Review article
Ανασκόπηση

# There is no safe threshold for lead exposure: A literature review

**Th. Vorvolakos, S. Arseniou, M. Samakouri**

*Department of Psychiatry, School of Medicine, Democritus University of Thrace, University General Hospital of Alexandroupolis, Alexandroupolis, Greece*

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Lead was one of the most dangerous environmental toxic substances for a long time in western countries, and this is still the case for many places on earth today. Its neurotoxic potential is highly significant but its secure blood level concentration remains unknown. The aim of this study was to approach the above issue from the perspective of social psychiatry. A systematic search was made of Dialog and Datastar interfaces for data regarding the neuropsychiatric complications of direct or chronic exposure to lead, and a review of the relevant literature was conducted using the databases Medline, Embase, CAB Global Health and Cochrane. Lead affects the cholinergic, dopaminergic and gloutamergic systems, thus intervening in the normal function of neurotransmion. The consequence of neurotoxicity in the central nervous system includes apoptosis and excitotoxicity. Direct as well as chronic exposure causes serious neurological symptoms and possibly constant cognitive impairment. Acute encephalopathy, the most serious expression of lead poisoning, occurs in blood level concentrations over 100 μg/dL in adults and 80–100 μg/dL in children. Early symptoms of lead neurotoxicity include irritability, headaches and difficulties in concentration in both children and adults. Continuous exposure in children produces neurobehavioral symptoms, such as decreased concentration, inability to follow instructions, difficulty to play games and low IQ, which are associated with concentrations of 10–35 μg/dL. However, some studies claim that cognitive decline and low IQ can occur in concentrations <10 μg/dL. The commonest symptom in adults is peripheral neuropathy with foot drop. Prenatal exposure to lead has been correlated with antisocial behavior and schizophrenia. Long-term lead exposure causing low and medium lead concentration in blood has been linked to depression as well as generalized anxiety disorder and other behavioral disorders. High blood level concentrations correlate with psychotic symptoms like delusions and hallucinations but more rarely with psychotic syndromes. Despite the fact that lead has been banned from gasoline, paint and water pipes, quite significant quantities of lead still exist, particularly in deprived areas of modern cities, in transition zones and city centers,

and there are also great concentrations around lead mines and in developing countries, but even for the remaining areas there is no safe threshold. CONCLUSIONS: Lead was and still is an environmental factor that increases neurologic and psychiatric morbidity. It also causes developmental disorders, especially in deprived areas. Prevention should be the single most important way of dealing with lead poisoning.

**Key words:** Lead, exposure, neurotoxicity, safe threshold.

## Introduction

Lead is a well known neurotoxicant that causes a variety of clinical conditions. Recent data now indicate that low level exposure (blood lead levels below 10 μg/dL) results in cognitive dysfunction, neurobehavioral disorders, neurological damage, hypertension and renal impairment.[1] Exposure to heavy metals early in development can predispose the brain to develop a neurodegenerative disease later in life. Alternatively, lead can exert their adverse effects through acute neurotoxicity or through slow accumulation during prolonged periods of life.[2] Inorganic and organic forms of lead are absorbed mainly by ingestion and inhalation; organic compounds may also be absorbed through the skin[3] and can cross the placental barrier.[4,5] In occupational settings, exposure through inhalation is more common, whereas in the general population it is largely through ingestion.[6]

## Exposure, absorption and distribution

Exposure to lead has been known to be neurotoxic since Roman times.[7] The removal of lead from paint in the 1970s and leaded gasoline in 1990 resulted in substantial lowering of mean blood lead levels. Between 1976 and 1991, levels fell from 15.8 to 2.8 μg/dL in adults and 13.7 μg/dL to 3.2 μg/dL in children.[8,9] Nowadays, common sources of lead exposure are lead-based paint in old houses, contaminated soil, household dust, old water pipes and lead-glazed ceramics.[10] Children are more susceptible to lead toxicity than adults, due to particular exposure pathways via hand-to-mouth activities like pica,[11,12] and because they have a developing system of cell differentiation and growth that is more vulnerable to inhibition and damage.[13]

It has been determined that lead can cross the placenta with fetal uptake beginning at 12 weeks of gestation and continuing up to birth. In fact, pregnant women with high blood lead levels may not display the toxic effects of lead poisoning, yet the development of the fetus can still be damaged in any trimester.[14–16]

## Mechanisms of lead neurotoxicity

Lead can affect the nervous system by multiple mechanisms, an important one of which competes with or mimics the action of calcium (influx) in neuron cells due to the chemical similarity. This disturbs calcium entry into cells and alters mitochondrial structure, leading to inhibited cellular respiration and altered calcium-based reactions and neuronal signalling.[17,18]

Calcium is the natural physiologic activator of Protein Kinase C (PCK), but the ability of lead to substitute calcium in the activation of PCK can lead to the impairment of brain microvascular formation and function, while high levels of lead exposure may disrupt the blood-brain barrier.[19,20] Excessive PCK activation can disrupt prefrontal cortical regulation of behavior and thought, possibly contributing to signs of prefrontal cortical dysfunction such as distractibility, impaired judgment and thought disorder.[21]

Lead also affects the glutamatergic, cholinergic and dopaminergic systems.[22] Most of the evidence available suggests that lead interferes with glutamate, which is critical for learning in the developing brain, by acting as an antagonist with its receptor (N-Methyl-D-Aspartate receptor-NMDAr).[23] It may also impair the regulation of dopamine synthesis and release, block evoked release of acetylcholine and decrease cholinergic function, and interfere

with γ-Amino Butiric Acid (GABA) neurotransmission by heme synthesis inhibition.[24] Furthermore, lead affects the levels and metabolism of serotonin[25] and the hypothalamic-pituitary-adrenal (HPA) axis which can lead to permanent HPA axis dysfunction.[26]

Lead can also cause neurotoxicity by increasing free radicals or by direct depletion of antioxidant reserves such as glutathione.[27] Lead-related oxidative stress can result in increased neuron vulnerability, activating the apoptosis program and inducing excitotoxicity, notably for astrocytes and microglia.

The dose-effect relationship of lead toxicity in the human brain seems to be associated with low level exposure in a biphasic pattern. Hence, in low blood lead level concentrations, it seems that there is a suppression of the glutamatergic system not seen in higher concentrations but which reappears in even higher concentrations following a pattern of reversed U.

Cecil[28] showed that a higher mean childhood blood lead concentration is related to region-specific reductions in adult gray matter volume, especially in the anterior cingulate cortex, which may affect mood regulation. Bellinger[29] confirmed that the greater lead-associated neurocognitive and behavioral findings in males suggest an underlying physiologic difference in how the brains of men and women respond to childhood lead exposure. The authors agree with previous studies suggesting that volume loss in both the cognitive and emotional territories of anterior cingulate cortex can explain the behavioral and cognitive problems with lead exposure. Bellinger observed that childhood lead exposure is associated with a significant and persistent impact on white matter microstructure.

## Neurologic and neurocognitive implications of lead intoxication

The toxic effects of lead vary greatly, ranging from potentially fatal encephalopathy in acute lead poisoning to subtle changes in neurocognitive function at low level exposure. As exposure progresses, symptoms may manifest differently.[30]

Brain damage (encephalopathy) is common at high exposure (blood levels above 100–120 μg/dL for adults and 80–100 μg/dL in children) and can be fatal or permanently disabling, resulting in dementia.[31,32]

Chronic exposure to high lead concentration induces cognitive deficits in the domains of viso-spatial perception, attention, recognition memory and new learning as well as neurological impairment such as gait ataxia, dysdiachokinesia and increased tendon reflexes, and can also lead to toxic encephalopathy.[33,34]

Moderate blood lead levels between 20–70 μg/100 mL can cause cognitive impairment as well as mood and behavioural disorders and other physical symptoms like anorexia, intermittent vomiting, abdominal pain, peripheral neuropathy with the characteristic foot drop, and lethargy. Results of more recent cross-sectional and prospective studies indicate that postnatal lead exposure resulting in blood levels as low as 25 μg/dL, and probably lower, are also associated with deficits in intellectual attainment and affect behavior.[35]

Baker reported various neurobehavioral effects in workers with blood lead concentrations between 40 and 60 micrograms/100 mL showing impaired performance in tests of verbal concept formation, visual/motor performance, memory, and mood. Furthermore, this impairment occurred in the absence of peripheral nervous system derangement and increased in severity with increasing lead concentrations.[36] Similar results were obtained by other studies that associated lead exposure with subclinical decrements of neurocognitive function.[37–39]

In the population-based sample of adults 20–59 years of age participating in the National Health and Nutrition Examination Survey III (NHANES III) study, no relationship was found between blood lead concentration (geometric mean 2,51 μg/dL) and covariate-adjusted performance assessment of neurocognitive function. However, significant associations have emerged in some studies involving older adults with slightly higher blood lead concentrations. A recent study with 991 participants,

which sought to determine whether long-term exposure to high levels of lead in the environment is associated with decrements in cognitive ability in older Americans, concluded that permanent cognitive decline is an effect of cumulative lead dose following previous environmental exposure and also that a portion of age-related decrements in cognitive function in this population might be associated with earlier lead exposure.[40] Wright[41] studied the association of lead exposure biomarkers with cognitive test scores as well as the modifying effects of age on the lead cognition relationship, and found that lead exposure might accelerate age-associated cognitive decline.

However, a meta-analysis of occupational studies by Goodman[42] suggested that none of the individual studies is adequate or conclusive in providing information on the subclinical neurobehavioral effects of lead exposure. Additionally, the authors claim that the studies do not provide adequate data for drawing firm conclusions about the biological effects of current lead exposure.

### Effect in children

The levels of lead considered tolerable for children have been repeatedly lowered over the past three decades. In the early 1960s, the toxic threshold was established as blood lead levels of 60 μg/dL.[43] In 1970, the threshold was reduced to 40 μg/dL;[44] it was further reduced to 30 μg/dL in 1975 and again to 25 μg/dL in 1985.

Finally, in 1991, CDC set the international level at 10 μg/dL.[45] According to Bellinger,[46] although this level only intends to serve as a risk guidance and management tool, it has been widely and incorrectly imbued with biological significance for the individual child. Indeed, the intervention level is often interpreted as a threshold; thus, a level lower than 10 μg/dL would be considered "safe," and a higher level "toxic." There is no safe level of lead exposure given that factors such as the endpoint of interest, age at exposure and at assessment, duration of blood lead elevation, and the characteristics of the child's rearing environment must also be considered.

Children are particularly vulnerable to lead poisoning. Some argue that the most detrimental effect of lead in children is neurotoxicity within the CNS.[47] Mild and moderate lead levels can also cause cognitive and behavioral problems. For each 10 μgr/dL increase in blood lead level, cognitive test scores decrease by 3.2 points.[48] Usually the effects are long-term and affect IQ scores, developmental delays, learning disabilities and other neurocognitive and behavioral effects.[49,50] The outcomes of four key studies of the neurobehavioral effects of low-level lead exposure in children were reviewed and analyzed by Davis[51] who concluded that blood lead levels of 10–15 μg/dL can cause impaired neurobehavioral activity. The results of a study involving 246 inner city young Afro-American children with a mean age of 7.5 years showed neurobehavioral deficits in areas of intelligence, reaction time, visual-motor integration, fine motor skills and attention, including executive function at levels <10 μg/dL.[52]

Blood lead levels above 10 μg/dL have been reliably associated with Attention Deficit Hyperactivity Disorder (ADHD), with the only real dispute being the magnitude of the effect.[53–55] Lead exposure is a plausible neurobiological candidate for ADHD involvement because it disrupts midbrain dopamine and other neurotransmission circuitry,[56] systems that are also implicated in ADHD.[57]

In a cross-sectional study of 756 children with a mean blood lead level of 11.4 μg/dL, Roy et al[58] noted that lead exposure affected behavior across multiple domains, including anxiety and social behavior. Their results also suggested that executive functions and attention are especially vulnerable to insult by lead among young children. They also observed that children with higher blood lead levels presented with more ADHD-type behaviors, especially the inattention component. However, it is not clear if behavioral changes precede lead exposure and could even induce lead exposure through behavioral pathways such as increased hand-to-mouth behavior. In contrast, Nigg et al[59] reported that even very low levels of blood lead exposure (<5 μg/dL) were associated with ADHD. They con-

firmed their previous findings and concluded that when applying DSM-IV ratings, blood lead was found to be reliably associated with hyperactivity but not inattention.

Furthermore, other studies suggested cognitive and behavioral deficits in children related to low and very low lead exposure. In prospective studies, it has been found that lead exposure in early life can cause neurocognitive deficits with no low-dose threshold.[60] The NHANES III findings lead to the conclusion that deficits in cognitive and academic skills associated with lead exposure occur at blood lead concentrations of less than 5 μg/dL.[61] However, there is some skepticism about the methodology of this study due to the fact that these findings proved difficult to be replicated.[62]

Latest studies also suggested that although the developing brain is vulnerable to the neurotoxic effects of lead, it is difficult to understand the exact correlation of lead neurotoxicity in infants, even in the case of lead exposure.[63]

## Psychiatric implications of lead poisoning

Despite the detailed knowledge regarding the effects of lead poisoning on neurocognition, there is significantly less and vague evidence in terms of psychiatric complications.

In a prospective study conducted in Cincinnati, prenatal and average childhood blood lead concentrations were reported to be associated with a greater risk of delinquent behavior later in life.[64] Prenatal lead exposure may increase the risk of other psychiatric disorders. The behavioral deficits associated with lead exposure strongly resemble certain premorbid features of schizophrenia, such as reduced attention and neurocognitive impairment. Opler[65] conducted a study of prenatal lead exposure and schizophrenia in 2004, using δ-aminolevulinic acid from maternal serum as an indirect biologic marker of lead exposure. The findings suggested a possible association of prenatal lead exposure and the development of adult-onset schizophrenia. In a second study in 2008 by the same group, the results provided further evidence for the role of early environmental exposure in the development of adult-onset psychiatric disorders.[66]

Using logistic regression models adjusted for age, alcohol intake, employment status, and education status, Rhodes et al found that long-term exposure is associated with depression, stress and behavioral symptoms.[67] The analysis of hair samples taken from ten symptomatic bipolar patients and from ten normal controls matched for age, sex and race suggested that a relatively high body lead burden may be associated with manic episodes of bipolar illness.[68]

In a cross-sectional epidemiologic survey, Bouchard[69] used NHANES data from 1999 to 2004 to investigate the relation between blood lead levels and the odds of major depressive disorder (MDD), panic disorder (PD) and generalized anxiety disorder (GAD) in a sample of US population aged 20 to 39 years. Increased blood lead levels were associated with a significantly higher risk of MD and PD in young adults with low levels of lead exposure but not GAD.

Stanley and Wakwe[70] measured serum lead levels in 21 depressive, 20 manic-depressive and 20 schizophrenic in-and outpatients of a mental health unit. Lead was found to be increased in depressives ($p<0.01$) and schizophrenics ($p<0.05$) but not in mania patients.

In contrast, a cross-sectional study by Golub et al[71] did not demonstrate a consistent association between environmental lead exposure and depression within the investigated blood lead levels. While their study found a statistically significant association between blood lead level and depression, when exposure was modeled as a categorical variable and only age, gender and sex were considered, the effect was small with a relative risk around 1.3. In addition, when education level and poverty income ratio were added to the model, no clear trends emerged to show that the risk of depression increases with the increase in blood lead levels. The authors underline the importance of considering the effects of socio-economic measures, such as education and poverty income ra-

tio in the investigation of lead effects on health. Longitudinal studies will be necessary to examine more fully the effect of environmental lead exposure on depression, including measures of HPA axis function, to help elucidate potential biological mechanisms.

Higher levels of lead concentrations are associated with psychotic symptoms such as hallucinations or delusions and more rarely with psychotic syndromes.

Rajan[72] evaluated the association between lead burden and psychiatric symptoms and its potential modification by genetic polymorphism in a longitudinal study with 1,075 elderly male participants. Increased lead burden was significantly associated with increased somatization, hostility and global distress. Participants with the allele 1-1 Aminolevulinic Acid Dehydrate (ALAD 1-1) genotype appeared to be at greater risk, particularly with regard to phobic anxiety symptoms, than those participants who were carriers of at least one variant ALAD allele.

Condray[73] investigated the relationship between chronic solvent exposure and adult lifetime psychiatric disorders as well as the relationship between solvent exposure and personality changes. In this study, 29 male painters and 32 male non-painter control subjects underwent semi-structured diagnostic interviews for DSM-III-R Axis I and Axis II disorders. Results showed that the probability of being diagnosed with a mood disorder differed significantly between painters (41%) and control subjects (16%). The groups did not differ in regard to personality disorders involving an onset before 25 years of age. In contrast, painters exhibited a subclinical pattern of personality dysfunction involving symptomatology and particularly increased difficulties in the domains of interpersonal relationships and impulse control that was measured allowing for onset after the age 25. Finally, a significant dose-response relationship was observed between career solvent exposure, blood lead level, and personality symptoms. These data showed an increased rate of psychological disturbance in a significant and substantial number of painters. However, not all painters were so characterized. This latter pattern raises the question of the potential role of differential vulnerability. ALAD-1 allele is also suggested as being partly responsible for this phenomenon.

Despite the above evidence, mainly deriving from epidemiological studies, no clear cause-effect relationship between lead poisoning and psychiatric symptoms has been established. Clinical improvement after lead burden reduction treatment can be helpful in providing some evidence regarding a potential relationship, although it is moderately effective as single treatment in the majority of reported cases.

An older study, regarding 1,113 autistic or hyperactive children with a mean blood lead value of 15.6 mgc following a program to reduce lead burden, resulted in clinical improvement of their symptoms.[74] In another study, Dimercaptosuccinic Acid (DMSA) was used to diminish the body burden of lead in clinically depressed patients after chronic lead exposure; few cases of documented clinical improvement following treatment have been reported. One case, involving a long-term lead worker with moderate to severe depression, appeared to respond dramatically to DMSA.[75] In another case study, a 52-year old male artisan of stained glass was admitted to hospital for depression twice, with one suicidal attempt and without neurological symptoms, cognitive or memory problems. His depression was lifted once the body burden of lead was reduced.[76]

Although there is strong evidence that lead burden can be related to anxiety, depressive and behavioral symptoms, the degree to which psychiatric symptoms cluster together to constitute psychiatric syndromes is not certain. Furthermore, most studies suggest that individual vulnerability due to genetic, socio-economic or other confounding factors must be considered before drawing any certain conclusions. Bouchard et al suggest that when assessing the role of lead as a risk factor for mental health outcomes, an indicator of long-term lead exposure, such as bone lead level, is desirable. Bone lead level has a clearance half-life of years to decades.

As a general conclusion, it is worth considering lead exposure as an occupational or environmental hazard during the psychiatric interview, especially when anxiety, behavioral or depressive symptoms are apparent.

## Prevention

Prevention of lead poisoning, other than the obvious social benefit, can also prove cost-effective and can be accomplished with the implementation of policies aimed to control possible sources of lead in the environment, and/or with educational programs that place the burden of preventing exposure on the individual and the family. Phasing out lead from gasoline, paint and food containers has been highly effective in reducing average lead exposure, but racial and income disparities persist. Although enforcement and lead abatement have been shown to reduce the societal cost of lead exposure within the home, dust control has limited efficacy.[77] Surveys conducted to examine whether pamphlets can increase the awareness of lead preventive techniques have shown mixed results.[78,79] Similar results were obtained by Polivka[80] who found it difficult to raise the awareness in people with low income and low education. People in poor areas tend to suffer more often from mental health problems, mainly depression, which makes it more difficult to implement lead exposure prevention programs either for them or their children.[81] According to DeSilva,[82] the intellectual deficits caused by lead exposure promote behaviors that increase the exposure itself. Nevin[83] also found that violent crime rates, rates of pregnancy at the age of 15 or less and unwed pregnancies are related to societal lead exposure over the last 50 years.

Medical treatment of individuals with overt lead intoxication involves decontamination, supportive care and judicious use of chelating agents.[84] A variety of chelating agents have been demonstrated to decrease blood lead concentrations. A recent clinical trial of oral chelation in young children with blood lead concentrations raging from 22 to 44 μg/dL found that the drug succimer lowered blood concentrations transiently but did not improve cognitive function.[85,86] Although in some instances chelation therapy has proved effective in improving depressive symptoms and more rarely in treating depressive episodes, and anecdotal evidence suggests that chelation has been associated with improvement in symptoms and decreased mortality in patients with lead encephalopathy, controlled clinical trials demonstrating efficacy are lacking.[87,88]

Despite the available chelation treatment or other alternatives to reduce body lead burden, primary prevention will be the most important technique in the future for eliminating lead poisoning.

## Conclusions

Lead neurotoxicity may be a contributing factor for adverse mental health outcomes, even at levels generally considered to pose no risk. Studies continue to describe apparent effects that were previously unknown and show that these effects can be detected at increasingly lower levels of exposure.

The well-known pharmacokinetics of lead in the nervous system combined with the epidemiological data mentioned above are in accordance with recent theories regarding schizophrenia.[89]

These data rate lead exposure as a severe environmental hazard that needs to be addressed through health policies and also to be taken into account in the differential diagnosis of neurological and mental health disorders.

The implementation of measures concerning lead poisoning prevention within the home lies mainly in the hands of individuals, despite various national policies. Awareness must be raised regarding lead poisoning and related protective techniques, especially in those that have been exposed the most. In addition, simple measures like pica management can be effective,[90] especially since routine screening for blood lead levels in all children admitted to a psychiatric inpatient unit appears to be neither efficacious nor cost effective.[91]

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# Δεν υπάρχει όριο ασφαλείας για την έκθεση στον μόλυβδο: Μια βιβλιογραφική ανασκόπηση

**Θ. Βορβολάκος, Στ. Αρσενίου, Μ. Σαμακουρή**

*Τομέας Ψυχιατρικής, Τμήμα Ιατρικής, Δημοκρίτειο Πανεπιστήμιο Θράκης, Πανεπιστημιακό Γενικό Νοσοκομείο Αλεξανδρούπολης, Αλεξανδρούπολη*

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Ο μόλυβδος αποτέλεσε έναν από τους πιο επικίνδυνους τοξικούς περιβαλλοντικούς παράγοντες στον δυτικό κόσμο, και εξακολουθεί να αποτελεί κίνδυνο σε πολλές περιοχές του πλανήτη. Η νευροτοξική του δράση είναι πολύ έντονη και σε μεγάλο βαθμό τα όρια ασφαλείας της συγκέντρωσής του στο αίμα παραμένουν άγνωστα. Σκοπός της παρούσας εργασίας είναι η βιβλιογραφική ανασκόπηση του θέματος από τη μεριά της κοινωνικής ψυχιατρικής. Δομημένη –με τη χρήση του περιβάλλοντος Dialog Datastar– βιβλιογραφική ανασκόπηση στις βάσεις δεδομένων MEDLINE, EMBASE, CAB Global Health, Cochrane Library γύρω από τις νευροψυχιατρικές εκδηλώσεις της άμεσης και μακροχρόνιας έκθεσης του οργανισμού στον μόλυβδο. Ο μόλυβδος επιδρά στο χολινεργικό, ντοπαμινεργικό και γλουταμινεργικό σύστημα, επεμβαίνοντας με αυτόν τον τρόπο στη φυσιολογική λειτουργία των νευροδιαβιβαστών. Οι νευροτοξικές επιδράσεις του μολύβδου στο κεντρικό νευρικό σύστημα περιλαμβάνουν απόπτωση και τοξικότητα από υπερδιέγερση (excitotoxicity), επιδρώντας στην αποθήκευση και απελευθέρωση νευροδιαβιβαστών και μεταβάλλοντας τους υποδοχείς τους. Τόσο η άμεση όσο και η μακροχρόνια έκθεση στον μόλυβδο προκαλεί σοβαρά νευρολογικά συμπτώματα και πιθανώς μόνιμα γνωσιακά ελλείμματα. Η πιο σοβαρή επίπτωση της δηλητηρίασης από μόλυβδο στα παιδιά είναι η οξεία εγκεφαλοπάθεια, σε συγκεντρώσεις πλάσματος >100 μg/dL στους ενήλικες και 80–100 μg/dL στα παιδιά. Πρώιμα συμπτώματα νευροτοξικότητας από μόλυβδο περιλαμβάνουν ευερεθιστότητα, κεφαλαλγία, διαταραχές προσοχής, τόσο στους ενήλικες όσο και στα παιδιά. Όσο η έκθεση στα παιδιά αυξάνεται, παρουσιάζονται νευροσυμπεριφορικές διαταραχές, όπως μείωση της προσοχής, αδυναμία να ακολουθήσει οδηγίες και εντολές, μειωμένη ενασχόληση με παιχνίδια, χαμηλός δείκτης νοημοσύνης σε επίπεδα πλάσματος 10–35 μg/dL. Μερικές έρευνες υποστηρίζουν πως η γνωσιακή έκπτωση και η μείωση του δείκτη IQ στα παιδιά μπορεί να προκληθεί και σε χαμηλότερες συγκεντρώσεις μολύβδου στο πλάσμα, ακόμη και <10 μg/dL. Το πιο κοινό νευρολογικό σύμπτωμα στους ενήλικες αποτελεί η περιφερική νευροπάθεια, με πτώση καρπού ή/και άκρου ποδός. Μελέτες έδειξαν συσχέτιση μεταξύ προγεννητικής έκθεσης στον μόλυβδο με αντικοινωνική συμπεριφορά και σχιζοφρένεια. Η μακρά έκθεση στον μόλυβδο που καταλήγει σε χαμηλή με μεσαίου μεγέθους συγκέντρωση μολύβδου στο πλάσμα έχει συσχετισθεί με κατάθλιψη, γενικευμένη αγχώδη διαταραχή και άλλες συμπεριφορικές διαταραχές. Υψηλές συγκεντρώσεις μολύβδου στο πλάσμα έχουν συσχετισθεί με ψυχωσικά συμπτώματα, όπως ψευδαισθήσεις και παραληρητικές ιδέες, και πιο σπάνια με ψυχωσικά σύνδρομα. Παρά την απαγόρευση της χρήσης του μολύβδου στη βενζίνη, στα χρώματα και στις σωληνώσεις του νερού, σημαντικές ποσότητες μολύβδου παραμένουν σε υποβαθμισμένες περιοχές σύγχρονων μητροπόλεων, κυρίως στις ζώνες μετάβασης, στα κέντρα των πόλεων, καθώς και σε περιοχές εξόρυξης μολύβδου και στις αναπτυσσόμενες χώρες, ενώ οι ασφαλείς συγκεντρώσεις στο περιβάλλον δεν είναι ακόμα σαφώς καθορισμένες. Ο μόλυβδος αποτελούσε αλλά και εξακολουθεί να αποτελεί έναν περιβαλλοντικό παράγοντα που αυξάνει τη νευ-

ρολογική και ψυχιατρική νοσηρότητα. Επίσης συμβάλλει ιδιαίτερα στην πρόκληση αναπτυξιακών διαταραχών κυρίως σε υποβαθμισμένες περιοχές. Η πρόληψη θα πρέπει να αποτελεί το σημαντικότερο μέσον αντιμετώπισης της δηλητηρίασης από μόλυβδο.

**Λέξεις ευρετηρίου**: Μόλυβδος, έκθεση, νευροτοξικότητα, όριο ασφαλείας.

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*Corresponding author:* Th. Vorvolakos, Department of Psychiatry
GR-681 00 Dragana Alexandroupolis, Alexandroupoli, Greece
Tel: (+30) 694 656 6186
e-mail: tvorvola@med.duth.gr