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Review article

The effect of environmental lead exposure on human health and the contribution of inflammatory mechanisms, a review

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ABSTRACT

Lead (Pb) pollution has been considered as a major threat for human health due to induction of inflammatory cascades in various tissues. The aim of present review is to summarize the literature on the effects of lead exposure on respiratory, neurologic, digestive, cardiovascular and urinary disorders and the role of inflammation as an underlying mechanism for these effects.

Various databases such as ISI Web of Knowledge, Medline, PubMed, Scopus, Google Scholar and Iran Medex, were searched from 1970 to November 2017 to gather the required articles using appropriate keywords such as lead, respiratory disorders, neurologic disorders, digestive disorders, cardiovascular disorders, urinary disorders and inflammation.

Disorders of various body systems and the role of inflammation due to lead exposure has been proven by various studies. These studies indicate that lead exposure may cause respiratory, neurologic, digestive, cardiovascular and urinary diseases. The results were also indicated the increased inflammatory cells and mediators due to lead exposure including cytokines and chemokines due to lead exposure which suggested to be the cause various organ disorders.

1. Introduction

Lead (Pb) is one of the most important environmental pollutants, and several studies have demonstrated that lead is a trigger for health problems. Lead is a natural component of the earth's crust with unique properties such as softness, high malleability, ductility, low melting point that poses a major threat to human health in several aspects (Jacobs et al., 2009). Lead is a persistent metal in all parts of the environment, in air, water, soil and primarily deriving from a variety of manufactured products like leaded gasoline, paints, ceramics, solders, water pipes, hair dye, cosmetics, airplanes, farm equipment, shielding for x-ray machines, etc. (Fortoul et al., 2005) (Fig. 1). Lead is considered as a potent environmental toxin with non-biodegradable nature and its toxic effects are well studied (Chen et al., 1997). In additional, alternative medicines (Ayurvedic drugs) is an important cause of symptomatic lead toxicity in humans. Ayurvedic medicines are the oldest classification of medicine in the world, including two main types of herbal and rasa shastra drugs. In rasa shastra, a mixture of heavy metals, minerals and jewelry is used as a combination of therapies. However, abdominal pain is one of the common symptoms due to lead toxicity, using this non-allopathic medicine. Mehta et al. (2017) reported severe recurrent abdominal pain due to lead toxicity in Indian cases using Ayurvedic medicines.

It was indicated that blood lead levels were significantly increased with age, smoking status, and alcohol consumption. Human exposure to lead occurs mainly via digestive and respiratory tracts (Fig. 1). Lead is widely distributed in the body, and interferes with several biochemical processes by its binding to sulfhydryl and other nucleophilic functional groups and contributing to oxidative stress (Kasten-Jolly et al., 2010) (Fig. 2). Lead may disturb physiological functions and induce numerous adverse effects in respiratory system such as Chronic obstructive pulmonary disease (COPD) like changes in the lung (Khazdair et al., 2012), asthma (Ho et al., 1998) lung cancer (Anttila et al., 1995), nervous system (Jusko et al., 2008), cardiovascular (Vaziri and Rodríguez-

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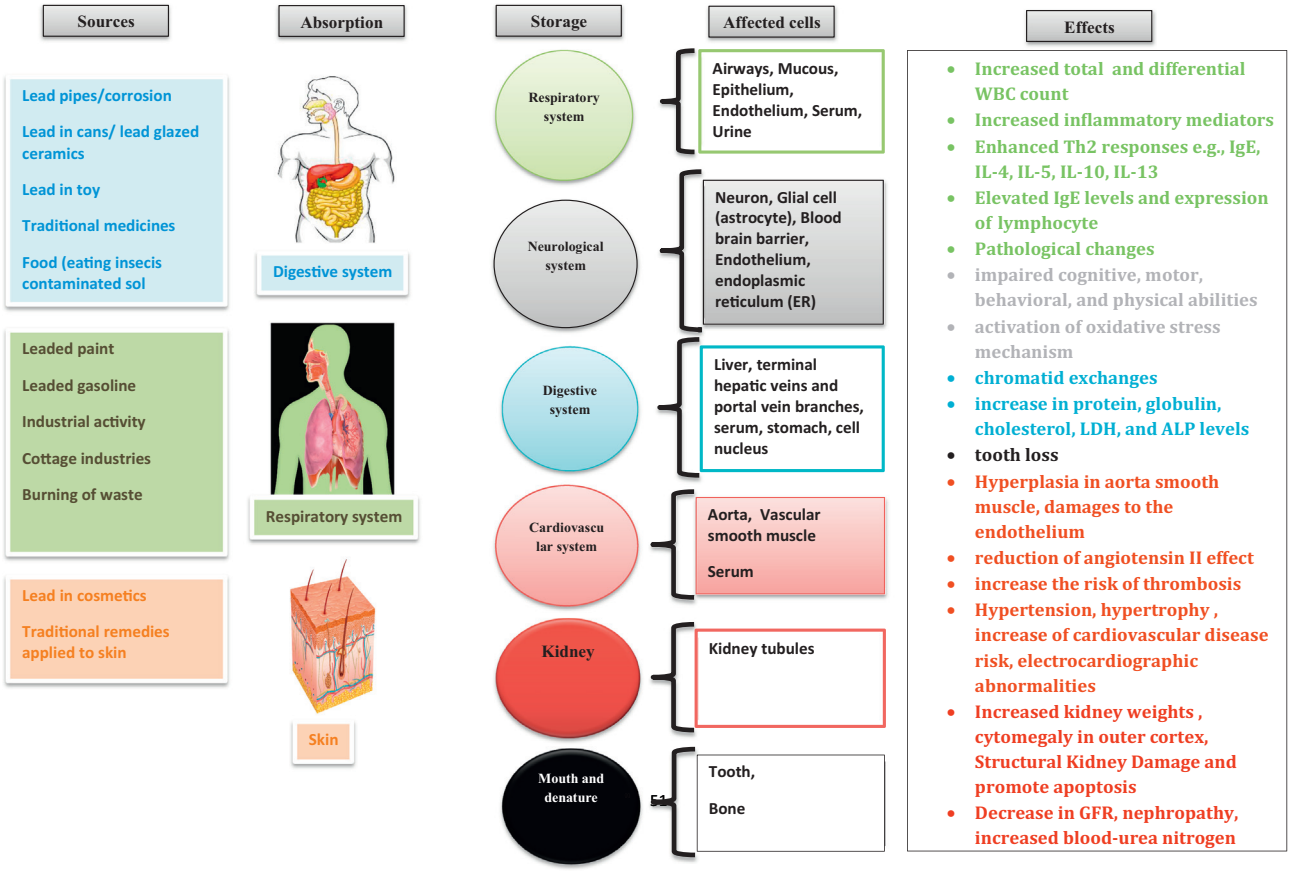

Fig. 1. Sources, absorption, storage and various effect of environmental lead.

Iturbe, 2006), digestive (Van de Wiele et al., 2007) and kidney (Fowler et al., 1980) disorders.

Lead has been found to induce oxidative stress by over production of free radicals, and cause cell membrane damage, via lipid peroxidation, which mediated the activation of inflammatory signaling cascades (Zelikoff et al., 1993) (Fig. 2). Inflammation process has an essential role in the adverse health effects induced by lead (Kurabi et al., 2016). This review article provides an overview of studies about association between lead exposure and inflammatory responses in respiratory, nervous, digestive, cardiovascular and urinary disorders due to lead toxic effects.

1.1. Pharmacokinetic and toxicology of lead

Respiratory and gastrointestinal (GI) tracts are the main rout of exposure to lead (Levin and Goldberg, 2000), but tetraethyl lead (leaded gasoline) also passes through the skin. Almost 35–40% of inhaled lead particles is deposited in the lungs, 37% of all lead particles ≤ 1 μm are deposited in alveolar region and 50% of the lead deposited in the respiratory tract is absorbed and enters the systemic circulation (Levin and Goldberg, 2000). Five to 15% of ingested inorganic lead is absorbed through the gastrointestinal mucosa (Fig. 1); however, this percentage depends on the age, pregnancy and nutritional factor such as calcium, zinc, iron magnesium and phosphate status (Russell Jones, 1989).

It has been indicated that lead absorption in children is faster than adults. Calcium, zinc, iron, magnesium and phosphate deficiency increased gastrointestinal absorption of lead (Russell Jones, 1989). Tetraethyl or alkyl-lead (leaded gasoline) among inorganic lead can only absorbed through the skin (Bolanowska, 1968).

About 99% of circulating lead is bound to erythrocytes and is diffused into the brain, liver, renal cortex, aorta, lungs, spleen, teeth, and bones for 4–6 weeks (Hohnadel et al., 1973). In adults, about 80–95% of lead is deposited in the bone while in children about 70% is deposited in bone. Lead is deposited in bone up to 30 years and increased with age. Inorganic lead is not metabolized and excreted unchanged in the urine. The fecal excretion of absorbed lead may occur through secretion into the bile, gastric fluid, and saliva (Barltrop and Meek, 1979). It was indicated that lead can also excreted through the nails and sweat (Omokhodion and Crockford, 1991), (Fig. 1). Blood lead level equal or > 10 μg/dl is unsafe for infants, children, and women of childbearing age and blood levels equal or > 30 μg/dl is unsafe for workers in occupational exposure (Barry, 1975).

The lead toxicity mainly related to the ability of lead metal ions to replace other bivalent cations such as Ca^{2+}, Mg^{2+}, Fe^{2+} and monovalent cations like Na^{+}, which finally disturbs the cell hemostasis and changes in various biological processes including cell adhesion, cellular signaling, protein folding, maturation, apoptosis, ionic transportation, enzyme regulation, oxidant-antioxidant balance and inflammatory responses (Jaishankar et al., 2014) (Fig. 2).

The recommended lead dose by the Joint Food and Agriculture Organization of the United Nations (FAO)/WHO Expert Committee on Food Additives (JECFA) for identify the magnitude of effect associated with lead exposure in different in drinking-water is 10 μg/l (WHO, 2008) and in air is 0.5 μg/m^3 (WHO, 2001). The threshold dose of lead for the effects on intelligence quotient (IQ) is from blood lead levels as low as 5 μg/dl (50 μg/l).

2. Method

Online literature resources were checked using different search engines such as ISI Web of Knowledge, Medline, Pub Med, Scopus, Google Scholar and Iran Medex, from 1970 to November 2017 to identify articles, editorials, and reviews about the contribution of