Arsenic Exposure and Its Impact on Health in Chile

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ABSTRACT

The problem of arsenic in Chile was reviewed. In Chile, the population is exposed to arsenic naturally via drinking-water and by air pollution resulted from mining activities. The sources of arsenic were identified to estimate the exposure of population to arsenic through air, water, and food. Health effects, particularly early effects, observed in children and adults, such as vascular diseases (premature cardiac infarct), respiratory illnesses (bronchiectasis), and skin lesions have been described. Chronic effects, such as lung and bladder cancers, were reported 20 years after peak exposure and persisted 27 years after mitigation measures for removing arsenic from drinking surface water were initiated. Although the effects of arsenic are similar in different ethnic and cultural groups (e.g. Japanese, Chinese, Indian, Bangladeshi, American, and Taiwanese), variations could be explained by age at exposure, the dose received, smoking, and nutrition. Since health effects were observed at arsenic levels of 50 μg/L in drinking-water, it is advised that Chile follows the World Health Organization's recommendation of 10 μg/L. The Chilean experience in removal of arsenic suggests that it is feasible to reach this level using the conventional coagulation process.

Key words: Arsenic; Arsenic exposure; Health effects; Impact studies; Chile

INTRODUCTION

Arsenic is present in most eco-systems in northern Chile and in some parts of central Chile, either naturally or by man-made causes, the latter derived from mining activities (1,2,3). The most extensive contamination of arsenic lies in the region between 17° 30' and 26° 05' South Latitude and between 67° 00' West Longitude and the Pacific Ocean (Fig.). Naturally-occurring arsenic in Chile is associated with the volcanic activity of the Tertiary and Quaternary periods in the Andes Mountains (4). This activity still continues as evidenced in lava flows, geysers, fumaroles, thermal waters, and other geothermal phenomena relating to the Pacific's so-called 'Ring of Fire'. These geological conditions explain the particular chemical characteristics of water in the zone: high pH, variable alkalinity, hardness, moderate-to-high salinity, high silica, and variable concentrations of boron, fluoride, and arsenic (5).

Arsenic present in sources of surface water for human consumption corresponds to the species arsenic(V) (6). Historically, concentrations of arsenic in water for human consumption vary, depending on sources of water or arsenic-removal treatments used. The soils of the northern zone also exhibit elevated and variable levels of arsenic and scant plant cultivation in the area (7-10).

Intense mining activity, principally copper smelting, generates significant emissions of arsenic into the atmosphere, which, in turn, precipitates downwind in soils, snow, and waters. The air of some cities in the area is contaminated with arsenic, and such concentrations are directly related to nearby copper smelting (3,7,11,12).

Arsenic exposure

Continental Chile is 5,000 km long. The population of 15,000,000 is distributed among the northern, central and southern zones, which account for 12%, 74%, and 14% of the population respectively (13). Only the inhabitants of the northern zone have been exposed to high concentrations of arsenic.

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The experience of northern Chile regarding arsenic exposure in drinking-water is a quasi-experiment, marked by a sudden increase in arsenic levels that lasted a few decades until an arsenic-removal plant was built. In as much as this zone is desert, drinking-water supplied by the water-treatment facility is the only source of water for the population (14). At its foundation in 1860, the

the first arsenic-removal plant began operation, and the arsenic content in drinking-water rapidly dropped to 110 µg/L (17). In 1979, a second water-treatment plant started functioning, and concentrations of arsenic were reduced to 40 µg/L. Since 2003, levels of arsenic have further dropped, reaching 10 µg/L in 2004 (18) (Table 1).

Fig. Locations of some main cities and population distribution in Chile
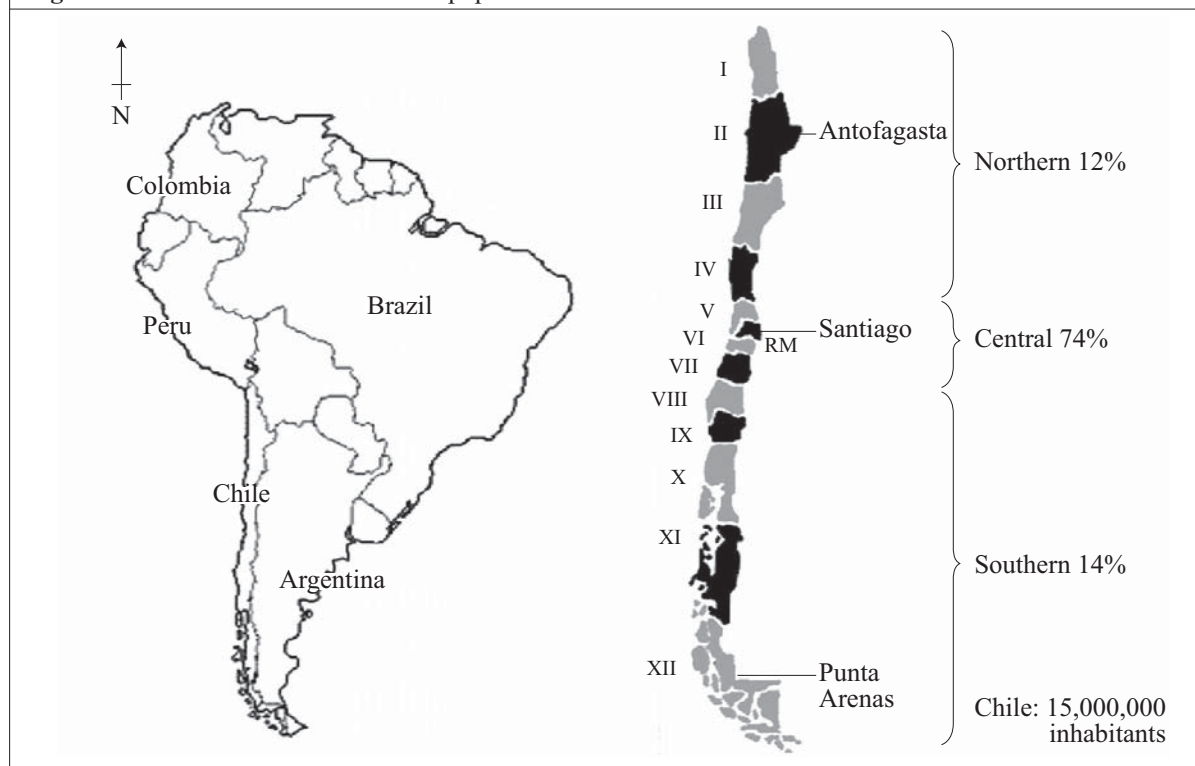
city of Antofagasta obtained its drinking-water by distillation of sea water. As the population grew, they obtained water from rivers coming from mountains. The Siloli River with levels of arsenic between 90 and 100 µg/L was used until the mid-1950s, when the population reached 100,000; the scarcity of drinking-water forced the use of a new water source—the Toconce River with levels of ar-senic ranging from 800 to 900 µg/L. The exception was a few households whose water was supplied since 1871 by the Railway Company which brought water from the Siloli River. In 1892, they represented only 5% of water consumption in Antofagasta; as the population grew, the percentage covered by the Siloli river decreased to negligible amounts (15). During 1950-1978, inhabitants of the northern region were exposed to average concentrations of arsenic from 90 to 860 µg/L. The highest exposure began abruptly in 1958, when the source of water for most of the region's population changed to the Toconce River and the Hojalar River, both with very high concentrations of arsenic (16). In May 1970,

Given both geological and anthropogenic conditions in the northern zone of Chile described above, arsenic exposure is multimedia and, perhaps, unique, and certain interesting questions arise: which pathway of the intake of arsenic is the most critical for human population and on which pathway should mitigation measures be focused within the context of a nation with limited economic resources? (19).

To answer these questions, an arsenic-exposure study of the entire Chilean population was conducted between 1994 and 1998 (20). An estimate of daily ambient exposure was made by combining the information obtained through environmental monitoring, i.e. arsenic concentration per exposure source—air, water, and food—with estimations of volume of air inhaled, water ingested, and foods consumed. The results demonstrated that drinking-water was the principal source of arsenic exposure in the northern and central zones, while foodstuffs were the principal pathway in the rest of the country (Table 2).

In numeric terms, arsenic contamination by air was the least significant of the three pathways. Arsenic contamination from foodstuffs, except for some isolated cases in the northern altiplano, is relatively constant throughout Chile, largely because the vegetables grown in the central zone and the animal meat, dairy, and wheat produced in the southern zone are supplied to the entire country. Most vegetables cultivated in the northern altiplano are only traded in the local markets for approximately 4,000 people, of mainly atacameños and quechuas ancestors (local indigenous people). For this specific population, food makes a substantial contribution to their total intake of arsenic (7-9). Various studies have demonstrated that foods are the main contribution to total intake of arsenic only when arsenic in water and air is negligible (21-24).

Table 1. Average concentration of arsenic in drinking-water (µg/L) in the main cities in northern Chile, 1950-2004

Years	Antofagasta (257,976*) (µg/L)	Tocopilla (43,565*) (µg/L)	Calama (141,422*) (µg/L)
1930-1957	90	250	150
1958-1970	860	250	150
1971-1977	110	636	287
1978-1979	110	110	110
1980-1987	70	110	110
1988-1994	40	40	40
1995-2003	40	40	40
2004-2005	10	10	10

* Size of population
Authors' elaboration based on references: 13-14,18,41

Table 2. Contribution of total arsenic by pathway of intake: Chilean cities, 1994-1995

Zone	City	Water (%)	Air (%)	Food (%)
Northern	Arica	56.91	1.58	41.51
	Iquique	89.15	0.40	10.45
	Antofagasta	81.77	1.46	16.78
	Calama	82.91	2.77	14.32
	Copiapó	33.21	12.29	54.50
	Coquimbo	46.82	1.95	51.23
Central	San Felipe	25.3	1.3	73.4
	Santiago	72.7	0.9	26.4
	Rancagua	69.3	2.0	28.7
	Talca	46.2	0.3	53.5
Southern	Concepción	19.2	1.3	79.5
	Temuco	19.4	0.4	80.2
	Coyhaique	19.4	0.4	80.2
	Punta Arenas	19.4	0.4	80.2

Authors' elaboration based on references: 20,41

HEALTH IMPACTS

There have been a series of reports concerning both early and chronic deleterious health effects attributed to arsenic contamination of water in north Chile.

Early health effects

Infant deaths

Promptly after the peak exposure years, there was an increase in infant mortality rate in Antofagasta (Region II). This excess was estimated at 18-24% of deaths for the 1958-1965 period (25).

Skin lesions

In Region II, since 1919, there have been reports of arsenicosis—leukoderma, melanoderma, and hyperkeratosis—but only associated with workers of nitrate mines (17); two years after the increase of arsenic exposure in drinking water, began reports of children presenting arsenicosis (26,17) and arsenicosis associated with respiratory symptoms, including diffuse and segmentary bronchiectasis (17). Twenty years after peak exposure, 12% of school children in Antofagasta presented arsenicosis, and 28% presented chronic bronchitis compared to only 4% among children of the non-exposed city of Iquique (16). In the city of Antofagasta, the number of children with arsenicosis bronco-pulmonary disease was 2.5 times higher than among children without such lesions. However, three years after the installation of the arsenic-treatment plant, the prevalence of cough or dyspnea dropped from 38% to 7%. In the general population, there was an excess of respiratory symptoms and vascular problems associated with arsenicosis (27).

Respiratory and cardiovascular diseases

A few years after peak exposure, children were reported to have peripheral vascular diseases, including Raynaud syndrome and ischaemia of the tongue. Twenty-two percent of patients hospitalized in Antofagasta presented peripheral vascular syndromes, such as achrocianosis, and 30% had Raynaud syndrome compared to none among Iquique patients (16,17). In 1973, researchers concluded that the most frequent clinical complications in children associated with arsenic in drinking-water were respiratory and cardiovascular diseases (28). Between 1967 and 1970, they described a younger age of cardiac infarct in the city of Antofagasta, where 10% of cardiac infarction cases were under the age of 41 years compared to only 1.5% in Santiago; 53% of these younger cases presented arsenicosis (29). In autopsies of children in Antofagasta, peculiar vascular lesions, consisting of intimal thickening of small and medium arteries, were found, mainly in the heart, gastrointestinal tract, skin,

liver, and pancreas (30). In 1980, a study comparing autopsies of children from Santiago and Antofagasta concluded that the morbid condition associated with ingestion of arsenic had resulted in: systemic occlusive arterial disease, diffuse hypertrophy of the myocardium, arterial hypertension, arterial thrombosis, bronchiectasis, hepatic cirrhosis, haemangioendotelioma of the liver, chronic diarrhoea, recurrent bronchopneumonia, and bilateral pneumonia. The author postulated that malnutrition interacts with arsenic to cause these morbid conditions (31).

Chronic effects

The first report of a higher risk of death due to lung cancer in Antofagasta was described for the 1976-1978 period, i.e. 20-25 years after the period of high exposure began. Standardized mortality ratios (SMRs) for lung cancer were 503 for Antofagasta and 449 for Tocopilla, i.e. five and four times higher, respectively, than the national average. The authors attributed this disparity to arsenic in drinking-water (32).

An ecological study conducted during 1994-1996 generated a database of arsenic exposure and deaths due to cancer for the 1950-1996 period, covering each of the 335 Chilean municipalities (33-35). For each municipality, the lifetime cumulative arsenic exposure (by air and water) was estimated for six age-groups (cohorts), and such exposure was related to mortality due to cancer in the 1985-1992 period. They studied cancer of the lung, bladder, kidney, skin, and liver, and gastric cancer not associated with arsenic, which was used as a comparison. Arsenic exposure through drinking-water was determined to be a highly significant risk factor (Poisson regression analysis) for all cancers associated with arsenic, but it showed no association with gastric cancer. Airborne arsenic could not explain the excess risks for any of the cancers. They concluded that the most important public-health impact of arsenic in drinking-water was lung cancer (33,35). The main relative excesses of mortality due to cancer, adjusted for age and sex, during 1985-1992, were for bladder cancer (SMR of 805 in Antofagasta), followed by lung cancer (SMR of 420 in Antofagasta). The risk of cancer in Antofagasta persisted high even 20-30 years after the treatment plants were in place; from 1993 to 2002, risks of dying from bladder and lung cancers in Antofagasta were four and seven times higher than the rest of Chile respectively (Table 3).

With a similar ecological approach, other authors estimated that arsenic might account for 7% of all deaths among those aged 30 years and above, indicating that this would be the greatest impact ever reported from environmental exposure to a carcinogen in the general population (36).

A case-control study of lung cancer conducted during 1993-1996 in North Chile demonstrated a dose-response effect of arsenic exposure in drinking-water and the risk of lung cancer, including a significant interaction between smoking and arsenic in the risk of lung cancer (14).

Table 3. Cancer standardized mortality ratios and 95% confidence intervals for selected cancers in various cities of Chile in two periods: 1985-1992 and 1993-2000

County arsenic average µg/L 1958-1970	Skin cancer SMR		Kidney cancer SMR		Liver cancer SMR		Lung cancer SMR		Bladder cancer SMR	
	1985-1992 (95% CI)	1993-2002 (95% CI)	1985-1992 (95% CI)	1993-2002 (95% CI)	1985-1992 (95% CI)	1993-2002 (95% CI)	1985-1992 (95% CI)	1993-2002 (95% CI)	1985-1992 (95% CI)	1993-2002 (95% CI)
Antofagasta 860 µg/L	318.9 (171.6-466.2)	298.5 (246.4-350.7)	230.3 (176.7-283.9)	233.1 (194.4-271.9)	154.2 (124.4-183.9)	137.7 (115.4-160.0)	420.1 (389.2-450.9)	406.1 (381.5-430.7)	805.0 (689.0-921.0)	740.1 (655.0-825.1)
Tocopilla 250 µg/L	397.4 (0.0-847.0)	329.1 (167.8-490.3)	125.0 (15.4-234.6)	201.9 (96.1-307.6)	127.5 (52.1-202.8)	121.8 (60.1-183.4)	479.1 (388.4-569.9)	397.2 (325.8-468.6)	683.5 (391.2-975.8)	782.8 (527.1-1038.5)
Calama 150 µg/L	156.3 (0.0-333.1)	115.6 (60.6-170.5)	216.8 (131.8-301.7)	89.3 (52.0-126.6)	109.0 (67.1-151.0)	110.9 (78.9-143.0)	140.7 (111.3-170.1)	112.5 (92.3-132.7)	128.4 (48.8-208.0)	211.9 (137.3-286.4)
Valparaiso <10 µg/L	97.0 (36.9-157.2)	96.5 (73.0-119.9)	138.9 (107.0-170.7)	137.9 (113.1-162.6)	102.8 (84.5-121.1)	113.0 (96.5-129.5)	136.6 (123.1-150.0)	131.8 (120.1-143.4)	96.7 (66.7-126.6)	121.8 (94.2-149.4)

Authors' elaboration based on official information from: Republic of Chile. Ministerio de Salud. Departamento de Estadísticas. Bases de datos de Mortalidad 1985-2002. See also references: 13-14,18,41); CL=Confidence interval; SMR=Standardized mortality ratio

Mitigation measures

In the 1970s, treatment processes to remove arsenic from drinking-water sources in the northern zone were initiated. Today, there are three arsenic-removal plants operating (two in Antofagasta and one in Calama). Combined, these installations treat 1,500 litres per second of surface water with average arsenic concentrations of 400-450 µg/L, and in 2004 reduced these to 10 µg [Cáceres A. Personal communication, 2005] of arsenic per litre (Table 1) (37). However, there are still problems of high concentrations of arsenic in water consumed by small, scattered, largely indigenous, communities in the northern Andes (3,000 inhabitants) that are being resolved as we write this report [Mr. Jorge Molina, Head of Regional Government. Seminario Internacional: El Arsénico en la Segunda Region. 17 November 2005. Universidad de Antofagasta] (38).

The Chilean experience in removal of arsenic at treatment plants by coagulation processes indicates that removal of arsenic is most efficient using $FeCl_3$ as a coagulant and that key factors in arsenic removal are: chemical species of the arsenic present, pH of water; and dosage of oxidizing agent and coagulant, velocity of agitation, and removal processes of the arsenic-flocs formed (5). At the level of individual households and small communities, the experience in Chile has not been so successful. In principle, the devices tested in the field, based on coagulation-filtration processes with low doses of coagulants, reduced arsenic to safer concentrations. In practice, however, this model has not been implemented in small communities due to lack of motivation of people in reducing arsenic because they do not see any health problem in their vicinity relating to drinking-water. Their main concern is about quantity of water, organoleptic characteristics, and sanitary quality (Unpublished observations).

DISCUSSION

Public-health and political management of the arsenic problem

Conversations and interviews conducted by the investigators in the study with principals in Antofagasta of an earlier era made it clear that the responsible officers of the water utility and health officials in the 1950s were advised that the new sources of water used contained arsenic in excess of the standards. The presence of a chemical, which did not change the colour or odour of water, nor produced any immediate evident health problem among the inhabitants, appeared at that time less of a problem than the need for providing sufficient quan-

tities of water of good microbiological quality. In those years, diarrhoea and malnutrition were the principal causes of infant deaths and shorter life-expectancy in Chile. The National Health Service had only recently come into existence and did not have epidemiologists in the region to initiate health surveillance. The first news and warning signs concerning the health effects attributable to arsenic were revealed by paediatricians and pathologists in hospitals in Santiago, 10 years after the onset of arsenic exposure (26,28,30). Following these reports and the resulting public alarm, mitigation measures were taken (27,39).

The case of arsenic in Chile can be explained in part by the sanitation priorities of that time, but also by insufficient understanding of the health risks posed by exposure to arsenic in water. This case underlines the critical importance of epidemiologic surveillance in environmental interventions and new housing projects from their outset. It also emphasizes the importance of the precautionary principle with potential health risks. On the positive side, the excellent response of the national health system in the 1970s should be highlighted. Under the leadership of Dr. J.M. Borgoño, a team of national and local epidemiologists undertook a study which enabled them to characterize the arsenic problem, describe the magnitude of the damage, and advocate the immediate installation of a plant to remove the contaminant. Simultaneously, the health system initiated a surveillance programme of drinking-water quality that is in place until today, determining arsenic at multiple points of the city, at different times, every day (18).

Characterization of arsenic risk: lessons learnt

Excess of lung cancer in the general population was caused by exposure to arsenic in drinking-water

In the early 1990s—30 years after the initial arsenic exposures and 15 years after installing treatment plants—high rates of lung cancer in Region II sparked new concerns among health officials and the public. The suspected cause was airborne arsenic coming from mining activities. At that time, the people did not associate ingested arsenic with lung cancer (40). In 1994, Chilean research agencies (41) funded a multidisciplinary team, which in just three years, demonstrated that the principal source of arsenic exposure for the general population was naturally-occurring arsenic in drinking-water and that past exposure was the main cause of the current excess of lung cancer in Region II (14,33-35).

Results of various studies showed that most population of Region II had similar levels of arsenic in air and food as the rest of Chile; content of arsenic in drinking-

water was the main difference among the regions (20,42). Although some mining areas of Region II had elevated levels of arsenic in air, as in the copper mine at Chuquicamata, only 3% of its inhabitants presented arsenicosis compared to 50% of people in the coastal city of Tocopilla, the latter with high levels of arsenic in water (39). This review, which has focused principally on exposure to arsenic in the general population in Chile, did not consider workers in the copper smelters who are exposed to inorganic arsenic in the air, which is known to increase the risk of lung cancer (43,44). When the contamination of drinking-water has been solved in the whole of Region II, arsenic in the air will emerge as a public-health priority in some mining areas and cities of Region II (i.e. the city of Calama).

Arsenic interacts with smoking to increase the risk of lung cancer

In 1981, Pershagen demonstrated the multiplicative effects of tobacco and arsenic exposure in air among smelter workers (45). Results of our studies showed a significant interaction between smoking and arsenic exposure in drinking-water (14). Rates of smoking and lung cancer in Chile are increasing countrywide; it is possible that the rate of lung cancer in II Region will not decrease because the past exposure to arsenic will interact with the growing smoking rates. An active anti-smoking campaign should be put in place in the region.

Paradoxical effect of arsenic in risk of bladder cancer

In our case-control study of bladder cancer (manuscript in preparation), we found that bladder cancer odds ratio (OR) for arsenic in drinking-water were smaller (OR: 2.2, 95% confidence interval [CI] 1.2-4.3) than the SMR for bladder cancer seen in Antofagasta (SMR: 743, 95% CI 527.1-1,038.5). We hypothesize that arsenic may not increase the incidence of bladder cancer but cause a more serious evolution of the disease (33-35); further research is needed to clarify this issue.

Arsenic may interact with nutritional status to increase health effects

Cases of bronchopneumonia among arsenic-exposed children have been associated with severe malnutrition (29). In his description of arsenicosis in Antofagasta, Zaldivar concluded that malnutrition interacted with arsenic, increasing the prevalence of bronchiectasis and recurrent bronchoneumonia (31). Mazunder, in 1998, found that skin lesions were a little higher in people with poor nutrition, although not statistically significant (46). A recent case-control study in West Bengal demonstrated that low intake of calcium, animal protein, folate, and fibre increased susceptibility to arsenic-caused skin

lesions, doubling the risk in the lowest intake (47). Studies in Chile have not provided sound data about the association between nutrition and arsenic due to lack of nutritional research in the high-risk period and high uncertainty in current research based on retrospective assessment of nutrition.

Skin lesions present a dose-response relationship with arsenic exposure; effects of arsenic may be partly reverted

In the high-exposure period, 35% of the population of Antofagasta presented skin lesions (17,28,39). Zaldivar estimated that the incidence rate of skin lesions in 1968 was 145.5 and 168 per 100,000 males and females respectively, dropping to 9 and 10 per 100,000 respectively in 1971, only one year after the operation of the treatment plant (29). Soon after treatment was in place, a marked reduction in arsenicosis and respiratory symptoms was also described by Borgoño (27). Concentration of arsenic in drinking-water has also been associated with skin lesions in a dose-response manner in West Bengal, India (46,48-49), and Mexico (50). Recent studies have demonstrated that the peripheral vascular effects seen at exposures of 180 μg/L of arsenic are also reverted after arsenic dropped to 37 μg/L (51). Dose-response and reversal of effects (skin, respiratory, and vascular) after removal of the agent are strong causal criteria not frequently found in environmental research.

Skin lesions may be a marker of arsenic susceptibility

Coldness of fingers, abdominal cramps, and respiratory signs in Chile were significantly higher among people who presented arsenicosis of the skin (28,39). Mazumder, also with same observation in West Bengal, demonstrated that respiratory symptoms were associated with skin arsenicosis (52). Among patients treated with Fowler's solution, the excess of bladder cancer only occurred in cases with arsenicosis (53). In Chile, 44% of lung cancer cases and 8% of controls presented skin lesions; 3.3% of cases and 0.2% of controls had previously been diagnosed with skin cancer (54). People with skin lesions deserve medical advice to avoid other risk factors and proper follow-up for early detection of an arsenic-associated malignancy.

Andean communities do not differ in susceptibility to arsenic

Some researchers reported that Andean communities exposed to high levels of arsenic did not present arsenicosis or cancers when assessed in cross-prevalence studies, concluding that indigenous people may have some genetic resistance to arsenic (55,56). Nevertheless, a few pieces of information indicate that they, in fact, may have the same risk as the general population in

Region II: in our case-control studies of lung and bladder cancers (14,33-35), we identified two cases of bladder cancer and six of lung cancer in individuals who had lived in San Pedro; twice as many as expected (unpublished observations). Smith showed that skin lesions were as frequent as expected among this population (57), and results of methylation studies suggest that their metabolism is similar to that of other populations (58-59). Some data suggest that methylation patterns aggregate in families and are correlated in siblings (r=0.3-0.8) (60), which could, in part, explain why skin lesions also aggregate in families (57). Although the high risk may not be evident in small communities, public-health officers should offer them the same protection as they do in large urban communities.

Health effects are very similar in different ethnic and cultural groups

Populations exposed to arsenic in drinking-water have been reported in the USA (61,62), Mexico (50,63,64), Argentina (65-67), India (52,68), Bangladesh (69-71), Taiwan (72-77), and Japan (78). Skin, vascular and respiratory effects, and cancers seen in this Chilean population have also been described in those populations (79-84). We have not seen an increase in risk of diabetes, hypertension, or neurological diseases described by others (69,75,83). Data from the 2003 National Health Survey in Chile showed that the prevalence of hypertension and diabetes in Region II are either similar to or lower than the national average, adjusting for age and sex (85). We have not studied the impact of arsenic on the intellectual function of children, which some authors have recently described (86). We do not have evidence regarding the effects of calcium, animal protein, folate, and fibre in susceptibility to arsenic-induced skin lesions as others have postulated (47). We have seen peripheral necrosis (27-30) but have not found the Blackfoot disease as described in Taiwan (87). Some differences in reported health effects may be due to study design and some may be real, and due to interaction of arsenic with genetic and environmental factors.

Biomarkers of arsenic

The Andean populations exposed to arsenic have an increase in micronuclei in exfoliated bladder cells, indicating that arsenic is inducing genetic damage (88-89) as also described in West Bengal (90) and reviewed by Chen (91). A recent report described elevated—but not statistically significant—micronuclei in buccal cells in exposed populations in Region II; micronuclei were unrelated to ethnic background (92). The differences in findings among studies may be related to variations in the study methods, the type of tissue studied, or to the chemical form of arsenic. It is necessary to learn more at the molecular level to identify early biological markers of exposure, susceptibility, and results.

Current standard of 50 µg/L of arsenic in drinking-water may not be a safe level for Chile

Our studies showed a decrease in birth-weight (-57 g) among newborns of mothers exposed to water with 40 µg/L of arsenic (93). We recommend that the arsenic-removal plants currently operating in Chile continue to be closely monitored to optimize, in a sustained manner, the efficiency of the present arsenic-removal processes. These have very recently been shown to be capable of producing water with 10 µg/L residual arsenic, i.e. at the maximum concentration recommended by the World Health Organization (94). The key parameters in efficient removal of arsenic are strict control of pH and accurate doses of the coagulant agent, controls for which technology is available (95,96).

Arsenic is not a new contaminant in Chile. The original American settlers of these lands were exposed to this chemical element. Arsenic has been being removed from drinking-water in the northern region for 35 years using coagulation processes with simple technology and at a reasonable cost. This has enabled the control of arsenic exposure in drinking-water in urban areas, reducing it between 1988 and 2003 to concentrations averaging 40 µg/L. More recently (2004-2005), arsenic levels have fallen to 10 µg/L through the automatization of the dosage levels of chemical agents—Cl_2 and $FeCl_3$—and better control of the pH of water treated. Despite our broad arsenic-removal experience and the great progress achieved to date, it has not yet been possible to resolve satisfactorily the problem of arsenic exposure in drinking-water of small, isolated Andean communities. These small communities of people in the northern Altiplano, until recently, continued without adequate solution due to technical or economic limitations. In our field work, it has become apparent that removal of arsenic is just one of the problems for which these populations require solutions. First and foremost, they need to be able to count on sound programmes of environmental sanitation and health education which could facilitate the acceptance and commitment of the community to the programme of arsenic removal from their water.

REFERENCES

1. Henriquez A. Causas del alto contenido de arsénico en los ríos Toconce y Hojalar. Santiago: Instituto de Investigaciones Geológicas, 1968. 10 p.

2. Alonso H. Arsenic enrichment in superficial waters, II Region Northern Chile. *In*: Sancha A, editor. Proceedings of the International Seminar on Arsenic in the Environment and Its Incidence on Health. Santiago: Universidad de Chile, 1992:101-8.

3. Romero L, Alonso H, Campano P, Fanfani L, Cida R, Dabea D *et al*. Arsenic enrichment in waters and sediments of the Río Loa (Second Región, Chile). *Appl Geochem* 2003;18:1399-416.

4. Enriquez H. Relación entre el contenido de arsénico en agua y el volcanismo cuaternario en Chile, Bolivia y Perú. Documentos Técnicos en Hidrología. Montevideo: United Nations Educational, Scientific and Cultural Organization, 1978:1-27.

5. Sancha A. Removing arsenic from drinking water. A brief review of some lessons learned and gaps arisen in Chilean water utilities. *In*: Chappell W, Abernathy C, Calderon R, Thomas D, editors. Arsenic exposure and health effects. New York: Elsevier B.V., 2003:471-81.

6. Arenas V, Jara M, Pastenes J, Escobar H, Salgado M. Monitoreo de arsénico en agua potable de la ciudad de Antofagasta. Proceedings Congreso Chileno de Ingenieria Sanitaria y Ambiental. *AIDIS* 1993:265-76.

7. Queirolo F, Stegen S, Mondaca J, Cortes R, Rojas R, Contreras C, Munoz L, Schwuger MJ, Ostapczuk P. Total arsenic, lead, cadmium, copper, and zinc in some salt rivers in the northern Andes of Antofagasta, Chile. *Sci Total Environ* 2000;255:85-95.

8. Munoz O, Diaz OP, Leyton I, Nunez N, Devesa V, Suner M *et al*. Vegetables collected in the cultivated Andean area of northern Chile: total and inorganic arsenic contents in raw vegetables. *J Agric Food Chem* 2002;50:642-7.

9. Diaz OP, Leyton I, Munoz O, Nunez N, Devesa V, Suner MA *et al*. Contribution of water, bread, and vegetables (raw and cooked) to dietary intake of inorganic arsenic in a rural village of Northern Chile. *J Agric Food Chem* 2004;52:1773-9.

10. Pastenes J, Acevedo E, Valladares I, Iracher R. Relaciones del contenido de arsénico en el sistema agua-suelo-planta en el valle de Chiu-Chiu. *Bol Soc Chil Quim* 1983;28:480-2.

11. De Gregori I, Fuentes E, Rojas M, Pinochet H, Potin-Gautier M. Monitoring of copper, arsenic and antimony levels in agricultural soils impacted and non-impacted by mining activities, from three regions in Chile. *J Environ Monit* 2003;5:287-95.

12. Queirolo F, Stegen S, Restovic M, Paz M, Ostapczuk P, Schwuger MJ *et al*. Total arsenic, lead, and cadmium levels in vegetables cultivated at the Andean villages of northern Chile. *Sci Total Environ* 2000; 255:75-84.

13. Chile, República de. Instituto Nacional de Estadísticas de Chile. CENSO 2002. (http://www.ine.cl/ine/canales/chile_estadistico/demografia_y_vitales/proyecciones/MenPrincOK.xls, accessed on 27 May 2006).

14. Ferreccio C, Gonzalez C, Milosavjlevic V, Marshall G, Sancha A, Smith A. Lung cancer and arsenic concentrations in drinking water in Chile. *Epidemiology* 2000;11:673-9.

15. Blakemore H. Historia del Ferrocarril de Antofagasta a Bolivia 1888-1988/ editor: Mercedes Gaju. Santiago: Impresos Universitarios S.A., 1996:103-14.

16. Borgoño J, Greiber R. Epidemiological study of arsenicism in the city of Antofagasta. *In*: Hemphill, editor. Trace Substance in Environmental Health Symposium. Columbia: University of Missouri, 1972:13-24.

17. Borgoño J, Greiber R. Epidemiologic study of arsenic poisoning in the city of Antofagasta (Estudio epidemiológico del arsenicismo en la ciudad de Antofagasta). *Rev Méd Chil* 1971;99:702-7.

18. Chile. Ministerio de Salud. SEREMI de Salud II Región. Laboratorio de acción sanitaria 1995-2004. Antofagasta: Ministerio de Salud, 2005. 10 p.

19. O'Ryan R, Sancha A. Controlling hazardous pollutants in a developing contex: the case of arsenic in Chile. *In*: Jay H. Lehr, editor. McGraw-Hill Standard handbook of environmental science, health and technology. Chapter 22. Global perspectives and trends. New York: McGraw-Hill, 2000;22:13-28.

20. Sancha A, Frenz P. Estimate of the current exposure of the urban population of northern Chile to arsenic. *In*: Reichard E, Hauchman F, Sancha A, editors. Interdisciplinary perspectives on drinking water risk assessment and management. Wallingford: International Association of Hydrological Sciencies, 2000:3-8. (IAHS Press publication no. 260).

21. Roychowdhury T, Tokunaga H, Ando M. Survey of arsenic and other heavy metals in food composites and drinking water and estimation of dietary intake by the villagers from an arsenic-affected area of West Bengal, India. *Sci Total Environ* 2003; 308:15-35.

22. Uchino T, Roychowdhury T, Ando M, Tokunaga H. Intake of arsenic from water, food composites and excretion through urine, hair from a studied population in West Bengal, India. *Food Chem Toxicol* 2006;44:455-61.

23. Del Razo LM, Garcia-Vargas GG, Garcia-Salcedo J, Sanmiguel MF, Rivera M, Hernandez MC *et al*. Arsenic levels in cooked food and assessment of adult dietary intake of arsenic in the Region Lagunera, Mexico. *Food Chem Toxicol* 2002;40:1423-31.

24. Schoof RA, Yost LJ, Eickhoff J, Crecelius EA, Cragin DW, Meacher DM *et al*. A market basket survey of inorganic arsenic in food. *Food Chem Toxicol* 1999;37:839-46.

25. Hopenhayn-Rich C, Browning S, Hertz-Picciotto I, Ferreccio C, Peralta C, Gibb H. Chronic arsenic exposure and risk of infant mortality in two areas of Chile. *Environ Health Perspect* 2000;108:667-73.

26. Bruning W. El problema del hidrarsenicismo crónico regional endémico en Antofagasta. *Rev Chile Ped* 1968;39:49-51.

27. Borgoño JM, Vicent P, Venturino H, Infante A. Arsenic in the drinking water of the city of Antofagasta: epidemiological and clinical study before and after the installation of a treatment pant. *Environ Health Perspect* 1977;19:103-5.

28. Puga F, Olivos P, Greiber R, Gonzalez I, Heras E, Barrera S *et al*. Hidroarsenicismo crónico en Antofagasta. Estudio epidemiológico y clínico. *Rev Chil Ped* 1973;44:215-22.

29. Zaldivar R. Arsenic contamination of drinking water and foodstuffs causing endemic chronic poisoning. *Beitr Path Bd* 1974;151:384-400.

30. Rosenberg H. Systemic arterial disease and chronic arsenicism in infants. *Arch Pathol* 1974;97:360-5.

31. Zaldivar R. A morbid condition involving cardio-vascular, broncopulmonary, digestive and neural lesions in children and young infants after dietary arsenic exposure. *Zbl Bakt, I Abt Orig B* 1980;170: 44-56.

32. Haynes R. The geographical distribution of mortality by cause in Chile. *Soc Sci Med* 1983;17:355-64.

33. Ferreccio C, González C, Milosavljevic V, Marshall G, Sancha A. Riesgo poblacional de cáncer por exposición a arsénico: Chile 1985-1992 (abstract) *in*: Book of proceedings of the III Congreso Chileno de Epide-miología, Viña del Mar. Santiago: Sociedad Chilena de Epidemiología, 1997:22.

34. Ferreccio C, González C, Milosavljevic V, Marshall G, Sancha A. Exposure to arsenic in air and drinking water: results of two epidemiologic studies in Chile. *In*: Arsenic: health effects, mechanisms of actions, and research issues. Hunt Valley, Maryland: National Cancer Institute, National Institute of Environmental Health Sciences, 1997:S14.

35. Ferreccio C, González C, Milosavljevic V, Marshall G, Sancha A. Exposure to arsenic in air and drinking water: results of a study in Chile. *In*: Reichard E, Hauchman F, Sancha A, editors. Interdisciplinary perspectives on drinking water risk assessment and managment. Wallingford: International Association of Hydrological Sciences, 2000:29-30. (IAHS Press publication no. 260).

36. Smith A, Goycolea M, Haque R, Biggs M. Marked increase in bladder and lung cancer mortality in a region of northern Chile due to arsenic in drinking water. *Am J Epidemiol* 1998;147:660-9.

37. Wiertz J, Gutierrez M. Arsenic: a Chilean approach in mining. *Environ Manage* 1996;4:20-21.

38. Sancha A. Removal of arsenic from drinking water supplies: Chilean experience. *J Wat Supply* 2000; 18:621-5.

39. Borgoño JM, Vicent P, Venturino H. Estudio clínico epidemiológico de hidroarsenicismo en la II region 1977. *Rev Med Chil* 1980;108:1039-48.

40. Rivara MI, Cebrian M, Corey G, Hernandez M, Romieu I. Cancer risk in an arsenic-contaminated area of Chile. *Toxicol Ind Health* 1997;13:321-38.

41. Fondo Nacional para el Desarrollo de la Ciencia y Tecnologia: Protección de la competitividad de los productos mineros en Chile. Santiago: Universidad de Chile, 1994. 30 p. (Proyecto FONDEF.2-24).

42. Caceres DD, Pino P, Montesinos N, Atalah E, Amigo H, Loomis D. Exposure to inorganic arsenic in drinking water and total urinary arsenic concentration in a Chilean population. *Environ Res* 2005;98:151-9.

43. Sancha A. Full-scale application of coagulation processes for arsenic removal in Chile: a successful case study. *In*: Chappell W, Abernathy C, Calderon R, editors. Arsenic exposure and health effects. New York: Elsevier Siences B.V., 1999:373-8.

44. Ferreccio C, González C, Solari J, Noder C. Cáncer broncopulmonar entre trabajadores expuestos a arsénico: un estudio de casos y controles. *Rev Méd Chile* 1996;124:119-23.

45. Pershagen G, Wall S, Taube A, Linnman L. On the interaction between occupational exposure and smoking and its relationship to lung cancer. *Scand J Work Environ Health* 1981;7:302-9.

46. Mazumder G, Haque R, Ghosh N, De B, Santra A, Chakraborti D *et al*. Arsenic levels in drinking water and prevalence of skin lesion in West Bengal, India. *Int J Epidemiol* 1998;27:871-7.

47. Mitra SM, Guha Mazumder DN, Basu A, Block G, Haque R, Samanta S *et al*. Nutritional factors and susceptibility to arsenic-caused skin lesions in West Bengal, India. *Environ Health Perspect* 2004;112: 1104-9.

48. Chakraborty AK, Saha KC. Arsenical dermatosis from tubewell water in West Bengal. *Indian J Med Res* 1987;85:326-34.

49. Haque R, Mazumder DN, Samanta S, Ghosh N, Kalman D, Smith MM *et al*. Arsenic in drinking water and skin lesions: dose-response data from West Bengal, India. *Epidemiology* 2003;14:174-82.

50. Cebrian ME, Albores A, Aguilar M, Blakely E. Chronic arsenic poisoning in the north of Mexico. *Hum Toxicol* 1983;2:121-33.

51. Pi J, Yamauchi H, Sun G, Yoshida T, Aikawa H, Fujimoto W *et al*. Vascular dysfunction in patients with chronic arsenosis can be reversed by reduction of arsenic exposure. *Environ Health Perspect* 2005; 113:339-41.

52. Mazumder G, Haque R, Ghosh N, De B, Santra A, Chakraborti D *et al*. Arsenic in drinking water and prevalence of respiratory effects in West Bengal, India. *Int J Epidemiol* 2000;29:1047-52.

53. Cuzick J, Sasieni P, Evans S. Ingested arsenic, keratoses, and bladder cancer. *Am J Epidemiol* 1992; 136:417-21.

54. Ferreccio C, González C, Milosavlevic V, Marshall G, Sancha AM. Lung cancer and arsenic exposure in drinking water: a case-control study in northern Chile. *Cad Saúde Publica Rio de Janeiro* 1998;14 (Suppl 3):193-8.

55. Aposhian HV, Arroyo A, Cebrian ME, del Razo LM, Hurbut KM, Dart RC *et al*. DMPS-arsenic challenge test. I: Increased urinary excretion of monomethylarsonic acid in humans given dimercaptopropane sulfonate. *J Pharmacol Exp Ther* 1997;282:192-200.

56. Kaiser J. Toxicologists shed new light on old poisons. *Science* 1993;279:1850-1.

57. Smith A, Arroyo A, Mazumder G, Kosnett M, Hernandez A, Beeris M *et al*. Arsenic induced skin lesions among Atacameño people in northern Chile despite good nutrition and centuries exposure. *Environ Health Perspect* 2000;108:617-20.

58. Hopenhayn-Rich C, Biggs ML, Kalman DA, Moore LE, Smith AH. Arsenic methylation patterns before and after changing from high to lower concentrations of arsenic in drinking water. *Environ Health Perspect* 1996;104:1200-7.

59. Hopenhayn-Rich C, Biggs ML, Smith AH, Kalman DA, Moore LE. Methylation study of population environmentally exposed to arsenic in drinking water. *Environ Health Perspect* 1996;104:620-8.

60. Chung JS, Kalman DA, Moore LE, Kosnett MJ, Arroyo AP, Beeris M *et al*. Family correlations of arsenic methylation patterns in children and parents exposed to high concentration of arsenic in drinking water. *Environ Health Perspect* 2002;110:729-33.

61. Bates MN, Smith AH, Cantor KP. Case-control study of bladder cancer and arsenic in drinking water. *Am J Epidemiol* 1995;141:523-30.

62. Calderon RL. Drinking water arsenic in the United States: a cohort mortality study. *Environ Health Perspect* 1999;107:359-65.

63. Chávez A, Perez C, Tovar E, Garmilla M. Estudios en una comunidad con arsenicismo cronico endemico. *Salud Publ Mex* 1964;8:435-41.

64. Wyatt CJ, Fimbres C, Romo L, Mendez RO, Grijalva M. Incidence of heavy metal contamination in water supplies in northern Mexico. *Environ Res* 1998; 76:114-9.

65. Hopenhayn-Rich C, Biggs ML, Fuchs A, Bergoglio R, Tello EE, Nicolli H *et al*. Bladder cancer mortality associated with arsenic in drinking water in Argentina. *Epidemiology* 1996;7:117-24.

66. Hopenhayn-Rich C, Biggs ML, Smith AH. Lung and kidney cancer mortality associated with arsenic in drinking water in Córdoba, Argentina. *Int J Epidemiol* 1998;27:561-9.

67. Concha G, Nermell B, Vahter MV. Metabolism of inorganic arsenic in children with chronic high arsenic exposure in northern Argentina. *Environ Health Perspect* 1998;106:355-9.

68. De BK, Majumdar D, Sen S, Guru S, Kundu S. Pulmonary involvement in chronic arsenic poisoning from drinking contaminated ground-water. *J Assoc Physicians India* 2004;52:395-400.

69. Rahman M, Tondel M, Ahmad SA, Axelson O. Diabetes mellitus associated with arsenic exposure in Bangladesh. *Am J Epidemiol* 1998;148:198-203.

70. Rahman MM, Sengupta MK, Ahamed S, Chowdhury UK, Lodh D, Hossain A *et al*. Arsenic contamination of groundwater and its health impact on residents in a village in West Bengal, India. *Bull World Health Organ* 2005;83:49-62.

71. Milton AH, Rahman M. Respiratory effects and arsenic contaminated well water in Bangladesh. *Int J Environ Health Res* 2002;12:175-9.

72. 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. *Natl cancer Inst* 1968;40:453-63.

73. Chiang HS, Guo HR, Hong CL, Lin SM, Lee EF. The incidence of bladder cancer in the blackfoot disease endemic area in Taiwan. *Br J Urology* 1993; 71:274-8.

74. Guo HR, Chiang HS, Hu H, Lipsitz SR, Monson RR. Arsenic in drinking water and urinary cancers: a preliminary report. *In*: Chappell WR, Abernathy CO, Cothern CR, editors. Arsenic: exposure and health. Northwood: Science and Technology Letters, 1994: 119-28.

75. Chen CJ, Hsueh YM, Lai MS, Shyu P, Chen SY, Wu M *et al*. Increased prevalence of hypertension and long-term arsenic exposure. *Hypertension* 1995; 25:53-60.

76. Chiou HY, Hsueh YM, Liaw KF, Horng SF, Chiang MH, Pu YS *et al*. Incidence of internal cancers and ingested inorganic arsenic: a seven-year follow-up study in Taiwan. *Cancer Res* 1995;55:1296-1300.

77. Chiou HY, Huang WI, Su CL, Chang SF, Hsu, YH, Chen CJ. Dose-response relationship between prevalence of cerebrovascular disease and ingested inorganic arsenic. *Stroke* 1997;28:1717-23.

78. Tsuda T, Babazono A, Yamamoto E, Kurumatani N, Mino Y, Ogawa T. Ingested arsenic and internal cancer: a historical cohort study followed for 33 years. *Am J Epidemiol* 1995;141:198-209.

79. International Agency for Research on Cancer. Some drinking water disinfectants and contaminants, including arsenic. V. 84. Lyon: International Agency for Research on Cancer, 2004:97-156.

80. Wang CH, Jeng JS, Yip PK, Chen CL, Hsu LI, Hsueh YM *et al*. Biological gradient between long-term arsenic exposure and carotid atherosclerosis. *Circulation* 2002;105:1804-9.

81. Yu HS, Lee CH, Chen GS. Peripheral vascular diseases resulting from chronic arsenical poisoning. *J Dermatol* 2002;29:123-30.

82. Chen CJ. Blackfoot disease (letter). *Lancet* 1990; 336:442.

83. Rahman M, Tondel M, Ahmad SA, Chowdhury IA, Faruquee MH, Axelson O. Hypertension and arsenic exposure in Bangladesh. *Hypertension* 1999; 33:74-8.

84. Tchounwou PB, Centeno JA, Patlolla AK. Arsenic toxicity, mutagenesis, and carcinogenesis—a health risk assessment and management approach. *Mol Cell Biochem* 2004;255:47-55.

85. Chile. Ministerio de Salud de Chile. Departamento de Epidemiología. Informe final. Santiago: Encuesta Nacional de Salud, 2003. (http://epi.minsal.cl/epi/html/invest/ENS/ENS.ht m, accessed on 27 May 2006).

86. Wasserman GA, Liu X, Parvez F, Ahsan H, Factor-Litvak P, van Geen A *et al*. Water arsenic exposure and children's intellectual function in Araihazar, Bangladesh. *Environ Health Perspect* 2004;112: 1329-33.

87. Chen CJ, Chuang YC, You SL, Lin HY. A retrospective study on malignant neoplasms of bladder, lung and liver in blackfoot disease endemic area in Taiwan. *Br J Cancer* 1986;53:399-405.

88. Moore LE, Smith AH, Hopenhayn-Rich C, Biggs ML, Kalman DA, Smith MT. Decrease in bladder cell micronucleous prevalence after intervention to lower the concentration of arsenic in drinking water. *Cancer Epidemiol Biomarkers Prev* 1997; 6:105-6.

89. Moore LE, Smith AH, Hopenhayn-Rich C, Biggs ML, Kaman DA, Smith MT. Micronuclei in exfoliated bladder cells among individuals chronically exposed to arsenic in drinking water. *Cancer Epidemiol Biomarkers Prev* 1997;6:31-6.

90. Basu A, Ghosh P, Das JK, Banerjee A, Ray K, Giri AK. Micronuclei as biomarkers of carcinogen exposure in populations exposed to arsenic through drinking water in West Bengal, India: a comparative study in three cell types. *Cancer Epidemiol Biomarkers Prev* 2004;13:820-7.

91. Chen CJ, Hsu LI, Wang CH, Shih WL, Hsu YH, Tseng MP *et al*. Biomarkers if exposure, effect, and susceptibility of arsenic-induced health hazards in Taiwan. *Toxicol Appl Pharmacol* 2005;206:198-206.

92. Martinez V, Creus A, Venegas W, Arroyo A, Beck JP, Gebel TW *et al*. Micronuclei assessment in buccal cells of people environmentally exposed to arsenic in northern Chile. *Toxicol Lett* 2005;155:319-27.

93. Hopenhayn-Rich C, Ferreccio C, Browning S, Huang B, Peralta C, Gibb H *et al*. Arsenic exposure from drinking water and birth weight. *Epidemiology* 2003;14:593-602.

94. World Health Organization. Guidelines for drinking water quality. Geneva: World Health Organization, 1984. 2 v.

95. Hering J, Chen P, Wilkie J, Elimelech M. Arsenic removal from drinking water during coagulation. *J Environ Engineering* 1997;123:800.

96. Edwards M. Chemistry of arsenic removal during coagulation and Fe-Mn oxidation. *J Am Water Works Assoc* 1994;86:64-78.