Zeitschrift: Mitteilungen aus Lebensmitteluntersuchungen und Hygiene = Travaux de chimie alimentaire et d'hygiène

Herausgeber: Bundesamt für Gesundheit

Band: 96 (2005)

Heft: 2

Artikel: Occurrence of arsenic in drinking water of the canton of Valais. Part II, Epidemiological comparison between arsenic concentrations and cancer incidence rates

Autor: Brüschweiler, Beat J. / Schlatter, Josef R. / Weck, Daniel de

DOI: https://doi.org/10.5169/seals-981941

Occurrence of arsenic in drinking water of the canton of Valais

Part II: Epidemiological comparison between arsenic concentrations and cancer incidence rates

Beat J. Brüschweiler[1], Josef R. Schlatter[1], Daniel de Weck, MD[2], Frédéric Favre[2], Jean-Christophe Luthi, MD, MPH, PhD[2]

[1]Swiss Federal Office of Public Health, Food Toxicology Section, 8004 Zurich
[2]Tumor Registry, Health Observatory, Canton of Valais, Av. Grand-Champsec 86, 1950 Sion

Received 18 December 2004, accepted 15 March 2005

Introduction

A systemic survey of arsenic levels in drinking water in the canton of Valais was performed by the Swiss Federal Office of Public Health (SFOPH) in 2003 and reported as part I of the present study (1). In short, a total of 1297 drinking water samples were analysed from all 160 communes of the canton of Valais. Arsenic levels were found to be ≥10 µg/l in 89 samples. The Swiss legal limit of 50 µg As/l (2) was exceeded in 7 drinking water samples from Sion, Vex und Oberwald with a maximum value of 101 µg/l in Oberwald.

The World Health Organisation (WHO) recommended a provisional guideline value of 10 µg As/l in drinking water in 1993 (3). The European Commission (EC) followed this recommendation in 1998 and implemented this value as a limit value in its directive on quality of water intended for human consumption (4). Inorganic arsenic is classified as carcinogenic to humans which can cause tumors in bladder, lung, skin, liver and kidney after oral exposure (5, 6). In several epidemiological studies such as the one from Taiwan, an association between high arsenic levels in drinking water and increased cancer incidence or cancer mortality in the exposed population was found (6, 7) (Table 1).

Table 1
Age-adjusted mortality rates from various cancers depending on the arsenic concentration in drinking water (7)

	Median arsenic concentration in well water	*Bladder cancer*	*Kidney cancer*	*Lung cancer*	*Liver cancer*	*Prostate cancer*
	(µg/l)	*(per 100000 person-years)*				
Males	<300	22.6	8.4	49.2	47.8	1.0
	300–599	61	18.9	100.7	67.6	9.0
	≥600	92.7	25.3	104.8	86.7	9.2
Females	<300	25.6	3.4	36.7	21.4	–
	300–599	57.0	19.4	60.8	24.2	–
	≥600	111.3	58	122.2	31.8	–

Mortality rates and population data in 42 villages of the blackfoot disease endemic area in Taiwan during 1973–1986; arsenic concentrations in well water in 1964–1966

The health risks of arsenic from food or drinking water was evaluated by the Joint FAO/WHO Expert Committee on Food Additives (JECFA). JECFA has derived a provisional tolerable weekly intake (PTWI) for inorganic arsenic of 15 µg/kg body weight (b.w.) in 1983 by using a threshold approach. This PTWI corresponds to a daily intake of approx. 130 µg per person weighing 60 kg (8) and is based on epidemiological studies from regions with high arsenic concentrations in the drinking water (e.g. Taiwan) where dermal diseases such as keratosis and hyperpigmentation have been shown to be the most sensitive effects. The evaluation in 1983 was confirmed in 1989 with the clear understanding that the margin between the PTWI and intakes reported to have toxic effects in epidemiological studies was narrow (9). With a mean inorganic arsenic intake of approx. 10 µg per person from food in Switzerland (10), drinking water could contain 80 µg/l without exceeding the PTWI assuming a water consumption of 1.5 liter per person and day. Based on the same epidemiological studies in Taiwan (7, 11, 12), the US National Research Council (NRC) has calculated the risk of developing cancer after lifetime exposure to arsenic in drinking water at lower concentration in the US assuming no threshold for the effects of arsenic (13). For the extrapolation to the lower dose range, NRC used an additive Poisson model with a linear term for dose. After considering the NRC analysis and conducting their own internal assessment, US Environmental Protection Agency (EPA) lowered the maximum contaminant level (MCL) for arsenic in drinking water from 50 µg/l to 10 µg/l. According to EPA's risk assessment, this level is associated with mean population cancer risk of $0.63–2.99\times10^{-4}$ (14).

Part II is an ecologic study to analyse, whether increased cancer incidences are observable in relation to higher arsenic concentrations in drinking water in the canton of Valais. Incidences of arsenic-specific tumors in the canton of Valais are compared with other cantons having low arsenic concentrations in drinking water.

Methods

Cancer incidence data

Incidence data of tumors associated with As exposure between 1989 and 1998 were used from the Tumor Registry of the canton of Valais. Cancers were coded according to the International Classification of Diseases 9 (ICD-9). All new cases of these cancer diagnosed between 1989 and 1998 were included in the study. These data include liver cancer (230 cases in men and 49 in women with ICD-9 Code 155); trachea, bronchus and lung cancer (867 cases in men and 232 in women with ICD-9 Code 162); skin cancer without melanoma (1424 cases in men and 1335 in women with ICD-9 Code 173); bladder cancer (263 cases in men and 72 in women with ICD-9 Code 188); cancer of the kidney and of other organs of the urinary tract (173 cases in men and 128 in women with ICD-9 Code 189). Cancer cases not being residents of the canton of Valais were excluded from the study.

As denominator we used the population of the canton of Valais in 1993. We applied the method described by Benhamou and Laplanche for estimating population by age between two censuses (15). We obtained data from censuses 1990 and 2000 from the Swiss federal statistical office. The population size of the canton of Valais in 1993 was 256000.

Water samples and analytical measurements

Sampling and analytical measurements are described in part I of this study (1).

Arsenic levels within communes were found to be perfectly lognormally distributed (e.g. *Staldenried, Visperterminen),* approximately lognormally distributed (e.g. *Bagnes, Evolène)* or distributed in subsets (e.g. *Sion)* (data not shown).

Arsenic was determined as total arsenic and no speciation was performed. The stability of total arsenic in drinking water is known to be high (M. Haldimann, personal communication).

Water in the canton of Valais originates mainly from springs and is less influenced by rainfall than fountain water. Since variability of arsenic concentrations over time was studied in part I and correlation between 2003 and 1999 was found to be high (1), the same trend is assumed to an earlier time point (such as 1989).

Epidemiological comparisons

Cancer incidences were compared between:

A) communes with mean drinking water concentrations ≥10 µg As/l *(Dorenaz, Eisten, Finhaut, Oberwald, Salvan, St-Nicklaus, Vernayaz)* and communes with mean drinking water concentrations <10 µg As/l
B) communes with incidental drinking water samples ≥10 µg As/l *(Bagnes, Collonges, Dorenaz, Eisten, Embd, Ernen, Finhaut, Grächen, Hérémence, Les Agettes, Leuk, Martigny, Martigny-Combe, Mühlebach, Oberwald, Randa, Riddes, Saas-Grund, Salvan, Simplon-Dorf, Sion, Staldenried, Steg, St-Martin, St-Nicklaus, Törbel, Trient, Ulrichen, Unterbäch, Vernayaz, Vex, Veysonnaz, Wiler)* and communes with drinking water concentrations of all samples <10 µg As/l
C) communes with incidental drinking water samples ≥50 µg As/l *(Oberwald, Sion, Vex)* and communes with drinking water concentrations of all samples <50 µg As/l.

Statistical analysis

For subjects with the type of cancer under investigation, we calculated crude rates and standardized age-adjusted incidence rates for the three groups described above for the entire time period 1989–1998 and separately for men and women. Cancer incidences were age-adjusted according to a standard European population. We further calculated the standardized age-adjusted rate ratio comparing areas with different cut-off point values for high and low arsenic levels in drinking water.

Finally, we assessed the correlation in each commune between standardized incidence rates of kidney cancer in women and mean arsenic levels in drinking water using Pearson correlation coefficient. Kidney cancer was chosen, because this tumor localisation has fewer confounding factors than the other types of cancer associated with arsenic exposure. For statistical reasons, we excluded communes with less than 1000 inhabitants. All analyses were done with SAS software (SAS Institute Inc. Cary, NC, USA).

Results and discussion

Standardized incidence rates in communes with mean concentrations ≥10 µg As/l and <10 µg As/l (comparison A) were found as shown in Table 2. Corresponding standardized rate ratios (SRRs) and 95 % confidence intervals (CI) were calculated. None of the differences were statistically significant. Given the fact that the number of cancer cases in communes with mean drinking water concentrations of ≥10 µg As/l were very small, this result is not surprising, also in view of the fact that at least for lung cancer there are confounding factors, such as tobacco smoking, air pollution, radon exposure and socio-economic status.

The results of comparison B, in which incidence rates of communes with and without incidental arsenic levels in public drinking water ≥10 µg As/l were compared, are shown in Table 3. A slight, but not significant increase of incidence rates

of cancer of kidney and other organs of the urinary tract was detected with SRRs for males and females of 1.17 (95 % CI=0.86–1.59), and 1.13 (95 % CI=0.73–1.76), respectively.

For the measurement of any arsenic values ≥50 µg/l (comparison C), only three communes were involved; Sion, with 27000 inhabitants, and Oberwald and Vex with 260 and 1300 inhabitants, respectively. The results are given in Table 4. In males, incidence of skin cancer (without melanoma) was statistically significantly increased (SRR=1.21; 95 % CI=1.04–1.41).

Table 2
Comparison A: Cancer incidences in the canton of Valais in communes with mean arsenic levels in public drinking water (≥10 µg/l and <10 µg/l), 1989–1998

Cancer	*Mean level ≥10 µg/l*		*Mean level <10 µg/l*			
Males	*Population size =3100*		*Population size =123434*			
	N	*SR*	*N*	*SR*	*SRR*	*95 % CI*
Liver	7	20.7	223	18.8	1.10	0.48–2.49
Trachea, bronchus, lung	31	91.2	836	71.0	1.28	0.87–1.90
Skin (without melanoma)	30	93.5	1386	115.8	0.81	0.56–1.17
Bladder	6	18.4	257	21.5	0.86	0.37–2.01
Kidney and other organs of the urinary tract	4	15.1	169	14.4	1.05	0.45–2.45
Females	*Population size =3023*		*Population size =126519*			
	N	*SR*	*N*	*SR*	*SRR*	*95 % CI*
Liver	1	4.2	48	2.9	1.44	0.30–6.94
Trachea, bronchus, lung	8	25.2	224	16.6	1.52	0.73–3.19
Skin (without melanoma)	29	78.2	1303	85.0	0.92	0.59–1.45
Bladder	5	11.5	72	4.6	2.48	0.68–9.07
Kidney and other organs of the urinary tract	5	11.5	123	8.6	1.34	0.37–4.81

N: total number of tumor cases
SR: standardized incidence rate using an European standard population (per 100000 person-years)
SRR: standardized rate ratio
CI: confidence interval

Table 3

Comparison B: Cancer incidences in the canton of Valais in communes *with* and *without* incidental arsenic levels in public drinking water (≥10 µg/l), 1989–1998

Cancer	*With incidental levels ≥10 µg/l*		*Without incidental levels ≥10 µg/l*			
Males	*Population size =34117*		*Population size =92418*			
	N	*SR*	*N*	*SR*	*SRR*	*95% CI*
Liver	64	18.9	166	18.8	1.01	0.76–1.33
Trachea, bronchus, lung	244	73.0	623	70.9	1.03	0.89–1.19
Skin (without melanoma)	378	111.7	1038	116.5	0.96	0.85–1.08
Bladder	67	20.5	196	21.8	0.94	0.72–1.23
Kidney and other organs of the urinary tract	52	16.1	121	13.8	1.17	0.86–1.59
Females	*Population size =35601*		*Population size =93942*			
	N	*SR*	*N*	*SR*	*SRR*	*95% CI*
Liver	12	2.6	37	3.1	0.84	0.37–1.94
Trachea, bronchus, lung	64	15.7	168	17.2	0.91	0.66–1.26
Skin (without melanoma)	372	84.9	960	85	1.00	0.86–1.16
Bladder	24	5.1	48	4.3	1.17	0.62–2.21
Kidney and other organs of the urinary tract	42	9.4	86	8.4	1.13	0.73–1.76

see Table 2

Table 4

Comparison C: Cancer incidences in the canton of Valais in communes *with* and *without* incidental arsenic levels in public drinking water (≥50 µg/l), 1989–1998

Cancer	*With incidental levels ≥50 µg/l*		*Without incidental levels ≥50 µg/l*			
Males	*Population size =13127*		*Population size =113408*			
	N	*SR*	*N*	*SR*	*SRR*	*95% CI*
Liver	25	20.1	205	18.7	1.07	0.72–1.59
Trachea, bronchus, lung	74	60.1	793	72.8	0.83	0.66–1.03
Skin (without melanoma)	169	136.6	1247	112.8	1.21	1.04–1.41
Bladder	26	21.3	237	21.5	0.99	0.68–1.45
Kidney and other organs of the urinary tract	22	18.3	151	14.0	1.31	0.87–1.99
Females	*Population size =14105*		*Population size =115420*			
	N	*SR*	*N*	*SR*	*SRR*	*95% CI*
Liver	5	2.78	44	3.0	0.93	0.28–3.04
Trachea, bronchus, lung	22	13.7	210	17.2	0.80	0.48–1.31
Skin (without melanoma)	154	92.7	1178	83.9	1.10	0.90–1.35
Bladder	9	5.0	63	4.5	1.11	0.45–2.72
Kidney and other organs of the urinary tract	17	10.0	111	8.5	1.18	0.64–2.17

see Table 2

In the evaluation of a potential correlation between standardized incidence rates of kidney cancer in women and mean arsenic drinking water concentrations by commune with more than 1000 inhabitants (n=62), the Pearson correlation coefficient was –0.062, showing no correlation (Figure 1).

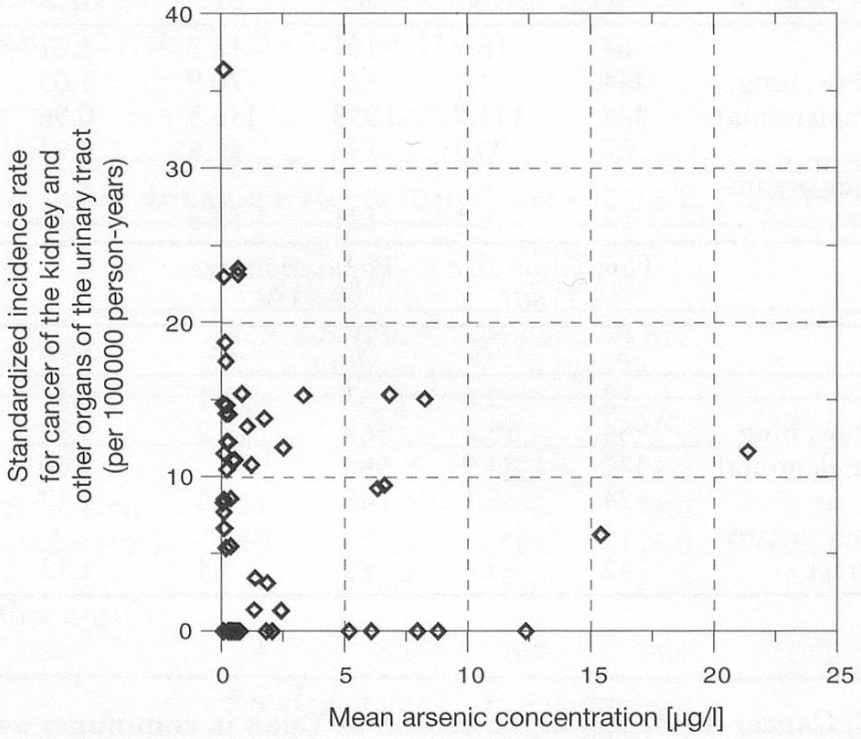

Figure 1 **Standardized incidence rates for cancer of the kidney and other organs of the urinary tract in women from communes in the canton of Valais with more than 1000 inhabitants (n=62). Pearson correlation coefficient=–0.062**

Interpretation of these results from the canton of Valais needs to be done with caution. First, we assumed that the arsenic concentrations in public drinking water in the communes correlate with the arsenic intakes of the population. In reality, however, there are differences in arsenic concentrations inside the communes, and in the consumption rate of public drinking water among individuals. Second, drinking water samples were not collected in an uniform way. Number of samples varied between 1 and 53 depending on the commune. Third, data from the Tumor Registry are only descriptive for an ecologic study. Potential relations between arsenic concentrations in public drinking water and cancer incidence observed in the communes might not exist at the level of individuals (ecologic fallacy). Fourth, we did not take into account known confounding factors for the different cancer types that we analyzed, such as tobacco and alcohol consumption, UV-light exposure, diet or socio-economic status. Recently, joint effects of environmental arsenic ingestion through drinking water and tobacco smoking in relation to lung cancer incidence

were found to be more than additive in a prospective cohort study in Taiwan (16). Last but not least, for several cancer types, the number of cases is very low and therefore it is difficult to interpret these results.

Table 5
Comparison of bladder cancer and kidney cancer incidences with other cantons

	Bladder	*Kidney and other organs of the urinary tract*	*Population size*	*Reference*
Males	*SR*	*SR*		
Canton of Valais: communes *with* incidental arsenic levels in public drinking water ≥10 µg/l (1989–1998)	20.5	16.1	34117	this study
Canton of Valais: communes *without* incidental arsenic levels in public drinking water ≥10 µg/l (1989–1998)	21.8	13.8	92418	this study
Canton of Valais (1989–1998): Total	21.4	14.4	126535	this study
Cantons of Grisons/Glarus (GR/GL) (1995–1999)	24.3	15.7	111166$^{\Delta}$	(22)
Canton of Ticino (TI) (1996–1998)	26.5	15.9	148317$^{\Delta}$	(22)
Cantons of Basle City/Basle Country (BS/BL) (1995–1999)	18.0	14.3	215837$^{\Delta}$	(22)
Canton of Geneva (GE) (1995–1999)	24.5	14.1	194732$^{\Delta}$	(22)
Canton of Vaud (VD) (1992–1996)	22.5	14.5	299184$^{\Delta}$	(22)
Females	*SR*	*SR*		
Canton of Valais: communes *with* incidental arsenic levels in public drinking water ≥10 µg/l (1989–1998)	5.1	9.4	35601	this study
Canton of Valais: communes *without* incidental arsenic levels in public drinking water ≥10 µg/l (1989–1998)	4.3	8.4	93942	this study
Canton of Valais (1989–1998): Total	4.5	8.7	129543	this study
Cantons of Grisons/Glarus (GR/GL) (1995–1999)	5.5	6.2	114124$^{\Delta}$	(22)
Canton of Ticino (TI) (1996–1998)	5.3	5.9	161898$^{\Delta}$	(22)
Cantons of Basle City/Basle Country (BS/BL) (1995–1999)	4.6	5.9	231866$^{\Delta}$	(22)
Canton of Geneva (GE) (1995–1999)	5.5	5.8	214088$^{\Delta}$	(22)
Canton of Vaud (VD) (1992–1996)	5.5	7.4	321110$^{\Delta}$	(22)

SR: standardized incidence rate using an European standard population (per 100000 person-years)
$^{\Delta}$: status in year 2000

Incidence rates of bladder and kidney cancer in the canton of Valais in 1989–1998 were compared with those in the cantons of Grisons/Glarus, Ticino, Basle City/Basle Country, Geneva and Vaud (Table 5). Specific regions of the cantons of Ticino (Sotto Ceneri) and Grisons (upper Engadin and Val Poschiavo) are known to have higher arsenic concentrations in their drinking water (17, 18). For males, the highest incidence rate of bladder cancer was observed in the canton of Ticino. Small differences between cantons were seen, which might be mainly related to smoking pattern across Switzerland. The highest incidence rate of kidney cancer in males was observed in the canton of Valais in communes with arsenic levels in public drinking ≥10 µg (16.1 per 100000 person-years) followed by Ticino and Grisons (15.9 and 15.7 per 100000 person-years). In the total canton of Valais it was found to be 14.4 per 100000 person-years, which is in the range of the other cantons (Basle, Geneva and Vaud). Since the number of people affected by increased arsenic exposure in the Ticino and Grisons is small, it is difficult to draw meaningful conclusions from these slight differences. For females, differences in incidence rates of bladder and kidney cancer between cantons were also small and no trend with respect to arsenic exposure was apparent.

Conclusion

A few small differences in tumor incidences between population exposed to higher and lower arsenic concentrations in public drinking water could be observed which were, however, with one exception not statistically significant. These results need to be interpreted with caution, since they are based on a descriptive ecologic study, which does not take into account the individual arsenic intake and the individual development of cancer, the different risk factors for each cancer site, including those who are not known in the literature to be related to arsenic.

Several possible toxicological mechanisms are under discussion which might be most relevant for arsenic toxicity in the low-dose range. These mechanisms include induced chromosomal abnormalities, altered DNA repair, altered DNA methylation patterns, and promotion/progression (19, 20). The latter three mechanisms would give strong evidence for a non-linear dose-response relationship. There is still an open discussion whether a threshold value exists or not. The choice of the extrapolation method is the most decisive for the assessment of the health risks in the low-dose range (21).

Acknowledgements

The authors thank Max Haldimann and Vincent Dudler (both SFOPH) for providing the analytical data of arsenic in drinking water (part I of this study).

Summary

In this study, it is examined whether a possible correlation between arsenic concentrations in public drinking water in the canton of Valais and cancer incidence

rates is apparent. A total of 1297 drinking water samples were analysed from all 160 communes of the canton of Valais in 2003. Incidence data of tumors associated with arsenic exposure (liver cancer, lung cancer, skin cancer excluding melanoma, bladder cancer, kidney cancer) between 1989 and 1998 were used from the Tumor Registry of the canton of Valais. Cancer incidences were compared between: A) communes with mean drinking water concentrations ≥10 µg As/l and communes with mean drinking water concentrations <10 µg As/l, B) communes with drinking water concentrations with at least one sample ≥10 µg As/l and communes without drinking water concentrations with at least one sample ≥10 µg As/l, and C) communes with drinking water concentrations with at least one sample ≥50 µg As/l and communes without drinking water concentrations with at least one sample ≥50 µg As/l. While some differences in cancer incidences between population with higher and lower arsenic exposure were seen, they were not statistically significant with one exception. Overall, no association between arsenic in drinking water and cancers in the canton of Valais was seen. Due to the limitations of ecological study design and small number of cancer cases, the data should be interpreted with caution.

Zusammenfassung

In der vorliegenden Studie wurde untersucht, ob im Kanton Wallis eine mögliche Korrelation zwischen erhöhten Arsenkonzentrationen im Trinkwasser und erhöhten Krebsinzidenzen bei der exponierten Bevölkerung festgestellt werden kann. Die Arsenkonzentrationen wurden im Jahr 2003 in insgesamt 1297 Trinkwasserproben aus allen 160 Walliser Gemeinden im Jahr 2003 gemessen. Bei den Krebsfällen bezogen wir uns auf Tumorarten, die mit Arsen-Exposition assoziiert sind (Leberkrebs, Lungenkrebs, Hautkrebs ohne Melanome, Blasenkrebs, Nierenkrebs), welche zwischen 1989 und 1998 vom Walliser Krebsregister neu erfasst wurden. Es wurden verschiedene Gruppen von Gemeinden miteinander verglichen: A) Gemeinden mit mittleren Arsenkonzentrationen ≥10 µg As/l mit solchen mit mittleren Konzentrationen <10 µg As/l, B) Gemeinden mit einzelnen Trinkwasserproben ≥10 µg As/l mit solchen ohne Trinkwasserproben ≥10 µg As/l, sowie C) Gemeinden mit einzelnen Trinkwasserproben ≥50 µg As/l mit solchen ohne Trinkwasserproben ≥50 µg As/l. Es konnten einige Unterschiede zwischen Bevölkerungsgruppen mit höheren und niedrigen Arsenexpositionen beobachtet werden, wobei diese mit einer einzigen Ausnahme nicht statistisch signifikant waren. Insgesamt konnte keine Assoziation zwischen Arsen im Trinkwasser und Krebs im Kanton Wallis gefunden werden. Wegen der begrenzten Aussagekraft von ökologischen Studien und der geringen Anzahl Krebsfälle sollten die Daten mit Vorsicht interpretiert werden.

Résumé

Dans cette étude, nous avons examiné s'il existait une corrélation entre les concentrations d'arsenic dans l'eau potable et les taux d'incidence de certains cancers dans le Canton du Valais. Au total, 1297 échantillons d'eau potable provenant de 160 communes du Canton du Valais ont été récoltés au cours de l'année 2003. Les taux d'incidence des cancers associés à l'arsenic (cancer du foie, du poumon, de la peau en excluant les mélanomes, de la vessie et du rein) ont été obtenus du Registre valaisan des tumeurs pour les années 1989 à 1998. Les comparaisons de l'incidence des cancers ont été faites pour: A) les communes ayant des concentrations moyennes d'arsenic dans l'eau potable ≥10 µg As/l et les communes ayant des concentrations moyennes <10 µg As/l, B) les communes ayant des concentrations dans l'eau potable comportant au moins un échantillon à ≥10 µg As/l et les communes ne comportant pas au moins un échantillon à ≥10 µg As/l, et C) les communes ayant des concentrations dans l'eau potable comportant au moins un échantillon ≥50 µg As/l et les communes ne comportant pas au moins un échantillon ≥50 µg As/l. Seules quelques petites différences dans l'incidence des cancers ont été observées entre les populations présentant différents niveaux d'exposition à l'arsenic. Aucune de ces différences n'était statistiquement significative à l'exception d'une seule. En conclusion, il n'est pas possible de conclure qu'il existe une association entre l'arsenic dans l'eau potable et les cancers dans le Canton du Valais. Au vu de la force probante limitée des études écologiques et du petit nombre de cas de cancer, il faut interpréter les résultats avec prudence.

Key words

Arsenic in drinking water, toxicity, epidemiology, tumor incidences, liver cancer, lung cancer, skin cancer, bladder cancer, kidney cancer

References

1 *Haldimann M., Pfammatter E., Venetz P.M., Studer P. and Dudler V.:* Occurrence of arsenic in drinking water of the canton of Valais. Part I: Overview of arsenic concentration and geographic distribution. Mitt. Lebensm. Hyg. **96**, 89–105 (2005)

2 *Anonymous:* Ordinance on food contaminants and components. Federal Dept. of Home Affairs, Bern. RS 817.021.23 (1995)

3 *World Health Organisation (WHO):* Arsenic. WHO guidelines for drinking-water quality. 156–167 (1996)

4 *Anonymous:* Council directive 98/83/EC on the quality of water intended for human consumption. European Commission. Official Journal L 330. 05/12/1998. p. 32–54 (1998)

5 *International Agency for Research on Cancer (IARC):* Some drinking-water disinfectants and contaminants, including arsenic. IARC Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Vol. **84**, 41–267 (2004)

6 *World Health Organisation (WHO):* Arsenic and arsenic compounds. Environmental Health Criteria **224**, p. 1–521 (2001)

7 *Wu M.M., Kuo T.L., Hwang Y.H. and Chen C.J.:* Dose-response relation between arsenic concentration in well water and mortality from cancers and vascular diseases. Am. J. Epidemiol. **130**, 1123–1132 (1989)

8 *Joint FAO/WHO Expert Committee on Food Additives (JECFA):* Arsenic. Geneva. WHO Food Add. Ser. **18**, 176–202 (1983)
9 *Joint FAO/WHO Expert Committee on Food Additives (JECFA):* Arsenic. WHO Geneva. WHO Food Add. Ser. **24**, 155–162 (1989)
10 *Zimmerli B., Bosshard E. and Knutti R.:* Occurrence and health risk evaluation of toxic trace elements in the diet. Mitt. Geb. Lebensm. Hyg. **80**, 490–518 (1989)
11 *Chen C.J., Chuang Y.C., Lin T.M. and Wu H.Y.:* Malignant neoplasms among residents of a blackfoot disease-endemic area in Taiwan: high-arsenic artesian well water and cancers. Cancer Res. **45**, 5895–5899 (1985)
12 *Chen C.J., Chen C.W., Wu M.M. and Kuo T.L.:* Cancer potential in liver, lung, bladder and kidney due to ingested inorganic arsenic in drinking water. Br. J. Cancer **66**, 888–892 (1992)
13 *National Research Council (NRC):* Arsenic in drinking water: 2001 update. p. 1–225. Washington DC, National Academy Press (2001)
14 *U.S. Environmental Protection Agency (EPA):* Arsenic in drinking water. Final rule. Table III.D-2(c). Fed. Regist. **66**, 7000–7010. January 22 (2001)
15 *Benhamou E. et Laplanche A.:* Estimation de la population à risque entre deux recensements pour le calcul d'un taux d'incidence ou de mortalité par cancer: comparaison de quatre méthodes. Rev. Epidemiol. Santé Publique **39**, 71–77 (1991)
16 *Chen C.L., Hsu L.I., Chiou H.Y., Hsueh Y.M., Chen S.Y., Wu M.M. and Chen C.J.:* Ingested arsenic, cigarette smoking, and lung cancer risk: a follow-up study in arseniasis-endemic areas in Taiwan. JAMA **292**, 2984–90 (2004)
17 *Pfeifer H.R., Hansen J., Hunziker J., Rey D., Schafer M. and Serneels V.:* Arsenic in Swiss soils and waters and their relation to rock composition and mining activities. Paris, Colloque **85**, INRA. Contaminated soils: 3rd Intern. Conf. Biogeochemistry of Trace Elements (1995)
18 *Beatrozzotti G., Berthoud J., De Rossa M., Gueye-Girardet A., Jaeggli M., Lavanchy J.-C., Pfeifer H.-R., Reymond D., Schlegel C., Schmit V. e Temgouma E.:* Contaminazione naturale da arsenico di acque superficiali e sotteranee in Ticino (Svizzera meridionale). Geol. Insubr. **7**, 1–16 (2002)
19 *Kitchin K.T.:* Recent advances in arsenic carcinogenesis: modes of action, animal model systems, and methylated arsenic metabolites. Toxicol. Appl. Pharmacol. **172**, 249–261 (2001)
20 *Schoen A., Beck B., Sharma R. and Dube E.:* Arsenic toxicity at low doses: epidemiological and mode of action considerations. Toxicol. Appl. Pharmacol **198**, 253–267 (2004)
21 *Daniel O., Schlatter J. und Zimmerli B.:* Arsen in Umwelt, Lebensmitteln und Mensch: Eine Übersicht. Mitt. Geb. Lebensm. Hyg. **89**, 123–146 (1998)
22 *Vereinigung Schweizer Krebsregister (VSRT):* Homepage. http://www.asrt.ch/ (2004)

Corresponding address: Dr. Beat Brüschweiler, Bundesamt für Gesundheit, Sektion Lebensmitteltoxikologie, Stauffacherstrasse 101, CH-8004 Zürich, e-mail: beat.brueschweiler@bag.admin.ch