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Review

Process and Prospect for Control and Prevention Impairment of Water-Borne Iodine Excess in China

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Abstract: Since the water-borne iodine excessive goiter was firstly discovered and reported on in 1978 in the Hebei Province, it has been confirmed successively. The national water-borne investigation carried out in 2005 demarcated the water-borne iodine-excess areas and water-borne iodine-excess endemial areas. The high iodine water well was found in 129 counties of 11 provinces, and about 30.98 million people lived in water-borne iodine-excess areas and water-borne iodine-excess endemial areas. In these areas, the measures of prevention and control were effectively implemented. In 2016, the new standard for iodine-excess areas was issued; the iodine-excess areas should be redrawn, non-iodized salt should be supplied in these areas, the drinking water should be gradually improved, and the damage of water-borne iodine excess should be controlled at an early date.

Keywords: water-borne; iodine excess; impairment; control and prevention

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1. Introduction

Iodine is a micronutrient that is essential for the production of thyroid hormones. The recommended daily iodine intake is 120 μg for adults who are not pregnant or lactating. The ingestion of iodine or exposure above this threshold is generally well tolerated. However, in certain susceptible individuals, including those with a pre-existing thyroid disease, the elderly, fetuses and neonates, or patients with other risk factors, the risk of developing iodine-induced thyroid dysfunction might be increased [1]. Excessive iodine intake may cause thyroid goiter, overt hyper- and hypothyroidism, subclinical hyper- and hypothyroidism, autoimmune thyroid diseases, iodine allergies and iodine poisoning, mental impairment, etc. [2–7]. Although few articles presented the relationship between iodine excess and thyroid carcinoma, concrete evidence is still needed. Iodine excess can be separated into water-borne and food-borne, according to its source. In some particular places, the source of the excess iodine might not be readily apparent [8–9]. China is the first country to find water-borne iodine excess which has been found in 13 provinces, municipalities and autonomous regions since 1978 [10–14].

2. The Discovery and Confirmation of the Water-Borne Iodine Induced Goiter

In 1978, high goiter prevalence caused by drinking water iodine excess was first discovered in Huanghua, a county of the Hebei Province, China. The Hebei Medical College primarily investigated this phenomenon. After comparing the chemical composition in deep groundwater and shallow-well water and investigating the thyroid morphology and function, and iodine metabolic states of local residents, they found that the goiter prevalence was 7.3% in 4344 residents who drink deep groundwater; the iodine content in deep groundwater was 961.2 μg/L; and the urine iodine concentration was 1645.3 μg/g cr and 2560 μg/g cr for men and women, respectively.

Since 1978, the existence of iodine-induced goiter has been confirmed successively through epidemiology, clinical and animal experiments. A number of studies by the Hebei Medical College investigated the decline of goiter rates before and after improving water through changing the well depth. People who lived in Zhangjuhe Village, a coastal village in the Hebei Province, had been drinking shallow well water which contained 34.5 μg/L iodine until 1978. The prevalence of goiter was 2.83% respectively in these individuals. However, after changing to deep groundwater in 1978, the water iodine content was raised to 306–450 μg/L and the prevalence of goiter rate elevated to 19.86%, respectively, which almost arrived at the level of a serious public health issue.

In order to further demonstrate the relationship between iodine-rich water and thyroid enlargement, surveys about drinking water iodine contents and goiter prevalence were undertaken in several counties. Associations between water iodine levels and thyroid enlargement were: When the water iodine was lower than 95.5 μg/L, goiter rate was generally low (<5%). When water iodine exceeded 200 μg/L, endemic goiter occurred in this area. The prevalence of goiter was positively related to the iodine content in drinking water; the trend was significant ($p < 0.05$) and the correlation coefficient was 0.93.

It showed that the iodine content in drinking water had a dose-response relationship with endemic goiter in the population. According to a series of epidemiological investigations, the reason of why endemic goiter became more prevalent in one area than others was attributed to the excessive iodine intake from the drinking water.

To verify that the endemic goiter in those areas was caused by iodine excess, and confirm there was a dose-response relationship between iodine and goiter prevalence, animal experiments on Leghorn chickens and Kunming mice were conducted by the Hebei Medical College. These experiments also showed positive results between high iodine and goiter.

Water improvement decreased the prevalence of iodine-induced goiter. In Xinglong Village, which is located in the central plain of the Hebei Province, before improving water to reduce iodine, the water iodine content was 559.0 μg/L and the urine iodine content was 1053.64 μg/g cr, the goiter rate in citizens was 4.5% and the goiter rate in children aged 8–10 was 29.03%. However, after drinking the optimal iodine water (the water iodine content was 44.0 μg/L) for seven months, the urine iodine content declined to 102.05 μg/g cr, and the goiter rate in the citizens dropped to 0.62%, the goiter rate in children aged 8–10 fell to 13.41% which indicates that the iodine excess was corrected. In the meantime, the water iodine, urine iodine and goiter prevalence did not change at all in the control area.

Based on these mentioned epidemiological surveys, animal experiments and observational studies on water improvement, it was concluded that endemic goiter occurred in coastal villages near Bohai Bay and in parts of the plain was induced by high iodine drinking water. In order to separate it from food-borne iodine excess induced by seaweed, this type of goiter was named endemic "Water-borne Iodine-Excess Goiter".

3. Water-Borne Iodine-Excess Area Discovery

In 1985, an investigation about the water-borne iodine-excess goiter in the Hebei Province demonstrated that in the "Plain-Type Iodine-Excess Area" of the Hebei Province, iodine-excess goiter was found in some low-lying and obstructed plains, including Xincheng and Xiong County in the Baoding area, Yongqing and Gu'an in the Langfang area, Guangzong and Wei County in the Xingtai area. This type of goiter was named "Plain-Type Iodine-Excess Goiter" because it was being found in plains.

In 1986, the "Inland-Type Iodine-Excess Goiter" was discovered in the Shanxi Province. Qian Qidong reported that the iodine content in shallow groundwater was 533.8 μg/L, the median of urine iodine concentration was 2428.5 μg/L and the goiter rate was about 32.54% in Xiaoyi County of the Shanxi Province [15]. As it was found in the west of the Taihang Mountain, it was also called "Inland-Type Iodine-Excess Goiter". "Water-Borne Iodine-Excess Goiters" were also found in some low-lying villages in more than 10 counties which are located in the Jinzhong Basin according to Liu Derun's report.

From 1983 to 2003, the water-borne iodine-excess areas were found in Shandong, Xinjiang, Fujian, Henan, Inner Mongolia, Anhui, Jiangsu, Beijing, Tianjin and Shaanxi. In 2013, the median of water iodine was over 150 μg/L in 14 villages of five counties near the Jianjiang river basin in the Guangdong Province. In 2017, during the project of national drinking water iodine investigation in China, high water iodine wells were found in Chengbu county of the Hunan Province.

4. National Investigation of Water-Borne Iodine-Excess Areas

In 2005, in order to explore the distribution of drinking water with high iodine in China, a national water-borne iodine-excess areas survey was launched by the Center for Endemic Disease Control, Chinese Center for Disease Control and Prevention. This survey was granted by the Public Health Fund and sponsored by the central government. The results showed that iodine excess is mainly naturally occurring in drinking water with high iodine in. Wells with high water iodine were found in 129 counties of 11 provinces, municipalities and autonomous regions, include: Anhui, Beijing, Fujian, Hebei, Henan, Jiangsu, Inner Mongolia, Shandong, Shanxi, Tianjin and Xinjiang. Water-borne iodine-excess areas (goiter prevalence <5%) exist in all these provinces except Fujian and Xinjiang, and water-borne iodine-excess endemial areas (goiter prevalence >5%) exist in all these provinces except Fujian, Xinjiang, Beijing and Inner Mongolia. A total of 96 counties contained water-borne iodine-excess villages and 64 counties contained water-borne iodine-excess endemial villages, Table 1. About 30.98 million people lived in the water-borne iodine-excess or endemial areas [9].

Table 1. The distribution of water-borne iodine-excess areas in 2005.

Province	Counties with HWI well	Counties with HWI townships	Counties with HWI endemial townships	Townships with HWI well	Townships with HWI area	Population in HWI area（thousand）	Townships with HWI endemial area	Population in HWI endemial area（thousand）
Beijing	1	1	0	6	1	30	0	0
Tianjin	2	2	1	19	11	110	4	320
Hebei	38	26	22	243	108	3780	63	2020
Shanxi	10	7	6	42	18	470	11	410
Inner Mongolia	2	1	0	18	2	40	0	0
Jiangsu	6	6	5	127	40	1520	48	2300
Anhui	10	3	2	90	15	880	21	1090
Fujian	1	0	0	3	0	0	0	00
Shandong	40	33	19	442	189	8800	58	3650
Henan	18	17	9	312	104	3240	41	2320
Xinjiang	1	0	0	2	0	0	0	0
Total	129	96	64	1304	488	18870	246	12110

Note: HWI, high water iodine.

5. Investigation on Other Iodine-Excess Impairments

The follow-up studies found that high iodine intake could increase the prevalence rate of hyperthyroidism, thyroid hypofunction and autoimmune thyroid diseases other than goiter.

It is controversial about whether high iodine intake can cause children's intellectual impairment. Qian et al. reported that the mean effect size of iodine excess on intelligence was 0.21, and iodine excess had not shown a significant role in children’s intelligence in a meta-analysis [16]. Ren et al.

reported that iodine content greater than 600 μg/L would reduce the intellectual level of children in a computerized literature research [17].

It is also found that high iodine content may improve the prevalence of cardiovascular diseases. Guo et al. found that there was a link between the Budd–Chiari syndrome and high iodine in external environment [18].

Studies have demonstrated that subclinical hypothyroidism was related to miscarriage, premature birth, stillbirth, fetal intrauterine growth retardation and a series of adverse pregnancy outcomes. Therefore, iodine excess may be an important factor which causes the adverse pregnancy outcomes.

6. National Criterion of the Delimitation and Demarcation of Water-Borne Iodine-Excess Areas and Endemial Areas

"Determination and classification of the areas of high water iodine and the endemial areas of iodine-excess goiter" (GB/T 19380-2003) was led by Liu, a chief physician in the Institute for Endemic Disease Control and Research of the Shanxi Province [19]. According to this standard, an area can be considered as high water iodine area if it complies with: ⅰ) When the median of iodine content in drinking water is more than 150 μg/L; ⅱ) the median urinary iodine of children aged 8–10 is over 400 μg/L. An endemial area of iodine-excess goiter complies with: i) When the median of iodine content in drinking water is more than 300 μg/L; ⅱ) the median urinary iodine of children aged 8–10 is over 800 μg/L; ⅲ) the goiter rate of children aged 8–10 is greater than 5%. These areas are delimitated on the basis of townships considered in the distribution characteristics and the applicability of intervening measures such as supplying non-iodized salt.

Jia, a chief physician in the institute for endemic disease control and research of the Shanxi Province, has led the revision of the standard since 2007. The revision complied: i) the name was corrected as "Definition and demarcation of water-borne iodine-excess areas and iodine-excess endemial areas" (GB/T 19380-2016) [20]; ⅱ) the areas were defined as villages instead of townships; ⅲ) the indicators of water-borne iodine-excess area were altered to: When the median of iodine concentration in drinking water is more than 100 μg/L instead of 150μg/L; ⅳ) the indicators of endemial areas of iodine-excess goiter were altered to: When the median of iodine content in drinking water is more than 100μg/L (compulsory indicator); the goiter rate of children aged 8–10 is higher than 5% (compulsory indicator); the median urinary iodine of children aged 8–10 is over 300 μg/L (reference indicator). The revised standard was released in 2016, Table 2.

Table 2. The old and new standard of iodine-excess area and endemial area.

Standard	Iodine-excess area	Iodine-excess endemial area
GB/T 19380-2003 Determination and classification of the areas of high water iodine and the endemial areas of iodine-excess goiter	① the median of iodine content in drinking water is more than 150 μg/L; ② the median urinary iodine of children aged 8–10 is over 400 μg/L	① the median of iodine content in drinking water is more than 300 μg/L; ②the median urinary iodine of children aged 8–10 is over 800 μg/L; ③the goiter rate of children aged 8–10 is greater than 5%
GB/T 19380-2016 Definition and demarcation of water-borne iodine-excess areas and iodine-excess endemial areas	the median of iodine concentration in drinking water is more than 100 μg/L	① the median of iodine content in drinking water is more than 100 μg/L (compulsory indicator); ②the goiter rate of children aged 8–10 is higher than 5% (compulsory indicator);

③the median urinary iodine of children aged 8–10 is over 300 μg/L (reference indicator)

7. Fulfillment of Intervention Measures

In order to prevent iodine deficiency disorders, comprehensive prevention and control measures including universal salt iodization have been implemented since 1995 in China.

China's "Regulation on Edible Salt Iodization as a Means to Eliminate IDD" specifies that iodine salt should not be distributed in iodine-excess areas. The scopes of water-borne iodine-excess areas are more explicit than before. So far, non-iodized salt has been supplied in these areas instead of iodized salt, and they were surveyed from 2007 as a prevention and control measure, Table 3.

Table 3. Coverage rate of non-iodized salt in water-borne iodine-excess areas from 2007 to 2016 surveillance.

Year	No. of province	No. of Counties	Sample size of salt	No. of non-iodized salt	Coverage rate of non-iodized salt (%)
2007	5	78	21,321	15,594	73.1
2008	8	84	19,462	16,114	82.8
2009	8	84	19,062	17,262	90.6
2010	8	110	24,692	19,334	78.3
2011	7	109	24,492	22,245	90.8
2012	8	110	25,961	23,923	92.1
2013	8	110	26,040	24,919	95.7
2014	8	110	25,679	24,545	95.6
2015	8	110	25,597	24,640	96.3
2016	8	110	26,280	25,339	96.4

Water improvement measures were also taken in order to reduce the high iodine intake from water in some areas. This work had already been completed in Beijing, Fujian, Inner Mongolia and Shaanxi.

In other provinces, the construction of water supply systems have been developed with the funds supplied by "Drinking Water Safety Projects in Rural Areas in the Eleventh-five Year" and "Preventing and Controlling High Fluorine and High Arsenic Project" of the National Development and Reform Commission. However, water iodine is not an indicator for choosing a water source in those projects.

8. Implementation of National Surveillance in Water-Borne Iodine-Excess Areas and Endemial Areas

Water-borne iodine-excess areas surveillance programs have been conducted in water-borne iodine-excess areas and endemial areas in the relevant provinces by the National Center for Endemic Disease Control from 2012. The purpose of this surveillance program included: Knowing the consumption of non-iodized salt in water-borne iodine-excess areas and endemial areas timely; learning the current situation of iodine changes in the environment and the status of iodine-excess goiter; maintaining the health of the people who live in water iodine-excess areas, and providing a scientific basis for the government's prevention and control strategy. This surveillance program is conducted once a year, and monitoring includes iodine in household salt, drinking water iodine and iodine-excess goiter.

9. The Major Issues during Control and Prevention of Water-Borne Iodine-Excess Impairments

There were also several issues during the prevention and control of water-borne iodine-excess impairments. First, the distribution of the water-borne iodine-excess areas in the village level in most

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provinces remains obscure although new standards for the water iodine-excess areas have been issued. The water iodine-excess areas and endemial areas should be determined and classified timely. Second, prevention and control measures should be strengthened to make sure that the edible non-iodized salt can be provided to all citizens living in water iodine-excess areas. Third, except Beijing, Inner Mongolia, Xinjiang, Shaanxi and Fujian, other provinces have not yet improved water to reduce iodine in water iodine-excess areas. The manner in which the water-improvement program functions as a project for the water department in these areas is a main problem. Forth, health education in water iodine-excess areas has not been carried out. Fifth, the impact of iodine excess for health is not clear, and it needs further scientific research.

10. Prospective and Suggestion on Control and Prevention of Water-Borne Iodine-Excess Impairments

10.1 Redrawing the High Water Iodine Areas According to the New Standard

In the current version of "Definition and demarcation of water-borne iodine-excess areas and iodine-excess endemial areas" (GB/T 19380-2016), the endemic area was defined by village instead of township, and the criteria of water iodine changed from iodine levels higher than 150 μg/L to any area where the iodine content is higher than 100 μg/L. Reducing the cut-off for high water iodine areas will increase the number of affected areas. It is important to check the water iodine distribution on a village level and know how many villages will be categorized as high water iodine under the new cut-off level.

10.2 Improving Water to Reduce Iodine in Water-Borne Iodine-Excess Areas

The method of improving water to reduce iodine can effectively prevent and control the prevalence of endemic goiter in water-borne iodine-excess endemial areas. Therefore, the water iodine distribution should be checked out at a village level by the health department and then provided to the local water conservancy department. The water conservancy department should take the water improvement program as an important project in water-borne iodine-excess areas, and control the impairments of iodine excess as early as possible.

10.3 Improving the Salt Market Supervision and Guaranteeing the Non-Iodized Salt Supplementation

As the intersection of water-borne iodine-excess areas, with the iodine deficiency areas and optimal iodine areas, it brought some difficulties for salt supplementation. In recent years, the rate of non-iodized salt consumption remained about 90% in water-borne iodine-excess areas, this number implied that there are some citizens who still choose iodized salt. Iodine-excess water and iodized salt will bring double hazards for the citizen. Therefore, the market supervision department of the salt industry should strengthen the market management to ensure that all residents of the water-borne iodine-excess areas eat the non-iodine salt.

10.4 Developing the Surveillance in Water-Borne Iodine-Excess Areas, Improving the Surveillance System

As the implementation of "Definition and demarcation of water-borne iodine-excess areas and iodine-excess endemial areas" (GB/T 19380-2016), the Center for Endemic Disease Control will revise the surveillance program, and the water-borne iodine-excess areas will be defined by village in future.

10.5 Carrying out Health Education and Health Promotion in Water-Borne Iodine-Excess Areas

Material of health education for water-borne iodine-excess areas should be made according to the current situation of prevention and control in water-borne iodine-excess areas. Health education and health promotion should be carried out for protecting from iodine-excess impairments. Through acknowledging the harm of iodine excess, citizens can choose non-iodized salt and drink low iodine water consciously. Improving the health education and promotion among leaders and relevant departments, and supervising water departments improving water to reduce iodine in these areas should be fulfilled as soon as possible.

10.6 Conducting Scientific Research about the Impairments of Iodine Excess

As water-borne iodine-excess areas was first been found in China, many people lived in the water-borne iodine-excess areas until now and because the impairment of iodine excess is still not very clear, it is suggested that epidemiological investigations on iodine-excess hazards and pathogenesis research should be strengthened in future.

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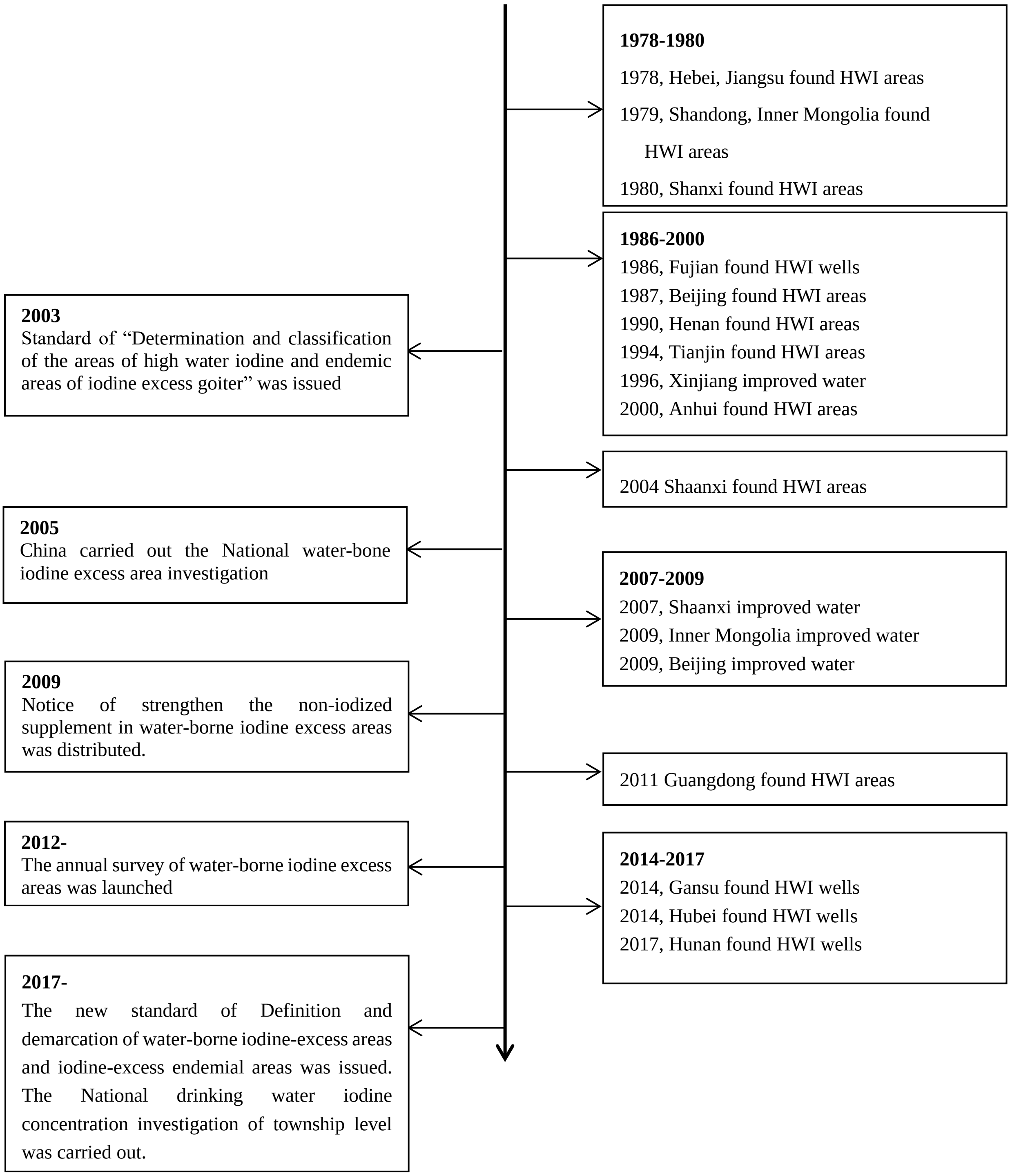

Figure 1. The process of Control and Prevention Impairment of Water-Borne Iodine Excess in China.