# Environmental Exposures, Socioeconomics, Disparities, and the Kidneys

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**Kidney disease disproportionately affects racial and ethnic minority populations, the poor, and the socially disadvantaged. The excess risk of kidney disease among minority and disadvantaged populations can only be partially explained by an excess of diabetes, hypertension, and poor access to preventive care. Disparities in the environmental exposure to nephrotoxicants have been documented in minority and disadvantaged populations and may explain some of the excess risk of kidney disease. High-level environmental and occupational exposure to lead, cadmium, and mercury are known to cause specific nephropathies. However, there is growing evidence that low-level exposures to heavy metals may contribute to the development of CKD and its progression. In this article, we summarize the excess risk of environmental exposures among minority and disadvantaged populations. We also review the epidemiologic and clinical data linking low-level environmental exposure to lead, cadmium, and mercury to CKD and its progression. Finally, we briefly describe Mesoamerican nephropathy, an epidemic of CKD affecting young men in Central America, which may have occupational and environmental exposures contributing to its development.**



**Key Words:** Cadmium, Chronic kidney disease, Health disparities, Lead, Mercury

## Introduction

Kidney disease disproportionately affects racial and ethnic minority groups. Compared with whites, there is a 4-fold risk of ESRD among African Americans and nearly double the risk for Native Americans, Asian Americans, and Hispanics in the United States.[1] Poverty and social disadvantage are associated with a higher risk of CKD and CKD progression.[2-5] Additionally, it appears that the relationship between poverty, low socioeconomic status, and kidney disease may be different among racial and ethnic minorities compared with whites.[6,7]

Most cases of ESRD worldwide are due to diabetes mellitus and hypertension. However, the etiology of ESRD in a significant percentage of patients is never clearly established, and the diagnosis of kidney disease because of environmental or occupational nephrotoxicants is rarely considered.[8-10] The kidneys are especially vulnerable to environmental exposures as approximately 20% of the cardiac output goes to the kidneys, and a fraction is then filtered. Along the nephron, the filtrate is largely reabsorbed, concentrated, and acidified. Thus, environmental toxins can be highly concentrated in the kidney, and some toxins can exist in ionic forms as the pH of the filtrate changes in different segments of the nephron. These factors help to explain the pathophysiologic mechanisms involved in certain toxins. For example, lead and cadmium cause much of their kidney ultrastructural damage in the proximal tubule, where two-thirds of the filtered load is reabsorbed.[8]

It is well known that high levels of exposure to occupational or environmental toxicants, such as lead, mercury, and cadmium, can cause specific nephropathies. However, more recent literature has examined low levels of environmental exposures to nephrotoxicants as risk factors for albuminuria and CKD.[11-14] In the case of low-level lead exposure, there is growing evidence of its role as an independent risk factor for progression of CKD regardless of the cause of CKD.[15-17] Race, ethnicity, low socioeconomic status, and poverty contribute to a higher burden of exposure to potential environmental nephrotoxicants which in turn may partially explain the excess risk of kidney disease.[12,13,18-21]

In this overview, we discuss the available data showing potential socioeconomic, racial, and ethnic disparities in the burden of exposure to nephrotoxicant heavy metals. We also discuss the evidence linking exposure to lead, cadmium, and mercury and kidney disease. We also briefly describe Mesoamerican nephropathy, an epidemic affecting young and poor men working in lowland sugarcane cultivation in Central America.

## Lead Exposure

### *Pathophysiology and Mechanism of Kidney Injury*

Lead is a toxic metal with no known biologic function that can affect almost any organ system including the kidneys. Lead is absorbed from the lungs and the gastrointestinal tract and marginally through the skin. After absorption, lead is distributed approximately 4% in the blood (bound to erythrocytes) with a 30-day half-life and 2% in the soft tissues with a 40-day half-life, and more than 90% accumulates in both trabecular and cortical bone with a half-life of 1 to 16 and 10 to 30 years, respectively.[22,23] The potential mechanisms of lead-induced kidney injury are shown in Figure 1.[24]

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Whole-blood lead levels represent both exogenous exposure and endogenous exposure from the bioavailable lead stored in soft tissues and bone.[8,25] Cumulative lead exposure and the bioavailable pool of lead in the body can be estimated by measuring cortical bone lead through in vivo X-ray fluorescence.[25] Because bone lead is not easily measured, the pool of bioavailable body lead has also been estimated by measuring urine lead levels after the administration of a single dose of calcium disodium EDTA (EDTA-chelatable lead).[26]

### *Historical Trends in Lead Exposure*

Tetraethyl lead, a form of organic lead, was previously added as an "antiknock" agent in gasoline, and its combustion products represented the most important source of environmental lead exposure.[8] The use of leaded paints and lead solder in food cans was also a significant source of environmental exposure to lead.[27] With the removal of lead in gasoline, paint, and can solder, there has a been a significant decline in the overall US population's blood lead levels over the past 40 years; however, these sources of exposure continue to play a significant role in poor and developing countries.[13,21,27,28] Other significant sources of exposure include living near or working in metal ore smelters, ceramic lead-glazing shops, lead battery factories, or recycling plants, particularly in poor countries without environmental or occupational hygiene regulations and active monitoring.[29-34]

**CLINICAL SUMMARY**

- Kidney disease disproportionately affects racial and ethnic minority populations and poor and socially disadvantaged groups.
- There is growing evidence that low-level environmental exposure to lead, cadmium, and mercury may increase the risk for kidney disease.
- Race, ethnicity, low socioeconomic status, and poverty contribute to a higher burden of exposure to environmental nephrotoxicants and may explain some of the excess risk for kidney disease.
- Mesoamerican nephropathy is a disease likely related to occupational and environmental exposures affecting young men working in lowland sugarcane cultivation in Central America.

### *Disparities in Lead Exposure by Race, Ethnicity, and Socioeconomic Status*

Despite successful reductions in the level of environmental exposure to lead in the overall US population, disparities persist. The National Health and Nutrition Examination Survey (NHANES) has shown that although blood lead levels in the US adult population have decreased significantly from the periods 1988 to 1994 and 1999 to 2002, significant differences in exposure remain among racial and ethnic minority groups, and the poor.[13] The geometric mean blood lead levels in US adults decreased by 41% between 1988 to 1994 and 1999 to 2002 and the proportion of adults with a blood lead level of 10 μg/dL or more decreased by 79%.[13] However, the age-adjusted prevalence of blood lead levels of 5 μg/dL or more for the 1999 to 2002 was higher for Mexican Americans (8.7%) and non-Hispanic blacks (8.1%) compared with non-Hispanic white adults (4.3%). A nearly 3-fold higher prevalence of blood lead levels of 10 μg/dL or more was also reported among non-Hispanic blacks (1.8%) and Mexican Americans (1.7%) compared with non-Hispanic white adults (0.6%; Fig 2).[13] Similarly, adults with a low socioeconomic status had a higher burden of exposure. Specifically, after adjusting for age, race, ethnicity, and gender, the odds ratio of having a blood lead level of 5 μg/dL or more was 1.74 (95% confidence interval [CI], 1.23-2.46) for adults with an annual household income less than $20,000, 2.62 (95% CI, 1.95-3.52) for adults lacking health insurance, 2.17 (95% CI, 1.61-2.93) for adults living in housing built before 1978, and 2.67 (95% CI, 1.83-3.90) for adults with less than a high school education.[13]

Data from the New York City Health and Nutrition Examination Survey (NYC HANES) collected in 2004 suggests that Asian Americans have the highest mean blood lead levels, with foreign-born Chinese having the highest levels and the highest proportion of adults with a blood lead level of 5 μg/dL or more.[35] The NYC HANES 2004 also reported higher geometric mean blood lead levels associated with lower income, lower levels of education, and shorter length of residence in the United States for the foreign born ($P < .004$ for trend tests).[35]

During the period 2007 to 2010, the NHANES reported similar disparities in lead exposure among children aged 1 to 5 years, with non-Hispanic black children having a significantly higher geometric blood lead level (1.8 μg/dL [95% CI, 1.6-19]) compared with Mexican American (1.3 μg/dL [95% CI, 1.2-1.4]) and non-Hispanic white children (1.3 μg/dL [95% CI, 1.1-1.4]).[21] Children living in poverty had higher blood lead levels compared with children not living in poverty (1.6 vs 1.2 μg/dL, respectively [$P < .01$]), and there was also a significant difference comparing children enrolled in Medicaid with those not enrolled (1.6 μg/dL [95% CI, 1.5-1.7] vs 1.2 μg/dL [95% CI, 1.2-1.3], respectively).[21]

Racial and ethnic minority groups, and those who have recently migrated to the United States, may also be at higher risk of lead exposure from several sources including ayurvedic medicine, traditional Mexican and Asian remedies, lead-glazed pottery, cosmetics, imported tamarind candy, and others.[35-39]

### *The Association between Lead Exposure and CKD and Its Progression*

Chronic high-level exposure to lead in the environment or in the occupational setting is known to cause lead nephropathy, a chronic tubulointerstitial nephritis.[40,41] With the advent of industrial hygiene regulations and the removal of lead as an additive to gasoline, paint, and can solder, cases of overt lead nephropathy are exceedingly rare in developed countries. However, there is growing data