Inorganic arsenic is well known as an environmental carcinogen. Reports from several countries show that an elevated exposure to arsenic, mainly through ingestion of arsenic-contaminated drinking water, is associated with several diseases, especially neoplasia. Increased incidences of skin, lung, liver, bladder, and kidney cancers and cardiovascular phenomena such as blackfoot disease could be identified (1–6). On the other hand, inhalation of arsenic, relevant mainly in workplaces, was shown to increase the risk of mainly lung cancer (7,8). Recently, evidence for increased risks of other types of cancers, mainly located in bone and kidney, was reported (9). In addition, increased rates of lung and skin cancers were noticed in winegrowers consuming wine contaminated with arsenic pesticides (10). Biomarkers of effect such as sister chromatid exchanges, micronuclei, and chromosomal aberrations were found at increased levels after elevated environmental exposure to arsenic (11–13). Moreover, several studies report an increased exposure to arsenic due to its release in the air from smelting activities (14–17).

Arsenic is a naturally occurring element found at relatively high levels in some drinking water sources and in soils. On the other hand, antimony is less widely distributed in the environment (18,19) but, like arsenic, it is known to be a genotoxic agent in vitro and in vivo (20,21) and has been shown to cause lung tumors in female rats (22). However, it is not known whether antimony is carcinogenic to humans (23,24). Reports on elevated human exposure to inorganic antimonial compounds are of occupational exposures only (24–27). Knowledge is scarce concerning the transfer of antimony from the environment to humans and the related hazards to human health.

Soil contamination with arsenic and antimony in the northern Palatinate region in midwestern Germany is due to the presence of faehrole (copper arsenic sulfides and copper antimony sulfides; gray copper) sources. Cinnabar ore (mercury sulfide) is also found in these sources. A large range of concentrations of elements in the soil exists even in small areas because, in former centuries, intense mining activities caused elements to be unhomogeneously distributed as rubble. Today, the region is characterized by housing and agriculture. In a biomarker study, the transfer of mercury from the environment to the residents could not be detected (19). The purpose of the present study was to investigate the transfer of arsenic and antimony from the environment to humans in the northern Palatinate region. Unlike the studies on arsenic previously described in which the main sources of exposure were arsenic-contaminated drinking water and industrial emissions, this study focuses on soil contaminated with arsenic and antimony as the main source of exposure.

Because humans excrete arsenic and antimony mainly via the kidneys (28–30), urinary concentrations were used as valid biomarkers of exposure. Biomonitoring of scalp hair was performed as additional screening to record cumulative exposures.

**Methods**

**Study design and study population.** This study was preceded by a project that sought to determine the contents of arsenic and antimony in soil and in plant and animal samples from the northern Palatinate region of Germany. Residents for whom the soil contents of arsenic and antimony in their housing areas were known (one to three soil samples per individual) were asked to participate in the study. To minimize a selection bias, a maximum participation rate was achieved by convincing those residents who did not reply to our first written request to participate. Nonexposed subjects from a rural area in south lower Saxony (Germany) were chosen as the reference group.

A six-page questionnaire served to assess factors of interest and confounding variables. All study subjects were interviewed concerning demographic characteristics, tobacco smoking, and alcohol drinking habits, and medical, occupational, and residential histories. Information on average and recent consumption of seafood, wild mushrooms and game, home grown vegetables, poultry, and eggs was requested throughout the questionnaire. A standardized analysis served to assign exact scores to the extent of seafood and home-grown produce consumption. For example, concerning seafood consumption, we asked how often seafood had been eaten during the previous week, when it had been eaten.

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eaten the last time, and how often in general seafood was eaten. We assigned 3 points to every meal of seafood. The examinations and collection of urine and scalp hair (50–100 mg, sampled oscillatory with a length of 3–5 cm) were performed from June to September in the homes of the study participants. Collection of 24-hr urine was deemed appropriate to determine metal/metalloid biomarkers (33); relating these biomarkers to urine creatinine could lead to decreased accuracy of data (32). During the following weekend, participants of the study collected 24-hr urine in flasks containing 50 ml 60% acetic acid (suprapure) for stabilization. All flasks and other materials used had been previously tested and were free from any detectable amounts of arsenic and antimony. The samples were portioned and kept frozen at -20°C until atomic absorption analysis was performed. Urine creatinine was determined with the help of purchased test kits. Fourteen adult samples with a volume of less than 0.75 1/24 hr and a creatinine content of less than 0.5 g/l urine were considered non-24 hr urine and therefore excluded from the study evaluations. Soil data for 10 subjects from the exposed collective was not available, and we could only obtain hair samples from children who were not toilet trained. For these reasons, group numbers given in the tables and figures may differ slightly. The committee of ethics of the University of Goettingen gave written consent to the study design and proceedings.

**Soil and scalp hair samples.** Soil samples were taken from a 0–30-cm level, mixed, crushed (particle size <0.01 mm), and decomposed in 1:1 (v/v) nitric acid/sulfuric acid and detected by atomic absorption spectroscopy (AAS) as described below. Additional measurements were performed for a number of samples after the soil had been sieved; in this case the fraction with a particle size of less than 2 mm was used for analysis.

Hair samples were broken down in a closed system using a microwave apparatus (MLS mega 1200; MLS Leutkirch, Germany) with 25–50 mg hair added to 1 ml 65% (v/v) nitric acid and 0.5 ml 30% (v/v) hydrogen peroxide. The samples were mineralized with 450 W for 10 min. The hair samples were not rinsed before analysis because of the well-known impossibility of removing an external contamination without reduction of their internal mineral content (33).

**Atomic absorption spectrometry (AAS).** Arsenic in urine was determined by means of the hydride technique using a Perkin Elmer AAS 400 (Perkin Elmer, Ueberlingen, Germany) with deuterium background compensation and an MHS 10 hydride generator. This technique is deemed the best approach to determine the arsenic species relevant to human toxicology because it only detects inorganic trivalent and pentavalent arsenicals, i.e., As(III), As(V), and the mono- (MMA; monomethylarsonic acid) and dimethylated species (DMA; dimethylarsonic acid) of arsenic. On the other hand, it does not detect arsenobetaine, arsenocholine, and other organoarsenicals from seafood, which leave the human body unchanged (28,29,34). As(V), As(III), and MMA are recovered to 100% with this method, and DMA to approximately 80%. Arsenic and antimony in scalp hair and antimony in urine were determined by the graphite furnace technique with an atomic absorption spectrometer (Perkin Elmer SIMAA 6000) with Zeeman background compensation. The detection limits were 0.5 µg/l for arsenic using hydride AAS and 0.5 µg/l (urine) and 0.005 µg/g (scrap hair) for arsenic and antimony using graphite furnace AAS. The corresponding replicate precisions were 3%, 5%, and 8%, respectively. Samples were analyzed in random order. Validity of the analyses was guaranteed by participation in a biannual interlaboratory quality control program organized by the German Society of Occupational Medicine for analyses in occupational and environmental toxicology and by internal and external standards (analytical grade) determined in each analytical run.

**Statistical evaluations.** Statistical evaluations were performed with the software WinStat 3.1 (Kalma Company, Cambridge, MA) (35). AAS results below the limit of detection were included in the statistical evaluations as an estimated 50% of the detection limit value.

Age, profession, sex, tobacco smoking, and seafood consumption were included in this study as possible confounding factors that can influence the contents of arsenic and antimony in urine and scalp hair. For the northern Palatinate subjects who were potentially exposed to higher levels of arsenic and antimony, we evaluated the soil contamination in their respective individual housing areas for any influence on the levels of urinary or scalp hair arsenic and antimony. Moreover, consumption of home-grown produce was included in the analysis.

**Statistically significant outlying samples** (p<0.05; no more than two for each element in urine or hair) were excluded from the study evaluation because they are not representative and they distorted the data. This proceeding did not change the statistical results, which had been proven by analysis using the whole data set. None of these outliers could point to any factor of interest in an individual analysis, and the source of elevated exposure of these subjects could not be identified.

In general, the statistical evaluations were conducted comparing the study subjects by region and by sex. Selected confounding factors like seafood consumption, sex, and age were included in an additional evaluation in which the two study collectives were combined. In case of equal sex distribution between strata, results are shown without stratification by sex for reasons of clarity. Multiple regression analyses were performed after logarithmic transformation, in which case the Pearson correlation coefficient is given.

**Results**

None of the study participants had an occupation that involved an elevated exposure to arsenic, antimony, or other heavy metals. The drinking water analyses conducted during the study period showed arsenic and antimony contents that were generally below 0.015 mg As/l and 0.002 mg Sb/l. Small drinking water systems and private wells used for drinking water had been included for the routine measurements. Thus, elevated exposures to arsenic and antimony by drinking water can be excluded; increased exposures could have been caused via the soil and home-grown produce only.

Special attention was given to skin conditions in the arsenic-exposed collective. Two subjects had dermatological manifestations. One of these subjects agreed to an additional examination by a dermatologist, and arsenic was excluded as the cause of his skin manifestation. No further indication of any adverse health effect that could be attributed to arsenic and antimony was found among the study participants.

Compared to its natural range, high concentrations of arsenic and antimony are present in the northern Palatinate soil (Table 1). The contaminated soil in northern Palatinate is greatly scattered because of mining activities in the past that distributed these elements as rubble. On the other hand, soil samples from our southern Saxony reference area revealed nonelevated concentrations of arsenic and antimony (data not shown).

| Table 1. Range of arsenic and antimony in northern Palatinate soil versus natural range soil contents |
| --- | --- | --- |
| Natural range | Total soil contents | Northern Palatinate |
| Soil (particle size <2 mm) | | |
| Arsenic | <20 | <2–605 | 76–592 |
| Antimony | <0.1 | <0.2 | 19–266 |

Values are given in milligrams per kilogram dry matter.

*Total soil contents in the housing area.

Data from one highly contaminated village only (Stalburg); soil samples were sieved before analysis.
The exposed group consisted of 218 people from the northern Palatinate region and the reference group of 76 people from south lower Saxony. Their general characteristics are shown in Table 2. A slightly higher percentage of people from south lower Saxony (67%) was willing to participate in the study in comparison to northern Palatinate. Study subjects from both regions had long residence times, with means of 29 and 23 years. Age range and smoking habits showed a similar distribution among the two groups. A higher number of older people in northern Palatinate participated in the study than in south lower Saxony, indicated by a median age of 53 versus 45 years, respectively.

To gain data on the transfer from arsenic and antimony from the soil to humans, the northern Palatinate study participants were grouped into four strata depending on the arsenic and antimony contents found in the soil of their respective housing areas (Fig. 1 and Fig. 2). The classifications were natural range soil content (see Table 1), slightly elevated (20–50 mg As/kg soil or 0.5–5 mg Sb/kg soil), or contaminated (>50 mg As/kg soil or >5 mg Sb/kg soil) (36). A highly exposed subgroup was chosen with the help of the 90th percentile of all soil data available for this study. A slight but significant correlation was noticed between the 24-hr arsenic excretion in urine and the content of arsenic in the soil (Fig. 1); the same was noticed for scalp hair (Fig. 2). The results of the respective statistical evaluations performed on an individual basis are presented in Table 3. Neither urine nor scalp hair showed increasing antimony levels with increasing contents of antimony in the soil. When the extent of home-grown produce consumption was included in the multiple regression analysis, only the level of urinary arsenic was very slightly but significantly correlated with this factor (Table 3).

Surprisingly, the reference subjects showed significantly higher levels of urinary arsenic and antimony (Table 4). However, data of both groups correspond to normal range reference data described by others (17,29,37–42). In a separate analysis, the children from the northern Palatinate region did not show higher contents of arsenic or antimony in urine or in scalp hair than the children of south lower Saxony. Thus, a special hazard to these children by an increased intake of contaminated soil did not seem evident.

Only arsenic in urine was significantly correlated with age in the multiple regression analysis (Table 3). However, when comparing the study participants over 18 years of age with the younger ones, we found that except

| Table 2. General characteristics of study subjects by region |
|-----------------|-----------------|-----------------|
|                  | Northern Palatinate | South lower Saxony |
| Participation rate (%) | 60               | 67               |
| Number of subjects    | 218              | 76               |
| Female                | 121              | 38               |
| Male                  | 97               | 38               |
| Mean (median) age (years) | 46.2 (53.0)      | 43.4 (45.0)      |
| Age range (years)     | 1–89             | 2–84             |
| Mean residence time (years) | 29              | 23               |
| Smokers               | 48               | 16               |
| Ex-smokers            | 46               | 22               |
| Nonsmokers            | 124              | 38               |
for antimony in scalp hair, a lower level of urinary arsenic and antimony predominated among the young subjects (p<0.001 two-sided U-test for arsenic and antimony in urine and p = 0.055 for arsenic in scalp hair (Fig. 3).

When the potentially exposed and the nonexposed groups were analyzed together in the statistical evaluation, the contents of arsenic in urine were positively associated with the extent of seafood consumption (Spearman coefficient of correlation r = 0.31; p<0.001) (Fig. 4 and Table 3). These findings correspond with those of other authors (14,40).

The determination of elevated exposures to antimony is hindered by low antimony body burdens in the population in general. In this study, this is indicated by a high percentage of samples below the limit of analytical detection. In 89 out of 196 samples from the northern Palatinate collective and 57 out of 75 urine samples from the reference group, antimony levels were found to be below 0.5 µg/l in urine.

In the collective-combined multiple regression analysis, male sex was positively associated with the contents of arsenic and antimony in urine and the contents of arsenic in scalp hair (Table 3). Antimony in scalp hair was not associated with sex, age, or with any other factor included in the analysis. Further associations in the multiple regression analysis could be found for arsenic in urine, which was correlated with seafood consumption and tended to be related with age. Consumption of home-grown produce revealed an association with arsenic in urine in the northern Palatinate collective only. Furthermore, the content of arsenic in the soil was associated with the 24-hr excretion of arsenic in urine and with the content of arsenic in scalp hair samples.

The arsenic contents in scalp hair were correlated with the antimony contents in scalp hair in the combined evaluation (Spearman correlation coefficient r = 0.44, p<0.001) (Fig. 5 and Table 5), although antimony in scalp hair was not associated with any of the factors included in the analysis (Table 5). Thus, there are unidentified sources, maybe dietary factors other than seafood, that cause both arsenic and antimony to be ingested in higher amounts. Furthermore, the arsenic contents in urine and scalp hair were positively correlated (Table 5), which is in agreement with another report (15).

Tobacco smoking did not have any influence on the contents of arsenic and antimony in urine or hair. Our results agree with other biomonitoring studies (17,40,43).

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**Table 3.** Multiple linear regression analysis (additional model)

| Parameter | Variable | r²      | p-Value |
|-----------|----------|---------|---------|
| **Arsenic in urine** | | | |
| Northern Palatinate (n = 189) | Age | 0.084 | 3.6 x 10⁻⁵ |
| | Soil content | 0.032 | 0.0053 |
| | Consumption of home-grown food | 0.014 | 0.046 |
| | Seafood | 0.034 | 0.0046 |
| | Total | 0.164 | |
| South lower Saxony (n = 74) | Sex | 0.086 | 0.004 |
| | Age | 0.103 | 0.003 |
| | Total | 0.199 | |
| Combined (n = 273) | Sex | 0.023 | 0.003 |
| | Age | 0.069 | 3.6 x 10⁻⁶ |
| | Seafood | 0.044 | 1.2 x 10⁻⁴ |
| | Total | 0.136 | |
| **Antimony in urine** | | | |
| Northern Palatinate (n = 188) | Sex | 0.035 | 0.004 |
| | Seafood | 0.016 | 0.044 |
| | Total | 0.051 | |
| South lower Saxony (n = 74) | Age | 0.05 | |
| | Total | 0.05 | |
| Combined (n = 272) | Sex | 0.025 | 0.009 |
| | Total | 0.025 | |
| **Arsenic in scalp hair** | | | |
| Northern Palatinate (n = 201) | Sex | 0.014 | 0.0048 |
| | Soil content | 0.047 | 0.0009 |
| | Seafood | 0.034 | 0.005 |
| | Total | 0.095 | |
| South lower Saxony (n = 74) | Sex | 0.128 | 0.001 |
| | Age | 0.055 | 0.019 |
| | Total | 0.183 | |
| Combined (n = 285) | Sex | 0.04 | 0.0006 |
| | Total | 0.04 | |

No significant correlation was seen in the analysis of antimony in scalp hair (n = 285).

a) In the combined evaluation, the 19 persons from northern Palatinate from whom no soil data was available were included.

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**Table 4.** Levels of urinary and scalp hair arsenic and antimony by region

| Region | As in urine (µg/24 hr) | As in hair (µg/g) | Sb in urine (µg/24 hr) | Sb in hair (µg/g) |
|--------|------------------------|------------------|------------------------|------------------|
| Palatinate | Saxony | Palatinate | Saxony | Palatinate | Saxony | Palatinate | Saxony |
| Median | 3.21 | 6.20 | 0.016 | 0.053 | 0.46 | 1.11 | 0.028 | 0.044 |
| Mean | 3.96 | 7.58 | 0.028 | 0.069 | 0.86 | 1.53 | 0.038 | 0.060 |
| Maximum | 18.32 | 23.78 | 0.154 | 0.682 | 4.73 | 5.86 | 0.317 | 0.459 |
| Minimum | <0.1 | 0.29 | <0.005 | 0.013 | <0.5 | <0.5 | <0.005 | <0.005 |
| Included | 199 | 75 | 211 | 74 | 196 | 75 | 211 | 74 |
| Outliers | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 |
| Excluded as non-24-hr urine | 13 | 1 | 13 | 1 | |

U-test (two-sided) p<0.001 p<0.001 p<0.001 p<0.001
and with recent trace element analyses of cigarette smoke that show low arsenic and antimony contents (44).

Discussion

Because of stringent environmental laws in industrialized countries, contamination levels of public concern are often too low to cause an increase in the incidence of disease that is large enough to be detected by epidemiological studies. Thus, the determination of biomarkers of exposure is a more appropriate method of assessment than to take the respective diseases as an endpoint.

Hydride AAS is the analytical method recommended to determine arsenic species of toxicological relevance, i.e., As(V), As(III), MMA, and DMA. Organoarsenicals and trimethylated arsenic compounds can be found at high concentrations in seafood, but they leave the human body metabolically unchanged. These species are thus not relevant for toxicological risk assessment and cannot be detected with the hydride technique (28,29). However, in this study we found an association between seafood consumption and increased arsenic contents in urine, which had been described previously (14,40). This may be explained by the prevalence of low quantities of inorganic arsenicals and DMA in seafood (reviewed by Phillips (45)). Certain marine species like crustacea or shellfish may have a greater impact on the release of inorganic arsenic (40,46). Freshwater fish seem to have lower arsenic contents, as do bottomfeeding fish and crustacea (47,48). Additionally, it seems likely that a certain portion of DMA or even inorganic arsenic can be released from seafood organoarsenicals (46).

Consumption of fish seems to play a more important part in the internal exposure to toxicologically relevant arsenicals than previously thought. We, like others (14,49), think that when determining arsenic as biomarker, seafood consumption should be included as a confounding variable, even when there is a low consumption of seafood in a population, as was the case in this study. Because inorganic arsenic is some orders of magnitude more genotoxic than DMA (50,51), it is important to know which species of arsenic are released from seafood in high amounts and whether differences exist depending on the type of seafood. Further research is necessary to determine the impact of seafood consumption on the exposure to toxicologically relevant arsenicals.

The reference subjects showed a significantly higher arsenic excretion in urine combined with a significantly higher mean value for seafood consumption (medians 15.0 vs. 9.0; ranges 0–42 and 0–45, respectively; p = 0.001, two-sided U-test). Thus, the differences in arsenic excretion between the two study groups may be explained by differences in seafood consumption. In contrast, the differences in antimony excretion in urine between the two study groups, as well as after stratification by sex, cannot be explained by differences in fish consumption because antimony in general was not associated with this factor in the statistical analysis. Unidentified regional differences in dietary habits and differing contents of antimony in food may be more plausible reasons.

Six subjects (5–56 years of age), among them one from northern Palatinate, showed a drastic short-time peak of arsenic in urine up to maximum values of 140 μg/l. This short-time peak of urinary arsenic was documented by others (40,52,53) and was suggested to be caused by enhanced consumption of seafood (52). Our findings, together with those of others (14,40), showed that seafood consumption is associated with but does not lead to an extreme increase in the urinary excretion of arsenic. Moreover, the six subjects were moderate consumers of seafood (range 1.5–18; median 9.0); one of these six had eaten fish the day before urine sampling, and the other five had not eaten seafood the last 10 days. There was no other source known for their elevated exposure to arsenic. We conclude that there may be other, presumably dietary, sources of arsenic, which still need to be identified.

Previous studies found a sex-specific higher urinary excretion of arsenic for men (17,42). Bucher et al. (17) proposed that male persons had higher levels of urinary arsenic because they absorb more dust-borne arsenic than females because they may do more gardening and farming. Different sex-related toxicokinetics or dietary habits were suggested as further possible reasons (17). However, these authors had not investigated whether there were sex differences in seafood consumption. In the present study, the score for seafood consumption proved to be not significantly different between the sexes [medians were 9.0 vs. 9.0 (northern Palatinate) and 16.5 vs. 15.0 (south lower Saxony) for females and males, respectively]. Thus, seafood consumption is presumably not the reason for the observed sex differences in arsenic excretion. Also, in this study we noticed that men seemed to have a higher burden of antimony in comparison to women.
We, like others (14,17), found that arsenic excretion in urine was slightly associated with age. With respect to the comparatively short biological half-life of arsenic of 30–40 hr (28,29,54,55), it cannot be explained why older people showed higher concentrations of arsenic and antimony in urine and in scalp hair.

In Tacoma, Washington, residents were exposed to arsenic via a former copper smelter (14), but an increase in arsenic excretion was found mainly in children up to 6 years of age living at a maximum distance of a half-mile from the smelter. Moreover, twofold and 10-fold elevated levels of arsenic in urine and scalp hair, respectively, were reported for children exposed by smelter emissions in Mexico (15). Binder et al. (56) reported elevated arsenic burdens only in children living near a former copper smelter. In contrast, in a biomarker study conducted by Hewitt et al. (57), no evidence for an increased body burden of arsenic was found in workers exposed to arsenic-contaminated soil. Ingestion of dust by hand-to-mouth contact seems to be the relevant exposure pathway (14); thus, the exposure may be higher for children than for adults because of ingestion of soil. Nevertheless, in the present study, a slight association between arsenic exposure and the levels of arsenic in urine as well as in scalp hair was also found for the adults.

The validity and quality of the data gained by scalp hair biomonitoring is not comparable to that gained by urine and blood biomonitoring. First of all, the analysis of scalp hair is not standardized. Its validity has a minor drawback in that a scatter of data is caused by various factors such as length and color of hair and the use of hair coloring and permanents. Nevertheless, on the level of intergroup differentiation, it is a valuable screening tool. In this study, the results of scalp hair biomonitoring confirm the results of urine as biomarker. Scalp hair proved to be affected by increased arsenic contents in the soil, as was arsenic excretion in urine. External contamination of hair is not likely to have been relevant because scalp hair did not reveal increasing contents of antimony with increasing exposure to antimony-contaminated soil.

Gastrointestinal absorption of antimony (5–20%) is far lower than of arsenic (60–80%) (28,54,55,58–60). This could explain why the internal exposures to antimony were not associated with increasing exposure to antimony-contaminated soil. However, it has to be taken into account that very little is known about the enteral absorption of these elements when they are soil bound.

The transfer rate of arsenic and antimony to vegetables and animals was found to be low in northern Patalane (L. Steubing, personal communication). Furthermore, we recently found that sheep bred on grounds contaminated with arsenic and antimony did not reveal elevated contents of these elements in blood and wool or was there evidence of an increased DNA damage (18). The results of this study indicate that mere exposure to contaminated soil in the northern Patalane area did not lead to a severe human exposure. However, it can be presumed that, in case of geogenic exposure, arsenic is more easily transferred from the environment to man than is antimony. Nevertheless, the transfer rate is low and leads to slightly, yet presumably not hazardous, elevated arsenic contents in urine and scalp hair. We can justly presume that an elevated risk of cancer should not be expected for the residents of the northern Patalane region.

REFERENCES

1. Tseng WP, Chu HM, How SW, Fong JM, Lin CS, Yeh S. Prevalence of skin cancer in an endemic area of chronic arsenicism in Taiwan. J Natl Cancer Inst 40:453–463 (1968).
2. Tseng WP. Effects and dose–response relationships of skin cancer and blackfoot disease with arsenic. Environ Health Perspect 19:105–118 (1977).
3. Chen CJ, Chua WS. Malignant neoplasms among residents of a blackfoot disease endemic area in Taiwan: high-arsenic arteriosclerotic heart disease and cancer. Cancer Res 45:5895–5899 (1985).
4. Chen CJ, Kuo TL, Wu MM. Arsenic and cancer (letter). Lancet 1:414–415 (1988).
5. Das D, Chatterjee A, Mandal BK, Samanta G, Chakraborti D, Chanda B. Arsenic in ground water in six districts of West Bengal, India: the biggest arsenic calamity in the world. Part M. Arsenic concentration in drinking water, hair, nails, urine, skin-scale and liver tissue (biopsy) of the affected people. Analyst 120:917–924 (1995).
6. Tsuda T, Nagira T, Yamamoto M, Kume Y. An epidemiological study on cancer in certified arsenic poisoning patients in Tokoro. Ind Health 28:53–62 (1990).
7. Ott MG, Holder BB, Gordon HL. Respiratory cancer and occupational exposure to arsenicals. Arch Environ Health 29:250–255 (1974).
8. Pershagen G. Lung cancer mortality among men living near an arsenic-emitting smelter. Am J Epidemiol 122:684–693 (1985).
9. Enterline PE, Day R, Marsh GM. Cancers related to exposure to arsenic at a copper smelter. Occup Environ Med 52:28–32 (1995).
10. Luehrheith R. The consequences of chronic arsenic poisoning among Moselle wine growers. Pthenoautoanatomical investigations of post-mortem examinations performed between 1960 and 1977. J Cancer Res Clin Oncol 105:173–182 (1983).
11. Nilsson R, Jha AN, Smith AH, Aylward LE, Natarajan AT. Chromosomal aberrations in humans exposed to arsenic in the Srednogorie area, Bulgaria. Fresen Environ Bull 25:49–53 (1986).
12. Larda D. Sister-chromatid exchange (SCE) among individuals chronically exposed to arsenic in drinking water. Mutat Res 312:111–120 (1994).
13. Moore LE, Warfield SM, Novak Z, Natarajan AT, Smith MT. Use of the fluorescent micronucleus assay to detect the genotoxic effects of radiation and arsenic exposure in exfoliated human epithelial cells. Environ Mol Mutagen 23:75–81 (1994).
14. Poisson L, Lowry Cible K, Kalman DA, Hughes JP, van Belle G, Covert DS, Burbacher TM, Bolgiano D, Mottet NK. Pathways of human exposure to arsenic in a community contaminated with a copper smelter. Environ Res 53:23–47 (1990).
15. Diaz Barriga F, Santos MA, Mejia JJ, Bataes L, Yanez L, Carriazes L, Vera E, del Roso LM, Cabrian ME. Arsenic and cadmium exposure in children living near a smelter complex in San Luis Potosi, Mexico. Environ Res 62:242–250 (1993).
16. Bancho V. Use of human hair as a biomarker in the assessment of exposure to pollutants in occupational and environmental settings. Toxicology 101:29–39 (1995).
17. Buchet JP, Saussens J, Roels H, Lauwerys R, Fagar R. Geographical and temporal differences in urinary excretion of inorganic arsenic: a Belgian population study. Occup Environ Med 53:230–237 (1996).
18. Gebel T, Kevekerdors S, Schafer J, van Plateen H, Dunkelberg H. Assessment of a possible genotoxic environmental risk in sheep bred on ground with strongly elevated contents of mercury, arsenic and antimony. Mutat Res 398:267–274 (1996).
19. Gebel T, Suchenwerth RHR, Behmke C, Piegaw A, Claudius K, Schulze E, Dunkelberg H. Biomonitoring – Untersuchung bei Personen in Wohngebieten mit erhöhtem Bodenanteil an Quecksilber, Arsen und Antimon. Gesundheitswesen (in press).
20. Hashem N, Shawki R. Carcinogenesis of peripheral lymphocytes: one biologic indicator of potential drug hazard. Afr J Med Sci 5:155–163 (1976).
21. Kuroda K, Endo G, Okamoto A, Yoo YS, Horiguchi S. Genotoxicity of benzylidene, galilium and antimony in short-term assays. Mutat Res 264:163–170 (1991).
22. Groth OH, Stettler LE, Burg JR, Busey WM, Grant GC, Wong L. Carcinogenic effects of antimony trioxide and antimony are concentrate in rats. J Toxicol Environ Health 18:607–626 (1988).
23. Newton PE, Bolte HF, Daly IW, Pillsbury BD, Terrill JB, Drew RT, Ben Dyke R, Sheldon AW, Rubin LF. Subchronic and chronic inhalation toxicity of antimony trioxide in the rat. Fundam Appl Toxicol 22:561–576 (1994).
24. Jones RD. Survey of antimony workers: mortality 1961–1992. Occup Environ Med 51:772–776 (1994).
25. Bailly R, Lauwerys R, Buchet JP, Malou P, Koningis J. Experimental and human studies on antimony metabolism: their relevance for the biological monitoring of workers exposed to inorganic antimony. Br J Ind Med 46:93–97 (1989).
26. Gerhardsson L, Brune D, Nordberg GF, Wester PD. Antimony in lung, liver and kidney tissue from deceased smelter workers. Scand J Work Environ Health 8:201–208 (1982).
27. Kanner M, Lainemann M, Schaller KH, Welte D, Lehnert G. External and internal antimony exposure in starter battery production. Int Arch Occup Environ Health 67:119–123 (1995).
28. Cercaussius EA. Changes in the chemical speciation of arsenic following ingestion by man. Environ Health Perspect 18:147–150 (1977).
29. Buchet JP, Lauwerys R, Roels H. Comparison of several methods for the determination of arsenic compounds in water and in urine. Their application for the study of arsenic metabolism and for the monitoring of workers exposed to arsenic. Int Arch Occup Environ Health 46:21–29 (1980).
30. Ludersdorff R, Fuchs A, Mayer P, Skulsukasi G, Schack G. Biological assessment of exposure to antimony and lead in the glass-producing industry. Int Arch Occup Environ Health 59:469–474 (1987).
31. Araki S, Aono H. Effects of water restriction and water loading on daily urinary excretion of heavy metals and organic substances in metal workers. Br Ind Med 46:389–392 (1989).
32. Boeniger MF, Lowry LK, Rosenburg J. Interpretation of urine results used to assess chemical exposure with emphasis on creatinine adjustments: a review. Am Ind Hyg Assoc J 54:61–67 (1993).
33. Chittleborough G. A chemist’s view of the analysis of human hair for trace elements. Sci Total Environ 14:53–75 (1980).
34. Schaller KH. Analyse in biologischem Materiael: Arsen, in: Analytische Methoden zur Prüfung gesundheits- schädlicher Arbeitsstoffe, vol 2 (Henschler D, ed). Weinheim, Germany/VCH Verlagsgesellschaft, 1981.
35. Kalmia Company I. Winstat 3.1. Cambridge, MA: Kalmia Company, 1995.
36. Anonymous. Leidraad Bodemsanering Deel II. Technisch-Inhoudelijk Deel. The Hague: Staatsuitgeverij, 1998.
37. Toa V, Colombi A, Maroni M, Buratti M, Calzaferri G. The speciation of the chemical forms of arsenic in the biological monitoring of exposure to inorganic arsenic. Sci Total Environ 34: 241–250 (1984).
38. Lanzer E. Aktivierungsanalyse von Umwelt-Metallen in menschlichem Kopfhaut. J Radioanal Chem 58:69–72 (1980).
39. Minioa C, Sabbioni E, Apostoli P, Pietra R, Pozzoli L, Gallinini M, Nicoleau G, Alessio L, Capodaglio G. Trace element reference values in tissues from inhabitants of the European Community I. A study of 46 elements in urine, blood and serum of Italian subjects. Sci Total Environ 85:89–105 (1989).
40. Vaher M, Lind B. Concentrations of arsenic in urine of the general population in Sweden. Sci Total Environ 54:1–12 (1986).
41. Yamato N. Concentrations and chemical species of arsenic in human urine and hair. Bull Environ Contam Toxicol 40:633–640 (1988).
42. German Federal Health Office, ed. Umwelt-Survey, Studienbeschreibung und Humanbiomonitoring. WeBoLu-Heft 5 (1995).
43. Hopenhain-Rich C, Biggs ML, Smith AH, Kalman DA, Moore LE. Methylation study of a population environmentally exposed to arsenic in drinking water. Environ Health Perspect 104:620–628 (1996).
44. Schneider G, Krivan V. Multi-element analysis of tobacco and smoke condensates by intramolecular neutron activation analysis and atomic absorption spectrometry. Int J Environ Anal Chem 53:87–100 (1993).
45. Phillips DJH. Arsenic in aquatic organisms: a review, emphasizing chemical speciation. Aquat Toxicol 16:151–186 (1990).
46. Buchet JP, Paubels S, Lauverys R. Assessment of exposure to inorganic arsenic following ingestion of marine organisms by volunteers. Environ Res 68:44–51 (1994).
47. Lunde G. Occurrence and transformation of arsenic in the marine environment. Environ Health Perspect 19:47–52 (1977).
48. Muro IC. Naturally occurring toxicants in foods and their significance. Clin Toxicol 5:947–963 (1978).
49. Arbouine MW, Wilson HK. The effect of seafood consumption on the assessment of occupational exposure to arsenic by urinary arsenic speciation measurements. J Trace Elem Electrolytes Health Dis 8: 135–160 (1992).
50. Gebel T, Christensen S, Dunkelberg H. Comparative and environmental genotoxicity of antimony and arsenic. Anticancer Res 17(4A):2603–2607 (1997).
51. Yamanaka K, Okada S. Induction of lung-specific DNA damage by metabolically methylated arsenicals via the production of free radicals. Environ Health Perspect 102 (suppl 3):37–46 (1994).
52. Schmid K, Lederer P, Schaller KH, Angerer J, Strebl H, Weber A. Internal exposure to hazardous substances of persons from various countries of origin—Investigations on exposure to lead, mercury, arsenic and cadmium. Zbl Hyg 199:24–37 (1996).
53. Trepka MJ, Heinrich J, Schulz C, Krause C, Popescu M, Wist M, Wichmann HE. Arsenic burden among children in industrial areas of eastern Germany. Sci Total Environ 190: 95–105 (1996).
54. Pomroy C, Charbonneau SM, McCullough RS, Tam GK. Human retention studies with \textsuperscript{75}As. Toxicol Appl Pharmacol 53:550–556 (1980).
55. Tam GK, Charbonneau SM, Bryce F, Pomroy C, Sandi E. Metabolism of inorganic arsenic \textsuperscript{75}As in humans following oral ingestion. Toxicol Appl Pharmacol 50:319–322 (1979).
56. Binder S, Forney D, Kaye W, Paschal D. Arsenic exposure in children living near a former copper smelter. Bull Environ Contam Toxicol 38:114–121 (1987).
57. Hewitt DJ, Milliner GC, Nye AC, Simmons HF. Investigation of arsenic exposure from soil at a superfund site. Environ Res 68:73–91 (1995).
58. Dieter MP, Jameson CW, Ewell MR, Lodge JW, Hejtmancik M, Grumblain SL, Ryan M, Peters AC. Comparative toxicity and tissue distribution of antimony potassium tartrate in rats and mice dosed by drinking water or intraperitoneal injection. J Toxicol Environ Health 34:51–62 (1991).
59. Lauwers LF, Roelants A, Rosselle PM, Heyndrickx B, Baute L. Oral antimony intoxications in man. Crit Care Med 18:324–326 (1990).
60. Zellhuis RL, Wilbowo AAE. Standard setting and metal speciation: arsenic. In: Changing Metal Cycles and Human Health (Nriagu JO, ed). Berlin, Heidelberg, New York:Springer 1984;323–344.

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