• ESOPHAGEAL CANCER •

# Research and control of well water pollution in high esophageal cancer areas

Xiu-Lan Zhang, Bing Zhang, Xing Zhang, Zhi-Feng Chen, Jun-Zhen Zhang, Shuo-Yuang Liang, Fan-Shu Men, Shu-Liang Zheng, Xiang-Ping Li, Xiu-Lan Bai

Xiu-Lan Zhang, Zhi-Feng Chen, Shuo-Yuang Liang, Cancer Institute, the Fourth Hospital of Hebei Medical University, Shijiazhuang 050011, Hebei Province, China

**Bing Zhang, Xing Zhang,** School of Public Health, Hebei Medical University, Shijiazhuang 050017, Hebei Province, China

**Jun-Zhen Zhang**, the Fourth Hospital of Hebei Medical University, Shijiazhuang 050011, Hebei Province, China

Fan-Shu Men, Shu-Liang Zheng, Xiang-Ping Li, Cixian Cancer Institute, Cixian County, Hebei Provence, China

Xiu-Lan Bai, Chichen Health Center, Chichen County, Hebei Province, China

Supported by Ministry of Education of China, No.85-914-01-01 Correspondence to: Dr. Xiu-Lan Zhang, Cancer Institute, the Fourth Hospital of Hebei Medical University, 12 Jian Kang Lu, Shijiazhuang 050011, Hebei Province, China. czf@xinhuanet.com Telephone: +86-311-5825709 Fax: +86-311-6077634

Received: 2002-10-08 Accepted: 2002-12-22

## Abstract

**AIM:** In order to detect risk factors for esophageal cancer, a national research program was carried out during the Eighth Five-Year Plan (from 1991 to 1995).

**METHODS:** Cixian County and Chichen County in Hebei Province were selected as the index and the control for the study fields with higher or lower incidence of esophagus cancer in China, respectively. In these areas, we investigated the pollution of three nitrogenous compounds in well water for drinking and the use of nitrogen fertilizer in farming.

**RESULTS:** In well water, nitrate nitrogen, nitrite nitrogen and ammonia nitrogen were 8.77 mg/L, 0.014 mg/L and 0.009 mg/L in Cixian County in 1993, respectively. They were significantly higher than their levels (3.84 mg/L, 0.004 mg/L and 0.004 mg/L) in Chichen County (P<0.01, t=6.281, t=3.784, t=3.775). There was a trend that the nitrogenous compounds in well water increased from 1993 to 1996. The amount of nitrogen fertilizer used in farming was 787. 6 kg per hectare land in Cixian County in 1991, significantly higher than 186 kg per hectare in Chichen County (t=9.603, P<0.001).

**CONCLUSION:** These investigations indicate that the pollution of nitrogenous compounds in well water for drinking is closely related to the use of nitrogen fertilizer in farming, and there is a significantly positive correlation between the level of three nitrogenous compounds in well water and the mortality of esophageal cancer (correlation coefficient =0.5992). We suggest that improvement of well system for drinking water quality should be an effective measure for esophageal cancer prevention and control in rural areas.

Zhang XL, Zhang B, Zhang X, Chen ZF, Zhang JZ, Liang SY, Men FS, Zheng SL, Li XP, Bai XL. Research and control of well water pollution in high esophageal cancer areas. *World J Gastroenterol* 2003; 9(6): 1187-1190

http://www.wjgnet.com/1007-9327/9/1187.asp

## INTRODUCTION

It is well known that the chief causes of most cancers are environmental, dietary and lifestyle factors. In China, there is a special area around the Taihang Mountain with the highest incidence of esophageal cancer. Esophageal cancer has been studied in this rural area for a long time<sup>[1-3]</sup>. These studies indicate some relationship between local environmental factors and esophageal cancer<sup>[4-8]</sup>. Among these, nitrogenous compounds in well water for drinking is considered as a possible risk factor for esophageal cancer because of its close relationship with local people's life<sup>[7, 8]</sup>. In this rural area, well is the main water source for drinking. It is polluted usually by nitrogenous compounds. In order to identify the effect of nitrogenous compound pollution on esophageal cancer, we designed a  $2\times 2$  cross-sectional study for factor analysis during the Eighth Five-Year Plan (from 1991 to 1995). The research program for investigating the relationship between drinking water pollution and esophageal cancer was carried out. It also included a step of improvement in well water quality and pollution control.

## MATERIALS AND METHODS

#### Study fields

According to mortality, two counties from Hebei Province were selected for the present study fields, Cixian County as index and Chichen County as control, respectively. From 1974 to 1976, the mortality per 100 000 of esophageal cancer standardized by Chinese population in Cixian County and in Chichen County was 147.7 and 8.3 in male, and 79.33 and 2.8 in female, respectively. Cixian County is located at the southern part of Hebei Province and the eastern foot of the Taihang Mountain. There are 354 villages under 35 local town governments in Cixian County. It covers an area of 1 015 Km<sup>2</sup> and has a population of 580 000.

## Well registration

Before the investigation, a team for the program was organized. The investigators and other work staff were trained based on the program guideline. From the end of 1991 to the beginning of 1992, we completed registration of the wells located in 101 villages (9 towns) in Cixian County and made well file. The registered items of well file included (1) position, (2) type, (3) depth, (4) enclosing wall, (5) wall structure, (6) pipeline, (7) pollution source within 10 meter distance, (8) served population, and (9) served time. According to the well registration, we started a consecutive monitor on the pollution of three nitrogenous compounds (nitrate nitrogen, nitrite nitrogen and ammonia nitrogen) in the selected wells. Meanwhile, we investigated the amount of nitrogen fertilizer used in farming per year in the study fields.

#### Nitrogenous compounds examination

The level of ammonia nitrogen in water was analyzed by Nessler's reagent method. The amount of nitrate nitrogen and of nitrite nitrogen was tested in terms of Cadmium column reduction method. The water samples were collected according to the routine method<sup>[9-12]</sup>.

#### Statistical analysis

Statistical analysis was performed by t test, and linear correlation was used for analysis on the relationship between three nitrogenous compounds and mortality of esophageal cancer. Two-tailed P value of less than 0.05 was defined as statistically significant.

## RESULTS

Among 9 towns in Cixian County, there were three types of well served for drinking water, manual-pump well, motor-pump well and non-pump well. Non-pump well was main type, about 554 were built in these areas. This type of well had a big opening mouth without pipe, enclosing wall and cover. Recently, some new motor-pump wells were built. They were 200 meter in depth with brick wall. These old and new wells provided drinking water for 130 952 people. In the control areas, 1/3 of wells was about 8 meters and 2/3 was less than 40 meters in depth. The depth of water varied with season. The served time of wells was different. The oldest one, for example, the Longwangmiao Well of the Xiguanglu Village of the Guanglu Town had a history of 300 years, and the new one was only 2 years.

The pollution of nitrogenous compounds in drinking water was a big health problem. We found that 41.2 % of the motorpump wells and 88.5 % of non-pump wells existed pollution sources within 10 meter distance, for example, excrement and urine from the residents and animals, and pollution sources increased year by year. The monitoring data from the sampled wells showed that nitrate nitrogen, nitrite nitrogen and ammonia nitrogen in Cixian County were significantly higher than those in Chichen County (P < 0.01), and the pollution increased gradually from 1993 to 1996 (Table 1). They were 20.6 %, 50.5 % and 33.3 % higher than the state permissive level, respectively. The amount of nitrogen fertilizer used in Cixian County's farming was significantly higher than in Chichen County (P<0.01), and there was an increasing trend (Table 2). The time trend of three nitrogen compounds in relation to the use of nitrogen fertilizer is shown in Figure 1, Figure 2 and Figure 3 for Cixian County and Chichen County, respectively.

**Table 1** Three nitrogenous compounds pollution (mg/L) ofthe well water in Cixian County and Chichen County from1993 to 1996

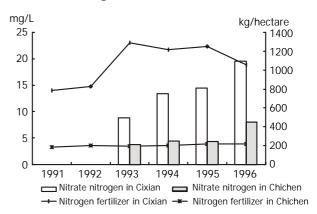
	Numbers of well	1993	1994	1995	1996
Nitrate nitrogen					
Cixian	33	$8.770^{\mathrm{b}}$	$13.381^{b}$	$14.473^{b}$	$19.554^{\mathrm{b}}$
Chichen	31	3.829	4.452	4.351	8.022
Ratio		2.29	3.00	3.33	2.44
(Cixian/Chichen)					
Nitrite nitrogen					
Cixian	33	$0.0144^{\text{b}}$	$0.0629^{\mathrm{b}}$	$0.0407^{\mathrm{b}}$	$0.0101^{\mathrm{b}}$
Chichen	31	0.0039	0.0094	0.0085	0.0020
Ratio		3.69	6.69	4.79	5.05
(Cixian/Chichen)					
Ammonia nitroge	n				
Cixian	33	0.0094 <sup>b</sup>	$0.0256^{\text{b}}$	0.0237	$0.0117^{b}$
Chichen	31	0.0039	0.0029	0.0230	0.0028
Ratio		2.41	8.82	1.03	4.18
(Cixian/Chichen)					

 $^{b}P<0.01$ , There was a significant difference between two counties.

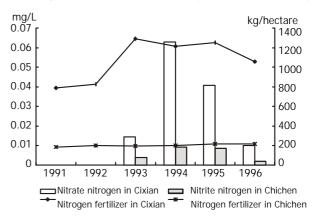
**Table 2** Farming use of nitrogen fertilizer (kg/hectare) inCixian County and Chichen County from 1991 to 1996

	1991	1992	1993	1994	1995	1996
Cixian Chichen	787.6 186.0 <sup> b</sup>	825.1 202.5 <sup>b</sup>	1293.1 196.5 <sup>ь</sup>	1213.6 201.0 <sup>ь</sup>	1251.1 220.5 <sup>ь</sup>	1053.1 219.0 <sup>b</sup>
Ratio (Cixian /Chichen)	4.20	4.07	6.58	6.04	5.67	4.81

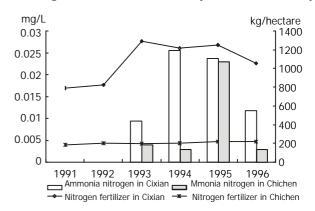
<sup>b</sup>P<0.01, There was a significant difference between two counties.



**Figure 1** Time trend of nitrate nitrogen in relation to the farming use of nitrogen fertilizer in Cixian County and Chichen County.



**Figure 2** Time trend of nitrite nitrogen in relation to the farming use of nitrogen fertilizer in Cixian County and Chichen County.



**Figure 3** Time trend of ammonia nitrogen in relation to the farming use of nitrogen fertilizer in Cixian County and Chichen County.

### DISCUSSION

It has been proven in animal experiments that nitrosamine compounds (NOC) are a kind of strong carcinogen and can cause tumor in different animal tissues and organs<sup>[13-21]</sup>. The epidemiological investigation has also demonstrated an increased risk of human gastric cancer with food intake polluted by nitrosamine compounds<sup>[22,23]</sup>. Nitrate and nitrite are precursors of NOC<sup>[24,25]</sup>.

If well water contains a large amount of three nitrogenous compounds, and serve as main water source, there may be two harmful effects on local people's health. One is that three nitrogenous compounds would accumulate in plants and in crops<sup>[25-29]</sup>. Usually, nitrate is easily reduced to nitrite, and then it is synthesized into NOC. The other harmful effect is that local people and livestock or poultry would have an increased intake of three nitrogenous compounds through the drinking water<sup>[30-32]</sup>. These nitrogenous compounds with ammonia can be changed to a strong carcinogen, NOC, in stomach since its pH value is 1-3 from gastric acid<sup>[33]</sup>.

The present investigation showed that the pollution of three nitrogenous compounds in the index area with high risk of esophageal cancer was significantly higher than that in the control area (P<0.01). The mortality ratio between Cixian County and Chichen County was 17.9 (147.7 per 100 000 /8. 3 per 100 000) in male, and 28.5 (79.3/2.8) in female in the period of 1974 through 1976. There was a positive correlation between the nitrate nitrogen, nitrite nitrogen in well water and mortality of esophageal cancer in the study fields. The present findings indicate that heavy pollution of nitrogenous compounds in drinking water in the index area is a possible risk factor for esophageal cancer.

There were two possible pollution sources of nitrogenous compounds for well in the investigated fields, living garbage or excrement and farming nitrogen fertilizer. In comparison of the two counties, we found that the amount of nitrogen fertilizer used in farming in Cixian County was significantly higher than that in Chichen County, and the pollution of nitrate nitrogen and nitrite nitrogen in well water had a similar trend (Figure 1 and Figure 2). It can be understood that the nitrate nitrogen and nitrite nitrogen in well water come mainly from the pollution of farming nitrogen fertilizer. The amount of ammonia nitrogen in well has not a regular change. Its pollution to the drinking water is possibly resulted from the excrement of local people and animals other than farming nitrogen fertilizer.

Based on these evidences, well water pollution control of three nitrogenous compounds will be one of the important measures for the primary prevention of esophageal cancer in the higher risk areas. The study revealed that water quality improvement had a beneficial effect on gastric cancer prevention<sup>[34]</sup>. At the beginning of the Ninth Five-Year Plan (1996-2000), a program for improvement of water supply system in the index area was started. Initial effect was observed (Table 3). There was a significant decline of three nitrogenous compounds in well water after several years' pollution control. These findings indicate that the program for improvement in water supply system is successful for pollution control. Whether pollution control of nitrogenous compounds contributes to incidence decline of esophageal cancer in the higher risk area, needs further study and more evidence.

 Table 3
 Three nitrogenous compounds (mg/L) in well water before and after well reconstruction

No. of well	Nitrate nitrogen		Nitrite nitrogen		Ammonia nitrogen	
	Before	After	Before	After	Before	After
12#	14.9621	8.0097	0.0077	0.0033	0.0131	0.0048
14#	8.9890	1.9099	0.0208	0.0067	0.0127	0.0053
29#	18.4929	0.0000	0.2929	0.0100	0.0459	0.0087

12#, 14#, 29# are the number of the sampled well.

Based on the presently investigated results, measures for pollution prevention and control in the areas with high risk of esophageal cancer should include: (1) The first measure is to improve the health consciousness of local people on drinking water, and to develop the type of deep well with pipeline. (2) The second is to focus on the environmental hygiene surrounding the well. It includes garbage control near water source, and sanitary management of excrement and urine. (3) The third is to establish and to improve the system management of water source, and to supply clean water with pipeline. (4) The fourth is to build high quality lavatory and to prevent its pollution to well water. (5) The fifth is to encourage local farmers to use rational formula fertilization in order to decrease effectively organic nitrogen pollution in the environment.

## REFERENCES

- Hou J, Lin PZ, Chen ZF, Wang GQ, Liu KG, Li SS, Meng FS, Du CL. Survey on esophageal cancer in Cixian County. *Zhongliu Fangzhi Yanjiu* 1998; 25: 73-75
- 2 Yokokawa Y, Ohta S, Hou J, Zhang XL, Li SS, Ping YM, Nakajima T. Ecological study on the risks of esophageal cancer in Cixian, China: the importance of nutritional status and the use of well water. *Int J Cancer* 1999; 83: 620-624
- 3 **Qiao YL**, Hou J, Yang L, He YT, Liu YY, Li LD, Li SS, Lian SY, Dong ZW. The Trends and preventive strategies of esophageal cancer in high-risk areas of Taihang Mountains, China. *Zhongguo Yixue Kexue Yuan Xuebao* 2000; **23**: 10-14
- 4 **Zhuo XG**, Watanabe S. Factor analysis of digestive cancer mortality and food consumption in 65 Chinese counties. *J Epidemiol* 1999; **9**: 275-284
- 5 Li WJ, Zhu MJ Chen PP, Lu WQ, Wang Q, Shi BQ. Study on dietary pattern and nutrients intakes of residents in areas of high and low incidence of esophageal cancer. *Weisheng Yanjiu* 1997; 26: 351-355
- 6 **Wang H**, Wei H, Ma J, Luo X. The fumonisin B1 content in corn from North China, a high risk area of esophageal cancer. *J Environ Pathol Toxicol Oncol* 2000; **19**: 139-141
- 7 Li WJ, Lu WQ, Zhu MJ, Shi BQ, Wang Q. Determination of copper, zinc, iron and calcium in wheat and maize and three nitrogen compounds in high and low risk areas of esophageal cnacer. Weisheng Yanjiu 1998; 27: 69-71
- 8 Zhang XL, Li SS, Zhang WZ. Investigation and study on drinking water in Cixian County. *Zhongguo Zhongliu* 1996; 5: 12-14
- 9 Hao CJ. The Practical handbook for environmental monitoring and water analysis. Harbin: Harbin Industrial University Press 1986
- 10 **Ministry of Public Health**. The people's republic of China, the standarded method for drinking water testing. *Beijing: China Standard Bureau Press* 1986
- 11 **Environmental Protective Bureau**. Ministry of urban and rural construction & environment protection analytical method for environmental monitoring. *Beijing: Chinese Environmental Science Press* 1986
- 12 **Chinese Environmental Monitoring Center**. The handbook of quality assurance for environmental monitoring on water. *Beijing: Chemical Industry Press* 1984
- 13 Opitz OG, Harada H, Suliman Y, Rhoades B, Sharpless NE, Kent R, Kopelovich L, Nakagawa H, Rustgi AK. A mouse model of human oral- esophageal cancer. J Clin Invest 2002; 110: 761-769
- 14 Fong LY, Nguyen VT, Farber JL. Esophageal cancer prevention in zinc- deficient rats: rapid induction of apoptosis by replenishing zinc. J Natl Cancer Inst 2001; 93: 1525-1533
- 15 Straif K, Weiland SK, Bungers M, Holthenrich D, Taeger D, Yi S, Keil U. Exposure to high concentrations of nitrosamines and cancer mortality among a cohort of rubber workers. *Occup Environ Med* 2000; 57: 180-187
- 16 **Qi GY**, Shu SC, You CF, Chen SW, Song Y. A case-control study on the influential factors of esophageal cancer. *Zhongguo Manxingbing Yu Fangyu Kongzhi* 2001; **9**: 15-14,34
- 17 Lin K, Shen ZY, Cai SS, Lu SX, Guo LP. Investigation on nitrosamines in the diets of the inhabitants of high-risk area for esophageal cancer in the southern China and analysis of the correlation factors. *Weisheng Yanjiu* 1997; 26: 266-269

- 18 Lin K, Shen W, Shen Z, Wu Y, Lu S. Dietary exposure ad urinary excretion of total N- nitroso compounds, nitrosamino acids and volatile nitrosamine in inhabitants of high- and low- risk areas for esophageal cancer in Southern China. *Int J Cancer* 2002; **102**: 207-211
- 19 Zhang GS, He YT, Hou J. A case control study on risk factor of esophageal cancer in Cixian County. *Sichuan Zhongliu FangZhi* 2000; 13: 65-67
- 20 Wilp J, Zwickenpflug W, Richter E. Nitrosation of dietary myosmine as risk factor of human cancer. *Food Chem Toxicol* 2002; 40: 1223-1228
- 21 **Siddiqi M**, Kumar R, Fazili Z, Spiegelhalder B, Preussmann R. Increased expoure to dietary amines and nitrate in a popalation at high risk of oesophageal and gastric cancer in Kashmir. *Carcinogenesis* 1992; **13**: 1331-1335
- 22 Cai L, Zheng ZL, Zhang ZF. Risk factors for the gastric cardia cancer: a case-control study in Fujian Province. World J Gastroenterol 2003; 9: 214-218
- 23 Ye WM, Yi YN, Luo RX, Zhou TS, Lin RT, Chen GD. Diet and gastric cancer: a casecontrol study in Fujian Province, China. *World J Gastroenterol* 1998; **4**: 516-518
- Rogers MA, Vaughan TL, Davis S, Thomas DB. Consumption of nitrate, nitrite, and nitrosodimethylamine and the risk of upper aerodigestive tract cancer. Cancer *Epidemiol Biomarkers Prev* 1995;
   4: 29-36
- 25 Yang XF, Wang KJ, Jia YS, Lian BQ, Li T, Li SD, Du C, Yan JG. Epidemiological investigation on cancer mortality of the workers exposed to nitrite compounds. *Zhonghua Laodongwei Shengzhi Yebing Zazhi* 1996; 14: 293-295
- 26 Li W, Lu W, Zhu M, Shi B. Determination of copper, zinc, iron and calcium in wheat and maize and three nitrogen compounds in high and low risk areas of esophageal cancer. *Weisheng Yanjiu* 1998; 27: 69-71

- 27 **Lu SH**, Camus AM, Ji C, Wang YL, Wang MY, Bartsch H. Mutagenicity in salmonella typhimurium of N-3-methylbutyl- N-1methyl-acetonyl-nitrosamine and N-methyl-Nbenzylnitrosamine, N-nitrosation products isolated from cornbread contaminated with commonly occurring moulds in Linshien County, a high incidence area for oesophageal cancer in Northern China. *Carcinogenesis* 1980; **1**: 867-870
- 28 Guo LP, Zhang FS, Wang XR, Mao DR, Chen XP. Effect of long-term fertilization on soil nitrate distribution. *J Environ Sci* 2001; 13: 58-63
- 29 Ramos C, Agut A, Lidon AL. Nitrate leaching in important crops of the Valencian Community region. *Environ Pollut* 2002; 118: 215-223
- 30 Barrett JH, Parslow RC, McKinney PA, Law GR, Forman D. Nitrate in drinking water and the incidence of gastric, esophageal, and brain cancer in Yorkshire, England. *Cancer Causes Control* 1998; 9: 153-159
- 31 **Lu WQ**, Chen JL, Li WJ, Wang Y, Ddong WZ, Zhu MJ, Wang Q. Analysis on three nitrogen compounds of the drinking water in high and low risk areas of esophageal cancer. *Zhongguo Zhongliu* 2000; **9**: 227
- 32 Shrestha RK, Ladha JK. Nitrate pollution in groundwater and strategies to reduce pollution. *Water Sci Technol* 2002; **45**: 29-35
- 33 Mayne ST, Risch HA, Dubrow R, Chow WH, Gammon MD, Vaughan TL, Farrow DC, Schoenberg JB, Stanford JL, Ahsan H, West AB, Rotterdam H, Blot WT, Fraumeni JF Jr. Nutrient intake and risk of subtypes of esophageal and gastric cancer. *Cancer Epidemiol Biomarkers Prev* 2001; 10: 1055-1062
- 34 Wang ZQ, He J, Chen W, Chen Y, Zhou TS, Lin YC. Relationship between different sources of drinking water, water quality improvement and gastric cancer mortality in Changle County-A retrospective-cohort study in high incidence area. World J Gastroenterol 1998; 4: 45-47

Edited by Wen CY and Wang XL