



# Considerable decrease of antibody titers against measles, mumps, and rubella in preschool children from an e-waste recycling area



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## HIGHLIGHTS

- Blood lead levels of children from e-waste recycling area were significantly higher.
- Antibody titers against MMR in children from e-waste recycling area significantly decreased.
- Vaccination strategies for children from e-waste recycling area should be modified.

## GRAPHICAL ABSTRACT



### Considerable decrease of antibody titers against measles, mumps and rubella vaccination

IgG antibody	Reference group	Exposed group	P value
Measles Ab (mIU/mL) [median (IQR)]	1046.79 (603.29–1733.10)	669.64 (372.88–1068.42)	<0.001
Mumps Ab (U/mL) [median (IQR)]	491.78 (183.38–945.96)	272.24 (95.19–590.16)	<0.001
Rubella Ab (IU/mL) [median (IQR)]	66.50 (25.32–105.59)	37.08 (17.67–66.66)	<0.001

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## ABSTRACT

Data on vaccination effects in children chronically exposed to heavy metals are extremely scarce. This study aims to investigate the immune responsiveness to measles, mumps, and rubella (MMR) vaccination in children from an e-waste recycling area. 378 healthy children from Guiyu (exposed group) and Haojiang (reference group) were surveyed. Blood lead (Pb) levels were measured by graphite furnace atomic absorption. Titers of antibodies against MMR were quantified by ELISA. Blood Pb levels of children from the exposed group were significantly higher than those from the reference group (5.61 µg/dL vs. 3.57 µg/dL,  $p < 0.001$ ). In contrast, the antibody titers against MMR of the children from the exposed group were significantly lower than those from the reference group. The median titer of the anti-measles antibody of the exposed group was 669.64 mIU/mL, with an interquartile range of 372.88–1068.42 mIU/mL; this was decreased by nearly 40% compared to that of the reference group (median 1046.79 mIU/mL, interquartile range 603.29–1733.10 mIU/mL). For antibody titers against mumps, there was an about 45% decrease in the exposed group (median 272.24 U/mL, interquartile range 95.19–590.16 U/mL), compared to the reference group (median 491.78 U/mL, interquartile range 183.38–945.96 U/mL). In the case of rubella, the median titer of the antibody was also significantly lower in the exposed group (median 37.08 IU/mL, interquartile range 17.67–66.66 IU/mL) compared to the reference

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group (median 66.50 IU/mL, interquartile range 25.32–105.59 IU/mL); the decrease in this case was nearly 44%. The proportion of children whose antibody titers against MMR were below protective level in the exposed group was higher than it was in the reference group. The present study demonstrates that the immune responsiveness to routine vaccination was suppressed in children chronically exposed to lead. Thus, the vaccination strategies for these children living in an e-waste recycling area should be modified.

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## 1. Introduction

Electronic and electric waste (e-waste), defined as end-of-life electronic products, including waste cathode ray tube (CRT) televisions, computers, CRT monitors, liquid crystal display monitors, cell phones, keyboards, printers, and copiers, has become a major environmental concern in China and other developing countries in the past two decades (Awasthi et al., 2016; Iqbal et al., 2015; Zeng et al., 2016a, 2016b; Grant et al., 2013; Suk et al., 2016). According to the report of the United Nations Environment Program (UNEP), approximately 50–80% of global e-waste products are shipped into Asia, and about 90% of them end up in China, where they are informally recycled in open workshops for profit. Guiyu, a town in southeast China, has become one of the largest e-waste destinations and recycling areas in the world during the past 30 years. To recycle precious metals, such as gold, silver, copper, and zinc, e-waste products are recycled predominantly by family-run open workshops using crude and informal extraction methods, such as heating circuit boards over a coal fire or strong acid leaching. During processing, large quantities of heavy metals and other toxic chemicals are released into the air, soil, and water (Huo et al., 2007). As a result, e-waste recycling became the most common cause of heavy metal pollution in developing countries.

Metals in e-waste include Pb, cadmium (Cd), mercury (Hg), chromium (Cr), iron, copper, aluminum, tin, nickel, silver, gold, arsenic, indium, ruthenium, selenium, vanadium, and zinc. Six substances, including Pb, Cd, Hg, hexavalent chromium, polybrominated biphenyls, and polybrominated diphenyl ethers (PBDE), are designated as hazardous substances by the EU's Restriction of Use of Certain Hazardous Substances (RoHS) (Howes, 2006). Our previous studies showed that the air, water, soil, and plants in Guiyu had been severely contaminated with Pb and Cd (Alabi et al., 2012; Guo et al., 2014), and that most children and neonates in Guiyu had blood Pb levels as high as 10 µg/dL (Huo et al., 2007; Liu et al., 2015; Xu et al., 2013; Yang et al., 2013). Our more recent studies showed that the levels of placental Pb, Cd, and PBDE in puerpera from Guiyu were significantly elevated and associated with fetal growth restriction (Xu et al., 2015b; Xu et al., 2016). Although it is well known that Pb affects the developing nervous system in children, no safe blood Pb level in children has been identified. Elevated blood Pb levels in childhood are associated with hyperactivity, attention problems, conduct problems, and impairment of cognition (Liu et al., 2014; Zhang et al., 2015). Elevated Pb in the blood also affects the immune system, blood system, and endocrine system (Zeng et al., 2016a, 2016b). The results of one study that had been carried out in schoolchildren showed that increased blood Pb levels may promote T-helper cell dysregulation and alter the availability of key T-helper1 and T-helper2 cytokines, effects that could ultimately contribute to the development of pulmonary allergic diseases (Hsiao et al., 2011). Another study carried out in 70 Pb-exposed workers demonstrated that occupational exposure to Pb might influence the immune system by impairing several mechanisms, which might ultimately produce deregulation of the immune response and diminish immunosurveillance in exposed individuals (García-Lestón et al., 2012). Additionally, our recent study demonstrated that the elevation of blood Pb level exerts adverse effects on natural killer cells in children chronically exposed to Pb (Zhang et al., 2016). The interaction of Pb with the immune system, leading to immunosuppression or immunodysregulation, may consequently cause increasing incidence of infectious disease. Vaccination responses are

strongly related to public health. Serum vaccine antibody concentration is an increasingly recognized parameter of the immune response to environmental contaminants in public health studies (Grandjean et al., 2012).

Routine immunization against hepatitis B virus, measles, mumps, and rubella (MMR) was initiated in the 1980s in China. Considering vaccination coverage has reached >95% in the Guangdong province of China in the last ten years, the quantification of antibody titers against hepatitis B virus and MMR can be a useful way to examine the immune function of children in a certain population. Previously, we evaluated associations between blood Pb and hepatitis B surface antibody (HBsAb) levels in children from Guiyu. We found that HBsAb levels are negatively associated with blood Pb levels; nearly 50% of chronically exposed children failed to develop sufficient immune responses to hepatitis B virus vaccination. This preliminary evidence suggests that Pb exposure is associated with heterogeneity in immunological responses (Xu et al., 2015a). Though the interaction between environmental contamination and children's immune responsiveness has become an emerging field of environmental epidemiological research, data on vaccination effects in children chronically exposed to heavy metals are extremely scarce. In order to further explore the effects of chronic Pb exposure on immune responsiveness, and to obtain more evidence for supporting the decision that vaccination strategies are needed to adjust for the children living in e-waste recycling areas, the present study was undertaken to investigate the immune responsiveness to MMR vaccination in children from e-waste exposed areas.

## 2. Materials and methods

### 2.1. Study population

The sampling site was located in Guiyu town, Shantou city, in the southeastern coast of the Guangdong province in China. Haojiang (the reference area) is located 31.6 km east of Guiyu.

A total of 378 healthy kindergarten children (263 from Guiyu and 115 from Haojiang), ranging in age from two to seven years, were enrolled as cross-sectional cumulative subjects in our study from December 2014 to March 2015. Haojiang, located 31.6 km east of Guiyu, was chosen as the reference area because of its lack of e-waste recycling workshops and its similar population, traffic density, residential lifestyle, cultural background, and socioeconomic status. According to the Chinese national immunity vaccination program for children, all children were administered the measles vaccine at eight months of age, and the MMR vaccine at two and six years of age. All children enrolled in this study had been administered the measles vaccine and MMR vaccine according to the national immunity vaccination program. Children who had any immune related diseases before, and had infectious disease in six months before blood sampling were ruled out. Informed written consent was obtained from each child's parents or guardians. The study was approved by the Human Ethics Committee of Shantou University Medical College, China.

### 2.2. Blood sample collection

A total of 4 mL of peripheral venous blood was collected from each participant and stored in two Pb-free tubes by well-trained nurses. The blood sample tube containing EDTA as an anticoagulant was used for Pb quantitation. The other blood sample tube was anticoagulant

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