

Preplanned Studies

Characteristics in the Distribution of Chronic Benzene Poisoning Associated Industries — 6 PLADs, China, 2005–2019

Jin Zhou^{1,8}; Lei Han^{2,8}; Jianxin Zhao¹; Xiurong Cheng¹; Fenxia Hou¹; Qiang Jia³; Juan Zhang⁴; Peiyu Xu⁵; Jing Liu⁶; Zihuan Wang⁷; Baoli Zhu²; Caihong Xing^{1,8}

Summary

What is already known on this topic?

Starting in the early 1950s, the main industries in China associated with chronic benzene poisoning (CBP) included painting, pharmaceuticals, and shoemaking. However, because of rapid socioeconomic development, the distribution of industries associated with CBP likely changed.

What is added by this report?

From 2005 to 2019, CBP has become an increasingly important type of chronic occupational poisoning (COP) in China. CBP was mainly found to have occurred in manufacturing industries, especially private enterprises and small and medium-sized enterprises. The sub-industry with the highest proportion of CBP cases was general and special equipment manufacturing, followed by chemical raw materials and chemical manufacturing.

What are the implications for public health practice?

CBP was found to be the main component of COP in China, so the supervision and management in manufacturing, especially in the medium-sized and small enterprises, need to be strengthened. Occupational benzene exposure limits should also be adjusted accordingly.

Chronic exposure to benzene causes poisoning, acute myeloid leukemia (AML), and other hematopoietic malignancies. While benzene exposure has an overall 7-fold risk for development of leukemia, chronic benzene poisoning (CBP) is associated with a 71-fold risk for development of AML or myelodysplastic syndromes in humans (1–2). CBP patients experience a strong and prolonged hematotoxicity characterized by significantly

reduced white blood cell counts. Malignant transformation in these CBP patients can take place in a short period of time (3). In this study, CBP data were obtained from the Occupational Disease and Occupational Health Monitoring Information System, a subsystem of the China Information System for Disease Control and Prevention. CBP patients from 6 provincial-level administrative divisions (PLADs)* were analyzed and characterized by age, enterprise scale†, ownership of the enterprise‡, and industry§ distribution. There was a total of 3,836 CBP patients across China during 2005–2019, of which 1,861 CBP in 6 PLADs were included in the analysis. This study suggests that a targeted occupational health survey is needed to determine the number of industries with CBP changes and strengthen the supervision and management of the industry with CBP.

CBP had been reported in China in the early 1950s with the main industries associated with CBP at the time being painting, pharmaceuticals, and distillation of coal and coal tar. In the 1970s, the prevalence of CBP was 1.1% (4). With the reduction of maximum allowable concentration (MAC) of benzene to 40 mg/m³ in 1979 and the improvement of hygiene conditions of workplaces, the prevalence of CBP decreased to 0.5%. The annual mean number of CBP cases decreased from 892 cases during 1979–1982 to 594 cases during 1984–1993 and 223 cases during 1996–2003. Correspondingly, the main industries associated with CBP had shifted to light industry and machinery (5–6). The permissible concentration-time weighted average (PC-TWA) of benzene in workplace in China was reduced to 6 mg/m³ in 2002. So far, whether the industrial distribution of CBP has changed with decreasing PC-TWA is unknown.

* Guangdong Province, Jiangsu Province, Shandong Province, Sichuan Province, Beijing Municipality, and Tianjin Municipality.

† Large, medium, small, and mini-sized enterprises.

‡ State-owned, collective, pooling, private, foreign, stock, and Hong Kong, Macao, and Taiwan of mainland China.

§ Chemical raw materials and chemical products manufacturing, general and special equipment manufacturing, non-mental mineral product industry, etc. More information about industry category is available at http://www.stats.gov.cn/tjsj/tjbz/hyflbz/201710/t20171012_1541679.html.

The 6 PLADs of Guangdong, Jiangsu, Shandong, Sichuan, Beijing, and Tianjin were selected because the number of CBP cases increased from 2005 to 2019 and accounted for more than half of the total number of new CBP patients in China after 2013. All CBP patients were diagnosed by local occupational disease diagnostic teams. To further refine the distribution of CBP in specific industries, the occupations of CBP patients in these PLADs were standardized using the *Industrial classification for national economic activities* (GB/T 4754–2017). Data were processed using Excel software (version Home and Student 2019, Microsoft Office).

From 2005 to 2019, the annual mean number of

CBP cases increased to 256 and the proportion of CBP in chronic occupational poisoning (COP) increased and reached 46% in 2019 (Figure 1A). As shown in Table 1, the number of medium-sized enterprises with CBP cases increased rapidly in the 6 PLADs from 2005 to 2012 and subsequently remained at a high level from 2009 to 2019. The number of small businesses with CBP cases continued to rise, and both small and medium enterprises eventually comprised 71% of all enterprises with CBP cases from 2017 to 2019. When enterprises with CBP cases were categorized according to ownership type, the number of CBP cases reported by private enterprises was the highest and increased rapidly. It was followed by foreign enterprises and

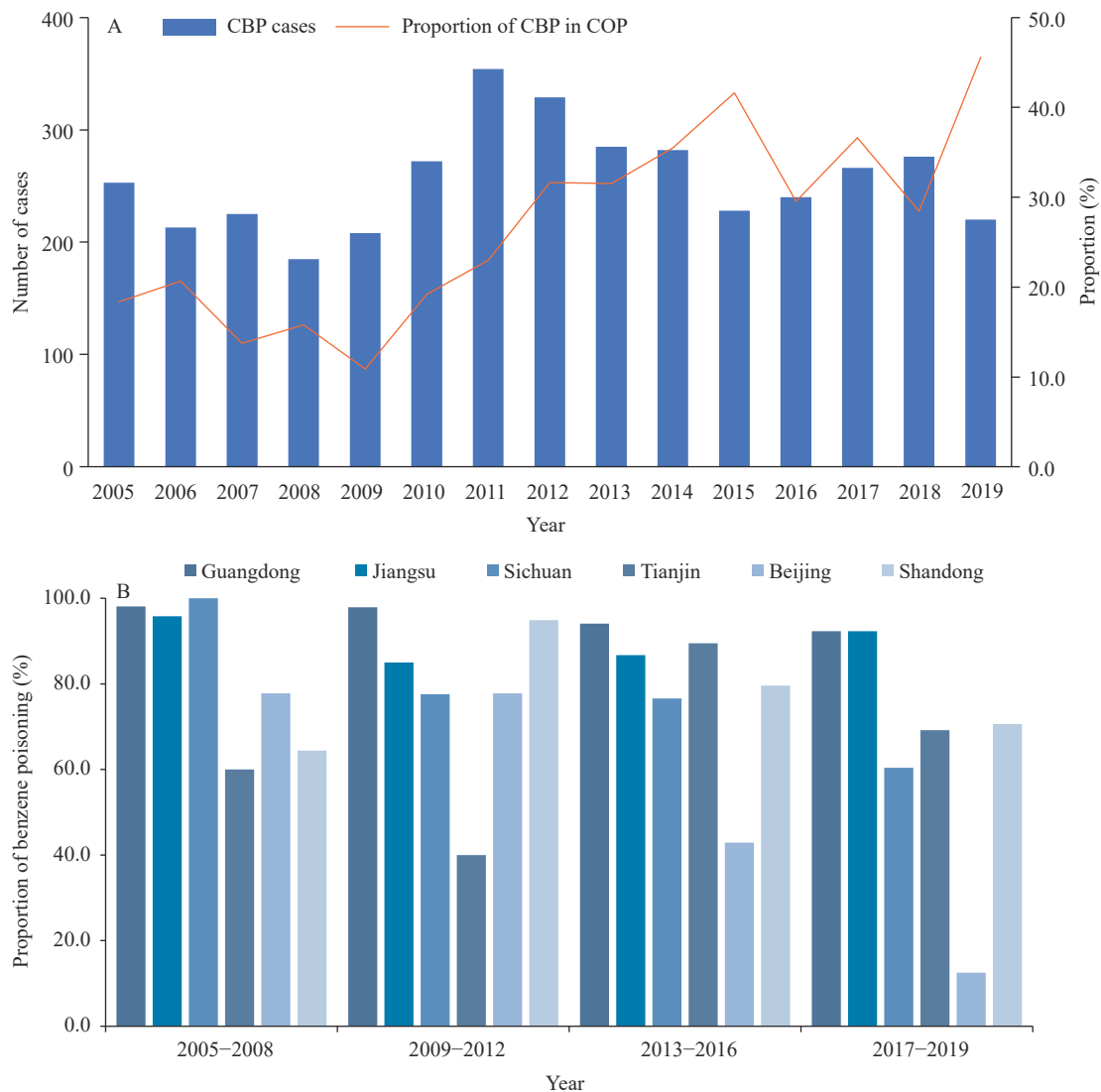


FIGURE 1. CBP in China, and manufacturing with CBP in 6 PLADs, 2005–2019. (A) New cases and proportion of reported CBP in China, 2005–2019; (B) The proportion of manufacturing with CBP in 6 PLADs in 4 periods of 4-years (2005–2008, 2009–2012, 2013–2016, 2017–2019).

TABLE 1. Distribution of enterprise scale and ownership type with chronic benzene poisoning (CBP) cases in 6 provincial-level administrative divisions (PLADs), 2005–2019.

Item	Number of CBP (%)			
	2005–2008	2009–2012	2013–2016	2017–2019
Total	252	464	595	550
Enterprise scale				
Large	59(23.4)	119(25.6)	157(26.4)	126(22.9)
Medium	73(29.0)	193(41.6)	190(31.9)	197(35.8)
Small	52(20.6)	111(23.9)	195(32.8)	195(35.5)
Mini-sized	0	0	6(1.0)	12(2.2)
Unrevealed	68(27.0)	41(8.8)	47(7.9)	20(3.6)
Ownership type				
State-owned	78(31.0)	74(16.0)	82(13.8)	38(6.9)
Collective	17(6.7)	20(4.3)	25(4.2)	4(0.7)
Pooling	9(3.6)	42(9.1)	46(7.7)	0
Private	72(28.6)	151(32.6)	237(39.8)	183(33.3)
Foreign	34(13.5)	77(16.6)	42(7.1)	140(25.5)
Hong Kong, Macao, and Taiwan of mainland China	16(6.3)	6(1.3)	6(1.0)	131(23.8)
Stock	0	20(4.3)	20(3.4)	22(4.0)
Unrevealed	26(10.3)	73(15.8)	137(23.0)	32(5.8)

Abbreviation: CBP=chronic benzene poisoning.

Hong Kong, Macao, and Taiwan of mainland China enterprises, they showed a sharp increase from 2017 to 2019.

For industry distribution, manufacturing was the industry in the 6 PLADs with the highest number of CBP cases during 2005–2008, accounting for 60% up to 100% of all cases. In 2009, the number of CBP cases related to manufacturing decreased in all PLADs except Shandong, but manufacturing was still the primarily associated industry. During 2013–2019, the proportion of CBP cases in 5 PLADs, excluding Beijing, related to manufacturing exceeded 60%, ranging from 60.4% to 94.1% (Figure 1B).

During 2005–2019, CBP mainly occurred in general and special equipment manufacturing, followed by raw chemical materials and chemical product manufacturing. Compared with the previous periods from 2005 to 2016, the number of CBP cases in these 2 industries decreased from 2017 to 2019, but they remain the main industries associated with CBP. The distribution of associated industries and characteristics of CBP in PLADs often differed: 1) in Jiangsu, chemical raw materials and chemical products manufacturing was always found to be the main industry associated with CBP during 2009–2019 (2009–2012: 11 cases, 27.5% of the total; 2013–2016:

26 cases, 35.6% of the total; 2017–2019: 9 cases, 34.6% of the total), followed by general and special equipment manufacturing (2009–2012: 10 cases, 25.0% of the total; 2013–2016: 13 cases, 17.8% of the total; 2017–2019: 7 cases, 26.9% of the total); 2) in Sichuan, the main industries associated with CBP were general and special equipment manufacturing during 2013–2016 (22 cases, 34.4% of the total) and was outpaced by paper products manufacturing and electrical equipment manufacturing during 2017–2019 (both 9 cases, 17.0% of the total); 3) in Shandong, the main industry associated with CBP was general and special equipment manufacturing during 2005–2008 (30 cases, 30.0% of the total)—which increased during 2009–2012 (39 cases, 33.3% of the total) and decreased during 2013–2016 (11 cases, 11.8% of the total) and during 2017–2019 (5 cases, 14.7% of the total) — and several industries were associated with CBP as 34 cases occurred in 25 industries during 2017–2019; and 4) in Tianjin, several industries were also associated with CBP, but transportation equipment manufacturing gradually became the most associated with CBP (2013–2016: 5 cases, 26.3% of the total; 2017–2019: 7 cases, 26.9% of the total) (Table 2).

TABLE 2. Characteristics in distribution of the top three industries with the most chronic benzene poisoning (CBP) cases in Jiangsu, Sichuan, Shandong, and Tianjin, 2005–2019.

PLAD	Year	Industry	Number of CBP (%)
Jiangsu	2005–2008	Leather, fur, feather products and shoemaking manufacturing	9(36.0)
		Plastics and rubber products manufacturing	5(20.0)
		General and special equipment manufacturing	5(20.0)
	2009–2012	Chemical raw materials and chemical products manufacturing	11(27.5)
		General and special equipment manufacturing	10(25.0)
		Non-ferrous metal product industry	3(7.5)
	2013–2016	Chemical raw materials and chemical products manufacturing	26(35.6)
		General and special equipment manufacturing	13(17.8)
		Metal product manufacturing	6(8.2)
	2017–2019	Chemical raw materials and chemical products manufacturing	9(34.6)
		General and special equipment manufacturing	7(26.9)
		Transportation equipment manufacturing	2(7.7)
Sichuan	2005–2008	Computer and electronic product manufacturing	6(60.0)
		General and special equipment manufacturing	3(30.0)
		Chemical raw materials and chemical products manufacturing	1(10.0)
	2009–2012	Transportation equipment manufacturing	13(27.5)
		Weapon and ammunition manufacturing	8(16.3)
		General and special equipment manufacturing	6(12.4)
	2013–2016	General and special equipment manufacturing	22(34.4)
		Transportation equipment manufacturing	9(14.1)
		Metal product manufacturing	5(7.8)
	2017–2019	Paper and paper products Manufacturing	9(17.0)
		Electrical equipment manufacturing	9(17.0)
		General and special equipment manufacturing	5(9.4)
Shandong	2005–2008	General and special equipment manufacturing	30(30.0)
		Transportation equipment manufacturing	11(11.0)
		Petroleum processing industry	9(9.0)
	2009–2012	General and special equipment manufacturing	39(33.3)
		Transportation equipment manufacturing	20(17.1)
		Chemical raw materials and chemical products manufacturing	10(8.5)
	2013–2016	Chemical raw materials and chemical products manufacturing	13(14.0)
		General and special equipment manufacturing	11(11.8)
		Transportation equipment manufacturing	6(6.5)
	2017–2019	General and special equipment manufacturing	5(14.7)
		Computer and electronic product manufacturing	5(14.7)
		Chemical raw materials and chemical products manufacturing	3(8.8)
Tianjin	2005–2008	Chemical raw materials and chemical products manufacturing	5(33.3)
		Petroleum processing industry	5(33.3)
		General and special equipment manufacturing	2(13.3)
	2009–2012	Petroleum processing industry	8(54.3)
		Computer and electronic product manufacturing	2(13.3)
		General and special equipment manufacturing	2(13.3)

TABLE 2. (Continued)

PLAD	Year	Industry	Number of CBP (%)
	2013–2016	Transportation equipment manufacturing	5(26.3)
		Metal product manufacturing	2(10.5)
		General and special equipment manufacturing	2(10.5)
	2017–2019	Transportation equipment manufacturing	7(26.9)
		General and special equipment manufacturing	3(11.5)
		Petroleum exploitation	3(11.5)

DISCUSSION

The number of new cases of CBP and the increased proportion of CBP in COP during 2005–2019 suggested that CBP may be the most important diseases in COP in China. The increasing number of cases may result from an increase in benzene-exposed workers; the increasing proportion of CBP in COP may result from a decrease in other occupational poisonings. The number of CBP cases needs to be further reduced due to the carcinogenicity of benzene.

In this study, we found that CBP mainly occurred in manufacturing industries, especially in private enterprises and small and medium-sized enterprises. The number of CBP cases in private and small enterprises have exceeded that of the large state-owned companies after 2013. This is probably due to the rapid development of small and medium-sized enterprises in recent years. Moreover, the production equipment and occupational health conditions in small and medium-sized enterprises are not as good as those of large state-owned enterprises. Therefore, it makes the occurrence of CBP increased and scattered. The supervision and management of small and medium-sized enterprises need to be strengthened.

In the past 15 year, the production and use of benzene was mainly in manufacturing, which accounts for one-third of all industries in China (GB/T 4754–2017). We further analyzed the manufacturing sub-industry and found that most industries with CBP were general and special equipment manufacturing, as well as chemical raw materials and chemical products manufacturing. Studies reported that the median benzene exposure level for general equipment manufacturing was 4.32 mg/m³ (range: 0.03–244.51 mg/m³) and was 3.52 mg/m³ (range: 0.79–8.30 mg/m³) for chemical raw materials and chemical products manufacturing during 1983–2014 (7). Though these exposure levels were lower than the 6 mg/m³ required by the PC-TWA in China, there was no significant decrease in the average number of new

cases from 2005 to 2019 compared to 1996–2003, suggesting that the occupational exposure limit of benzene at 6 mg/m³ may need to be reconsidered. Furthermore, in high-income countries like the United States, benzene exposure levels are well below this occupational exposure limit (3.25 mg/m³), so CBP cases were relatively rare (8). There was an average of only 10 CBP cases per year among 240,000 occupational benzene-exposed workers in the United States (9). By comparison, 186 of the 342,212 workers exposed to benzene in 5 PLADs in China in 2017 suffered from CBP.

During 1979–1981, CBP patients mainly occurred in spray paint workers (34.1%), painters (20.8%), and shoemakers (12%) (4). Less than 1% of shoemakers had CBP cases in the 6 PLADs by 2019. The number of CBP cases in computer and electronic product manufacturing began to increase, while the leather, fur, feather products, and shoe manufacturers were no longer the main industry for CBP (Table 2). Differing from China, the International Agency for Research on Cancer report states that synthetic rubber, paint, and ink manufacturing and painting are important sub-industries within manufacturing with serious CBP hazards. It can be seen that the distribution of industries associated with CBP in China is still quite different from that in other countries.

This study was subject to at least some limitations. First, this study included more than 50% of total CBP patients in China among 6 PLADs, but the descriptive statistics on the distribution of these cases may not be comprehensive, which could lead to an imprecise estimation of the distribution. Further investigation could include more patients and other PLADs. Second, the number of reported CBP cases was lower than the actual number of cases due to the lack of obvious clinical symptoms in CBP patients and the lack of full coverage of workers by physical examination, which may have led to an underestimation of the extent of CBP cases.

All enterprises and industries can benefit from a

comprehensive approach to CBP prevention. A hierarchy of controls needs to be fully implemented. First, elimination and substitution: using non-toxic and low toxic substances instead of toxic or high toxic substances is the first choice to reduce exposure to toxic hazards. Second, engineering controls: strengthening ventilation and other engineering controls to bring the concentration of benzene in the workplace within the occupational exposure limit. Third, administrative controls: decreasing occupational benzene exposure limits to a safer concentration. Fourth, personal protective equipment (PPE): proper use of PPE to protect benzene workers. Other community-based strategies include strengthening economic supports, health education, and early finding, diagnosis, and treatment.

Acknowledgment: Guangdong Provincial Key Laboratory of Occupational Disease Prevention and Treatment staff.

Conflicts of Interest: No conflicts of interest were reported.

Funding: The study was funded by the Project of Occupational Health Risk Assessment and National Occupational Health Standard Formulation of National Institute of Occupational Health and Poison Control (Project No.: 131031109000150003).

doi: [10.46234/ccdcw2020.243](https://doi.org/10.46234/ccdcw2020.243)

Corresponding author: Caihong Xing, xingch@niohp.chinacdc.cn.

¹ Key Laboratory of Chemical Safety and Health, National Institute for Occupational Health and Poison Control, Chinese Center for Disease Control and Prevention, Beijing, China; ² Jiangsu Provincial Center for Disease Control and Prevention, Nanjing, Jiangsu, China; ³ Shandong Academy of Occupational Health and Occupational Medicine, Shandong First Medical University & Shandong Academy of Medical Sciences, Jinan, Shandong, China; ⁴ Key Laboratory of Environmental Medicine Engineering of Ministry of Education, School of Public Health, Southeast University, Nanjing, Jiangsu, China; ⁵ Department of Nutrition, Food Safety and Toxicology, West China School of

Public Health, Sichuan University, Chengdu, Sichuan, China; ⁶ Tianjin Centers for Disease Control and Prevention, Tianjin, China; ⁷ Beijing Center for Disease Prevention and Control, Beijing Research Center for Preventive Medicine, Beijing, China.
[&] Joint first authors.

Submitted: October 19, 2020; Accepted: November 18, 2020

REFERENCES

1. Yin SN, Li GL, Tain FD, Fu ZI, Jin C, Chen YJ, et al. Leukaemia in benzene workers: a retrospective cohort study. *Br J Ind Med* 1987; 44(2):124 – 8. <http://dx.doi.org/10.1136/oem.44.2.124>.
2. Rothman N, Smith MT, Hayes RB, Traver RD, Hoener B, Campleman S, et al. Benzene poisoning, a risk factor for hematological malignancy, is associated with the NQO1 609C-->T mutation and rapid fractional excretion of chlorzoxazone. *Cancer Res* 1997;57(14):2839 – 42. <https://pubmed.ncbi.nlm.nih.gov/9230185/>.
3. Mehlman MA, Upton A. The identification and control of environmental and occupational diseases: asbestos and cancers. Princeton: Princeton Scientific Publishing Co. 1994; p. 291 – 2. <https://www.amazon.com/Identification-Control-Environmental-Occupational-Diseases/dp/0911131515>.
4. Yin SN, Li Q, Liu Y, Tian F, Du C, Jin C. Occupational exposure to benzene in China. *Br J Ind Med* 1987;44(3):192 – 5. <http://dx.doi.org/10.1136/oem.44.3.192>.
5. Qu GE. Investigation and etiological analysis of occupational poisoning by lead, benzene, mercury, organophosphorus pesticides and trinitrotoluene in China. *Chin J Ind Hyg Occup Dis* 1984;2(1):25 – 30. <http://www.cnki.com.cn/Article/CJFDTOTAL-ZHLD198401009.htm>. (In Chinese).
6. Chen SY, Gao Y, Pang D, Wang HF, Zhang HC. National notification of incidence of chronic occupational poisoning during 1984–1993. *Chin J Prev Med* 1995;29(5):286 – 9. <http://d.wanfangdata.com.cn/periodical/zhfyx199505110>. (In Chinese).
7. Wen CJ, Li RZ, Xu HJ, Liu M, Su SB, Wen XZ. Meta regression analysis on evaluation of occupational benzene exposure. *J Environ Occup Med* 2018;35(8):750 – 5. <http://dx.doi.org/10.13213/j.cnki.jeom.2018.18153>. (In Chinese).
8. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, International Agency for Research on Cancer. IARC monographs on the evaluation of carcinogenic risks to humans, No. 120. IARC. 2018. <https://www.ncbi.nlm.nih.gov/books/NBK550161/>. [2020-11-17].
9. Yu JN, Zhang CY, Wu SS, Li XL. The control and management of occupational benzene poisoning in United States. *Chin J Ind Hyg Occup Dis* 2013;31(1):65 – 7. <http://dx.doi.org/10.3760/cma.j.issn.1001-9391.2013.01.020>. (In Chinese).