelial cells lining the convoluted tubules, desquamation of the epithelium, protein masses in tubular lumina and shrunken glomeruli were observed. However, in a second group injected subcutaneously with antimony trioxide (at an equivalent dose of antimony), few pathological changes of significance were found, suggesting that at least some of the changes observed with antimony trifluoride were attributable to the presence of fluorine.[49] Severe diarrhoea was observed in dogs administered antimony trioxide at a dose of 84 mg Sb/kg bw per day for 32 days. No effects were observed in rats exposed to 501 mg Sb/kg bw per day or less as antimony trioxide for 20 days.[50]

Rats, rabbits and dogs were exposed to the dust of antimony trisulphide for seven hours per day, five days per week, for at least six weeks, at concentrations of 3.07, 5.6 and 5.32 mg/m^3, respectively.[41] Rats and rabbits developed parenchymatous degeneration of the myocardium and functional disorders of the heart, accompanied by ECG alterations (e.g., flattened T-wave pattern); these findings were not as pronounced in dogs.

In a range-finding test for "subacute" oral toxicity,[51] rats (five per sex per group) were fed a diet containing antimony trioxide at doses ranging from 60 to 1070 mg/kg bw per day for 30 days. The animals showed reduced growth and appetite as well as unspecified micropathological changes in the liver, kidney, spleen or testes at the highest dose. No effects were observed at or below 270 mg/kg bw per day.

Growth retardation as a result of subchronic oral exposure via feeding has also been suggested by a decrease in body weight gain in a study in which antimony or antimony trioxide was administered in the diet (0.1% or 1.0% antimony, 1.0% antimony trioxide) of 10 male Wistar rats for 12 weeks. The average weights of the rats at the end of the experiment were 438.0 ± 22.3 g (0.1% antimony), 401.0 ± 18.3 g (1.0% antimony) and 454.3 ± 38.8 g (1.0% antimony trioxide), compared with 489.5 ± 60.5 g for rats in the control group. Body weights returned to normal after 12 weeks on an antimony-free diet.[52]

In a recently completed study,[53] male and female Sprague-Dawley rats (15 per sex per group) were exposed to a soluble trivalent antimony salt (potassium antimony tartrate) in tap water at concentrations of 0.5, 5, 50 or 500 mg/L for 13 weeks. Calculated antimony intakes ranged from 0.06 to 42.17 mg/kg bw per day in males and from 0.06 to 45.69 mg/kg bw per day in females (although the actual "absorbed" doses were closer to 0.006–4.5 mg/kg bw per day based on the estimation of a 10% gastrointestinal absorption of potassium antimony tartrate). Control rats received unsupplemented tap water as drinking water. An additional 10 male and 10 female rats were included in each of the control and 500 mg/L groups and were given tap water for a further four weeks following the 13-week exposure period. All animals survived the treatment and recovery periods with no clinical signs of toxicity. Rats exposed at the highest dose level consumed significantly (35%) less water than rats in the control and lower dose groups and showed suppressed body weight gain. During recovery, water intakes were quickly restored to that of the control groups, and body weight gain was accelerated. At necropsy, one male in the 5 mg/L dose group and three males in the highest dose group had gross haematuria. A male rat in the highest dose group had a cirrhotic liver, and a female rat in the lowest dose group had a nodular, fibrotic spleen; because this effect was not observed at higher doses, the authors considered it to be not biologically significant.[54] Females in the 50 mg/L dose groups had a significant decrease in thymus to body weight ratios compared with controls. Significantly increased kidney to body weight ratios were observed in the highest dose group of both males and females compared with the control males and females. Both males and females in the highest dose group had decreased alkaline phosphatase activity and creatinine serum levels, whereas only males at 500 mg/L had decreased red blood cell and platelet counts and a slight increase in mean corpuscular volume. Females showed a dose-related decrease in serum glucose starting at 5 mg/L. Mild adaptive histological changes were observed in the highest dose groups in the thyroid, liver and pituitary glands of both sexes and in the spleen of male rats and thymus of female rats. After a four-week recovery period, the pituitary gland appeared largely normal, and the changes in the liver and thyroid of both sexes became less severe. On the other hand, minimal changes persisted in the spleen of both sexes and in the thymus of males. Tissue antimony levels were dose-related in the following (descending) order: red blood cells >> spleen, liver > kidney > brain, fat > serum. Following the recovery period, the antimony level in the highest-dose animals decreased in all tissues (antimony levels in red blood cells were not determined) except the spleen. A no-observed-adverse-effect level (NOAEL) of 0.5 mg antimony/L in drinking water, equivalent to an average intake of 0.06 mg/kg bw per day, was established based on the histological changes observed at 5 mg/L.

Decreases in haematocrit, haemoglobin and plasma protein levels were observed in rats exposed to 500–1000 mg Sb/d for 12–24 weeks.[52,55] Sunagawa[55] observed a decrease in red blood cell count in rats exposed to 418 mg Sb/kg bw per day as antimony trioxide for 24 weeks. Cloudy swelling of the hepatic cords was also observed at a dose of 418 mg Sb/kg bw per day as antimony trioxide or to 500 mg Sb/kg bw per day as metallic antimony. However, lower concentrations of antimony trioxide or potassium antimony tartrate did not produce the effects mentioned above.[50,56]

When dogs were treated with 6644 mg Sb/kg bw per day for 32 days, weakness and difficulty in moving hind limbs were observed.[50]

Chronic Toxicity and Carcinogenicity

There are only two studies available on the chronic toxicity of antimony.[56,57] In the first,[56] potassium antimony tartrate was provided in drinking water (5 mg/L as antimony) of Charles River CD strain mice (54 per sex per group) from the time of weaning until natural death. The animals were weighed weekly up to eight weeks and then monthly. The daily intake of antimony was calculated by the authors to be 350 µg/kg bw. Antimony did not significantly suppress growth in either male or female mice during the first year but did result in weight loss in males after 18 months ($p < 0.025$) and decreased weight gain in females measured at 12 and 18 months ($p < 0.005$). The median life spans and 75% life spans of female mice were shortened by 49 and 86 days, respectively. Effects on the life span were minimal in males.

In the second study,[57] potassium antimony tartrate was provided in drinking water (5 mg/L as antimony) to Long-Evans rats (50 per sex per group) from the time of

weaning until natural death. Water consumption by the rats was not reported. However, water consumption for rats of the same strain handled in the same laboratory was reported as 7.5 mL/100 g bw per day for females and 6.8 mL/100 g bw per day for males.[58] These would correspond to estimated doses of 340 µg/kg bw per day and 375 µg/kg bw per day for male and female rats, respectively. Antimony was more toxic to rats than to the mice in the first study. The life spans of the exposed rats were shortened significantly (the median life span was 106–107 days less than controls, and the 90% life span was 70 and 165 days less than controls for males and females, respectively). Longevity, the mean age of the last surviving 10%, was also significantly reduced compared with control rats. There were no measurable differences in the body weights between exposed and control rats. However, antimony accumulated in soft tissues with age. The mean concentration of antimony in five tissues (kidney, liver, heart, lung and spleen) of all rats analysed was 13.1 µg/g. As antimony was innately toxic to rats at 5 mg/L (which corresponded to 0.340 and 0.375 mg Sb/kg bw per day for males and females, respectively), this level was a lowest-observed-adverse-effect level (LOAEL) in this study.

The same two oral lifetime studies in mice[56] and rats[57] have suggested that antimony is not a carcinogen. In the mouse study,[56] dead animals were necropsied, gross lesions were recorded and tissues were examined histologically. Tumours identified at necropsy were also examined microscopically. Tumours were found in 34.8% of control animals and 18.8% of antimony-exposed animals. No reason was given for the high tumour incidence in controls. In the rat study,[57] antimony was not tumorigenic, as evidenced by a comparison of visible tumours in controls and treated animals at necropsy. Tumour frequencies in male and female control rats were 20.0% and 35.9%, respectively, whereas frequencies in treated male and female rats were 12.0% and 38.3%, respectively. In a third study, administration of 5 mg Sb/L (as the potassium tartrate) in drinking water to Charles River CD-1 strain mice for life did not result in any significant differences in the incidence of spontaneous or malignant tumours.[58] It should be noted that these studies are old and inadequate by modern standards. Major deficiencies of all three studies included the lack of complete histology, administration of only one dose level and limited reporting of pathology.

The induction of lung neoplasms was reported in female CDF rats, but not in male CDF rats, following the inhalation of antimony trioxide or antimony ore concentrate (concentrations ranged from 1.6 to 45 mg/m^3 in the two studies) for periods of up to a year, followed by surveillance from 20 weeks to 15 months.[59,60]

Mutagenicity

Several antimony compounds showed mutagenic potential in short-term *in vitro* tests. They have caused chromosome breaks in cultured human leukocytes[61] and enhanced the transformation of hamster cells by SA virus 7.[62] Three antimony compounds (antimony trioxide, antimony trichlorides and antimony pentachloride) were positive in the *Bacillus subtilis* rec assay, inhibiting the cellular growth of a recombinant-deficient strain of *B. subtilis* more strongly than that of a wild one.[63]

Reproductive and Developmental Toxicity

The information gathered from very limited animal studies on reproductive and developmental effects suggests that prenatal exposures to antimony can lower the rate of conception.[33] Female rats were exposed either to antimony dust via a single intraperitoneal injection of 50 mg/kg bw (acute exposure) or to antimony trioxide dust for four hours per day for 1.5–2 months at a concentration of 250 mg/m^3 (subchronic exposure).[33] The females were mated 3–5 days following injection, whereas inhalation exposure was continued throughout the gestation period. Following mating, only 15 of 30 acutely exposed females and 16 of 24 subchronically exposed females conceived, compared with nine of 10 females and 10 of 10 females in the two control groups. Fewer offspring were born in both exposed groups (average 6.2 per litter) than in the control group (8.3 per litter). No morphological changes were observed in the foetuses. Resorption and foetal deaths were not discussed.

In a study to evaluate the effect of antimony on development of vasomotor reactivity in the pups,[64] female albino rats (30 per group) were given antimony trichlorides at 0, 0.1 or 1 mg/100 mL (0, 1 or 10 mg/L) in drinking water *ad libitum* from the first day of pregnancy until weaning of the pups (22 days after delivery). The pups (10 per dam) received antimony at 0, 1 or 10 mg/L in their drinking water *ad libitum* from weaning to day 60. The dams showed a significant dose-related decrease ($p < 0.05$) in body weight on gestational day 20, but not on day 10. The pups in the high-dose group also had significantly reduced body weight ($p < 0.05$) from the 10th to the 60th day of age. Because food and water consumption data were not provided, it is not possible to determine if the effects on body weight were due to the direct toxicity of the chemical or to reduced food and/or water intake. The response of pups to hypertension- and hypotension-inducing drugs was altered at both antimony doses.

No foetal abnormalities were observed on gestational day 20 in pregnant rats after intramuscular administration of a solution containing antimony dextran glycoside (125 or 250 mg Sb/kg bw) on five occasions between the eighth and 14th days of gestation. Antimony was not detected in the foetuses.[65]

Classification and Assessment

Antimony is classified as having inadequate data for the evaluation of its carcinogenicity (Group V). For compounds classified in this way, the tolerable daily intake (TDI) is derived on the basis of division of the NOAEL or LOAEL in an animal study by an appropriate uncertainty factor.

Based on the available information, it is clear that antimony affects many organs and systems in the body. In a recently completed 13-week study using the most appropriate route and vehicle of administration (i.e., drinking water), groups of rats were exposed to potassium antimony tartrate in drinking water at concentrations of 0.5, 5, 50 or 500 mg/L.[53] A NOAEL of 0.5 mg Sb/L in drinking water, equivalent to an average intake of 0.06 mg/kg bw per day, was established based on the histological changes observed at 5 mg/L. For antimony, the TDI is derived as follows:

$$\text{TDI} = \frac{0.06 \text{ mg/kg bw per day}}{300} = 0.0002 \text{ mg/kg bw per day}$$

where:

- 0.06 mg/kg bw per day is the NOAEL in a 13-week study in rats[53]
- 300 is the uncertainty factor (×10 for intraspecies variation; ×10 for interspecies variation; and ×3 for the use of a short-term study).

Rationale

The maximum acceptable concentration (MAC) for antimony in drinking water is derived from the TDI as follows:

$$\text{MAC} = \frac{0.0002 \text{ mg/kg bw per day} \times 70 \text{ kg} \times 0.38}{1.5 \text{ L/d}} \approx 0.004 \text{ mg/L}$$

where:

- 0.0002 mg/kg bw per day is the TDI, as derived above
- 70 kg is the average body weight of an adult
- 0.38 is the proportion of total daily intake allocated to drinking water (as calculated in the "Exposure" section)
- 1.5 L/d is the average daily consumption of drinking water for an adult.

The calculated MAC for antimony in drinking water is 0.004 mg/L, which is below the practical quantitation level. The maximum acceptable concentration for antimony in drinking water has therefore been set at the practical quantitation level of 0.006 mg/L.

Because antimony may leach from materials in the distribution system, sampling should be carried out on flushed samples at the point of consumption.

References

1. McCutcheon, B. Antimony. In: 1995 Canadian minerals yearbook. Review and outlook. Minerals and Metals Sector, Natural Resources Canada. pp. 55.1–55.5 (1995).

2. Statistics Canada. Canada's mineral production. Preliminary estimates 1997. Catalogue No. 26-202-XPB, Manufacturing, Construction and Energy Division. pp. 8–9 (1997).

3. Canadian Council of Resource and Environment Ministers. Canadian water quality guidelines. Environment Canada (1987).

4. U.S. Environmental Protection Agency. Ambient water quality criteria for antimony. EPA 440/5-80-020 (NTIS PB81-117319), Criteria and Standards Division, Office of Water Regulations and Standards, Washington, DC (1980).

5. Cyr, F., Mehra, M.C. and Mallet, V.N. Leaching of chemical contaminants from a municipal landfill site. Bull. Environ. Contam. Toxicol., 38: 775–782 (1987).

6. Subramanian, K.S., Connor, J.W. and Meranger, J.C. Leaching of antimony, cadmium, copper, lead, silver, tin and zinc from copper piping with non-lead-based soldered joints. J. Environ. Sci. Health, A26(6): 911–929 (1991).

7. Monitoring and Assessment Research Centre (MARC). Exposure commitment assessments of environmental pollutants. Vol. 3. MARC Report No. 30, Chelsea College, University of London. pp. 32–52 (1983).

8. Parker, C.L., McKeon, K. and Livshits, E. Antimony removal technology for mining industry wastewaters. Report No. EPA-600/7-79-129, U.S. Environmental Protection Agency (1979)., cited in reference 12.

9. McKee, J.E. and Wolf, H.W. Water quality criteria. 2nd edition. Resources Agency of California, State Water Quality Control Board. pp. 138–139 (1963).

10. Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological profile for antimony. TP-91/02, Public Health Service, U.S. Department of Health and Human Services (1992).

11. National Water Quality Data Bank (NAQUADAT), 1985. Water Quality Branch, Inland Waters Directorate, Environment Canada, Ottawa (1987), cited in reference 3.

12. SENES Consultants Ltd. Drinking water criteria review for antimony. Prepared for Ontario Ministry of the Environment, Toronto (1986).

13. Dominie, K. Personal communication. Newfoundland and Labrador Department of Environment (1995).

14. Ecobichon, D.J. Personal communication. New Brunswick Department of Health and Community Services (1995).

15. Schroeder, H.A. Municipal drinking water and cardiovascular death rates. J. Am. Med. Assoc., 195: 81 (1966).

16. Greathouse, D.G and Craun, G.F. Cardiovascular disease study — Occurrence of inorganics in household tap water and relationships to cardiovascular mortality rates. In: Trace substances in environmental health XII. Proceedings of the University of Missouri's 12th Annual Conference on Trace Substances in Environmental Health (1978).

17. World Health Organization. Guidelines for drinking-water quality. Vol. 2. Health criteria and other supporting information. Geneva (1996).

18. Hopper, J.F. and Barrie, L.A. Regional and background aerosol trace elemental composition observed in eastern Canada. Tellus, 40B: 446–462 (1988), cited in reference 10.

19. Kowalczyk, G.S., Gordon, G.E. and Rheingrover, S.W. Identification of atmospheric particulate sources in Washington, D.C. using chemical element balances. Environ. Sci. Technol., 16: 79–90 (1982), cited in reference 10.

20. Murthy, G.K., Rhea, U. and Peeler, J.T. Levels of antimony, cadmium, chromium, cobalt, manganese, and zinc in institutional total diets. Environ. Sci. Technol., 5: 436–442 (1971).

21. Friberg, L., Nordberg, G.F. and Vouk, V. Handbook on the toxicology of metals. Amsterdam. 709 pp. (1979).

22. Iyengar, G.V., Tanner, J.T., Wolf, W.R. and Zeisler, R. Preparation of a mixed human diet material for the determination of nutrient elements, selected toxic elements and organic nutrients: a preliminary report. Sci. Total Environ., 61: 235–252 (1987).

23. Goulden, P.D. and Brooksbank, P. Automated atomic absorption determination of arsenic, antimony, and selenium in natural waters. Anal. Chem., 46: 1431–1436 (1974).

24. Rubel, F., Jr. Personal communication. January 31 (1978), cited in reference 25.

25. Sorg, T.J. and Logsdon, G.S. Treatment technology to meet the interim primary drinking water regulations for inorganics: Part 2. J. Am. Water Works Assoc., 70(70): 379 (1978).

26. Health and Welfare Canada. Guidelines for Canadian drinking water quality. Water treatment principles and applications. A manual for the production of drinking water. Canadian Water and Wastewater Association, Ottawa (1993).

27. Thomas, R.G., Felicetti, S.W., Lucchino, R.V. and McClellan, R.O. Retention patterns of antimony in mice following inhalation of particles formed at different temperatures. Proc. Exp. Biol. Med., 144: 544–550 (1973), cited in reference 10.

28. Waitz, J.A., Ober, R.E., Meisenhelder, J.E. and Thompson, P.E. Physiological disposition of antimony after administration of ^{124}Sb-labelled tartar emetic to rats, mice and monkeys, and the effects of tris (p-aminophenyl) carbonium pamoate on this distribution. Bull. W.H.O., 33: 537–546 (1965).

29. Felicetti, S.A., Thomas, R.G. and McClellan, R.O. Metabolism of two valence states of inhaled antimony in hamsters. Am. Ind. Hyg. Assoc. J., 35(5): 292–300 (1974).

30. Moskalev, Y.I. Materials on the distribution of radioactive antimony. Med. Radiol., 4: 6–13 (1959). Cited in U.S. Environmental Protection Agency. Drinking water criteria document for antimony. NTIS/PB 92-173293, prepared for Criteria and Standards Division, Office of Drinking Water, Washington, DC (1992).

31. Van Bruwaene, R.E., Gerber, G.B., Kirchmann, R. and Colard, J. Metabolism of antimony-124 in lactating cows. Health Phys., 43(5): 738–743 (1982). Cited in U.S. Environmental Protection Agency. Drinking water criteria document for antimony. NTIS/PB 92-173293, prepared for Criteria and Standards Division, Office of Drinking Water, Washington, DC (1992).

32. Abdalla, A. and Saif, M. Tracer studies with antimony-124 in man. In: Bilharziasis. G.E.W. Walstenhalne and M. O'Conner (eds.). Little, Brown and Co., Boston, MA. p. 287 (1962), cited in reference 4.

33. Belyaeva, A.P. The effect of antimony on reproduction. Gig. Tr. Prof. Zabol., 11: 32 (1967).

34. Gerber, G.B., Maes, J. and Eykens, B. Transfer of antimony and arsenic to the developing organism. Arch. Toxicol., 49(2): 159–168 (1982).

35. Clemente, G.F., Ingrao, G. and Santaroni, G.P. The concentration of some trace elements in human milk from Italy. Sci. Total Environ., 24: 255–265 (1982).

36. Otto, G.F. and Maren, T.H. Studies on the excretion and concentration of antimony in blood and other tissues following the injection of trivalent and pentavalent antimonials into experimental animals. Am. J. Hyg., 51: 370–385 (1950).

37. Stemmer, K.L. Pharmacology and toxicology of heavy metals: antimony. Pharmacol. Ther. A, 1: 157–160 (1976).

38. Venugopal, B. and Luckey, T.D. Metal toxicity in mammals. Vol. 2. Plenum Press, New York, NY (1978).

39. Werrin, M. Chemical food poisoning. Association of Food and Drug Officials, Hussock Food and Drug Office, U.S. Q. Bull., 27: 28–45 (1963).

40. Chopra, R.N. Experimental investigation into the action of organic compounds of antimony. Indian J. Med. Res., 15: 41 (1927). Cited in Browning, E. Toxicity of industrial metals. 2nd edition. Butterworths, London (1969).

41. Brieger, H., Semisch, C.W., Stasney, J. and Piatnek, D.A. Industrial antimony poisoning. Ind. Med. Surg., 23: 521–523 (1954).

42. Schnorr, T.M., Steenland, K., Thun, M.J. and Rinsky, R.A. Mortality in a cohort of antimony smelter workers. Am. J. Ind. Med., 27: 759–770 (1995).

43. Jones, R.D. Survey of antimony workers: mortality 1961–1992. Occup. Environ. Med., 51: 772–776 (1994).

44. Hayes, W.J. and Laws, E.R. Handbook of pesticide toxicology. Vol. 2. Classes of pesticides. Academic Press, New York, NY (1991).

45. Bradley, W.R. and Fredrick, W.G. The toxicity of antimony — animal studies. Ind. Med., 10(4): 15–22 (1941).

46. Ercoli, N. Chemotherapeutic and toxicological properties of antimonyl tartrate-dimethylcysteine chelates (33304). Proc. Soc. Exp. Biol. Med., 129: 284–290 (1968).

47. Oelkers, H.A. Zur Pharmacologies des Antimons. Arch. Exp. Pathol. Pharmakol., 187: 56 (1937). Cited in Browning, E. Toxicity of industrial metals. 2nd edition. Butterworths, London (1969).

48. Pribyl, E. Nitrogen metabolism in experimental subacute arsenic and antimony poisoning. J. Biol. Chem., 74: 775 (1927). Cited in Browning, E. Toxicity of industrial metals. 2nd edition. Butterworths, London (1969).

49. Levina, E.N. and Chekunova, M.P. Toxicity of antimony halides. Fed. Proc., 24: T608–T610 (1965) (translation of Gig. Tr. Prof. Zabol., 8(7): 25, 1964).

50. Fleming, A.J. The toxicity of antimony trioxide. OTS215027. Sponsored by E.I. Du Pont de Nemours and Co., Wilmington, DE (1982).

51. Smyth, H.F., Jr. and Carpenter, C.P. Further experience with the range finding test in the industrial toxicology laboratory. J. Ind. Hyg. Toxicol., 30: 63–68 (1948).

52. Hiraoka, N. The toxicity and organ-distribution of antimony after chronic administration to rats. J. Kyoto Prefect. Univ. Med., 95(8): 997–1017 (1986) (in Japanese with English abstract and tables).

53. Poon, R., Chu, I., Lecavalier, P., Valli, V.E., Foster, W., Gupta, S. and Thomas, B. Effects of antimony on rats following 90-day exposure via drinking water. Food Chem. Toxicol., 36: 21–35 (1998).

54. Poon, R. Personal communication. Environmental Health Directorate, Health Canada, Ottawa (1998).

55. Sunagawa, S. Experimental studies on antimony poisoning. Igaku Kenkyu, 51: 129–142 (1981).

56. Schroeder, H.A., Mitchener, M., Balassa, J.J., Kanisawa, M. and Nason, A.P. Zirconium, niobium, antimony and fluorine in mice: effects on growth, survival and tissue levels. J. Nutr., 95(1): 95–101 (1968).

57. Schroeder, H.A., Mitchener, M. and Nason, A.P. Zirconium, niobium, antimony, vanadium and lead in rats: life term studies. J. Nutr., 100(1): 59–68 (1970).

58. Kanisawa, M. and Schroeder, H.A. Life term studies on the effect of trace elements on spontaneous tumors in mice and rats. Cancer Res., 29(4): 892–895 (1969).

59. Watt, W.D. Chronic inhalation toxicity of antimony trioxide: validation of the threshold limit value. Diss. Abstr. Int., 44(3): 739-B–740-B (1983).

60. Groth, D.H., Stettler, L.E., Burg, J.R., Busey, W.M., Grant, G.C. and Wong, L. Carcinogenic effects of antimony trioxide and antimony ore concentrate in rats. J. Toxicol. Environ. Health, 18: 607–626 (1986).

61. Paton, G.R. and Allison, A.C. Chromosome damage in human cell cultures induced by metal salts. Mutat. Res., 16: 332–336 (1972).

62. Castro, B.C., Meyers, J. and Di Paolo, J.A. Enhancement of viral transformation for evaluation of the carcinogenic or mutagenic potential of inorganic salts. Cancer Res., 39: 193–198 (1979).

63. Kanematsu, K. and Kada, T. Mutagenicity of metal compounds. Mutat. Res., 53: 207–208 (1978).

64. Rossi, F., Acampora, R., Vacca, C., Maione, S., Matera, M.G., Servodio, R. and Marmo, E. Prenatal and postnatal antimony exposure in rats: effect on vasomotor reactivity development of pups. Teratogen. Carcinogen. Mutagen., 7: 491–496 (1987).

65. Casals, J.B. Pharmacokinetic and toxicological studies of antimony dextran glycoside (RL-712). Br. J. Pharmacol., 46: 281–288 (1972).