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Abstract

Environmental pollution always threatens the public health of our country, and the incidence of diseases closely related to environmental pollution has continued to rise in recent years. With the rapid urbanization and industrialization, the pollutions of persistent toxic substances (PTS) in air, water, and soil constitute a major hidden danger, which are urgent to be investigated for ecological safety and environmental health risks. In order to solve realistic environmental issues, the potential health hazards of PTS desire to be uncovered through interdisciplinary research. In this article, we review the background and development history of environmental health research on PTS, as well as the current status and recent trend in this field. We also discuss the main scientific issues and challenges in this aspect, and elaborate policy recommendations for the development of environmental health research on PTS.

Keywords

persistent toxic substances; health effect; frontier scientific issue; planning proposal

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Current Status and Thinking of Environmental Health Research on Persistent Toxic Pollutants

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Abstract: Environmental pollution always threatens the public health, and the incidence of diseases closely related to environmental pollution has continued to rise in recent years. With the rapid urbanization and industrialization, the pollutions of persistent toxic substances (PTSs) in air, water, and soil constitute a major hidden danger, which are urgent to be investigated for environment and health safety. In order to solve realistic environmental issues, we uncovered the potential health hazards of PTSs through interdisciplinary research. In this article, we review the background and development history of research on the effects of PTSs on the environment and human health, as well as the current status and recent trend in this field. We also discuss the main scientific issues and challenges in this aspect and elaborate policy recommendations for the development of research on PTSs.
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1 Effects of persistent toxic pollutants on the environment and human health

1.1 Persistent toxic pollutants

Persistent toxic pollutants (PTSs) are considered to be a major environmental issue that affects human survival and health in the 21st century, including persistent organic pollutants (POPs, e.g., polychlorinated biphenyls, polycyclic aromatic hydrocarbons, polybrominated diphenyl ether, and dioxins) and organometallic compounds (e.g., organic mercury compounds, organic tin compounds, and organic lead compounds) [1,2]. Since PTSs are difficult to degrade in the environment, they can migrate over a long distance and be accumulated in organisms, which will bring long-term negative effects and hazards to human health and the environment. Therefore, PTSs have been kept a concern of governments and environmental scientists, becoming the frontier and hot topic in environmental sciences [3].

In recent decades, international environmental protection has successively focused on the control of conventional air and water pollution, the control of heavy metal pollution, and the reduction and control of PTSs [4]. In order to address the

environmental problems caused by anthropogenic emissions of PTSs, many countries have signed several global conventions, such as the Stockholm Convention on Persistent Organic Pollutants (Hereinafter referred to as Stockholm Convention) signed in 2001 and the Minamata Convention on Mercury signed in 2013. Over 30 chemicals have been listed in Stockholm Convention (Table 1) ^①. In the past two decades, China has stepped into the world's leading ranks in technical standards for environmental monitoring of POPs. However, the level, trend, and health risk of POPs in human body in China remain unclear [5]. With the increase of POPs included in Stockholm Convention, it will be a long-term and arduous task to comprehend the trends of POPs in the environment and human body in China.

1.2 Health risks and hazards

Air, soil, water, and sediment all can be contaminated by PTSs. PTSs can stay in the environment for a long time, be spread through air, water or food chain. Moreover, they can be accumulated in organisms to exert negative effects on human body, causing cancer, endocrine disorders, reproductive disorders, nervous system injury, and cardiovascular diseases ^②. The human exposure pathways of environmental

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① All POPs listed in the Stockholm Convention. <http://www.pops.int/TheConvention/ThePOPs/AllPOPs/tabid/2509/Default.aspx>.

② Persistent Organic Pollutants (POPs) and Pesticides. <https://www.unenvironment.org/cep/persistent-organic-pollutants-pops-andpesticides>.

Table 1 All POPs listed in the Stockholm Convention

Measures to be taken	Chemicals
Elimination	Aldrin, chlordane, chlordecone, decabromodiphenyl ether, dicofol, dieldrin, endrin, heptachlor, hexabromobiphenyl, hexabromocyclododecane, hexabromodiphenyl ether and heptabromodiphenyl ether, hexachlorobenzene, hexachlorobutadiene, α -hexachlorocyclohexane, β -hexachlorocyclohexane, lindane, mirex, pentachlorobenzene, pentachlorophenol and its salts and esters, polychlorinated biphenyls, polychlorinated naphthalenes, pentadecafluorooctanoic acid and its salts and related compounds, short-chain chlorinated paraffins, endosulfan and its related isomers, tetrabromodiphenyl ether and pentabrodiphenyl ether, toxaphene
Restriction	Dichlorodiphenyltrichloroethanes (DDTs), perfluorooctane sulfonic acid and its salts and perfluorooctane sulfonyl fluoride
Unintentional production	Hexachlorobenzene, hexachlorobutadiene, pentachlorobenzene, polychlorinated biphenyls, polychlorinated dibenzodioxins, polychlorinated dibenzofurans, polychlorinated naphthalenes

PTSs mainly include (1) inhalation of volatile or granular PTSs from the air, (2) ingestion of PTSs from contaminated drinking water, (3) edible agricultural and animal husbandry products or aquatic products from PTSs-contaminated areas, and (4) skin exposure. For a long time, the environmental exposure and human health effects of PTSs have been widely concerned, and researchers have carried out intensive research to confirm the potential health risks and hazards.

(1) Carcinogenicity. Malignant tumors are a group of diseases that seriously threaten the health of residents in China. The National Cancer Report 2019 released by the National Cancer Quality Control Center showed that over the past 10 years, the incidence of malignant tumors had increased by about 3.9% annually, showing a narrowing gap between urban and rural areas, which were closely associated with aging, industrialization, urbanization, lifestyle, and environmental pollution^③. It is estimated that about 16% of global cancer deaths are linked to environmental risk^[6]. The environmental exposure to PTSs is associated with the elevated risks of cancers in breast, prostate, colorectum, and thyroid^[7].

(2) Endocrine disruption. Most PTSs are endocrine disruptors and can act on multiple hormone receptors and thus interfere with hormone homeostasis^[8]. Relevant studies have shown that PTSs are significantly associated with thyroid hormone dyshomeostasis and insulin resistance. Moreover, they can interfere with substance and energy metabolism and affect the distribution of body fat^[9], thereby increasing the incidence of thyroid diseases^[10], obesity^[11], diabetes^[12], and metabolic syndrome^[13].

(3) Reproduction risk. PTSs can disturb the level of sex hormone to cause the impaired development of reproductive system and the premature decline of reproductive function. PTSs exposure may increase follicle-stimulating hormone, luteinizing hormone and total testosterone^[14], and decrease estradiol and anti-Mullerian hormone^[15]. Besides, it could lead to female primary ovarian insufficiency^[16], premature ovarian failure^[17], and male testicular dysgenesis syndrome^[18]. Furthermore, PTSs can be transmitted from mother to offspring through placenta, leading

to adverse birth outcomes, such as premature delivery and low birth weight^[19].

(4) Nervous system injury. PTSs can cause the injury of nervous system by blocking dopamine neurotransmission, affecting thyroid hormone and calcium-dependent signaling, and inducing oxidative stress^[20]. The PTSs exposure in early childhood development is connected with the abnormal development of nervous system, such as retarded neurodevelopment^[21], autistic spectrum disorder^[22], attention deficit and hyperactivity disorder^[23].

(5) Cardiovascular diseases. PTSs mainly attack the cardiovascular system by activating the aryl hydrocarbon receptor (AHR) signaling pathway, inducing oxidative stress, activating nuclear factor κ B and mediating inflammatory response, and impairing the regulatory function of the renin-angiotensin system^[24]. The exposure to PTSs change the lipid level of the circulatory system^[25] and up-regulate serum total cholesterol and low-density lipoprotein cholesterol^[26], which will then increase the risks of coronary heart disease^[27], hypertension^[28], stroke^[29], and carotid atherosclerosis^[30].

2 Current situation and development trend of research on the effects of PTSs on the environment and human health

2.1 International situation

(1) Development strategy and research plan. Western developed countries have been deploying environmental and health strategic research programs at the national level and have invested large funds to support the corresponding basic and application research to protect public health. In 2003, the European Commission issued the European strategy for the development of environment and health, attempting to establish a complete and effective policy and research framework for environmental and health issues, so as to reduce the health risk and disease burden caused by environmental factors. One year later, the European Commission approved

③ National Cancer Report 2019. <http://www.china-rt.cn/special/846.html>.

the European action plan on environment and health to strengthen cooperation among member states in environment and health and promote research on environmental risk factors and diseases. In 2007, the National Research Council of the United States published "Toxicity Testing in the 21st Century: A Vision and A Strategy," and launched Toxicology in the 21st Century (Tox21) program which aims to find out new molecular biological endpoints and reveal the toxic action mode based on pathway analysis. The Tox21 Consortium is a federal collaboration between the U.S. Environmental Protection Agency (EPA), National Toxicology Program (NTP) headquartered at the National Institute of Environmental Health Sciences (NIEHS), National Center for Advancing Translational Sciences (NCATS), and Food and Drug Administration (FDA). The main focuses of Tox21 are commercial chemicals, pesticides, and pollutants, including basic research, exposure research, translational science, health differences and global environmental health, training and education, communication and participation, as well as two cross research topics: knowledge management cooperation and integration method.

(2) Fundamental research. The international environmental health research is shifting toward low-dose exposure, with the goal of revealing the differences of human susceptibility at various biological levels by revealing the molecular mechanisms and signal pathways of oxidative stress, inflammation, gene damage, and epigenetic changes. From 1999 to 2019, the papers on environmental exposure and health effects of PTSs increased year by year, and the research developed steadily. The relevant papers were from 91 countries and regions in the world, and the top five countries were the United States, China, Japan, Canada, and Italy, with the paper number of 2 707, 1 743, 479, 443, and 398, respectively. The United States has taken the lead in the number of studies. The relevant papers published by Chinese scientists have increased from 2 (1% of the global total) in 1999 to 252 (29% of the global total) in 2019, showing exponential growth. The western developed economies have started in advance in environmental and health research, and their multidisciplinary cooperation has gradually established a mature communication mechanism.

2.2 Current situation and trend in China

In the 1970s, the research team of China had already done some research on PTSs and the construction of environmental monitoring standards. They carried out basic research on environmental analysis methods and equipment development, pollution distribution and evolution trend, pollutant morphology and environmental chemical behavior, and ecotoxicological effects, which laid a good foundation for the construction and development of this discipline, and provided a scientific basis for the management and control of PTSs in China. Since 2004, the International Symposium on Persistent Toxic Substances, sponsored and organized by the State Key Laboratory of Environmental Chemistry and Ecotoxicology,

Research Center for Eco-Environmental Sciences, Chinese Academy of Sciences, have been successfully held in China, the United States, Japan, Canada, and other countries and regions for 16 consecutive sessions, making a good international influence.

3 Scientific issues and challenges

The National Environment and Health Action Plan (NEHAP) issued in 2007 stipulates that by 2015, we should improve the assessment and warning of environmental and health risks, realize multi-department collaborative response to pollution emergencies, and primarily make all sectors participate in environmental and health work. Since 2011, the Ministry of Environmental Protection (now the Ministry of Ecology and Environment) and the National Health and Family Planning Commission (now the National Health Commission) have collaborated to carry out a special survey on environment and health in key areas involving 20 provinces of China. The survey aims to find out the main environmental problems and their impacts on the public health, on the basis of which the health risks caused by environmental pollution can be assessed and further the comprehensive prevention and control countermeasures be formulated. Despite the abundant resources allocated for environmental pollution and health research, China started late in this field compared with the developed countries, as manifested by the imperfect layout, insufficient research, and fragmented scientific problems. Especially in the field of life science and medical research, though the gap between China and developed countries has been narrowing, the talent team, innovation capacity, infrastructure and other aspects of China are behind those in developed countries, which limits the research of PTSs in China. Besides, the specific stage of social development, the lack of basic research data, and unreasonable discipline layout restrict the development of research on environmental pollution and health as well as the establishment of the systematic research system.

The ultimate goal of environment and health research is to explore how environment factors affect human health and to protect public safety by improving the environment. In view of the current environment and health problems in China, the following issues need to be addressed.

(1) Improving the identification and research method of PTSs with health hazards. We should study and develop the technologies for separation, identification and tracing of PTSs in the environment and biological samples, and establish a high-throughput toxicity evaluation platform for PTSs. Besides, efforts should be made to develop the method for computational prediction of PTSs toxicity, decipher the toxic pathway of high-risk PTSs, and mine new biomarkers to improve the identification of such pollutants (Fig. 1).

(2) Identifying the external and internal exposure risks of PTSs. PTSs in the environment present combined pollution.

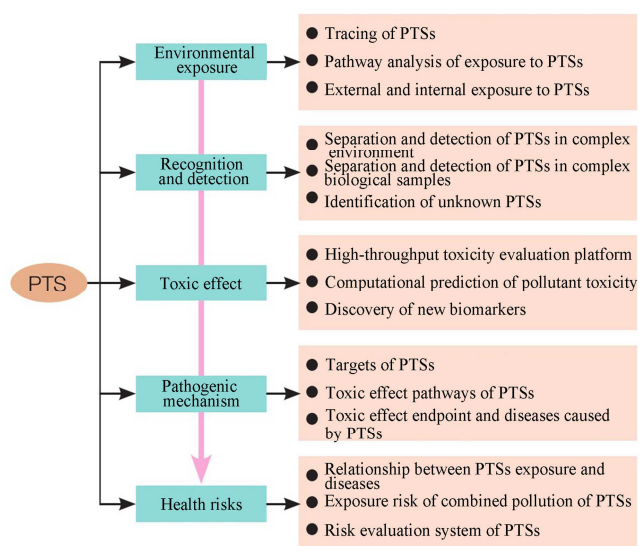


Fig. 1 Scientific issues and challenges of research on the effects of persistent toxic pollutants (PTs) on the environment and human health in China

On one hand, the toxic effects and disease risks of known PTs are not completely clear. On the other hand, there are many unknown PTs components whose toxicological and health effects remain unknown. Therefore, it is urgent to identify the key components that may have pathogenic risk based on the toxicological test, and clarify the process from PTs exposure to body injury and health hazards. According to epidemiological data, we are supposed to identify the responsible pollutants damaging human health and build a multidisciplinary research system of environmental analysis–biotoxicology–clinical medicine (Fig. 1).

(3) Revealing the toxic effects and pathogenic mechanisms of PTs. On the basis of clarifying the main health problems caused by high-risk PTs exposure, the pathogenic mechanism of pollutants and the interaction mechanism between pollutants and biomolecules should be revealed for the construction of the evaluation system of pollutants impacting the occurrence and progression of diseases (Fig. 1), and provide a theoretical basis for the prevention and control of high-risk PTs.

4 Policy recommendations

The discipline development and policy formulation of environmental pollution and health research, a key field in environmental science, are related to the construction of ecological civilization, social sustainable development and people health. Therefore, they are the major strategic needs of China.

(1) Establishing the monitoring system and management standard of high-risk PTs as soon as possible. (1) It is necessary to establish a national-level PTs monitoring network to comprehensively master the actual exposure level and

distribution characteristics of PTs in China, and objectively evaluate the risks and hazards of potential health problems and diseases caused by PTs. (2) We need to separately manage different health risks and implement strict and sound management standards (e.g., quality standards and emission standards) for high-risk PTs.

(2) Strengthening the interdisciplinary construction and talent cultivation in the field of environment and health effects of PTs. We should explore environment and health problems caused by PTs through the establishment of major special projects and promote the crossing of environmental science, public health, clinical medicine and other disciplines, so as to solve the alleviate the division of different disciplines, strengthen the construction of scientific research team and talent cultivation, and build a comprehensive research system and platform for PTs.

(3) Conducting scientific research on the environmental health problems of typical PTs-contaminated areas in China. Backed by scientific research institutions, we should focus on the typical areas or occupational groups of PTs exposure in China, clarify the correlation between human exposure to PTs and major diseases, determine the potential pathogenic factors, and improve the identification ability of health risks, so as to address the environmental problems.

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