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Review

Medical geology of arsenic, selenium and thallium in China

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ABSTRACT

Arsenic (As), selenium (Se) and thallium (Tl) are three trace metals (metalloids) of high concern in China because deficiency or excess expose can cause a range of endemic diseases, such as endemic arsenism, selenosis, Keshan disease (KD), Kashin–Beck disease (KBD) and thallotoxicosis. These specific endemic diseases were attributable for overabundance or deficiency (mainly referring to selenium) of these three elements in the local environment as a result of natural geochemical processes and/or anthropologic activities. The geochemistry and human health impacts of these three trace elements have been intensively studied since the 1970s in China, in terms of geochemical sources, distribution, transportation, health impact pathways, and prevention/remediation measures. Endemic arsenism in China are induced from the exposures of high As in either drinking water or domestic combustion of As-rich coals. Both endemic selenium deficiency and selenosis occurred in China. The KD and KBD were related to the deficiency of Se in the low-Se geological belt with Se contents in soil less than 0.125 mg/kg stretching from northeast to southwest of China. Endemic selenosis occurred in areas with high Se concentrations in soils derived from the Se-enriched black carbonaceous siliceous rocks, carbonaceous shale and slate. Endemic Tl poisoning occurred in southwestern China due to Tl contamination in local drinking water and vegetables surrounding the Tl-rich sulfide mineralized areas. Some measures have been taken to control and remedy the endemic diseases with significant effects in reducing health risk and damage of As, Se and Tl. However, the states of the endemic diseases of As, Se and Tl in China are still serious in some areas, and substantial research efforts regarding the health impacts of these elements are further required. This paper reviews the progress of medical geology of As, Se and Tl in China, and provides with some outlooks for future research directions.

Contents

1. Introduction

Deficiency and toxicity of trace elements can cause a range of endemic diseases. Arsenic (As), selenium (Se) and thallium (Tl) are important metal (metalloid) elements, which can induce some endemic diseases, such as endemic arsenism, selenosis, Keshan disease, and thallotoxicosis due to their overabundances or deficiencies in the local environments. In general, thallium is a toxic element, while selenium is an essential element but can be toxic in excessive level. Arsenic is debated whether it is essential or not to human health, but is known to be toxic. These three trace metals can be enriched in the environment through natural geochemical processes or anthropologic activities, and result in adverse impacts on human health. Many researches on the geochemical sources, distribution,

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Fig. 1. Map showing the areas distributing endemic arsenism in China (after Xia and Liu (2004), and Jin et al. (2003)).

transfer and transportation, exposure paths and adverse health impacts of the three elements have been conducted since the 1970s in China. However, some of the research outcomes are not well known in the international scientific communities because most of the documents were published in Chinese journals, especially in the 20th century. The monograph of "The Atlas of Endemic Diseases and Their Environments in the People's Republic of China" (Tan, 1989) was the main summary works on the distribution of endemic diseases and their relationships with environmental conditions in China before the 1990s. The problems of endemic diseases caused by metals (metalloids) have continued to attract increasing concerns of governments and scientists in China, and many effective measures have been taken to control and remedy the endemic diseases. However, the status of the endemic diseases of As, Se and Tl in China are still serious in some regions, and some new endemic areas are emerging in recent years. The purpose of this paper is to review the research progress of the human health impacts of these elements in China, particularly from the perspective of medical geology.

2. Arsenic impacts on human health in China

Except for some occupational exposure (Liu et al., 2001), high arsenic exposures in China are mainly from drinking water with elevated arsenic (mainly groundwater), indoor burning of high arsenic coal, and arsenic-bearing minerals mining. The spatial distribution of endemic arsenism in China is shown in Fig. 1.

Endemic arsenism via arsenic-rich drinking water (mainly groundwater) was first reported in Taiwan in 1968, then in Xinjiang in 1980, Inner Mongolia in 1989, Shanxi Province in 1994, and Ningxia, Jilin, Qinghai, Anhui and certain suburbs of Beijing in the 2000s (Xia and Liu, 2004);. In the mainland of China, more than 500,000 persons in 1047 villages of eight provinces are exposed to high arsenic drinking water (As>0.05 mg/L), and almost 8000 arsenism patients were diagnosed (Jin et al., 2003). According to the new national standard (GB 5749-2006) for arsenic concentration in drinking water, which decreases acceptable exposure from 0.05 mg/L to 0.01 mg/L, thus increasing the population defined as being at risk of arsenic exposure from drinking water in China.

In Taiwan, high groundwater arsenic concentrations have been found in both the southwest and northeast parts of the island (Tseng et al., 1968; Hsu et al., 1997). The arsenic concentrations in most groundwater samples from the arsenism prevalence areas in Taiwan were between 0.4 mg/L and 0.6 mg/L (Kuo, 1968; Tseng et al., 1968). In China mainland, high groundwater arsenic concentrations have been found mainly in the northern China (Fig. 1). Arsenic concentration in Shanyin County, the worst affected of the regions in Shanxi Province, is as high as 4.4 mg/L (Sun et al., 2001). Although the hydrogeological and geochemical conditions in the local affected aquifers vary, some specific features are apparent. Aquifers at high risk appear to be those overlain in large alluvial and delta plain sediments as well as large inland basins, the latter especially those formed in arid and semi-arid areas. In each case, the Quaternary aquifers are particularly prone to develop and preserve high-arsenic in groundwater (Smedley and Kinniburgh, 2005). Studies show that arsenic is present largely as As(III) in the high-arsenic groundwater with highly reducing conditions (Chen et al., 1994; Luo et al., 1997). The highly reducing and alkaline conditions favor arsenic desorption from oxide/oxyhydroxide surfaces, thereby increase the concentrations of As in the aqueous phase (Xie et al., 2008; Y.X. Wang et al., 2009).

Endemic arsenism due to burning high arsenic coal indoor have been found in Guizhou and Shaanxi provinces in China since 1953 and 2001, respectively (Jin et al., 2003; Zheng et al., 2005). Although As contents in the majority of the coals in Guizhou Province are similar to those in other parts of China (Wang et al., 2006), some local coals contain high As up to 3.5 wt.% (Ding et al., 2001). The high arsenic coals are in the Longtan formation of Late Permian, an alternating marine and terrestrial formation. The frequent eruptions of volcanic ashes during the Late Permian age (Wang, 1996; Chen et al., 2003) and epigenetic low-temperature hydrothermal fluids penetrating into coal seams after coal-formation have led to the geochemical and mineralogical anomalies of coal (Dai et al., 2004, 2005). Near the high As coals, some Au deposits as well as Sb, Hg, and Tl mineralization occurred. Dai et al. (2006) observed that the main carrier of As in the coal samples is an epigenetic getchellite

($AsSbS_3$) rather than syngenetic pyrite and clay minerals. Getchellite occurs only in the veined kaolinite of hydrothermal origin (Dai et al., 2006). This indicates that the high As, Sb, Hg, and Tl in coal are derived from an arsenic- and antimony-rich hydrothermal fluid. In the endemic prevalence areas, for daily domestic cooking and crop drying the high arsenic coals are burned indoors without chimneys. As a result, the polluted indoor air (As at 0.072 ± 0.043 mg/m^3 in bed room, 0.26 ± 0.18 mg/m^3 in living room, and 0.46 ± 0.30 mg/m^3 in kitchen), corn (As 5–20 mg/kg), chili (As 100–800 mg/kg) and other foods became the main sources of arsenic exposure (An et al., 2004; Zheng et al., 2005). About 48,000 people were at the risk of high arsenic exposure from high arsenic coal combustion (As>100 mg/kg) and 2402 patients were diagnosed to be chronic arsenism in 8 counties of Guizhou and Shaanxi provinces, but most of the cases occurred in Guizhou Province (Jin et al., 2003).

Arsenic is usually associated with gold, copper, lead, zinc, tin, nickel and cobalt in sulfide deposits. It could be released to the environment during the mining process. Until 2003 the amount of arsenic mined in China was reached to 1392 kt, 70% of which was discharged into tailings (Xiao et al., 2008). The deposits enriched with arsenic are mainly distributed in Yunnan, Guangxi and Hunan provinces, where the local population is at high risk to arsenic exposure from ground water leaching (Lu et al., 2000; Lu and Zhang, 2005; Xie et al., 2005; Xiao et al., 2008).

Arsenic concentrations in biological materials, such as hair, urine, nail, or blood are usually used to be biomarkers to evaluate the levels of arsenic exposure. The biomarkers could be dependent on various environmental conditions, and on individual variation, but the average concentrations in the biomarkers from endemic arsenism areas are usually much higher than those from the control areas. Arsenic concentrations in the biomarkers from some endemic arsenism areas and the control areas in China are shown in Table 1. According to an investigation on arsenic concentration in urine, hair and nail from three arsenic polluted areas, arsenic concentrations in nail and hair from the polluted areas were significantly higher than those form the control area except urine. Therefore, hair and nail are thought to be better biomarkers for arsenic exposure than urine (Wu et al., 1987). The total arsenic concentrations in biomarkers are affected by many factors. Therefore, arsenic species including inorganic arsenic (iAs), monomethylated arsenic (MMA), dimethylated arsenic (DMA), arsenobetaine (AsB) and As/creatinine were also tested to evaluate the exposure level and their health effects (Shraim et al., 2003). Some researches further suggested that urinary malondialdehyde (MDA) and porphyrins could be as useful biomarkers rather than the total arsenic for arsenic exposure from coal burning because positive correlations were observed between urinary As and porphyrins, MDA (Xie et al., 2001; Ng et al., 2005; J.P. Wang et al., 2009).

A large number of epidemiological investigations in China have confirmed that high arsenic exposure is associated with skin lesions (Tseng, 1997; Wang et al., 2002; Yang et al., 2002), peripheral vascular disease (Ma et al., 1995), polyneuropathy (Li et al., 1993), hypertension (Chen et al., 1995), black foot disease (Tseng, 1997) and high risk of skin cancer and other cancers (Luo et al., 1995; Chiou and Xue, 1996; Tseng, 1997). Among the diseases, skin lesions are one of the most common features of chronic arsenic poisoning, and are used as diagnostic criteria for endemic arsenism in Inner Mongolia, China (Guo et al., 2001). With high arsenic exposure from drinking water or coal burning, the grade of arsenism is determined by the degree of skin pigmentation, depigmentation and hyperkerotosis on palms of hands and soles of the feet (Sun, 2004). Some other Chinese researchers have also proved that arsenic exposure damaged pulmonary function (Chen et al., 1997), renal function (Hong et al., 2007), immune function (Li et al., 2007), antioxidation ability (G.L. Zhang et al., 1999), mental health (Fujino et al., 2004), cultured osteoblasts (Tang et al., 2009), and DNA synthesis and repair function (Zhang et al., 2000). Except for the adverse effects on human health from arsenic exposure, many researchers in China have also suggested that arsenic trioxide (As_2O_3) showed therapeutic effects on acute promyelocytic leukemia (APL) (Lu et al., 1999), solid tumors such as malignant lymphoma (Zhang and Nie, 2001), gallbladder carcinoma (Ai et al., 2007), ovarian carcinoma (Zhang and Wang, 2006), and cervical cancer (Yu et al., 2007).

3. Selenium impacts on human health in China

Selenium is essential to human health in trace amounts, but harmful in excessive levels. The range between dietary deficiency (<40 μg/day) and

Table 1
Arsenic concentrations in the biological materials from some endemic arsenism areas and the control areas in China.

Location and arsenism type	Biomarker	Average As concentration	References
Whole China	Hair	0.571 ± 1.213 mg/kg (n = 1313; normal population)	Yang et al. (1996)
Tongyu, Jilin (Drinking-water-type)	Hair	4.4 mg/kg (n = 33; suspected arsenism group)	Tang et al. (2001)
	Urine	0.16 mg/l (n = 132; suspected arsenism group)	
Xinjiang	Hair	1.68 mg/kg (arsenism area group)	Jin et al. (2003)
		0.65 mg/kg (control group)	
Beijing (Drinking-water-type)	Hair	1.54 mg/kg (arsenism area group)	
		0.57 mg/kg (control group)	
Bameng, Inner Mongolia (Drinking-water-type)	Urine	135.64 ± 2.73 μg/l (n = 214; arsenism area group)	Dong and Liu (2006)
	Blood	11.02 ± 3.17 μg/l (n = 63; control group)	
		16.04 ± 2.81 μg/l (n = 108; arsenism area group)	
		1.98 ± 6.52 μg/l (n = 84; control group)	
Guizhou (Coal-burning-type)	Hair	53.5 ± 15.9 mg/kg (Village A with arsenosis group)	Zheng et al. (2005)
	Urine	43.4 ± 33.5 mg/kg (Village B with arsenosis group)	
		48.6 ± 40.6 mg/kg (village C with arsenosis group)	
		10.8 ± 0.7 mg/kg (village D with arsenosis group)	
		0.60 ± 0.40 mg/kg (village A control group)	
		0.56 ± 0.55 mg/kg (village B control group)	
		1.34 ± 0.67 mg/l (Village A with arsenosis group)	
		1.07 ± 0.57 mg/l (Village B with arsenosis group)	
		1.24 ± 0.79 mg/l (village C with arsenosis group)	
		0.44 ± 0.27 mg/l (village D with arsenosis group)	
		0.07 ± 0.03 mg/l (village A control group)	
		0.06 ± 0.04 mg/l (village B control group)	
Anlong, Guizhou (Coal-burning-type)	Hair	27.76 ± 0.03 mg/kg (n = 112; arsenism patient group)	Zhong et al. (1999)
		0.70 ± 0.03 mg/kg (n = 46; control group)	
Nengshuijiang Hunan (Metals-mining)	Hair	4.21 mg/kg (n = 67; Antimony Mining Area group)	Liu et al. (2009)
		0.28 mg/kg (n = 22; control group from Guiyang)	

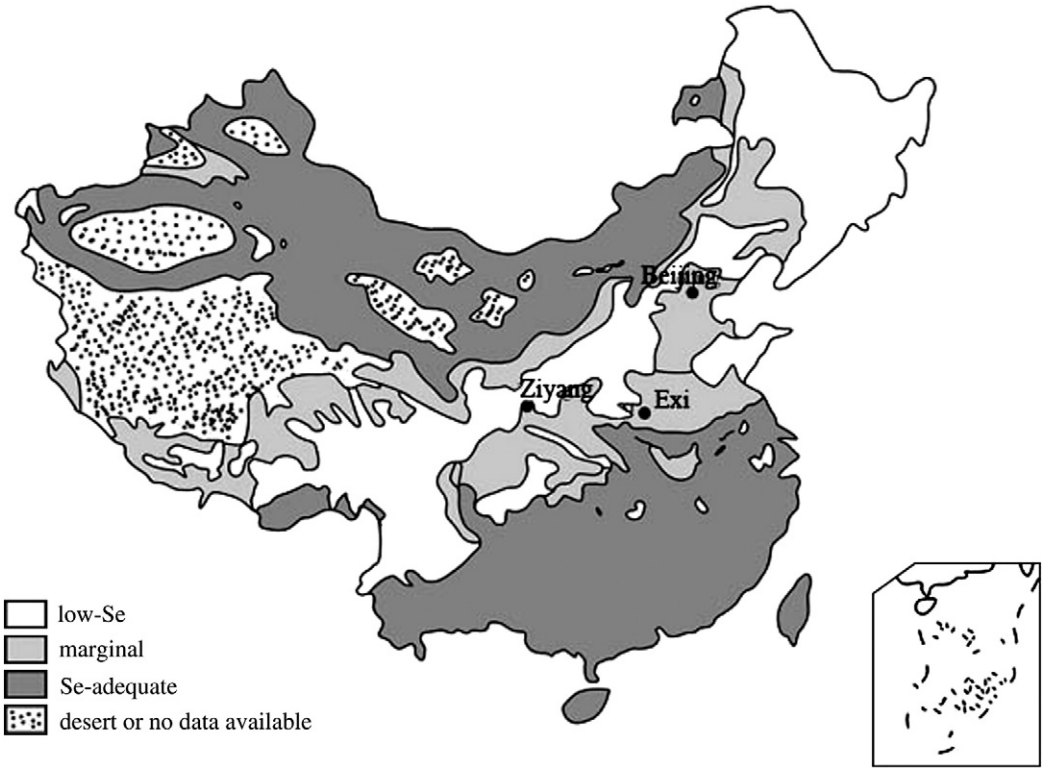

Fig. 2. Soil selenium distribution in China (low-Se: <0.125 mg/kg; marginal: 0.125–0.175 mg/kg; Se-adequate: 0.175–3.0 mg/kg. Exi and Ziyang are the Se-excessive areas where local soil Se content are higher than 3.0 mg/kg and have induced selenosis) (Tan, 1989; S.J. Li et al., 2009).

toxic levels (>400 μg/day) are narrow (Yang and Xia, 1995; WHO, 1996). Diet is the most important source of selenium for human. Geology exerts a fundamental control on the concentrations of selenium in soils, crops, and animals. Both the lowest and highest concentrations and the flux of Se in the environment are reported in China (Wang and Gao, 2001). As a result, both endemic selenium deficiency and selenosis occurred in China.

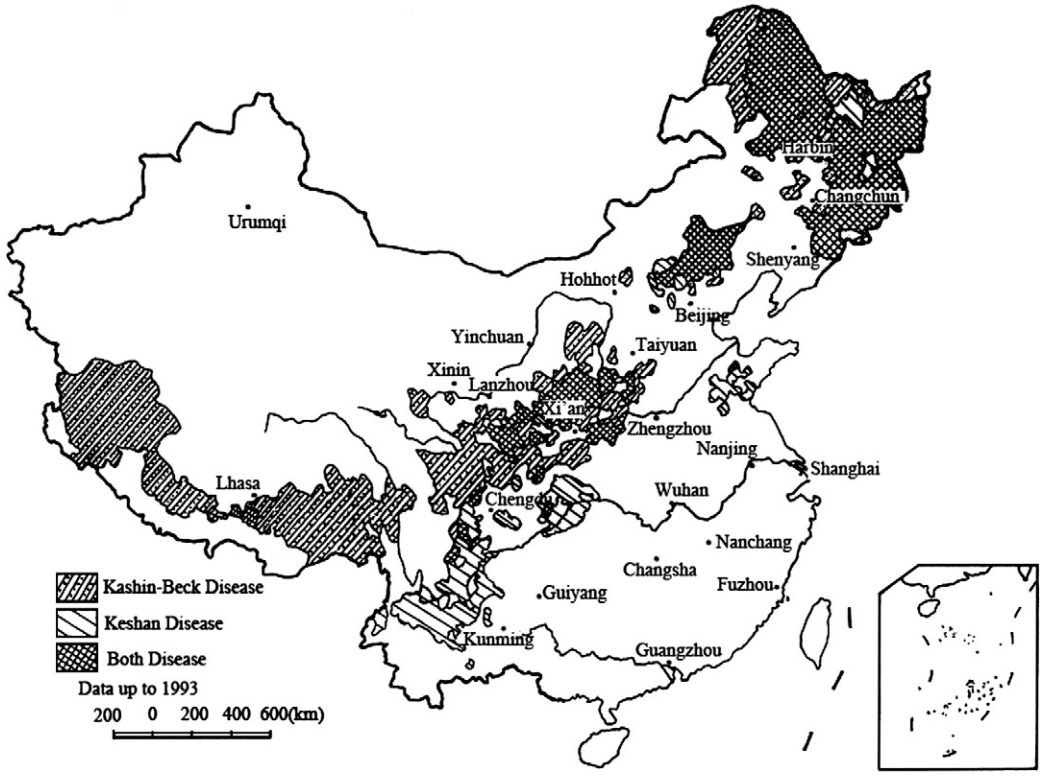

Fig. 3. Areas distribution of KD and KBD in China (by disease-affected counties) (Tan et al., 2002).

3.1. Health impacts of selenium deficiency in China

A low-Se belt, with Se contents in soil less than 0.125 mg/kg, stretching from Heilongjiang Province of Northeast China to Yunnan Province of Southwest China, was identified during the intensive geochemical surveys in the 1960s in China. Lots of epidemiological data on the human diseases, such as Kashin–Beck disease (KBD) and Keshan disease (KD) in this low-Se belt were obtained from the 1960s to 1970s. The data showed a close correlation between the concentration of selenium in the environment and incidences of the two diseases (Figs. 2 and 3) (Tan, 1989; Tan et al., 2002; S.J. Li et al., 2009). KBD and KD, especially KD, were later characterized as Se-responsive human diseases.

Keshan disease (KD) is an endemic cardiomyopathy (heart disease) that mainly affects children aged at 2 to 10, and to some extent women of child-bearing age (Hartikainen, 2005). The disease has been documented for over 100 years, but the name is derived from a serious outbreak in Keshan County, northeast China in 1935. This disease manifests as an acute insufficiency of the heart function or as a chronic moderate-to-severe heart enlargement and can result in death. It mainly occurred in the low-Se belt across China, and the affected areas were characterized by the remoteness of village locations, and a high proportion of farmers who were highly dependent on their local environment for their food supply. The local soils and crops contained quite low selenium. KD occurred in areas where grain crops contained <0.04 mg/kg of selenium and dietary selenium intakes was extremely low (e.g., 10–15 μg/day). Affected populations were characterized by low selenium contents in hair (<0.12 mg/kg) (Xu and Jiang, 1986; Tan, 1989; Yang and Xia, 1995) and in blood (<0.1–0.2 mg/L) (Gong and Ma, 2007). The worst affected years of KD were recorded in 1959, 1964, and 1970 when the annual prevalence exceeded 40 per 100,000 with more than 8000 cases and 1400–3000 deaths each year. During the 1980s the prevalence of KD dropped to less than 5 per 100,000 with less than 1000 cases reported annually (Tan, 1989). In recent years, the incidence of the disease in China has continued to decline as the results of the widespread selenium supplementation provided by the government and with residents increasingly less dependent on locally grown foodstuffs in the diet. Although the disease proved to be selenium responsive, the exact biological function of the element in the pathogenesis was still unclear. Lei et al. (2009) suggested that selenium deficiency in carriers with the glutathione peroxidase-1 (GPx-1) leucine-containing allele is associated with low GPx-1 enzyme activity, which may, in turn, increase the incidence of KD. However, the etiology of Keshan disease seems quite complicated. It is likely that numerous agents work synergistically to cause the disease (Li et al., 1985). Besides selenium, the deficiencies of vitamin E (Wang et al., 1991), calcium (Kang et al., 1992), molybdenum (Wang et al., 1982), and boron (Fang et al., 2002) were also considered to be the pathogenic factors.

Kashin–Beck disease (KBD), an endemic osteoarthropathy (stunting of feet and hands) causing deformity of the affected joints, is named after the Russian scientists who first described it between 1861 and 1899 (Fordyce, 2005). It is characterized by chronic disabling degenerative osteoarthrosis affecting the peripheral joints and the spine with apoptosis of the hyaline cartilage tissues. Impairment of movement in the extremities is commonly followed by bone development disturbances such as shortened fingers and toes and in more extreme cases, dwarfism (Tan, 1989). The etiology of KBD is still debated. In China, the pattern of disease incidence is concordant with KD in the north of the country (Fig. 3) and many reports suggested that the occurrence of KBD is related to the selenium-deficient environment (Li et al., 1982; Hou and Zhu, 1984; S.J. Li et al., 2009). However, other studies confirmed that there was no significant difference in selenium levels between the KBD patients and the control groups in the same area (Kang et al., 2006). This indicated that selenium deficiency could be one of the important but not the specific pathogenic factor for KBD. Other factors such as fungal contamination of grain, humic substances in drinking water and iodine-deficiency may also be the possible causes of KBD (Peng et al., 1999; Zhang et al., 2001). Nonetheless, selenium was confirmed to be a preventative factor in KBD in China (Wang et al., 1983; Zou et al., 2009).

Low selenium levels were also observed in biological samples such as hair, urine, blood or serum from patients with various cancers (Yu et al., 1985), including liver cancer (Wang et al., 1990; Lin et al., 1994), lung cancer (Chu et al., 1984; Pan and Zhang, 1998), galactophore cancer (He et al., 2003), esophageal cancer (Appleton et al., 2006), nasopharyngeal cancer (Pan et al., 1999), cervical cancer (Hou et al., 2006), colon cancer (Zhao et al., 1991), gastric cancer (Wu, 2007), cardiovascular disease (Jin, 2004), diabetes mellitus (Liu et al., 2002), cataract and hearing loss (Chuang et al., 2007), arsenic-associated skin lesions (Huang et al., 2008), and endemic goiter and cretinism (Su et al., 2002). These studies indicate that some relationships exist between these diseases and lower selenium, but whether low selenium levels are the causes of these diseases are less clear (Yang et al., 1988). Even so, many epidemiological and clinical studies have demonstrated that dietary supplementation of selenium could reduce the incidence of above diseases (Yu et al., 1990, 1997; Chen and Wong, 2009).

3.2. Selenosis in China

Intakes of excessive selenium can cause selenosis of human and animals. Many scientists suggested that Marco Polo was the first man who recorded selenium toxicity during raveling along the Silk Road in the named Suzhou region of western China (the present Hexi Corridor) in 1295, whose horse died from hair loss and hoof lesions which were the main symptoms of chronic selenium toxicity. However, recent research demonstrated that the geochemical baseline Se in this area is far lower than that in typical seleniferous areas, and that the horse most likely died from grazing poisonous grasses, mostly *Oxytropis DC*, *Stellera chamaejasme*, and *Achnatheru inebrians* (Shao and Zheng, 2008). There are two notable Se-excessive regions in China. They are the Exi seleniferous region in Western Hubei Province and the Ziyang seleniferous region in Southern Shaanxi Province (Fig. 2). The outbreaks of endemic human selenosis were reported in these two regions in the 20th century but the prevalence in Western Hubei Province was more serious and widespread.

Human selenosis in Western Hubei Province could be traced to 1923. Total 477 cases of human selenosis were reported from 1923 to 1987, and 70% cases occurred in 1959 to 1963. Ninety percent of the patients were located in the towns of Shadi, Xintang and Shuanghe in Enshi District, and the others patients were distributed in Laiwu Town in Enshi, Nantan and Houmen Towns in Badong County, Shatuo Town in Xuanen County (Mou et al., 2007). Among them, Yutangba in Shuanghe Town is the most serious village suffered from the endemic selenosis.

Studies proved that the endemic selenosis in Western Hubei Province was related to the occurrence of Permian Se-enriched carbonaceous strata (Yang et al., 1983). The selenium in local soil, drinking water, crops and vegetables all originated directly or indirectly from the surrounding seleniferous strata (Zheng et al., 1992). The average Se concentration in the local carbonaceous siliceous rocks and carbonaceous shales (known locally as “stone coal”) is 143.9 mg/kg (Mou et al., 2007) and the maximum content is up to 84,123 mg/kg (Yang et al., 1983), while the average Se content of shale in the world is only 0.06 mg/kg (Fordyce, 2005). In the Se-rich rocks, selenium mainly presents in native selenium and copper (iron) selenide assemblages including krutaite, klockmannite, mandarinoite, naumannite, Se-bearing pyrite, Se-bearing chalcopyrite and unidentified Fe–Se minerals (Zhu et al., 2004a,b).

Selenium was dispersed from the Se-enriched carbonaceous rocks to the food chain via complex biogeochemical cycling processes including weathering, rock–water interactions and biological activities. In addition, in the endemic selenosis areas, human activities such as stone coal conveyance by local villagers, mining of stone coal for use as a fuel or fertilizer, and discharging lime into cropland to improve soil, caused variable addition of Se to the soil and further accumulation of Se in the food chain. For example, Se concentration in 11 soil samples in the

Table 2
Se concentration in soil, corn and water in the selenosis area of Yutangba, Enshi.

Sampling time (yr)	Se in soil (mg/kg)		Se in corn (mg/kg)		Se in stream water (μg/L)		References
	A (±S.D.)	n	A (±S.D.)	n	A (±S.D.)	n	
1963	6.83		33.47				Mao et al. (1997)
1966	7.86 ± 0.69	6	14.6	5	139	4	Yang et al. (1981)
1987	3.45 ± 1.53	4	14.07 ± 7.26	4			Mao et al. (1997)
1989	5.48 ± 6.41	9					Zheng et al. (1993)
1992	4.06 ± 1.24	28	6.47 ± 4.29	130			Zhu and Zheng (2001)
1996	4.99 ± 2.38	5	3.24 ± 1.54	5	40.4	1	Fordyce et al. (1998)
1999	4.75 ± 7.43	150	1.48 ± 1.41	20	58.4 ± 16.8	12	Zhu et al. (2008)

A: arithmetic mean; S.D.: arithmetic standard deviation; n: number of samples.

town of Yutangba ranged from 346 to 2018 mg/kg with an average of 899 ± 548 mg/kg in the croplands and the discarded coal spoils (Zhu et al., 2008). Se concentrations in the local soil, corn and water determined in the past 40 years at the typical endemic selenosis area of Yutangba are listed in Table 2. It shows that selenium concentrations in soil were almost unchanged over the past 40 years. However, Se concentrations in corn have decreased gradually based on the sampling year. This indicates that Se availability to plants in Yutangba is gradually decreasing. In addition, The Se content in stream water has decreased from 139 μg/L in the 1960s to 58.41 ± 16.82 μg/L, and has not changed greatly in recent years (Zhu et al., 2008). This confirms that the strong Se releases observed in the past were dependent on human activities.

Naore Village, Shuang'an Town in Daba Moutain, Ziyang County, Southern Shaanxi Province is the second important region where endemic selenosis prevalence occurred (Cheng and Mei, 1980). More than ten cases of human selenosis and thousands of cases of swine selenosis have been reported in the region of Daba Moutain (Li et al., 2008). The selenium content of corn in some fields of Naore village is 6.6 mg/kg (Luo and Qiu, 1995), and horsebeans reach up to 48.84 mg/kg Se (Mei, 1985). The selenium content in the local soils was determined to be 15.74 mg/kg (Mei, 1985) and 26 mg/kg (Zhao et al., 1993). The sources of high selenium in this area are usually thought to be related to the early Silurian carbonaceous slate and stone coal (Mei, 1985; Fang and Wu, 2004). However, Luo et al. (2004) pointed out that the Early Cambrian and Late Neoproterozoic pyritic, black carbonaceous slate and volcanic tuff, in which selenium average concentration are 22 mg/kg and 32 mg/kg, respectively, should be the main sources of the high selenium content with 10–30 mg/kg Se in the local soil of Daba.

Hair and nail loss were the prime symptoms of endemic selenosis, but disorders of the nervous system, skin, poor dental heath, garlic breath, and paralysis were also reported. Although no health investigations were carried out in the peak prevalence years of 1961 to 1964 in Enshi District, subsequent studies in these areas carried out in the 1970s revealed very high dietary intakes of 3.2–6.8 mg/day with a range of selenium in the blood of 1.3–7.5 mg/L and hair selenium levels of 4.1–100 mg/kg (Yang et al., 1983; Tan, 1989). Due to increasingly less dependence on locally grown foodstuffs in the diet, no human cases of selenium toxicity have been reported since 1987 in these areas, but the local animals frequently suffer hoof and hair loss as a result of the high environmental selenium (Mou et al., 2007).

4. Thallium impacts on human health in China

Thallium is one of the most toxic metals and can cause chronic and acute poisoning (Zitko, 1975; Smith and Carson, 1977). It is widely distributed in the natural environment but generally present in low concentration, with 0.75 mg/kg in the earth's crust (Taylor and McLennan, 1985), 0.01–3 mg/kg in soil (Fergusson, 1990), 0.001–0.25 μg/L in water (Banks et al., 1995), and 0.03–0.3 mg/kg in food crops (Kabata-Pendias and Pendias, 1992). Thallium minerals are rare in nature, thus Tl is often excluded from the list of metals to be evaluated, and the environmental impact related to the natural occurrence of Tl has received relatively little attention in the world despite its high toxicity (Xiao et al., 2004a). However, a typical serious endemic thallotoxicosis occurred due to Tl pollution in local waters and food crops in southwestern China's Guizhou Province.

A rural area of Lanmuchang (105°30′23″E, 25°31′28″N) in southwest Guizhou Province was identified to have high Tl contents in local ecosystem due to the presence of Tl-bearing sulfide minerals (Chen, 1989a,b). In the 1960s–1970s, Lanmuchang, with a population of approximately 1000 people, was affected by endemic Tl poisoning (APASSGP and EGLIGCAS, 1974; Liu, 1983; Zhou and Liu, 1985). The poisoning, which affected a large portion of the population (over 400 cases) and caused symptoms, such as hair loss, body-aches, reduced vision and blindness, was thought largely to be due to Tl contamination in drinking water and vegetables (Zhou and Liu, 1985; Long and Zhang, 1996). High concentrations of Tl in bedrocks/ores (6–35,000 mg/kg), aquatic system (0.005–1100 μg/L in groundwater and 0.07–31 μg/L in surface waters), soil layers (1.5–124 mg/kg) and food crops (1–500 mg/kg, dry weight) were observed in this area (Xiao et al., 2004b). Even though Tl-free water was piped from outside of the area has provided with adequate drinking water since the early 1990s, a portion of the villagers (around 40% of the population) still rely on the cheaper dug-wells or springs close to the Tl mineralized area, and all rely on the natural water sources for agricultural and domestic uses. Therefore, the symptoms of chronic Tl intoxication still occur in the area in the 2000s (Xiao et al., 2003, 2007).

Previous studies demonstrated that Tl tended to accumulate in local food crops grown in Tl-polluted soils (Z. Zhang et al., 1999; Xiao et al., 2004a). In the Lanmuchang Tl-polluted area, Tl showed the highest concentration in green cabbage, ranging from 120 to 495 mg/kg with an average of 338 mg/kg (Xiao et al., 2004a). For other local crops, Tl presented at 0.87–5.4 mg/kg in Chinese cabbage, 0.8–5.3 mg/kg in chili, 1–5.2 mg/kg in shelled rice, and 0.78–3.1 mg/kg in granular corn (Xiao et al., 2004a). The high accumulation of Tl in the local food crops clearly implied that Tl in crop soil could easily transfer to crops. The daily intake of Tl from consumption of the local food crops was estimated at 1.9 mg/day for the local adult inhabitant in Lanmuchang (Xiao et al., 2004b). This high ingestion rate of Tl is 1000 times higher than the world average daily intake (2 μg/day) as indicated by Sabbioni et al. (1984), and also far above the element's "oral reference dose" of 0.056 mg/day (RAIS, 2003).

The excessive intake of thallium from the daily diet over the year induced accumulation of thallium in human tissues and harm to human health. The previous epidemiological investigations showed high Tl in urine of the local villagers, ranging from 600 to 3000 μg/L in the 1970s (Zhou and Liu, 1985), 77.7 to 2660 μg/L in the 1990s (Z. Zhang et al., 1999), and 2.51 to 2668 μg/L in 2003 (Xiao et al., 2007). These high urinary Tl levels were from 1 to 4 orders of magnitude higher than the accepted maximum urinary Tl concentration of <1 μg/L for "non-exposed" humans in the world. It is surprising to note that the high Tl levels in urine of the local villagers were nearly constant within the past four decades. This likely reflected a long-term exposure to Tl in the local environment, and the main cause was from the continuous ingestion of Tl from the food crops grown in the local Tl-polluted soils over the years (Xiao et al., 2004a, 2007), whereas the threat from the drinking water

Table 3
Thallium concentration in biological materials from endemic thallotoxicosis patients and control groups.

Biological materials	Range and mean of Tl concentration in different groups	References
	Range/A ± S.D.	
Urine (mg/l)	0.6–3.0/1.46 ± 0.15 (endemic thallotoxicosis patients)	Zhou and Liu (1985)
	0.0–1.0/0.39 ± 0.049 (healthy people from endemic thallotoxicosis area)	
	0.0–0.23/0.059 ± 0.004 (control group from thallium free area)	
Hair (μg/g)	6.0–50.0/23.6 ± 3.0 (endemic thallotoxicosis patients)	
	0.0–20/6.49 ± 1.27 (healthy people from endemic thallotoxicosis area)	
	0.0–0.75/0.166 ± 0.049 (control group from thallium free area)	
Blood (mg/l)	0.5–22.0/4.54 ± 1.80 (endemic thallotoxicosis patients)	
Urine (μg/l)	132.00–962.00/405.25 ± 267.18 (n = 22, endemic thallotoxicosis patients)	Huang et al. (1995)
	4.00–76.00/47.25 ± 30.29 (n = 23, healthy people from endemic thallotoxicosis area)	
	0–6.00/2.27 ± 1.39 (n = 105, control group from thallium free area)	
Hair (μg/g)	0.80–4.35/1.54 ± 0.69 (n = 22, endemic thallotoxicosis patients)	
	0.05–0.75/0.34 ± 0.19 (n = 43, healthy people from endemic thallotoxicosis area)	
	0–0.15/0.046 ± 0.032 (n = 122, control group from thallium free area)	
Nail (μg/g)	4.31–34.29/10.49 ± 6.93 (n = 22, endemic thallotoxicosis patients)	
	1.68–6.56/3.82 ± 1.29 (n = 23; control group from non thallium polluted area)	
	0–3.23/0.99 ± 0.92 (n = 60; control group from thallium free area)	
Urine (μg/l)	1220–2660/2073 (n = 4; seriously Hg–Tl-diseased patients in Lanmuchang)	Z. Zhang et al. (1999)
	150–660/394 (n = 5; slightly Hg–Tl-diseased patients in Lanmuchang)	
	18–106/91 (n = 4; normal inhabitants in Lanmuchang)	
Hair (μg/g)	6.10–12.24/8.43 (n = 6; seriously Hg–Tl-diseased patients in Lanmuchang)	
	4.19–7.85/6.16 (n = 7; slightly Hg–Tl-diseased patients in Lanmuchang)	
	0.45 (n = 1; healthy people)	
Nail (μg/g)	2.97–32.24/13.92 (n = 5; seriously Hg–Tl-diseased patients in Lanmuchang)	
	5.14–13.94/8.53 (n = 3; slightly Hg–Tl-diseased patients in Lanmuchang)	
	1.13–1.62/1.38 (n = 2; healthy people)	
Urine (μg/l)	2.50–2668/521.9 (n = 25; inhabitants in Lanmuchang Tl mineralized area)	Xiao et al. (2007)
	1.05–1.70/1.40 (n = 3; inhabitants in background area with no Tl mineralization)	
	0.387–0.96/0.651 (n = 4; inhabitants in Guiyang City)	

(0.12–0.38 μg/L Tl) has been eliminated by piping uncontaminated groundwater from outside the Lanmuchang area (Xiao et al., 2003, 2007).

A number of investigations showed that thallium concentrations in urine, hair, nail and blood from endemic thallotoxicosis patients were much higher than that from the control groups (Table 3). According to Xiao et al. (2007), the majority of the local population with urinary Tl concentrations above 4.5–6 μg/L from the Lanmuchang area might suffer from the early adverse health effects, and some of the villagers with urinary Tl concentrations over 500 μg/L could be considered as approaching clinical intoxication. The higher concentration of thallium in these biological materials can be used as indicators of thallium intoxication. Based on the investigation of Tl in urine of the villagers from endemic thallotoxicosis area, urinary thallium contents, Tl>1000, 100–1000 and <100 μg/L, were suggested to be used as preliminary criteria for distinguishing seriously thallotoxicosis patients, lightly thallotoxicosis patients and normal inhabitants, respectively, in China (Z. Zhang et al., 1999).

Table 4
Clinical manifestations of 30 patients suffered from chronic endemic thallotoxicosis. From Feng et al. (2001).

Symptoms		Cases number	Percentage (%)
Hair loss		30	100
Visual acuity	<0.01	8	27
	<0.1	3	10
	0.1–0.4	9	30
	0.5–0.7	4	13
	0.8–0.9	2	7
	>1.0	4	13
Optic nerve atrophy		8	27
Dullness of pupil reaction		8	27
Punctuate or nubby white opacity on eye lens		14	47
Sensory disturbance on distal part of extremities		7	23
Poor appetite		9	30
Lower extremity pain		6	20
Numbness of the extremities		6	20
Muscle atrophy		7	23
Muscle pain		5	17
Fatigue weakness		12	40
Dreaminess		9	30
Palpitation		5	17
Character change		4	13
Extremities tremor		3	10
Gait aberration		7	23
Linguistic dullness		4	13
Emaciation		13	43

The exact mechanism of thallium toxicity is still unclear (Peter and Viraraghavan, 2005). Possible toxic mechanisms of thallium include ligand formation with protein sulfhydril groups, inhibition of cellular respiration, interaction with riboflavin and riboflavin-based cofactors, and distribution of calcium homeostasis (Mulkey and Oehme, 1993). The major symptoms of chronic endemic thallotoxicosis in Lanmuchang include anorexia, headache, pain in abdomen, upper arms and thighs and even all over the body. In extreme cases, alopecia, blindness and even death were caused (Zhang et al., 1998). The results of a reexamination on 30 patients who suffered from the chronic endemic thallotoxicosis for 4 to 27 years showed that all of the patients had the history of hair loss and reduced vision in different degree. The alopecia could occur in a few days or even one night but the hair could re-grow in several months to two years if thallium poisoning was abated (Feng et al., 2001). However, the optic nerve damage revealed progressive severe with recurrent poisoning (Pan, 1986; Feng et al., 2001). Chronic endemic thallotoxicosis could also cause peripheral neuritis and induced to partial or even absolute loss of working capacity. Some details of clinical manifestations from chronic endemic thallotoxicosis patients in Lamuchang are shown in Table 4. The natural processes, exacerbated by human activities, such as mining and farming, may produce high enrichment of Tl in soil, water, and food chain, and finally result in endemic thallotoxicosis when the local population expose to Tl (Xiao et al., 2004b). Similar contexts, with high primary content of Tl in other areas related to sulfide mineralization in China have also arisen scientists' attention, such as Nanhua As–Tl deposit in Yunnan (Zhang, 1998), Yunfu Dajiangping pyrite deposit in Guangdong (X.P. Li et al., 2009; Yang et al., 2005), Xiangquan Thallium-

only deposit in Anhui (Hu et al., 2007; Zhou et al., 2008), Chenmenshan copper deposit in Anhui, Lanping lead–zinc deposit in Yunnan, Yilan mercury deposit in Guangxi, Getang Sb–Au deposit in Guizhou and Dongbeizai Au–As deposit in Sichuan (Zhang et al., 1998). In these naturally-occurring Tl enrichment areas, Tl could also be dispersed beyond a mineralized zone, and its abundances in local water, soil and crops may rise above permissible levels and result in adverse health effects.

5. Conclusions and outlook

Arsenic, selenium and thallium are the important elements which can induce serious endemic diseases due to its contamination or deficiency in China, have been attracting high environmental and medical concerns.

Endemic arsenism in China can be divided into drinking-water type and coal-burning type. Arsenism caused by drinking high-As groundwater mainly distributed in Taiwan and north part of China mainland. Coal-burning type arsenism is mainly caused by burning high-As coal in indoor environments without chimney and occurred in Guizhou and Shaanxi Province. Skin lesions are the most common features of endemic arsenism. Other diseases, such as peripheral vascular disease, polyneuropathy, hypertension, black foot disease, skin cancer and other cancers, can also be induced by high arsenic exposure. Both endemic selenium deficiency and selenosis due to the lower and higher concentrations in the environment occurred in China. The KD and KBD are usually thought to be related to the deficiency of Se in the low-Se belt stretching from northeast to southwest of China, but researches have proved that they should be multi-pathogeny diseases. Endemic selenosis occurred in Western Hubei and Southern Shannxi where high Se concentration in soil mainly derived from the local Se-rich rocks. The prime symptoms of endemic selenosis are hair and nail loss, but disorders of the nervous system, skin, poor dental heath, garlic breath, and paralysis were also reported. Endemic Tl poisoning occurred in Lanmuchang of Southwest China due to high Tl exposure from drinking water and vegetables in the Tl mineralized area. Hair loss, body-aches, reduced vision and blindness are the main symptoms of thallotoxicosis. Testing the urinary Tl concentration of Tl-affected population is a quick way of detecting Tl exposure.

Some measures have been taken to control and remedy the endemic diseases, such as supply with safe drinking water for residents in the endemic areas, prevention of using high arsenic or selenium coal, application of selenium fertilizer or selenium salt in low selenium areas, and public health education, and they have shown significant effects in reducing health risk and damage of As, Se and Tl. However, the status of the endemic diseases of As, Se and Tl are still serious in some locations, and some new endemic areas emerged in recent years due to intensive human activities combined with the natural biological geochemical processes, and lots of research projects are needed to study the human health impact in affected areas. For example, the mechanism of cancer occurrence caused by arsenic exposure is still unclear and different persons exposed to the same level of arsenic result in difference outcomes, so that it is necessary to study the molecular mechanisms of individual susceptibility using specific biomarkers. In addition, in some endemic areas in China, the environment is rich in multi-elements. Further studies on the combined interactions on human health of the metal (metalloid) elements such as As–F, As–Se, Tl–Hg–As, Se–I, and Se–Cd are also required. Furthermore, the endemic arsenism, selenosis and thallotoxicosis mainly occurred in the adults, but the studies on the health effects of these elements exposure to children are relative few. More attentions on the health impacts of metal (metalloid) elements on children should be conducted in the future work, especially the impact of exposures at young age to their health at later stage.

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