Reviews / Analyses

Toxic and trace elements in tobacco and tobacco smoke*

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While the harmful health effects of carbon monoxide, nicotine, tar, irritants and other noxious gases that are present in tobacco smoke are well known, those due to heavy metals and other toxic mineral elements in tobacco smoke are not sufficiently emphasized. Tobacco smoking influences the concentrations of several elements in some organs. This review summarizes the known effects of some trace elements and other biochemically important elements (Al, As, Cd, Cr, Cu, Pb, Mn, Hg, Ni, Po-210, Se, and Zn) which are linked with smoking. Cigarette smoking may be a substantial source of intake of these hazardous elements not only to the smoker but also, through passive smoking, to nonsmokers. The adverse health effects of these toxic elements on the fetus through maternal smoking, and on infants through parental smoking, are of special concern.

Introduction

The scientific literature is filled with evidence on the harmful health effects of carbon monoxide, nicotine, tar, irritants and other noxious gases emitted in tobacco smoke. Not enough attention, however, has been paid to the presence of heavy metals and other toxic and trace elements in tobacco smoke and their possible effects on biochemical processes in the human body. Once inhaled through smoking, heavy metals have a long biological half-life. Chronic adverse effects on human health may, therefore, in later years result from prolonged intake of such toxic elements, some of which are powerful carcinogens. Several of them accumulate in bone and may trigger disorders of mineral metabolism, e.g., osteoporosis. The body burden of heavy metals increases as a result of occupational exposure, and tobacco smoking enhances the adverse effects of such exposure.

In the tobacco plant, the concentration of elements varies along the stalk, being higher in the older leaves than in the younger, top leaves. In cigarettes, element concentrations vary among brands and even within the same brand. Besides tobacco, the main sources of trace and other elements in cigarettes are the paper and the filter.

Passage from tobacco to smoke

Elements pass from tobacco to the smoke and smoke condensate (the so-called tar). Cigarette filters succeed in retaining only a proportion of the element concentrations. Environmental smoke pollution consists not only of the smoke exhaled by the smokers but also of sidestream smoke emitted by the burning cigarette. Sidestream smoke, which is inhaled by nonsmokers (passive smoking), usually contains relatively high concentrations of many noxious substances including heavy metals. As particle sizes are smaller in sidestream smoke than in mainstream smoke, their deposition in the lung tissue of passive smokers reaches deeper into the alveolar spaces.

* This review is a condensed version of a more detailed report, Toxic and trace elements in tobacco (unpublished WHO document WHO/TOH/CLH/91.1, 1991). Readers are referred to this report for a complete reference list. The following abbreviations are used: mBq (millibecquerel) and pCi (picocurie) as units of radioactivity; Sv (sievert) and mrem (millirem) as units of radiation exposure; µg (microgram); ng (nanogram); µmol (micromole); IU (International Unit as enzyme activity).

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Biochemical effects

Aluminium

The concentration of aluminium in tobacco is relatively high, as shown in Table 1. In occupationally non-exposed male subjects, aluminium concentrations were found to be 5.1 µg/l in urine, 4.2 µg/l in plasma, and 1.8 µg/l in erythrocytes; these levels were not influenced by smoking or by age (*51*). Aluminium is interesting because of its alleged but still unproven association with Alzheimer's disease.

Arsenic

Unlike aluminium, the concentration of arsenic in tobacco is relatively low, usually below detectable limits (Table 1). No significant differences were found in As levels in liver, kidney cortex, lung, and hair among smokers and non-smokers. The median concentration of inorganic As in urine of adults was found to be 8 µg/g creatinine, and that of organic As was 12 µg/g. Neither of them was influenced by smoking. On the other hand, a positive association was found between urinary As levels in children and parental smoking habits. The mean As level in the urine of children of non-smoking parents was 4.2 µg/g creatinine, in children with one parent smoking it was 5.5 µg/g, and in children with both parents smoking it was 13 µg/g creatinine.

Cadmium

Tobacco plants have a special ability to absorb cadmium from soil and to accumulate it in unusually high concentrations in the leaves (ranging from 0.77 to 7.02 µg/g). In cigarettes, Cd concentrations range from 0.5 to 3.5 µg/g, with a mean level of 1.7 µg/g (*2, 3*). These are very high levels compared with those in food which are normally below 0.05 µg/g. Smoking 40 cigarettes a day provides about twice as much cadmium as that present in food. A large proportion of the Cd contained in the cigarette passes into the smoke. Since Cd concentration in the ash is practically constant (about 16% of that present in the unsmoked cigarette and a further 15% is retained by the filter), the greater part (nearly 70%) passes into the smoke (*4*). Most of the Cd passes into sidestream smoke, thus posing a risk to passive smokers.

Table 1: **Concentration range for main trace and heavy elements in cigarette tobacco of 12 American brands**[a]

Element	Concentration range (µg/g)
Al	699–1200
As	<1
Ba	40.7–56.6
Ca	1.39–1.96 (mg/100g)
Co	<0.01–0.94
Cr	<0.1–3.45
Fe	325–520
Mg	0.13–0.54 (mg/100g)
Mn	155–400
Ni	<2–400
Se	<0.007–0.091
Sr	29.7–49.5
Zn	16.8–30.5

[a] From: Iskander, F.Y. et al. (*1*).

Cadmium is highly toxic, and is one of the most important heavy metals when the adverse health effects of smoking are considered. Cd levels in the blood, urine, and organs of occupationally non-exposed non-smokers are very low, but increase in smokers. Schenker (*3*) estimated the weekly Cd intake from food and water in humans as 284 µg; smoking 40 cigarettes/day provides twice as much Cd as food. By comparison, Cd intake from air is insignificant. Not all of the ingested Cd is absorbed, however. Reddy & Dorn (*5*) estimated from 24-hr faecal sample analyses that the smoking-related increase in daily Cd intake of smokers was about 1 µg higher than that of non-smokers.

In all studies, blood Cd concentrations were found to rise with increasing smoking (*6, 7*). Possible relationships between smoking, Cd tissue levels, hypertension, and cardiovascular diseases have been reported (*8–10*). Smoking has an unclear or no influence on Cd urinary levels: about 2.47 µg/l in both non-smokers and smokers (*11*). In fat tissue, the mean Cd level was four times higher (10 ng/g) in smokers than in non-smokers (2.5 ng/g) (*12*).

Significant differences in Cd levels were found in kidney cortex, kidney medulla, lung, prostate, and muscle between non-smokers, ex-smokers, and smokers (*13*). The results are summarized in Table 2.

In the lungs of Finnish subjects Cd levels were 3.0 µg/g dry weight in smokers versus 1.1 in ex-smokers and 0.4 in non-smokers (*17*). The authors calculated the half-life of Cd in human lung to be 9.4 years. In German subjects Cd levels were 0.05 µg/g lung wet weight in non-smokers, 0.22 in ex-smokers, and 0.32 in smokers (*11*), while in the Chinese they were 1.07 µg/g dry weight in non-smokers and about 2.2 µg/g in smokers (*15*). The values reported in these three groups vary widely, probably because of ethnic differences.

A summary of a biopsy study of German male subjects (*11*) is presented in Table 3.

The effects of cadmium are evident in pregnancy. Blood Cd levels are higher in non-pregnant smokers than in pregnant smokers. Smokers had higher placental Cd levels than non-smokers. Schiele

Table 2: **Cadmium concentrations (μg/g) in kidney cortex and kidney medulla in non-smokers, light smokers and smokers**

	Non-smokers	Light smokers	Smokers	Reference
Kidney cortex	13.9	16.2	19.1 wet	*13*
	16.7		33.3 wet	*14*
	10.4	23.5	42.5 wet	*11*
	70	111	192 dry	*15*
	74		225 dry	*16*
Kidney medulla	7.0	8.3	9.7 wet	*13*
	1.9	9.1	14.5 wet	*11*

et al. (*18*) found that the mean Cd levels in the blood of newborns of smoking mothers were not significantly different from those of infants born from non-smoking mothers (0.4 μg/l vs 0.3 μg/l, respectively). These results suggest the existence of a placental barrier for Cd. The same authors found a significant relationship between smoking habits and blood Cd concentrations in women. The median value in non-smokers was 0.6 μg/l and that in smokers 1.1 μg/l.

On the other hand, others have suggested and ineffective placental barrier against this element, because they found no significant difference between Cd levels in cord blood and in maternal blood, and smokers did not have significantly higher Cd levels in amniotic fluid (*19*). Low infant birth weights were observed more frequently in female smokers (*20*).

In both the blood and milk of lactating mothers Cd concentrations increased with cigarette consumption. The median concentrations were 0.54 μg/l in blood and 0.07 μg/l in milk in non-smokers but increased to 1.54 and 0.16 μg/l, respectively, in women smoking more than 20 cigarettes per day (*21*).

Table 3: **Cadmium concentrations (μg/g wet weight) in German male subjects**[a]

	Non-smokers	Ex-smokers	Smokers
Colon	0.09	0.07	N.A.[b]
Liver	N.A.[b]	1.2	1.5
Lung	0.05	0.22	0.32
Muscle	0.052	0.054	0.061
Prostate	0.06	0.10	0.15
Blood	2.1 μg/l	2.8 μg/l	4.2 μg/l
Urine	2.47 μg/l	2.78 μg/l	2.47 μg/l

[a] Source: ref. *11*.
[b] N.A., data not available.

Chromium

Concentrations of chromium in urine are influenced by smoking habits. Average concentrations in lung tissue were 1.3 μg/g dry weight in non-smokers and 4.3 μg/g in smokers (*22*), increasing with age and smoking time but with no apparent decrease after stopping smoking (in ex-smokers, 4.8 μg/g). It must be borne in mind that the biological effects of chromium depend on its valency; in the trivalent form Cr is an essential element (*23*), in the hexavalent form it is carcinogenic.

Copper

The copper content in tobacco leaves was reported to be 15.6 μg/g (*2*). Smoking apparently increases the serum Cu levels from 1.14 mg/l in non-smokers, to 1.21 mg/l in light smokers, and 1.31 mg/l in smokers of more than 10 cigarettes/day (*24*). No significant differences due to smoking were found in Cu concentrations in the kidney cortex: 12.5 μg/g dry weight in non-smokers and 13.4 μg/g in smokers (*16*).

Lead

Average concentration of lead in filter-tipped cigarettes is 2.4 μg/g, about 6% passing into mainstream smoke (*2*). Japanese cigarettes contain 1,29 μg per cigarette (range, 0.96 to 2.00) (*25*) and Italian cigarettes about the same (0.6 to 2.00) (*26*).

Smokers and former smokers have higher blood Pb levels than non-smokers (Table 4) (*24, 25, 27, 28*).

It is interesting to note that while farmers have lower Pb concentrations in blood (3.8 μg/dl in non-smokers and 4.5 μg/dl in smokers (*25*)), taxi drivers had higher levels (27.4 and 29.4 μg/dl, respectively).

Cigarette consumption depresses the activity of the enzyme 5-aminolevulinic acid dehydratase (the most sensitive indicator of the lead burden to the body) in erythrocytes from 117.5 activity units in non-smokers to 88.8 in smokers of less than 20 cigarettes/day, to 74.1 in heavy smokers of more than 20 cigarettes/day (*26*). This was confirmed by other authors (*29*).

Table 4: **Lead concentrations in blood (μg/dl) (geometric means) and smoking habits**

	Non-smokers	Ex-smokers	Smokers	Reference
Males	10.3	10.8	11.7	*27*
	17.2 [a]		20.9 [a]	*24*
Females	6.9	7.6	8.3	*27*
	11.1		11.8	*25*
	15.8		17.3	*28*

[a] Arithmetic mean.

Passive smoking plays an important role in exposure of children to lead. Parental smoking, but no other environmental or dietary factors, was found to be related to the blood Pb level in children: 30 µg/l on average in children of non-smoking parents, 37 µg/l if only the father smoked, and 47 µg/l if the mother, or both parents, smoked (*30*). Even if children lived near a lead smelter parental smoking had a significantly stronger influence on blood lead levels (35 µg/l in children with non-smoking parents, 38 µg/l if only the father smoked, 43 µg/l if the mother or both parents smoked, and 46 µg/l if the mother smoked more than 15 cigarettes/day (*31*). The number of cigarettes smoked by the parents was negatively correlated with the British Ability Scales scores, which measure the ability and attainment of small children (*32*).

Manganese

Manganese concentrations in tobacco range from 155 to 400 µg/g (Table 1). Their concentrations in plant leaves increase with increasing Mn application rates in soil but decrease with increasing soil pH (*33*). In humans, no significant correlation was found between Mn levels in blood and smoking habits.

Mercury

In unsmoked cigarettes, the mercury content is, on average, 30±10 ng per cigarette, although Japanese brands contain as much as 60 ng. Upon burning, one cigarette may release 14 to 34 ng of mercury into the smoke (*34*). Smoking does not affect the Hg levels in urine, hair, blood, kidney cortex, liver, or lung, and had no influence on the levels in maternal and cord blood. However, smoking did influence the sister chromatid exchange (SCE)[a] index: for every 10 g of tobacco smoked per day the SCE per cell was 0.7 times higher than that for non-smokers (*52*).

Nickel

Tobacco plants tend to strongly absorb nickel from the soil and to accumulate it in the leaves (*35*). Average Ni concentrations were 0.64 µg/g in soil-grown tobacco and 1.15 µg/g in sludge-grown tobacco. During smoking, the Ni content averaged 72.6 ng in the mainstream smoke per cigarette produced from soil-grown tobacco and 78.5 ng per cigarette produced from sludge-grown tobacco (*35*). Other authors (*47*) found 5.5 µg/g in tobacco from Egyptian cigarettes, 27.8 µg/g in the ash, and 4 µg/g in the paper; foreign brands were found to contain 2.78 to 4.84 µg Ni per cigarette, and 3.14 to 4.61 µg in the ash from each cigarette (*47*).

Nickel forms a toxic carbonyl compound. Because of the high carbon monoxide level in tobacco smoke, Ni carbonyl thus produced is considered to be a potential carcinogen.

Polonium

Several investigators have provided evidence of the presence of Po-210 in tobacco and tobacco smoke. Po-210 in tobacco plants is derived from the radioactive decay of Pb-210 or Ra-226, or from Rn-222 daughters, which are present in soil and/or air. Po-210 levels were found to range between 1.5 and 10.7 mBq/g of tobacco (0.04 to 0.29 pCi/g), equivalent to 4.2 exp–18 to 3.10 exp–17 grams of polonium per gram of tobacco depending on the tobacco blend (*36*). Po-210 levels were on average 15.9 mBq (0.43 pCi) in a whole cigarette, 1.4 mBq (0.038 pCi) in the ash, and 4.4 mBq (0.12 pCi) in the butt (*37*). IARC has reported a range of 1.7 to 3.4 mBq (0.045 to 0.091 pCi) in the mainstream smoke of each cigarette (*50*).

The lung (peripheral parenchyma) in current smokers contains 0.27 mBq/g (0.0074 pCi/g wet weight) of Po-210, and the peribronchial lymph nodes contain 0.4 mBq/g (0.011 pCi/g). By comparison, the peripheral parenchyma samples from non-smokers contain only 0.06 mBq/g (0.0016 pCi/g) and the peribronchial lymph nodes only 0.22 mBq/g (0.006 pCi) (*38*). Since Po-210 was detected in higher concentrations in several tissues and biological fluids of smokers than non-smokers, it is thought that Po-210 could be a causal factor in carcinogenesis (*39, 40*). According to Westin (*41*), tobacco could be the largest, single worldwide source of carcinogenic ionizing radiation, and the bronchial region of smokers' lungs could be exposed to as much as 7x10 exp–5 Sv (7 mrem) with each cigarette.

Tobacco smoke containing Po-210 combines with household dust, settles on surfaces and clothing, and contributes to household radon-emitted alpha-radioactivity (*42*).

Selenium

Concentrations of selenium in 12 American cigarette brands ranged between 0.007 and 0.091 µg/g (Table 1), with an average of 0.087 µg/g in tobacco, 0.4 µg/g in the paper, and 0.09 µg/g in the filter (*1*). By comparison, Pakistani cigarette brands showed

[a] SCE is a measure of the exchange of DNA material within the chromosomes, and may be an indication of genotoxicity.

higher concentrations: 2.28 µg/g in tobacco and 2.16 µg/g in the paper (*43*).

Analyses of Se levels in serum tend to show slightly lower concentrations in smokers (1.60 µmol/l) than in non-smokers (1.70 µmol/l) (*44*). Lung cancer patients also had lower serum levels (0.099 µg/l) than non-smoking controls (0.122 µg/l) (*45*).

Maternal smoking may exert harmful effects on selenium metabolism in the developing fetus, especially on glutathion peroxidase, a Se-containing enzyme. The mean activity of this enzyme in cord blood from newborns of smoking mothers was significantly lower (22.1 IU/g of haemoglobin) than in those from non-smoking mothers (24.1 IU/g Hb) (*46*).

Zinc

Zinc concentrations, analysed in 12 American cigarette brands, range from 16.8 to 30.5 µg/g (Table 1). About 70% of the zinc contained in a cigarette's tobacco and paper is transferred to the smoke (*43*) and a part is trapped by the filter (*47*).

Smoking does not influence the zinc level in most human tissues and biological fluids. In kidney cortex, however, Zn concentrations were 234 µg/g dry weight in non-smokers and 328 µg/g in smokers, a statistically significant difference.

In relation to pregnancy, polymorphonuclear (PMN) cell Zn concentrations were found to be significantly lower in smoking mothers (1.00 ± 0.04 µmol Zn per 1x10 exp–10 PMN cells) than in non-smoking mothers (1.16 ± 0.06 µmol). Mononuclear (MN) cell Zn concentrations were also lower in smoking mothers (1.47 µmol Zn per 1x10 exp–10 MN cells) than in non-smokers (2.64 µmol). It is known that pregnant women who smoke and have low PMN Zn levels are at risk of delivering small-for-gestational-age babies (*48*).

Mean Zn and albumin levels in plasma in smoking women, 24 and 48 hours after delivery, were lower than in control non-smoking mothers (*22*). Newborns of smoking mothers have 5% less plasma Zn, 12% less cord-blood Zn, and a 13% decrease in the activity of alkaline phosphatase (a Zn enzyme), compared with newborns from non-smoking mothers (*49*). The Cd/Zn ratio was found to be related to birth weight. Smoking during pregnancy increases the risk of small-for-date neonatal weight. It is hypothesized that Cd inhaled with cigarette smoke may stimulate the synthesis of metallothionein, a protein which binds Zn, thus reducing its availability for intestinal absorption and placental transfer. This type of Cd-Zn interaction may occur in pregnant smoking women at the maternal-placental-fetal unit level, thus resulting in a less favourable zinc status in the neonate (*20*).

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Résumé

Eléments toxiques et éléments en trace dans le tabac et la fumée de tabac

Si on connaît bien les effets nocifs du monoxyde de carbone, de la nicotine, du goudron, des irritants et des autres gaz nocifs présents dans la fumée de tabac, on n'insiste pas assez sur ceux des autres éléments toxiques de la fumée. Le tabagisme influe sur la concentration de plusieurs éléments dans certains organes. On ne connaît qu'incomplètement les effets nocifs des métaux lourds et des autres éléments en trace inhalés par les fumeurs. Le présent article présente les effets connus de certains éléments en trace et d'autres éléments ayant un rôle biochimique important (aluminium, arsenic, cadmium, chrome, cuivre, manganèse, mercure, nickel, plomb, polonium-210, sélénium et zinc), liés au tabagisme. Les principales observations sont les suivantes:

Cadmium: Les plants de tabac ont une aptitude particulière à absorber le cadmium du sol et à le concentrer dans les feuilles. On retrouve environ 16% du cadmium présent dans les cigarettes dans les cendres, 15% dans le filtre, 17% dans le mégot et plus de 50% dans la fumée. Les concentrations de cadmium dans le sang, le cortex et la médullaire du rein, le foie, les poumons, la prostate et le tissu adipeux sont sensiblement plus élevées chez les fumeurs que chez les non-fumeurs, tandis que la relation entre sa concentration urinaire et le tabagisme est peu claire. La demi-vie biologique du cadmium dans le poumon est évaluée à 9,4 ans. La concentration de cadmium dans le placenta est plus élevée chez les mères fumeuses et présente une corrélation significative avec la valeur trouvée dans le sang du cordon. Le cadmium s'accumule dans le liquide amniotique et l'amnios. Dans le sang et le lait, les concentrations de cadmium augmentent avec la consommation de cigarettes.

Chrome: Les teneurs urinaires en chrome sont influencées par le tabagisme, en fonction du nombre de cigarettes fumées.

Mercure: 10 à 20% du mercure présent dans la cigarette sont émis dans la fumée. Les concentrations de mercure dans le sang, l'urine, les cheveux, les reins, le foie et les poumons ne sont pas corrélées au tabagisme.

Plomb: Les concentrations de plomb dans le sang sont influencées par le tabagisme. L'activité de l'acide delta-aminolévulinique-déshydratase dans le sang présente une corrélation négative marquée avec le nombre de cigarettes fumées. Chez l'enfant, le tabagisme des parents a un effet significatif sur la plombémie. Le tabagisme maternel a davantage d'impact que le tabagisme paternel.

Polonium: La concentration de Po-210 dans les poumons est significativement plus élevée chez les fumeurs et les ex-fumeurs que chez les non-fumeurs. On estime que chez les fumeurs, les régions bronchiques critiques peuvent être exposées à une radioactivité atteignant 7×10^{-5} Sv (soit 7 mrem) par cigarette.

Zinc: On estime qu'environ 70% du zinc présent dans les cigarettes (tabac et papier) passent dans la fumée. Les concentrations de zinc dans le sang du cordon sont influencées par le tabagisme maternel; on observe une diminution de 5% du zinc plasmatique et de 12% du zinc érythrocytaire dans le sang du cordon chez les nourrissons de fumeuses. Cette observation peut être associée au faible poids de naissance des nouveau-nés de mères fumeuses.

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