

REVIEW ARTICLE

Influence of organic and inorganic soil pollutants on modifiable cerebrovascular disease risk factors

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Abstract

Growing evidence indicates that chronic exposure to organic and inorganic soil pollutants may contribute to the development of cerebrovascular disease (CeVD) by modulating key, potentially reversible cardiometabolic risk factors. While the vascular consequences of air and water pollution are increasingly recognized, contaminated soils remain an underappreciated environmental reservoir of toxicants with potential health effects. Inorganic pollutants such as lead and cadmium, together with organic compounds including polycyclic aromatic hydrocarbons and polychlorinated biphenyls, can enter the human body through ingestion, inhalation of resuspended particulates, or, for some compounds, dermal absorption. Once absorbed, these pollutants disrupt metabolic and vascular homeostasis through converging mechanisms involving oxidative stress, endothelial dysfunction, and chronic low-grade inflammation. These processes promote the development of hypertension, insulin resistance, hyperglycemia, and dyslipidemia—well-established, modifiable risk factors for CeVD. Organic pollutants may further exacerbate metabolic toxicity through endocrine-disrupting effects and activation of the aryl hydrocarbon receptor, amplifying their cerebrovascular relevance. This review synthesizes experimental, epidemiological, and mechanistic evidence linking exposure to organic and inorganic soil pollutants with adverse alterations in blood pressure regulation, glucose metabolism, and lipid homeostasis. Despite growing concern, a critical knowledge gap remains in defining pollutant-specific associations with discrete cerebrovascular outcomes, largely due to limited integrative studies combining environmental exposure assessment with clinical biomarkers and longitudinal health data. Moreover, populations in industrially burdened or low-resource settings experience disproportionate exposure risks, reinforcing health inequities. Strengthening soil pollution surveillance, advancing remediation strategies, and incorporating environmental exposure histories into cardiovascular risk assessment may represent an upstream approach to reducing the global burden of CeVD.

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1. Introduction

Emerging epidemiological data underscore the role of environmental soil contaminants—both organic and inorganic—as potential contributors to the global burden of cerebrovascular disease (CeVD). Organic pollutants such as polycyclic aromatic hydrocarbons (PAHs), pesticides, and polychlorinated biphenyls (PCBs), along with inorganic pollutants including heavy metals such as lead, arsenic, and cadmium, are increasingly detected in agricultural and urban soils.¹ These pollutants can enter the human body through ingestion (e.g., contaminated crops and groundwater) and inhalation of resuspended particulates, and, for some compounds, through dermal contact.² Numerous population-based studies have demonstrated that chronic exposure to such contaminants is associated with modifiable risk factors, including hypertension, insulin resistance, systemic inflammation, and endothelial dysfunction—key antecedents of cerebrovascular pathology.³ Nonetheless, these associations remain underexplored in prospective studies, signaling a major gap in longitudinal data linking soil exposure directly to CeVD events.

The public health implications of soil pollution are particularly pronounced in low- and middle-income countries (LMICs), where environmental regulations and soil remediation infrastructure are limited. Populations residing near industrial zones, mining areas, and intensively farmed land face disproportionately high exposures to neurovascular toxicants.⁴ These exposures exacerbate existing health inequities, as affected communities often lack access to healthcare services and public health education. Furthermore, the cumulative burden of multiple environmental exposures—air, water, and soil—may synergistically worsen vascular outcomes across the lifespan.⁵ Current public health strategies largely omit soil pollution from environmental risk assessment frameworks, thereby missing an opportunity for upstream prevention in CeVD-related morbidity.

From a mechanistic standpoint, organic and inorganic soil pollutants promote oxidative stress, systemic inflammation, and vascular endothelial dysfunction—all key processes in the development of CeVD. Heavy metals such as cadmium and lead can disrupt calcium homeostasis, impair nitric oxide bioavailability, and activate proinflammatory signaling, contributing to vasoconstriction and increased arterial stiffness.⁶ Organic pollutants such as PAHs and dioxin-like PCBs can exert toxicity through activation of the aryl hydrocarbon receptor (AhR), which modulates vascular gene expression, disrupts lipid metabolism, and enhances cytokine production.⁷ These mechanisms may compromise blood-

brain barrier integrity and increase the risk of cerebral ischemia, microvascular damage, and neuroinflammation. The pathophysiologic effects may also amplify traditional risk factors such as smoking, diabetes, and obesity, adding complexity to cerebrovascular risk profiles.⁵

Recent advances in environmental neuroscience have started to illuminate the neurovascular consequences of chronic pollutant exposure. Animal models exposed to low-dose arsenic or persistent organic pollutants demonstrate cerebrovascular remodeling, microglial activation, and impaired cognitive function.⁸ Epidemiological studies have further linked proximity to contaminated soils with increased stroke mortality and subclinical atherosclerosis. To illustrate the population burden of CeVD, Marrugat *et al.*⁹ estimated that a cumulative incidence of CeVD of 218 per 100,000 (95% confidence interval [CI], 214–221) in Catalanian men and 127 per 100,000 (95% CI, 125–128) in Catalanian women.⁹ Despite these findings, the current knowledge base remains limited by a lack of well-controlled human studies, especially those incorporating personalized exposure assessments and accounting for pollutant mixtures. The integration of soil science, toxicogenomics, and cerebrovascular research is nascent, and standardized methodologies for exposure quantification are not yet widely implemented.¹⁰

This review aims to address critical knowledge gaps in understanding how chronic, low-level soil pollutant exposure contributes to modifiable cerebrovascular risk factors across diverse populations. Using epidemiological studies, we also examine public health implications and potential pathophysiological mechanisms underlying CeVD.

2. Methodology

This narrative review synthesized current evidence examining the impact of soil pollutants on modifiable risk factors for CeVD. The literature was comprehensively searched in major databases, including PubMed, SCOPUS, and Google Scholar, using search terms such as “stroke,” “cerebrovascular disease,” “organic and inorganic soil pollutants,” and “environmental determinants of health.” Peer-reviewed publications published through 2025 were considered eligible, with additional sources identified by screening reference lists of relevant articles. Priority was given to high-quality evidence, including large population-based cohort studies, disease registries, and meta-analyses. Consistent with the methodological approach of narrative reviews, no formal appraisal of study quality or risk of bias was undertaken. The primary objective was to synthesize and critically interpret existing findings to elucidate clinically relevant associations, potential mechanisms, and

cerebrovascular outcomes linked to environmental soil pollutant exposure.

3. Evidence synthesis

3.1. Overview of soil pollutants

Soil pollution refers to contamination of soil arising from natural and anthropogenic activities. Developed and developing nations experience unequal burdens of soil pollution driven by wildfires, mineral exploration and mining, industrial activities, poor waste disposal and management, and pesticide use, among other factors.¹¹ As an environmental stressor, soil pollution threatens ecosystems.¹

3.2. Types of soil pollutants

3.2.1. Organic soil pollutants

In a study by Moeckel *et al.*¹², organic pollutants such as chlorinated paraffins, PAHs, PCBs, and polybrominated diphenyl ethers were assessed in soil samples collected from an e-waste dumping site (Agbogloshie) in Ghana.¹² PCBs exhibited the highest soil concentrations and, in some samples, exceeded soil guideline levels, posing potential risks to mammalian health and safety.

In soils and sediments collected from an urbanized river floodplain site in Delhi, India, organochlorine pesticides, PAHs, and phenolic compounds were assessed in 2018.¹³ A total of 54 samples (27 soils and 27 sediments) were collected and analyzed. Soil concentrations of phenolic compounds, PAHs, and organochlorine pesticides were reported as 639–2,112 µg/kg, 473–1,132 µg/kg, and 13–41 µg/kg, respectively. Sediment concentrations were estimated as 553–20,983 µg/kg, 1,685–4,010 µg/kg, and 4.2–47 µg/kg, respectively. The predominant PAHs (51–76%) were four-ring compounds in both soils and sediments, while seven carcinogen PAHs accounted for 43–61% of total PAHs. Among organochlorine pesticides, p,p'-DDT was the most abundant in soils, whereas α-HCH was detected at the highest levels in sediments.

In China, Teng *et al.*¹⁴ determined soil levels of total petroleum hydrocarbons, 16 PAHs, and n-alkanes. Total petroleum hydrocarbon levels were high, reaching 12.8478%, and ranged from 1% to 2% at most sites. The average level of total organic compounds with carbon chain length between C16 and C34 across 30 sampling sites exceeded recommended limits considered hazardous to human health. Pyrogenic PAHs dominated at most sites, with evidence of petrogenic hydrocarbons at some locations.

In bio-based fertilizer-treated soils, Das *et al.*¹⁵ evaluated organic contaminants using samples from

poultry, agricultural, veterinary, and sludge sources. Organic contaminants were extracted using a QuEChERS-based method and analyzed by liquid chromatography-quadrupole time-of-flight mass spectrometry with an automated data-interpretation workflow optimized for bio-based fertilizer-treated agricultural soil. Three contaminants were detected in soil treated with bio-based fertilizer at 0.4–28.7 ng/g. For the veterinary and sludge sources, the contaminant profiles were similar.

Sun *et al.*¹⁶ evaluated PCB contamination in agricultural soils from the Yangtze River Delta, one of the largest economic zones in China. PCB concentrations ranged from <0.1 ng/g to 130 ng/g (dry weight). Although concentrations were low and did not significantly affect soil ecosystem function, they may still pose health risks to residents. In a related study, Sun *et al.*¹⁷ measured endocrine disruptors and contaminants, including organochlorine pesticides, phthalate esters, and polybrominated diphenyl ethers, in soils from the Yangtze River Delta. Residues of Σ15 organochlorine pesticides, Σ13 polybrominated diphenyl ethers, and Σ15 phthalate esters ranged 1.0–3,520 ng/g, <1.0–382 ng/g, and 167–9,370 ng/g, respectively.

An earlier study by Chen *et al.*¹⁸ was conducted in effluent-irrigated farmlands; the effluents originated from biological treatment plants receiving industrial discharges and sewage wastewater. Residues of organochlorine pesticides and PAHs were compared between soils irrigated with effluents and those irrigated with groundwater. In effluent-irrigated soils, contamination was characterized by predominant accumulation of high-molecular-weight PAHs. Zhang *et al.*¹⁹ examined soil contamination by organochlorine pesticides and other persistent organic pollutants from contaminated sites and assessed soil quality in the surrounding area. Eight persistent organic pollutant pesticides and related contaminants were analyzed in surface soils collected from new and old pesticide-factory sites in southeast China. Surface soils from residential areas near both sites exhibited varying degrees of contamination and may pose health risks.

3.2.2. Inorganic soil pollutants

Luo *et al.*²⁰ reported heavy metal contamination in soils resulting from lead and zinc smelting in China. Lead, cadmium, and zinc were the major heavy metals, with extremely high soil concentrations. These metals have documented carcinogenic, genotoxic, and neurotoxic effects and may pose risks to human health.

In Jebba, Nigeria, Oyebamiji *et al.*²¹ conducted a study on heavy metal contamination associated with agro-allied and non-agro-allied business activities. A total of 137 surface soil samples were collected and analyzed for 25

metals. Heavy metals were detected at levels that may pose threats to human health and ecosystems, with children more vulnerable to non-carcinogenic effects.

In Iran, Enjavinejad *et al.*²² investigated 77 farmlands in southeast Shiraz to assess heavy metals in vegetables and soils and to identify potential sources. Metals assessed included iron, manganese, copper, zinc, cadmium, nickel, and lead. Principal component analysis suggested that cadmium and lead were mainly influenced by anthropogenic activities, whereas manganese, iron, copper, and nickel were more strongly associated with natural sources. Cadmium and lead contributed the most to the total hazard index. Nickel showed the highest health risk index (20.42), indicating an extremely high risk for children.

In South Africa, Kapwata *et al.*²³ utilized a portable spectrophotometer to determine concentrations of arsenic, lead, cadmium, and mercury in residential soils in rural Giyani and to assess the distribution of soil metal concentrations. The majority (57%) of soil samples from the highly polluted site were extremely contaminated with arsenic. In another South African study, Shezi *et al.*²⁴ evaluated heavy metal contamination in soils at preschool facilities located near industrial operations. Average concentrations were estimated as 232, 16, 4,469, 137, 30, 176, and 1,547 mg/kg for zinc, arsenic, iron, manganese, lead, strontium, and titanium, respectively.

Marrugo-Negrete *et al.*²⁵ assessed heavy metals in 83 agricultural soils irrigated by the Sinú River in northern Colombia; the site was affected by mining and seasonal flooding. Mean concentrations of zinc, copper, nickel, lead, cadmium, and mercury were 1,365, 1,149, 661, 0.071, 0.040, and 0.159 mg/kg, respectively. Except for cadmium and lead, the other heavy metals exceeded reported global background levels.

In southwest Cameroon, Ngole-Jeme *et al.*²⁶ evaluated chromium, cadmium, cobalt, nickel, lead, zinc, and copper in soils along unpaved roads. Vehicular emissions were identified as a major source of soil contamination with heavy metals. A moderate health hazard was estimated for road users in areas with high traffic volume and intense anthropogenic activity.

3.3. Effects of soil pollutants on cardiovascular disease risk factors

3.3.1. Hypertensive effects of organic and inorganic soil pollutants

Hypertension is a sustained elevation of blood pressure. It is typically driven by increased systemic vascular resistance and/or increased cardiac output, which increases mechanical stress on arterial walls and may contribute to

endothelial injury, vascular remodeling, and reduced tissue perfusion.²⁷ Hypertension can impair cerebral perfusion and is an important risk factor for stroke. Organic soil pollutants (especially PCBs, dioxin, and bisphenol A) and inorganic contaminants (cadmium, lead, and arsenic) have been associated with higher blood pressure.⁹

For instance, Pavuk *et al.*²⁸ carried out a longitudinal community health survey in Anniston, Alabama, United States, to determine whether persistent chlorinated compounds were associated with hypertension in 338 people who lived near a polychlorinated biphenyl production plant. They reported an association between PCB exposure and hypertension. Goncharov *et al.*²⁹ investigated the relationship between blood pressure and PCBs in 758 people who lived in Anniston, Alabama, near a PCB manufacturing plant. A positive association was reported between serum PCB concentrations and both systolic and diastolic blood pressure. Cheng *et al.*³⁰ examined the influence of dioxin-like PCBs on blood pressure in children using a cross-sectional study conducted between 2023 and 2024 involving 5,240 children aged 7–10 years. PCB-77, PCB-81, PCB-118, PCB-126, PCB-167, and PCB-169 were reported to be associated with elevated systolic blood pressure, pulse pressure, and mean arterial pressure. Goncharov *et al.*³¹ also evaluated the relationship between blood pressure and serum total PCBs; serum total PCB level was reported to be a strong predictor of blood pressure.

Ilhan *et al.*³² utilized 2,3,7,8-tetrachlorodibenzo-p-dioxin to induce hypertension in rats; 500 ng/kg/day was administered orally using gavage for a period of 4 weeks. Marrugat *et al.*⁹ assessed the associations between total PCBs and hypertension risk in Inuit from Nunavik, Canada, using 315 participants aged ≥ 18 years. Higher plasma PCB levels were associated with higher hypertension risk. In a study by Kopf *et al.*³³, adult male C57BL/6 mice were administered 300 ng/kg of 2,3,7,8-tetrachlorodibenzo-p-dioxin through oral gavage three times per week for a period of 60 days. Blood pressure and endothelial function were assessed using radiotelemetry and acetylcholine-induced vasorelaxation. Mean arterial pressure and heart weight increased, along with concentric left ventricular hypertrophy and elevated superoxide anion production.

Bae *et al.*³⁴ evaluated whether increased bisphenol A exposure through canned beverage consumption affected blood pressure and heart rate variability using a randomized crossover trial involving adults aged ≥ 60 years. Urinary bisphenol A levels, blood pressure, and heart rate variability were measured two hours after beverage consumption. Urinary bisphenol A increased by $\geq 1,600\%$, while systolic blood pressure increased by

approximately 4.5 mmHg after consumption of a bisphenol A-enriched beverage. In a related study, Bae *et al.*³⁵ assessed associations between urinary bisphenol A, heart rate variability, and blood pressure in 521 noninstitutionalized older adults (≥ 60 years) in Seoul (2008–2010). A positive association was reported between urinary bisphenol A and blood pressure. In addition, Bae *et al.*³⁶ assessed the effect of prenatal bisphenol A exposure on blood pressure in 645 children aged 4 years, born to women enrolled during mid-pregnancy (2008–2011). Children's diastolic blood pressure was positively associated with maternal urinary bisphenol A concentration. Xiong *et al.*³⁷ determined serum bisphenol A concentrations in 88 patients with dilated cardiomyopathy and gender- and age-matched controls; bisphenol A concentrations were higher in patients than in controls.

An earlier study by Perry *et al.*³⁸ showed that rats continuously administered cadmium, with or without additional salt, exhibited persistent hypertension for a period of 20 months. However, the introduction of 0.35 ppm of selenium alleviated hypertension. Rossi *et al.*³⁹ studied the vascular effects of cadmium chloride exposure (100 mg/L in drinking water for seven days) in Wistar rats. Cadmium-exposed rats exhibited higher systolic blood pressure, increased contractile response to phenylephrine, reduced catalase activity, and elevated basal hydrogen peroxide production. Puri⁴⁰ investigated the effects of cadmium acetate administered intravenously (0.32, 1.0, and 3.2 mg/kg) and intracerebroventricularly (1, 3.2, 10 μ g) on blood pressure in male Sprague–Dawley rats anesthetized using urethane. Intravenous cadmium caused a brief drop in blood pressure followed by a sustained rise, whereas intracerebroventricular administration produced a hypertensive response. Pinheiro *et al.*⁴¹ investigated the cardiovascular effects of intraperitoneal cadmium (1 mg/kg) in three-month-old male Wistar rats and the underlying mechanisms. Cadmium increased systolic blood pressure, and this effect was mediated by cyclooxygenase-2, nicotinamide adenine dinucleotide phosphate oxidase, and the angiotensin II type 1 receptor.

Using the United States National Health and Nutrition Examination Survey (NHANES; 1999–2016), an analysis of 39,477 adults with blood lead and blood pressure measurements was conducted; hypertension was associated with each doubling of blood lead concentration. Gambelunghe *et al.*⁴² evaluated the relationship between blood lead, systolic and diastolic blood pressure, and hypertension in 4,452 Malmo residents aged 46–67 years. Low blood lead levels were associated with higher blood

pressure and may increase the risk of hypertension. Glenn *et al.*⁴³ followed 575 people occupationally exposed to lead in South Korea (1997–2001) and reported that higher blood lead was associated with higher systolic blood pressure. A mean annual increase of 0.9 was reported per 10 μ g/dL increase in blood lead. Hara *et al.*⁴⁴ analyzed NHANES data (2003–2010) from 12,725 participants (21.1% Black, 20.5% Hispanic, and 58.4% White) and reported that doubling of blood lead was associated with higher systolic and diastolic blood pressure.

Chen *et al.*⁴⁵ studied the association between prolonged inorganic arsenic exposure and the prevalence of hypertension in 382 men and 516 women residing in arseniasis-hyperendemic villages. A 1.5-fold increase in sex- and age-adjusted prevalence of hypertension was reported compared with residents in non-endemic areas. Ameer *et al.*⁴⁶ examined arsenic exposure and blood pressure in 225 women in the northern Argentinean Andes; with a median urinary arsenic concentration of 200 μ g/L, arsenic was inversely associated with diastolic blood pressure. In Bangladesh, Khatun *et al.*⁴⁷ examined whether there was a dose–response relationship between arsenic exposure and high blood pressure in 828 people from high- and low-arsenic-exposed regions, with vascular nitric oxide as a potential underlying mechanism. As arsenic levels increased in drinking water, hair, and nails, systolic and diastolic blood pressure increased; mediation analysis indicated a mediating effect of nitric oxide. Kaufman *et al.*⁴⁸ studied arsenic biomarkers and blood pressure in 1,910 American Indian participants from the Northern Plains, Southern Plains, and Southwest and reported a modest cross-sectional relationship between arsenic biomarkers and blood pressure. Wang *et al.*⁴⁹ investigated arsenic exposure and blood pressure in 233 participants with arsenicosis and 84 unexposed participants and reported that arsenic exposure was associated with hypertension and wider pulse pressure, indicating higher systolic blood pressure and pulse pressure.

Organic and inorganic soil pollutants, including PCBs, dioxin, bisphenol A, cadmium, lead, and arsenic, may increase systolic and diastolic blood pressure, mean arterial blood pressure, and pulse pressure (Figure 1). These effects may be attributed to reduced nitric oxide bioavailability, nicotinamide adenine dinucleotide phosphate oxidase, cyclooxygenase-related pathways, and oxidative stress.^{50,51} Other mechanisms may include altered baroreflex sensitivity and heart rate response.⁵² Hypertension contributes to vascular dysfunction and reduced cerebral perfusion, which may increase stroke risk.

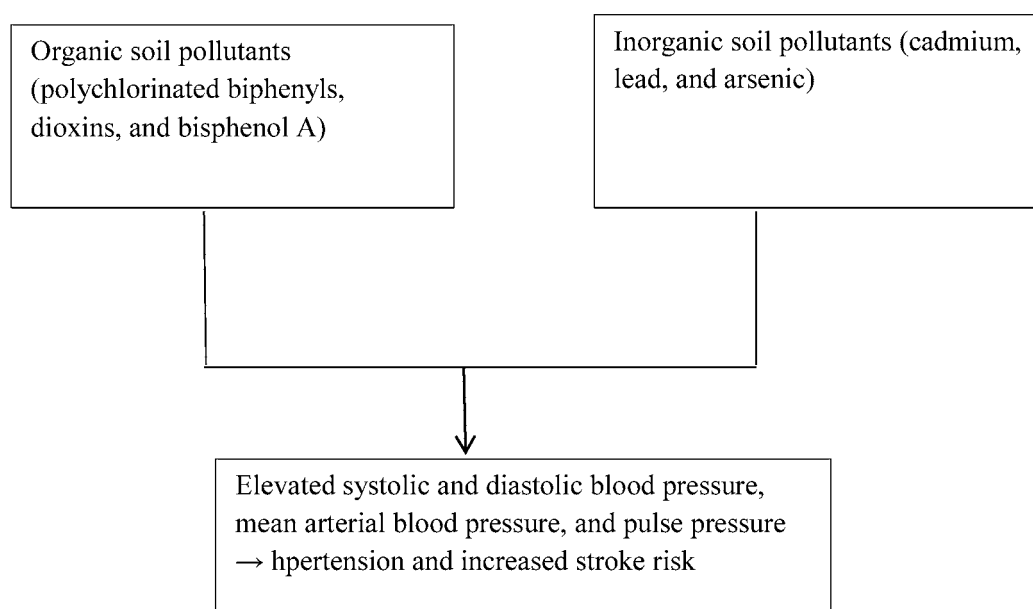


Figure 1. Effect of organic and inorganic soil pollutants on blood pressure. Organic soil pollutants (polychlorinated biphenyls, dioxin, and bisphenol A) and inorganic soil pollutants (cadmium, lead, and arsenic) are associated with higher systolic and diastolic blood pressure, mean arterial pressure, and pulse pressure, contributing to hypertension and increased stroke risk. Image created by the authors.

3.4. Hyperglycemia induced by organic and inorganic soil pollutants

Soils contaminated with organic pollutants (e.g., dioxins, bisphenol A, and PCBs) and inorganic contaminants (especially cadmium, lead, and arsenic) arise from both anthropogenic and natural sources. Warner *et al.*⁵⁴ included 426 adult offspring (≥ 18 years) with prenatal 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) exposure assessment and fasting blood measurements. A 10-fold increase in maternal TCDD estimated at pregnancy was inversely associated with fasting insulin among daughters, but not sons. Hoyeck *et al.*⁵⁴ examined the effects of a single high-dose TCDD injection (20 $\mu\text{g/kg}$) on glucose metabolism and beta-cell (β -cell) function in male and female C57Bl/6 mice. In males, TCDD exposure was associated with reduced fasting insulin concentrations (up to six weeks), decreased β -cell area, and increased delta-cell area.

In a study conducted by Matteo *et al.*⁵⁵, male and female mice were administered TCDD (20 ng/kg/day , twice per week) for a period of three months while being fed chow or a high-fat diet. TCDD accelerated the onset of high-fat diet-induced hyperglycemia, impaired glucose-induced plasma insulin responses, and decreased the proportion of islet β -cell area in females.

Moghaddam *et al.*⁵⁶ investigated the effects of bisphenol A on blood glucose and pancreatic oxidant/antioxidant

balance in mice using doses of 0.5 and 2 mg/kg for a period of four weeks. In a dose-dependent manner, bisphenol A increased blood glucose concentration, increased malondialdehyde, and decreased catalase, superoxide dismutase, glutathione, and total antioxidant status in the pancreas. Maternal bisphenol A exposure (10 $\mu\text{g/kg/day}$ and 10 mg/kg/day) in pregnant mice was associated with higher body fat and impaired glucose homeostasis in the first- and second-generation male offspring, but not females.⁵⁷ Proposed mechanisms included overexpression of the imprinted *Igf2* gene in the fetus and increased DNA methylation at the *Igf2* differentially methylated region 1. Bansal *et al.*⁵⁸ reported that maternal bisphenol A exposure (10 $\mu\text{g/kg/day}$ and 10 mg/kg/day) disrupted insulin production in first- and second-generation male offspring, but not females. At 10 $\mu\text{g/kg/day}$, β -cell mass decreased and β -cell death increased, with effects persisting into the second generation.

Weber *et al.*⁵⁹ demonstrated the effects of TCDD on key hepatic gluconeogenic enzymes in male Sprague-Dawley rats using 5, 15, 25, or 125 $\mu\text{g/kg}$. TCDD suppressed glucose-6-phosphatase activity. Phosphoenolpyruvate carboxykinase and pyruvate carboxylase activities decreased after two days of treatment, whereas pyruvate kinase activity was unaffected.

Baker *et al.*⁶⁰ examined the effects of coplanar PCBs for 4 weeks on insulin and glucose homeostasis and adipose

tumor necrosis factor- α (TNF- α) in lean and obese mice using *in vivo* and *in vitro* models. PCB exposure disrupted glucose/insulin homeostasis in low-fat-fed mice and increased adipose TNF- α expression. Zhang *et al.*⁶¹ examined PCB-related experimental diabetes and potential mechanisms. Daily exposure of polychlorinated diphenyl for 60 days increased fasting blood glucose and insulin resistance, and these effects were attributed to reduced expression of the insulin pathway (insulin receptor, insulin receptor substrate, phosphatidylinositol 3-kinase, protein kinase B) and glucose transporter-4 in muscle and liver.

Xi *et al.*⁶² examined oral exposure of 21-day-old C57BL/6 male mice to Aroclor 1254 (0.5, 5, 50, or 500 $\mu\text{g/kg}$, once every three days for 60 days). Exposure was associated with impaired glucose tolerance and elevated fasting serum insulin levels, along with increased pancreatic β -cell mass in mice administered 50 and 500 $\mu\text{g/kg}$. At 50 and 500 $\mu\text{g/kg}$, transcription of pancreatic insulin gene 2 was downregulated. Kim *et al.*⁶³ reported that both dioxin-like and non-dioxin-like PCBs induced insulin resistance *in vitro* and *in vivo*. These effects were mediated by increased expression of fat-specific protein 27, localized to lipid droplets, in 3T3-L1 adipocytes and in mice.

Nguyen *et al.*⁶⁴ investigated subcutaneous cadmium chloride (0.6 mg/kg) exposure in rats and in leptin receptor-deficient db/db mice. After two weeks of cadmium administration, animals underwent two weeks without dosing; at the end of the four-week period, cadmium exposure was associated with higher blood glucose when compared to lean mice. Jacquet *et al.*⁶⁵ conducted oral cadmium chloride exposure in adult Wistar rats via drinking water (0, 5, 50, or 500 $\mu\text{g/kg/day}$) for three months and reported increased fasting blood glucose and higher glucose-stimulated plasma insulin in females. Fitzgerald *et al.*⁶⁶ assessed the role of pancreatic islets in cadmium-mediated hyperglycemia using subcutaneous cadmium exposure (0.6 mg/kg) in male Sprague-Dawley rats for three months. A time-dependent increase in fasting blood glucose and altered insulin release *in vitro* were reported, together with bioaccumulation of cadmium in islets.

Tyrrell *et al.*⁶⁷ exposed adult female ZDF rats to lead in drinking water for 24 weeks. Hyperglycemia was observed after two months, and glucose intolerance occurred after three months. Lead-associated hyperglycemia was linked to increased expression of *PCK1* and *G6PC* genes. Wan *et al.*⁶⁸ reported that administering 0.05% lead in drinking water for 28 weeks increased fasting plasma glucose, hepatic glucose production, and expression of *G6PC*, *FBP1*, and *PCK1*. Paul *et al.*⁶⁹ investigated inorganic arsenic (25 and 50 ppm for 20 weeks) in high-fat-fed C57BL/6 mice and reported higher fasting blood glucose and worsened

glucose intolerance compared with the high-fat diet alone. Liu *et al.*⁷⁰ examined inorganic arsenic effects on glucose homeostasis in normoglycemic and diabetic C57BL/6LJ mice; arsenic exposure exacerbated islet β -cell dysfunction in normoglycemic mice and worsened glucose intolerance in diabetic animals, with hepatic oxidative damage and elevated gluconeogenesis reported.

3.5. Hyperlipidemia induced by organic and inorganic soil pollutants

Hyperlipidemia is an important modifiable risk factor for CeVD. Low high-density lipoprotein and elevated atherogenic lipoproteins, including non-high-density lipoprotein cholesterol (e.g., low-density lipoprotein, intermediate-density lipoprotein, and very low-density lipoprotein), increase the likelihood of atherosclerosis^{71,72}, a progressive vascular disorder characterized by arterial stiffening and narrowing. Cerebral atherosclerosis can reduce cerebral perfusion and increase stroke risk. Many studies suggest that organic pollutants (e.g., dioxin, bisphenol A, and PCBs) and inorganic contaminants (especially cadmium, lead, and arsenic) may promote dyslipidemia. For instance, Brewster *et al.*⁷³ reported that a single intraperitoneal administration of TCDD (1 $\mu\text{g/kg}$ or 50 $\mu\text{g/kg}$) led to a dose-dependent increase in triglycerides and reduced adipose tissue lipoprotein lipase activity in rabbits 10 days after administration. In pigs, rabbits, and hamsters, Brewster *et al.*⁷⁴ showed that reduced adipose tissue lipoprotein lipase activity after a single intraperitoneal administration of TCDD, with increased triglycerides (except in rats). Following a single administration of 1 μg TCDD to guinea pigs, suppression of adipose tissue lipoprotein activity was sustained for 10 days, with the greatest reduction observed after two days.⁷⁵

Wang *et al.*⁷⁶ conducted a Chinese cohort study of 1,872 dyslipidemia-free participants aged ≥ 40 years (enrolled in 2009) who were followed for four years. Serum lipid levels and urinary bisphenol A were measured at baseline and follow-up. Participants with elevated bisphenol A at both baseline and follow-up exhibited an additional 6.12% increase in triglycerides and 2.94% increase in low-density lipoprotein cholesterol compared with those with low bisphenol A. Marmugi *et al.*⁷⁷ examined prolonged bisphenol A exposure in adult mice and reported increased expression of key genes involved in cholesterol synthesis (including *Lss*, *Hmgcr*, *Mvd*, and *Sqle*) and sterol regulatory element-binding proteins 2. Samarghandian *et al.*⁷⁸ investigated bisphenol A effects on lipid profile and pancreatic oxidant/antioxidant balance in mice administered 0.5 or 2 mg/kg for four weeks. In a dose-dependent manner, bisphenol A reduced high-density lipoprotein cholesterol and increased malondialdehyde,

while decreasing catalase, superoxide dismutase, glutathione, and total antioxidant status in the pancreas. Guo *et al.*⁷⁹ evaluated the link between urinary bisphenol A and hyperlipidemia using NHANES data (2003–2016) and reported higher urinary bisphenol A in participants with hyperlipidemia than in those without. Moghaddam *et al.*⁵⁶ also reported that bisphenol A exposure increased body weight and altered pancreatic oxidative stress markers.

Azaïs-Braesco *et al.*⁸⁰ investigated the effect of a single intraperitoneal injection of 2,2',4,4',5,5'-hexachlorobiphenyl or 3,3',4,4'-tetrachlorobiphenyl at 300 µmol/kg on lipid metabolism in serum and liver of male Sprague–Dawley rats. 3,3',4,4'-tetrachlorobiphenyl increased triglycerides and total liver lipids, and both compounds increased phospholipid and cholesterol content in the liver microsomal fraction. Aminov *et al.*⁸¹ analyzed fasting serum lipid levels in 575 residents of Anniston who reported not taking lipid-lowering drugs. Serum concentrations of 35 PCB congeners and 9 chlorinated pesticides were measured, and higher serum lipid levels were associated with higher summed PCB and pesticide concentrations. Kania-Korwel *et al.*⁸² evaluated dose-related alterations in hepatic lipid content in male Sprague–Dawley rats administered PCB-126 for three months through intraperitoneal injections (0.01, 0.05, and 0.2 µmol/kg body weight). PCB-126 increased hepatic polar lipids and fatty acids incorporated into triglycerides; increasing the PCB-126 dose decreased phosphatidylserine levels and increased fatty acids incorporated into triglycerides. Arsenescu *et al.*⁸³ evaluated six-week intraperitoneal PCB-77 exposure (49 mg/kg) and reported serum dyslipidemia, adipocyte enlargement, body weight gain, and worsened atherosclerosis *in vivo* (C57BL/6 wild-type or AhR^{-/-} mice), supported by *in vitro* findings. Zhang *et al.*⁶¹ showed that daily PCB administration for 60 days increased body weight and pancreatic β-cell mass and reduced islet α-cell mass; resistin, TNF-α, and interleukin-6 were also increased. Kim *et al.*⁶³ reported that both dioxin-like (PCB-118) and non-dioxin-like (PCB-138) PCBs promoted *in vitro* adipocyte differentiation, increased lipid droplet size, increased adipose mass and adipocyte size. *In vivo*, C57BL/6 mice administered PCB-118 or PCB-138 (37.5 mg/kg, intraperitoneal) showed increased adipose mass and adipocyte size, and impaired whole-body insulin action.

Kim *et al.*⁸⁴ reported that incubating human high-density lipoprotein with cadmium chloride (24 µM) increased the formation of advanced glycation end products and promoted spontaneous development of multimeric apolipoprotein A-I. Cadmium-treated high-density lipoprotein increased oxidized low-density

lipoprotein uptake into macrophages. Samarghandian *et al.*⁷⁸ reported that chronic cadmium exposure (2 mg/L) increased serum total cholesterol, low-density lipoprotein, and triglycerides and decreased high-density lipoprotein; malondialdehyde increased and glutathione decreased. Zhou *et al.*⁸⁵ conducted a cross-sectional survey of 1,489 cadmium-exposed workers from cadmium smelting factories in central and southwestern China. Mean blood cadmium was estimated as 3.61 ± 0.84 µg/L, and dyslipidemia prevalence was 66.3%; workers with dyslipidemia had higher average blood cadmium levels. In the study by Nguyen *et al.*⁶⁴, cadmium was administered for two weeks, followed by a two-week no-dosing period, leading to increased body weight and epididymal and retroperitoneal fat pad weights.

Tyrrell *et al.*⁶⁷ showed that lead administration to ZDF rats for 24 weeks elevated hepatic triglyceride levels. Zhang *et al.*⁸⁶ assessed the association between blood lead concentrations and hyperlipidemia in 43,196 participants from NHANES (1999–2018); blood lead concentrations were measured using inductively coupled plasma mass spectrometry. Elevated blood lead concentrations were observed in participants with hyperlipidemia. Kristal-Boneh *et al.*⁸⁷ assessed associations between blood lead levels and serum lipids in 56 occupationally exposed individuals. Mean blood lead concentration was 42.3 ± 14.9 µg/dL, and total cholesterol was higher among lead-exposed participants.

Kuo *et al.*⁸⁸ assessed associations between early-life exposure to inorganic arsenic and lipid profiles in 237 adolescents in a 15-year birth cohort study in central Taiwan. Compared with the stable-low arsenic trajectory group, total cholesterol increased by 14% and low-density lipoprotein cholesterol by 23% in the rising-high trajectory group. Qu and Huang⁸⁹ assessed the association between urinary arsenic and lipid profiles (total cholesterol, low-density lipoprotein, and high-density lipoprotein) in 6,633 adults aged ≥20 years using NHANES data. Urinary arsenic concentration was positively correlated with total cholesterol. Yue *et al.*⁹⁰ evaluated urinary arsenic and lipid profiles in participants aged 12–17 years using NHANES data (2009–2016) and reported that creatinine-adjusted arsenic was positively correlated with total cholesterol. Karim *et al.*⁹¹ investigated the relationship between arsenic exposure and atherosclerosis-related biomarkers in 324 arsenic-exposed participants in Bangladesh. Higher oxidized low-density lipoprotein levels and increased intercellular adhesion molecule-1, C-reactive protein, and vascular cell adhesion molecule-1 were reported in arsenic-endemic subjects compared with unexposed subjects.

Polychlorinated biphenyls, dioxin, bisphenol A, cadmium, lead, and arsenic are environmental pollutants that can be found in soils. In experimental and observational studies, exposure to these pollutants has been associated with higher low-density lipoprotein, triglycerides, total cholesterol, very low-density lipoprotein, and hepatic triglycerides, and lower high-density lipoprotein.⁷⁴⁻⁷⁶ In experimental models, these exposures have been linked to adipocyte differentiation, increased lipid droplet size, oxidized low-density lipoprotein formation, adipose tissue enlargement, and weight gain. Proposed mechanisms included altered regulation of lipid metabolism (e.g., sterol

regulatory element-binding proteins 2 and HMG-CoA reductase) and oxidative stress.

In addition to hyperlipidemia, hypertension and hyperglycemia are important modifiable risk factors for CeVD (Figure 2). Hypertension, hyperglycemia, and hyperlipidemia can contribute to cerebral vascular dysfunction and reduced cerebral perfusion. Soil pollutants such as PCBs, dioxin, bisphenol A, cadmium, lead, and arsenic may adversely affect brain and cardiovascular health (Table 1), particularly in susceptible populations such as individuals with metabolic syndrome. In metabolic

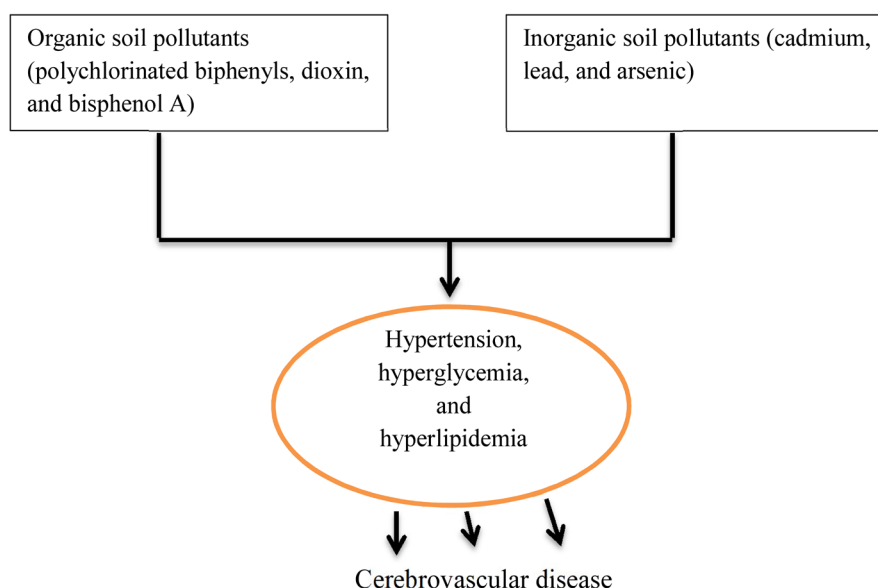


Figure 2. Exposure to organic soil pollutants (polychlorinated biphenyls, dioxin, and bisphenol A) and inorganic soil pollutants (cadmium, lead, and arsenic) may contribute to hypertension, hyperglycemia, and hyperlipidemia. Hypertension, hyperglycemia, and hyperlipidemia are important modifiable risk factors for cerebrovascular disease. Image created by the authors.

Table 1. Effect of exposure to organic and inorganic soil contaminants on cerebrovascular risk factors

Cerebrovascular disease risk factor	Organic and inorganic soil pollutants
Hypertensive effects ^{29,41}	A positive relationship was found between serum polychlorinated biphenyls concentrations and both systolic and diastolic blood pressure. Intraperitoneal cadmium administration (1 mg/kg) for 14 days in three-month-old male Wistar rats increased systolic blood pressure.
Hyperglycemic effects ^{54,65}	A single high-dose TCDD injection (20 µg/kg) reduced fasting insulin levels. Oral exposure of adult female Wistar rats to cadmium chloride (0, 5, 50, or 500 µg/kg/day) via drinking water for three months increased fasting blood glucose.
Hyperlipidemic effects ^{73,78}	A single intraperitoneal administration of TCDD (1 µg/kg or 50 µg/kg) led to a dose-dependent increase in triglycerides 10 days after administration. Chronic cadmium exposure (2 mg/L) increased serum total cholesterol, low-density lipoprotein, and triglycerides and decreased high-density lipoprotein.

Abbreviation: TCDD: 2,3,7,8-tetrachlorodibenzo-p-dioxin.

syndrome, exposure to these organic and inorganic soil pollutants may worsen cognitive decline and white matter alterations.^{8,92}

4. Conclusion and future perspective

Organic and inorganic soil pollutants significantly contribute to the development of modifiable CeVD risk factors, including hyperlipidemia, hyperglycemia, and hypertension, through complex and interrelated pathophysiological mechanisms. Heavy metals such as lead, cadmium, and arsenic have been linked to oxidative stress, impaired endothelial function, and disruption of calcium and nitric oxide signaling, which may contribute to vascular stiffness and elevated blood pressure. Organic pollutants such as PAHs and PCBs may alter lipid metabolism and promote insulin resistance, including via endocrine-disrupting effects and AhR-related pathways. These exposures may also promote systemic inflammation and atherogenesis, thereby increasing cerebrovascular risk. Given the chronic nature of soil-based pollutant exposure, impacts may be particularly relevant in socioeconomically disadvantaged and agriculturally dependent communities. Public health responses may benefit from strengthened environmental monitoring, remediation of contaminated soils, and improved regulation of industrial and agricultural sources. Incorporating environmental exposure assessment into cardiovascular risk screening and advancing interdisciplinary research will be vital to mitigating long-term cerebrovascular impacts of soil pollution.

Future studies should prioritize longitudinal cohort designs, broader pollutant coverage, and evaluation of health outcomes beyond CeVD. Integrating geospatial soil contamination data with individual biomonitoring and neurovascular health metrics may improve exposure assessment. Interdisciplinary approaches combining omics, exposome methods, and advanced imaging could help elucidate pollutant-specific and synergistic effects on cerebrovascular biology. Further investigation of age-related susceptibility, gene–environment interactions, and microbiome-mediated mechanisms may also identify preventive targets. As soil degradation intensifies with urbanization and climate-related ecological change, recognizing soil pollution as a potentially modifiable determinant of cerebrovascular health is imperative for precision public health.

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The authors declare no conflict of interest.

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