Potential relationships between exposure to arsenic (As) in the environment and endemic disease in southwestern China

Donglin Li¹, Hucai Zhang²*, Fengqin Chang², Lizeng Duan² and Yang Zhang²

1. Institute for International Rivers and Eco-security, Yunnan University, Kunming, 650504, China
2. Institute for Ecological Research and Pollution Control of Plateau Lakes, School of Ecology and Environmental Science, Yunnan University, Kunming 650504, Yunnan, China

*Corresponding author: Hucai Zhang

Donglin Li¹, E-mail: donglinli@mail.ynu.edu.cn
Hucai Zhang²*, E-mail: zhanghc@ynu.edu.cn
Fengqin Chang², E-mail: changfq@ynu.edu.cn
Lizeng Duan², E-mail: duanlizeng2019@ynu.edu.cn
Yang Zhang², E-mail: 414064473@qq.com

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Authors' contributions

HZ conceived and designed experiments. DL and YZ performed experiments. FC, LD and YZ performed statistical and chemical analysis. DL wrote manuscript. All authors read and approved the final manuscript.

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Abstract There have been many reported cases of a strange disease exhibiting clinical features of limb gangrene, blisters, ulceration and exfoliation in Daping village, Yunnan Province in southwestern China. The prevalence rate of the disease is very high compared to other places in Yunnan Province and greater China. The pathogenesis is unknown and has bewildered doctors for many years. In this study, the content of As in soil \( (n=31) \), water \( (n=55) \), and plants \( (n=7) \) were systematically measured. The results show a high As concentration in plants and soil samples from the area, and the source of As linked to the weathering of black shale strata. We assessed the risks of human exposure to As through six possible exposure pathways. Ingestion of soil and plants are found to be the two main ways that children and adults are exposed to As, and children have a higher health risk than adults. Our study sheds new light on the environmental geochemistry and health links of this disease.

Keywords: endemic disease; arsenic (As); health risk assessment; black shale; heavy metals; ecological risk

1 Introduction

Some metals and metalloids in the environment pose a serious threat to human health (Antoniadis et al. 2017; Mukherjee et al. 2019; Wallis et al. 2020). Arsenic (As) is one of the most ubiquitous elements in air, rocks, soil and water (Qu et al. 2020; Smedley and Kinniburgh 2002). Arsenic is classified as a highly toxic element in the ICH Q3D guidelines (ICH 2019) and also occupies the top of the most recent list of toxic substances released by the ATSDR (ATSDR 2019). China also added As in soil (CEPA 2018), water (HHCRC 2006) and foods (HHCRC 2005) to its lists of restricted toxicants.
Arsenic can induce a variety of cancers (lung, liver, and bladder), and Blackfoot disease (BFD) with gangrene and ulceration of the extremities (Ali et al. 2020; Chen et al. 1994; Wallis et al. 2020).

Approximately 14 million people in the world are exposed to high-As content living environments, and Arsenic has received widespread attention due to its extreme toxicity and widespread pollution (Ali et al. 2020; Chen et al. 1994; Wallis et al. 2020).

Sources of arsenic can be classified as natural sources, such as bedrock weathering enrichment (Mailloux et al. 2009), mining and smelting, and anthropogenic sources, e.g., fossil fuel combustion, pesticide and fertilizer application (Anawar et al. 2002). However, due to significant differences in geochemical background and spatio-temporal distributions of economic development and industrial activities, the degree of pollution, pollution sources, element transferability and bio-accessibility differ greatly from one location to another (Emenike et al. 2019; Fallahzadeh et al. 2017; Fendorf et al. 2010; Xu et al. 2020; Zeng et al. 2015). Therefore, it is important to investigate the sources, exposure pathways and influencing factors of As in areas with suspected arsenicosis in order to reduce residents' exposure to As and prevent endemic diseases induced by As accumulation.

In Daping village in Yunnan Province, southwestern China, some individuals exhibit phenomena including limb gangrene, blisters, ulceration and exfoliation in childhood (Hou 2013). These symptoms are similar to those of patients with long-term As exposure. Professional doctors had been trying for ten years but could not identify the cause of this disease when screening for infectious diseases and occupational diseases.

To probe the possible relationships between As exposure and this endemic disease, the As contents of soil, water and plants within and surrounding Daping village were sampled and analyzed.
comprehensively; based on the analyzed data, the possible sources, migration and enrichment processes of As are discussed in detail. We also assessed the risk of six exposure routes, and the potential relationships between As in the environment and this disease were investigated. This study may provide a scientific basis for the determination of geochemical sites with high background levels of toxic elements and shed new light on the relationships between environmental geochemistry and human health.

2 Materials and methods

2.1 The study area

Daping village (105°43'37"E, 23°33'15"N) is located in Banlun Township, Funing County, Yunnan Province, southwestern China (Fig. 1). The village is located in mountainous terrain with an average altitude of 1133 m above sea level (a.s.l.) and occupies an area of approximately 0.95 km². The annual temperature and precipitation are 16.9 °C and 1015 mm, respectively. The region has a subtropical monsoon climate, with distinct rainy and dry seasons. The lithological formation is mainly black mud shale, biolistic limestone, carbonate rock, basic intrusive rock and intrusive diorite.
Fig. 1 Map of sampling locations in Banlun Township, Funing County, Yunnan Province, southwestern China. (a) Map of China. (b) Map of Yunnan Province. (c) Map of study area. (d) Amputation patients have received prosthetic limbs.

According to a survey, there are 234 people in the village, including at least six patients with unusual diseases (blisters, wounds that are difficult to heal, and ulceration). Patients with severe symptoms were ultimately forced to undergo amputation multiple times to relieve pain, and they all showed symptoms in childhood (Tab. S1). No similar cases were found in adjacent areas.

2.2 Material collection and chemical analyses

2.2.1 Soil

Soil samples were collected randomly during the period of July 2016 and October 2017. Additionally, the lithological characteristics of bedrock were observed during soil collection. The soil of distinct land use types included farmland, non-farmland and water source sediment. More detailed
sampling locations are shown in Fig. 1. The samples were collected at depths of 1 to 10 cm, and approximately 1 kg of each soil was placed in a plastic bag and labeled properly after gravel, plant roots, leaves, and other materials were removed and discarded. Soil samples were further ground (<75 μm particle diameter), digested with HNO₃-HF (Hu et al. 2011), and measured with inductively coupled plasma mass spectrometry (ICP-MS, Varian 820-MS).

2.2.2 Water

Mountain streams, irrigation water and villagers’ drinking water were collected in plastic bottles; two of each sample (Fig. 1). Plastic bottles were cleaned with 2% nitric acid before sample collection. After the tap had run for one minute, drinking water samples were collected. Then, the correct label was placed on the bottle, and the bottle was plugged, placed in a box, and delivered to the laboratory.

All water samples were collected and stored in sterile polythene cans and filtered through a mixed cellulose ester micro porous filtration membrane with a pore size of 0.45 μm (Chen et al. 1994). To determine the total As (total), 1.25 mL of concentrated hydrochloric acid and 5 mL of thiourea-ascorbic acid mixed solution were added, and the mixture was prerduced at room temperature for 60 min for the analysis of As (total). To determine As (III), 15 mL samples were placed in a 25 mL brown volumetric flask. A total of 5 mL of citric acid aqueous solution (0.5 m/L) was added, the volume was fixed with pure water, and the mixture was shaken well. As (III) and As (total) in the samples were measured by atomic fluorescence spectrophotometry (Jitian AFS-8220).

2.2.3 Plants

Seeds of rice and corn that may have been eaten by patients in the village during the sampling
period were selected and packed in plastic zip-lock bags to ensure they were not cross contaminated with soil and water (Fig. 1). The plant samples were washed, dried, weighed and digested with HNO$_3$ and H$_2$O$_2$, and As was measured with an inductively coupled plasma mass spectrometer (ICP-MS, Varian 820-MS) after evaporation, atomization and ionization (Chen et al. 2014).

2.3 Health risk assessment

2.3.1 Non-carcinogenic risk assessment

Calculation of average daily intake of arsenic: There are six pathways of exposure to arsenic in soil, water and plants (Ali et al. 2020; Antoniadis et al. 2017). The calculation formulas of the arsenic average daily ingestion (AAD) from soil (ingestion, dermal absorption and inhalation of particulate matter in the air), water bodies (ingestion and dermal absorption) and plants (ingestion) are as follows (1 to 6):

$$ AADS_{ing} = C \times \frac{S \times EF \times ED \times BW \times AT}{10^{-6}} \quad (1) $$

$$ AADS_{de} = C \times \frac{SA \times SAF \times ABS_{w} \times EF \times ED \times BW \times AT}{10^{-6}} \quad (2) $$

$$ AADS_{inh} = C \times \frac{S \times inhR \times EF \times ED \times PEF \times BW \times AT}{10^{-6}} \quad (3) $$

$$ AADW_{ing} = C \times \frac{W \times ingR \times EF \times ED \times BW \times AT}{10^{-6}} \quad (4) $$

$$ AADW_{de} = C \times \frac{SA \times SAF \times ABS_{w} \times EF \times ET \times ED \times BW \times AT}{10^{-6}} \quad (5) $$

$$ AADP_{ing} = C \times \frac{P \times ingR \times FI \times EF \times ED \times BW \times AT}{10^{-6}} \quad (6) $$

Where $AADS_{ing}$, $AADS_{de}$ and $AADS_{inh}$ are ingestion, dermal absorption and inhalation intake from soil, respectively; $AADW_{ing}$ and $AADW_{de}$ are ingestion and dermal absorption intake from water, respectively; and $AADP_{ing}$ is ingestion from plants, with all units in mg As kg$^{-1}$ BW day$^{-1}$. $C$ is the total As concentration in soil, water and plants (mg kg$^{-1}$, mg L$^{-1}$, and mg kg$^{-1}$, respectively), and $S \times IngR,$
WIngR and PingR are the ingestion rates of soil (mg day\(^{-1}\)), water (L day\(^{-1}\)) and foods (mg day\(^{-1}\)), respectively. EF is exposure frequency (day year\(^{-1}\)); ED is exposure duration (year); BW is body weight (kg); AT is average time (day); ET is exposure frequency (hour day\(^{-1}\)); SA is surface area (cm\(^2\)), SAF is the skin adherence factor (mg cm\(^{-2}\)); ABS\(_S\) is the dermal absorption factor of soil (unitless); ABS\(_W\) is the dermal absorption factor of water (unitless); SinhR is the inhalation rate (m\(^3\) day\(^{-1}\)); PEF is the particle emission factor (m\(^3\) kg\(^{-1}\)); and FI is the fraction ingested from consumed foodstuffs (unitless). The factors and their values used in this work for AADS\(_{s\_ing}\), AADS\(_{s\_de}\), AADW\(_{s\_ing}\), AADW\(_{s\_de}\), AADS\(_{inh}\) and AADP\(_{s\_ing}\) are shown and explained in Tab. S2.

Hazard quotient (HQ) calculation: The hazard quotient (HQ, unitless) is the ratio of the average daily intake of arsenic to its reference dose (RfD), and it is used to quantify the non-carcinogenic risk of As (USEPA 1989). The hazard index (HI) approach was used to assess the overall potential of noncarcinogenic effects from all exposure pathways (Antoniadis et al. 2019; Fallahzadeh et al. 2017). Additionally, the HI can account for the cumulative risk of all arsenic sources combined, as described in formula (14). An HQ < 1 or HI < 1 indicates that there are no adverse health effects, and the risk is within the safe range. An HQ > 1 or HI > 1 indicates that adverse health effects may occur (Xiao et al. 2019). This paper includes ingestion (HQ\(_{s\_ing}\)), dermal absorption (HQ\(_{s\_de}\)) and inhalation (HQ\(_{s\_inh}\)) from soil, ingestion (HQ\(_{w\_ing}\)) and dermal absorption (HQ\(_{w\_de}\)) from water, and ingestion (HQ\(_{p\_ing}\)) from plants. They can be calculated by the following equations (7 to 14):

\[
HQ_{s\_ing} = \frac{AADS_{s\_ing}}{RfD_{s\_ing}}
\]

\[
HQ_{s\_de} = \frac{AADS_{s\_de}}{RfD_{s\_de}}
\]
\[ R_{fD_{s inh}} = R_{fC_{s inh}} \times 20(\text{m}^3/\text{day})/70(\text{kg}) \]  

(9)

\[ H_{Q_{s inh}} = \frac{AADS_{s inh}}{R_{fD_{s inh}}} \]  

(10)

\[ H_{Q_{w ing}} = \frac{AADW_{w ing}}{R_{fD_{w ing}}} \]  

(11)

\[ H_{Q_{w de}} = \frac{AADW_{w de}}{R_{fD_{w de}}} \]  

(12)

\[ H_{Q_{p ing}} = \frac{AADP_{p ing}}{R_{fD_{p ing}}} \]  

(13)

\[ H_{I} = H_{Q_{s ing}} + H_{Q_{s de}} + H_{Q_{s inh}} + H_{Q_{w ing}} + H_{Q_{w de}} + H_{Q_{p ing}} \]  

(14)

Where \( R_{fD_{s ing}} \) is the oral reference dose (ingestion from soil); \( R_{fD_{s de}} \) is the reference dose through dermal absorption (dermal absorption from soil); \( R_{fD_{s inh}} \) is the dose through inhalation of airborne particles (inhalation absorption from soil); \( R_{fC_{s inh}} \) is the inhalation reference concentration given for As; \( R_{fD_{w ing}} \) is the oral reference dose (ingestion from water); \( R_{fD_{w de}} \) is the reference dose through dermal absorption (dermal absorption from water); and \( R_{fD_{p ing}} \) is the oral reference dose (ingestion from plants). Their units are all the same (\( \mu \text{g kg}^{-1} \text{day}^{-1} \)). The values of \( R_{fD_{s ing}}, R_{fD_{s de}}, R_{fC_{s inh}}, R_{fD_{w ing}}, R_{fD_{w de}} \) and \( R_{fD_{p ing}} \) used in this study are 0.3 (Antoniadis et al. 2019), 0.3 (USEPA 2004), 15 \( \cdot \) 10\(^{-6} \) (Antoniadis et al. 2019), 0.3 (Xiao et al. 2019), 0.285 (Xiao et al. 2019) and 0.3 (Zang et al. 2017), respectively.

2.3.2 Carcinogenic risk assessment

The calculations of carcinogenic risk are based on the human intake values from six pathways \( (AADS_{s ing}, AADS_{s de}, AADW_{w ing}, AADW_{w de}, AADS_{s inh} \) and \( AADP_{p ing} \)). The carcinogenic risks (CR, unitless) of arsenic exposure are calculated as follows:

\[ CR_i = AAD_i \times SF_i \]  

(15)

Where \( SF_i \) is the slope factor (\( \text{mg kg}^{-1} \text{day}^{-1} \)) per exposure pathway. \( SF_{s ing}, SF_{s de}, \) and \( SF_{s inh} \) are
the slope factors related to soil ingestion, soil dermal absorption and inhalation of air particles, respectively. $SF_{Wing}$ and $SF_{Wde}$ is the slope factors related to water ingestion and water dermal absorption, respectively. $SF_{Ping}$ is the slope factor for plants ingestion. The value of $SF_i$ used in this work is shown in Tab. S3.

$$CR_{total} = CR_{Sing} + CR_{Sde} + CR_{Sinh} + CR_{Wing} + CR_{Wde} + CR_{Ping}$$  \hspace{1cm} (16)

Where $CR_{Sing}$, $CR_{Sde}$ and $CR_{Sinh}$ (all unitless) are cancer risks related to ingestion, dermal absorption and inhalation from soil; $CR_{Wing}$ and $CR_{Wde}$ (all unitless) are cancer risks related to ingestion and dermal absorption from water; $CR_{Ping}$ (unitless) is the cancer risks of plants ingestion. As for carcinogenic risk $CR > 1 \times 10^{-4}$, indicate significant cancer risk; if $CR < 1 \times 10^{-6}$, carcinogenic risk is negligible; and if the value of carcinogenic risk remain within the range of $1 \times 10^{-6} < CR < 1 \times 10^{-4}$, it is a tolerable risk to human health (Antoniadis et al. 2019; Wu et al. 2017).

2.4 Quality control

Program blank and standard samples were used in the process of testing and analysis to ensure accuracy of the results. The reference materials used are as follows: soil (GBW 07315-16), water (GSB 04-1767-2004) and plants (GSB-7). All chemical reagents were guaranteed reagents. The standard deviations of all elements were less than 5%. All glassware and plastic containers were soaked in HNO$_3$ for 24 hours before used and thoroughly washed with deionized water.

2.5 Statistical analysis

The chemical analysis data of soil, plants and water were statistically analyzed using SPSS 24.0 (IBM Corporation, Armonk, NY, USA) and Microsoft Excel 2010 (Microsoft Corporation, Redmond, USA) (Wang et al. 2017). A T-test was used to compare the two groups of data when they followed a
normal distribution, and a nonparametric test was used for those without a normal distribution. The Games-Howell and LSD methods were used for single-factor analysis of variance (ANOVA). The map of sampling sites was generated using CorelDraw X6 (Corel Corporation, Ottawa, Canada). The ordinary Kriging interpolations of As concentrations were computed with Surfer 16 (Zang et al. 2017).

3 Results

3.1 Arsenic content in soil

The range of arsenic contents in farmland and non-farmland soil are 2.84 to 176.48 (73.95±50.57 mg/kg, wet weight (ww), n=22) and 6.78 to 119.39 (46.58±41.84, mg/kg, ww, n=8), respectively. In the sediment of the fluvial water source, the content of As is extremely high, reaching 202.22 (mg/kg, ww) (Tab. S4, Fig. 2a). The proportion is 74.19% of As contents of soil higher than the Chinese threshold (30 mg/kg). The average content of As (71.03±54.2 mg/kg, ww, n=31) in all soil samples is higher than the average values for the world (6 mg/kg) and China (11.2 mg/kg), with these values being approximately 11.8 times and 6.3 times higher than those for the world and China (Bowen 1979; Wei 1990). It clearly shows that soil As pollution is severe (Fig. 2a).
Fig. 2 Arsenic content in different types of soil (a), water (b) and plants (c). The red line indicates Chinese limits for As contents in soil, water and plants.

3.2 Relationship between arsenic distribution and lithology

The bedrock outcrops around Daping village are black mud shale, biolistic limestone, carbonate rock, basic intrusive rock and intrusive diorite. The village of Daping is located on black mud shale, a large amount of strawberry pyrite was found in the black shale (Fig. 3a, 3d, e and f). In black shale, the As contents in soil are all higher than the Chinese soil threshold (30 mg/kg), except for those of S1, S2, S3, S4, S5 and S7 (Fig. 3a, b). The contents in samples of intrusive basic rocks and carbonate strata are lower than 30 mg/kg, except for that in S6. It is clear that the regional lithology is the main contributor to the As content in soil.
Fig. 3 Geological map and spatial distribution map of soil arsenic in Daping village. (a) Daping village is located in the distribution range of Black shale and the content of As is related to the spatial distribution of black shale (As=30 mg/kg is Chinese risk control standard for soil contamination of agricultural land). (b) Spatial distribution relationship between black shale region and the variety of content of As. (c) Photo of the outcrop of black shale. (d) Strawberry pyrite in black shale. (e) Backscattering map of strawberry pyrite.
3.3 Arsenic content in water

The range of As in all water samples was 0.01 to 2.58 μg/L (0.45±0.5, n=55). The As concentrations in mountain streams, irrigation water and villagers' drinking water are 0.08 to 1.65 μg/L (0.63±0.47, n=24), 0.13 to 2.58 μg/L (0.73±0.84, n=7) and 0.01 to 0.83 μg/L (0.20±0.20, n=24), respectively (Fig. 2b, Tab. S4). According to average concentration of As, the different water sources ranked as follows: irrigation water > mountain stream water > residential drinking water. Thus, the concentration of As (total) in the water is lower than the limit of 10 μg/L set by China and the WHO (HHCRC 2006), and it was also lower than that in the water of the Chinese Loess Plateau (15.16±86.8 μg/L) (Xiao et al. 2019) and Bangladesh (200 μg/L) (Anawar et al. 2002).

The detailed analysis results show that the As in the water column was dominated by As (III). The ranges of As (III)/As (total) in drinking water, mountain streams, and irrigation water are 36% to 87% (51%±56%, n=3), 39% to 72% (51%±53%, n=8) and 45% to 78% (62%±23%, n=3), respectively (Tab. S5). The ratio of As (III) to As (V) is much lower than that reported by Chen et al. (Chen et al. 1994).

3.4 Arsenic content in plants

The contents of As in corn seeds are lower than 0.05 (mg/kg, ww.), which are lower than the Chinese ecological security threshold of 0.2 mg/kg (Fig. 2c, Tab. S4). The range of As contents in rice seeds is 0.03 to 0.17 (mg/kg, ww.), and the content of As in some rice seeds was slightly higher than the Chinese ecological security threshold of 0.15 mg/kg (HHCRC 2005).

3.5 Risk assessments

3.5.1 Non-carcinogenic risk

The hazard quotient (HQ) of children and adults as a possible route of exposure to As show the
trend of ingestion from soil > ingestion from plants > dermal absorption from soil > water ingestion > inhalation of particulate matter in the air > dermal absorption from water (p<0.05) (Fig. 4a, Tab. S6). At the same time, for all exposure routes, the HQ of children is significantly higher than that of adults (p<0.05). The hazard index (HI) values of exposure to As in children and adults are 3.91 and 0.91, respectively (Fig. 4, Tab. S6). HQs of ingestion from soil, ingestion from plants and dermal absorption from soil take huge proportion for HI, and the values of HQ for children is 74.1%, 17% and 6.84%, while those for adults is 54.14%, 35.50% and 4.43%, respectively (Fig. 4b). It is clear that ingestion from soil and plants are the two main risk exposure routes (Fig. 4).

**Fig. 4** (a) Hazard quotient (HQ) values of six exposure routes of arsenic in children and adults. (b) Contribution of Hazard quotient (HQ) of each exposure route to hazard index (HI). *: p<0.05. Values of HQ or HI > 1 indicate that adverse health effects may occur.

### 3.5.2 Carcinogenic risk

The carcinogenic risks owing to exposure to As in the living environment are shown in Tab. S7.
The carcinogenic risks for children and adults exposure to pathways of ingestion of soil and plants, and the dermal absorption are high (CR > $10^{-4}$). The inhalation of particles in the air is safe (CR < $10^{-6}$), and the other exposure pathways are acceptable or tolerable risk to human health ($10^{-4} < CR < 10^{-6}$). Plant ingestion has some effects on human health, which is different to non-carcinogenic risk (Fig. 5a). The next is the soil ingestion and dermal absorption from soil. The risks of children and adults differ greatly among exposure pathways (e.g. inhalation of particles in the air (children < adults, p<0.05); dermal absorption from soil (adults < children, p<0.05)). The CR of As exposure in the same environment shows that children (CR$_{total}$=5.66E-04) have relatively higher risks than adults (CR$_{total}$=4.17E-04) (Fig. 5b) (Antoniadis et al. 2019; Wu et al. 2017).

**Fig. 5** (a) Carcinogenic risk (CR) values of six exposure routes of arsenic in children and adults. (b) Contribution of Carcinogenic risk (CR) of per exposure route to CR$_{total}$. *: p<0.05. Values of CR > $10^{-4}$ indicates high carcinogenic risks
4 Discussion

4.1 Geochemical sources of arsenic

Our results show that the proportion of soil samples with As content exceeding the Chinese upper limit for Daping was 74.19%, in which the content was much higher than the tolerable maximum value (23 mg/kg) for child exposure to As in soil (Antoniadis et al. 2019). The As concentrations in streams, irrigation water and villagers' drinking water are lower than the WHO and Chinese standards for water (Fig. 2b). The content of As in plants show significant variance between corn and rice (Fig. 2c). The contents of As in corn rice is higher than the Chinese standard for food. Where is the source of As in the village?

Previous studies have shown that As in soil can be derived from the following: (1) the weathering and enrichment of parent rocks (Kamata and Katoh 2019; Qu et al. 2020), (2) the combustion of fossil fuels (Dai et al. 2012; Finkelman et al. 1999), (3) irrigation with water with high concentrations of As (Brammer and Ravenscroft 2009), and (4) the use of pesticides and fertilizers (Kelepertzis et al. 2018). Various controlling factors caused significant differences in the soil As content among regions. However, the As in most areas derives from geochemical genesis, that is, environmental problems that are caused by the weathering, enrichment and migration of parent rocks (Kamata and Katoh 2019; Yan et al. 2018).

Ore mining or other enterprises that may cause soil As pollution have not been found near Daping village. Chemical fertilizers and pesticides are necessary for contemporary agricultural cultivation, but there is no significant difference (P<0.05) in the As content between farmland and non-farmland in the village of Daping (Fig. 2a); that is, the soil without human interference is also contaminated by As. At
the same time, there have been no reports of coal with a high As content near the village of Daping, and the area has a subtropical monsoon climate, is warm year round and has a low level of economic development, mainly involving the use of electricity and firewood for daily cooking. These comprehensive factors cause residents to essentially avoid fossil fuels, reducing the possibility of As settling into the soil due to coal combustion (Wang et al. 2020). Therefore, industrial activities, pesticides, chemical fertilizers and air deposition may not be the main sources of As in the soil.

The weathering of parent rocks can release a large amount of As into the soil (Duan et al. 2017; Emenike et al. 2019; Mailloux et al. 2009). There are significant differences in As content among different types of parent rocks (Qu et al. 2020). It has been reported that the As content in basic volcanic rocks is 2.3 mg/kg, that of carbonate rocks is 2.5 mg/kg (Qu et al. 2020), and that of black shale is 315 mg/kg, with a maximum of 490 mg/kg (Smedley and Kinniburgh 2002), which is closely related to the type and content of As-bearing minerals. The As content in sedimentary pyrite is significantly higher than that in bedrock (Li et al. 2005). Pyrite containing As in the stratum can release a large amount of As into the soil (Kamata and Katoh 2019). The lithological outcrops in Daping are mainly black mud shale, biolistic limestone, carbonate rock, basic intrusive rock and intrusive diorite (Fig. 3a). Our analyses revealed a significant correlation between the As content in soil and rock type (Fig. 3). The partial mismatch between As content values and rock types may be due to the influence of the landscape (Fig. 3 and 1c), thus causing the contents in samples (S1 to S5 and S7) to fall below the threshold (30 mg/kg) (Fig. 3b). Sample S6 has higher As content owing to soil with a high As content was transported and covered the soil with a low As content (Fig. 3a and 1c). The content of As in the soil of the village of Daping does not change with the types of soil usage, but it may be related to the
lithological properties of the bedrock; that is, it may be due to the weathering of pyrite rich in As in black shale (Fig. 3c, d, e), which releases a large amount of As into the soil and causes the difference under the action of physical transport such as gravity and water flow (Fig. 1c, 2a, 3). The subtropical monsoon climate aggravates the weathering process of bedrock that leads to soil formation.

4.2 Migration and enrichment of arsenic

Arsenic in soil can migrate into the water column and plants along with the precipitation and plant absorption processes, in turn causing serious environmental problems due to the transferability and bioaccessibility (Antoniadis et al. 2017; Nganje et al. 2020). Human exposure to water and to plants with high As contents are the two main routes of human As poisoning (Smedley and Kinniburgh 2002).

4.2.1 Migration of arsenic in soil

Physical and chemical conditions such as rainfall, temperature and soil properties control the intensity of soil leaching and weathering (Isimekhai et al. 2017). In moist, water-saturated soils, with the decrease in the Eh and pH, As is transformed into an unstable and transferable phase (Han et al. 2001), and the amount of As in soil could reach 1.8 mg m$^{-2}$ day$^{-1}$ with light rainfall (Roberts et al. 2009). The oxidative release of As from As-bearing pyrite in the black shale strata of Daping provides a source of As, and changes from dry soil to wet soil promote the transformation of As, which then transfers into the water body with precipitation, forming a complete "source, transportation and storage" process from the soil to water column (Han et al. 2001; Roberts et al. 2009). This is consistent with the migration model of endemic As poisoning in the Datong Basin, Shanxi Province (Wang et al. 2010).
4.2.2 Enrichment of arsenic in water

The analytical results of water samples showed that the concentration of As in drinking water in Daping village was lower than 10 μg/L during the rainy season sampling period (July 2016 and August 2017). This does not imply that the As in the water is lower than 10 μg/L for a long time. The concentration of As fluctuates due to climate change (Tondel et al. 1999).

During the dry season, most of the soluble As is leached and washed from the soil into drinking water, resulting in a high As concentration in the water column. At the same time, under conditions of long-term drought, intense evaporation undoubtedly strongly enriches As from several to hundreds of times in limited water and lead drinking water to rich high concentration of As (Isimekhai et al. 2017; Smedley and Kinniburgh 2002). An extremely high As content (202.22 mg/kg) is also found in the sediment of drinking water sources in the village of Daping, which may indirectly indicate that there was drinking water with a high concentration of As in the historical period (Fig. 2a).

4.2.3 Enrichment of arsenic in plants

Plants can absorb and accumulate As directly from soil and water. A previous study showed that the As contents in 13 kinds of rice seeds planted in 72.2 mg/kg soil ranged from 0.10 to 0.38 mg/kg and showed enrichment differences of root > stem > leaf > husk > milled rice (Chen et al. 2009). In the case of the village of Daping, the As content of maize seeds is lower than the Chinese limit of 0.2 mg/kg (HHCRC 2005), but the As content of some rice samples is slightly higher than the Chinese limit of 0.15 mg/kg (HHCRC 2005). Taking into account that the As content of cultivated soil is as high as 108.12 mg/kg, which is higher than that of the experiment of Chen and colleagues (72.2 mg/kg). Plants grown under high-As concentration stress show a reduction in crop yield (Das et al. 2004) and
As-enriched plants may be eaten by animals and increase the human absorption of As through plant-animal-human contact (Abedin et al. 2002).

4.3 Risk assessments of arsenic

The HI and CR_{total} of As exposure in the same environment shows that children (HI=3.91, CR=5.66E-04) have higher health risks than adults (HI=0.91, CR=4.17E-04) (Mukherjee et al. 2019; Xiao et al. 2019), which is consistent with the fact that children have lower immunity (Fig. 4 and 5).

The carcinogenic risk and non-carcinogenic risk assessment of six As exposure routes shows that soil and plant ingestion are the two main risk exposure routes (HQ > 1, CR > 10^{-4}), which was consistent with the results that soil and plants was contaminated by As (Fig. 4 and 5).

All the patients in the village of Daping developed the disease in childhood (Tab. S1), and the families and patients consumed the same food and drinking water; in other words, they had the same exposure pathways to As, but the prevalence rates were completely different. This may be due to individual differences in immune ability caused by age and sex (Emenike et al. 2019). Previous studies have shown stark differences in metal loading between members of the same household including twins, brother and sister etc. (Mitchell et al. 1996). It is worth noting that children have special behavioral habits (e.g., finger sucking and crawling), not observed in adults. In addition, based on the economic conditions, toys were covered in dirt soil or dust contaminated by As, which were leaded to that individuals have historically consumed considerable quantities of soil. At the same time, the range of activities of children was relatively fixed, while adults left the village to make money, leading to greater mobility. These combined factors cause children to have a greater chance and higher risk of exposure to As in the environment (Duan et al. 2017; Zhao et al. 2019).
4.4 Relationship between arsenic and endemic disease

As exposure related to outcomes like cancers of skin and lung, bladder, Blackfoot disease, etc. A large number of studies have shown that the causes of Blackfoot disease (e.g., China, Bangladesh, and West Bengal) are that patients consumed water (Brammer and Ravenscroft 2009; Smedley and Kinniburgh 2002) and plants (Brammer and Ravenscroft 2009; Das et al. 2004) with As contamination for a long time, which led to a large amount of As accumulation in the body. The symptoms (e.g., toe ulceration, necrosis and exfoliation) of patients in the village of Daping are extremely similar to the symptoms of Blackfoot (Brammer and Ravenscroft 2009; Chen et al. 2016; Sharma et al. 2014).

Verifying whether this disease is Blackfoot requires support from pathological and toxicological research. It is of little significance to identify whether it belongs to Blackfoot. There is no specific method used to treat arsenic poisoning. The best way to treat the condition is to eliminate arsenic exposure, such as strengthening the protection of children (e.g., improving water quality and washing hands frequently). In a word, the location of Daping village, the limitation of economic conditions and the unique behavioral habits of children lead to the occurrence of this endemic disease.

5 Conclusions and recommendation

The content of As in most soil and rice in the village of Daping was higher than the Chinese background and threshold value, and the source of As might be derived from the weathering and enrichment of black shale strata. The concentration of As in water is likely focused, especially during the dry season. Risk assessments show that ingested soil and plants have higher HQ and CR than other routes, which are two main risk exposure routes. Compared with adults (HI=0.91, CR=5.66E-04), children (HI=3.91, CR=4.17E-04) have a high ecological risk of As exposure in the same environment.
Based on pathological characteristics, geochemical characteristics and risk assessment, it has been revealed that the endemic disease in Daping village may potentially be related to As exposure in the environment and poses a significant health threat. We suggest that avoiding planting crops or choosing to plant crops with low enrichment factors, increasing the quality of water and the protection of children, such as encouraging frequent hand washing to reduce direct contact with soil.

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