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Lead (Pb), intellectual functioning and health

Dear Editor – The latest concerns raised by the Environmental Protection Agency (EPA) over lead (Pb) in water supplied in counties Galway, Donegal, Limerick, North Tipperary and Cork are a worrying, but not a new development in relation to exposure to Pb in Ireland. In recent years over 10 million toys have been recalled in Europe having found to be contaminated with Pb or Pb based paint (the brands involved are market leaders including Reebok, Mattel and Fisher-Price).

Concern about Pb and the effect on human health is considerable, but may be of particular concern to psychiatrists given its impact on IQ. Although most, if not all adults are aware of the dangers of Pb poisoning, it is often in a rather broad and non-specific sense. Complacency about this issue is common given that Pb is usually an unseen and insidious pollutant which many people believe is no longer a real health risk.

Sources of Pb

Pb pollution is ubiquitous in the environment and is detectable in all phases of the inert environment such as air, water and soil as well as in most biological systems. It is one of man's most valuable commodities and is mined and processed in over 60 countries.¹ It has been described as the most important toxic hazard in the development of civilisation and exposure of human populations was considered relatively low until the arrival of the industrial revolution of the 1920s and 1930s and large-scale mining.² Between the 1930s and 1970s, the Pb concentration measured in the Greenland ice sheet was 25 to 50 times higher than during the Roman times, due in large part to leaded petrol. This was evident in decreasing Pb concentrations in Greenland snow by a factor of 7.5 over a 20 year period from the late 1960s.³

Although the 1980s and 1990s have seen a large decrease in atmospheric Pb loads, mainly due to the phasing out of leaded petrol the problem remains.⁴ Most of the millions of tonnes of Pb burned in petrol in Europe in the 20th century remains in the soil, air and water. Since 1991, all new cars on the roads of Europe are required to run on unleaded petrol. In Ireland legislation recognising the toxicity of Pb paints was first introduced in 1921 with a ban on Pb paint for interior use passed in Europe in 1933 and Pb compounds were finally eliminated from household paints by 1960.

Exposure

Pb is a multimedia exposure problem. The occupational threats of working with Pb have long been recognised with certain occupations being at particular risk to Pb exposure such as painters, ironworkers, construction workers, cable-splicers, automobile radiator repair mechanics, firearms instructor, metal shop worker, stained glass artists and battery makers/recyclers. In addition, care may need to be taken in other industrial areas such as paint manufacturing, the crystal glass industries, certain ceramic and craft pottery industries and even elements of the plastic industry (which

use Pb additives), the electronics industry, demolition/salvage work, as well as some elements of the steel industry. Other non-occupational sources of Pb exposure include Pb dust (either from paint or mining/ tailings), batteries, ceramics, and certain hobbies such as making stained glass and furniture restoration.

Although Pb has been banned from paint and petrol for some years now, it remains a constant in our environment. The main avenues of lead uptake among humans are via ingestion and inhalation (and rarely by skin exposure). Many older homes may still have Pb pipes, and plumbing in newer homes may include Pb solder. Many people may erroneously assume for example that 'lead free' piping is in fact Pb free. However counsel from the US EPA indicates that the piping may in fact not be Pb free but contain < 8% Pb.

Other sources of potential contamination include Pb based paint that is peeling or cracking. Given improvements in legislation that have reduced Pb in pollutants such as paint and petrol it would be easy to be complacent on this issue. Today, in many parts of the world Pb toxicity from paint represents a major source of exposure for children.⁵ Children ingest dust and soil contaminated with Pb from paint, which flakes or chalks as it ages or is disturbed during home maintenance or renovation.⁶

Toxicity

Pb poisoning is an environmental disease that is the result of human activities. The hazards from Pb have long been recognised and indications of the consequences have been documented as far back as the 2nd century BC by Galen and in the 5th century by Hippocrates. Sub-clinical Pb toxicity defined by a whole blood concentration greater than or equal to 10 micrograms per decilitre ($\mu\text{g}/\text{dL}$) affects an estimated one in 20 children in the United States. Both children and adults are susceptible to health effects from Pb exposure, but the exposure pathways and effects are somewhat different. Although many body systems can be severely affected by high chronic and acute Pb exposure, Pb is a hazard mainly not because of the moderate or low exposure but the chronic exposure that can affect the developing nervous system of young children in more elusive and detrimental ways.

The recent decades have seen a continual reduction in what are deemed 'safe' levels of blood Pb levels (the intervention level for BPb in children declined from 60 $\mu\text{g}/\text{dL}$ in 1965 to 10 $\mu\text{g}/\text{dL}$ in 2000.⁷ Evidence of health impacts at lower and lower levels of exposure continue to emerge in the research literature.⁸ Perhaps most significantly it is important to note that there is no evidence to date that contradicts the suspicion that there may be no threshold below which lead does not exert a toxic effect. Although the current accepted intervention level for BPb in children is currently 10 $\mu\text{g}/\text{dL}$, this level is still disputed with some authors suggesting a reduction to 2 $\mu\text{g}/\text{dL}$.⁹

Adverse health and psychological effects

Although deaths from Pb pollution are extremely rare, psychologists should be aware of the potential threat to IQ it poses. Recent investigations examining the impact of lead on attention and IQ,¹⁰ including a meta-analysis of seven international population-based longitudinal cohort studies have noted a dose-response relationship between increasing lead and decreasing IQ, indicating the absence of a 'safe' blood lead level.¹¹

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ABBREVIATED PRESCRIBING INFORMATION: For full prescribing information refer to the Summary of Product Characteristics.

Name: Ebixa. **Active Substance:** Memantine Hydrochloride. **Indication:** Treatment of patients with moderate to severe Alzheimer's disease. **Dosage & Administration:** Treatment should be initiated and supervised by a physician experienced in the diagnosis and treatment of Alzheimer's dementia. Therapy should only be started if a caregiver is available who will regularly monitor the intake of the medicinal product by the patient. Treatment is orally either as tablets (10 mg) or solution (10 mg/g) taken with or without food at the same time every day. Maintenance dose is 20mg/day, (two tablets or 40 drops once a day). Treatment starts with 5mg/day (half a tablet or 10 drops once a day) for the first week; the 2nd week 10mg/day (one tablet or 20 drops once a day); the 3rd week 15mg/day (one and a half tablets or 30 drops once a day) and the 4th week 20mg/day (two tablets or 40 drops once a day). Moderate renal impairment 10mg/day (one tablet or 20 drops once a day), if well tolerated after 7 days the dose can be titrated up to 20mg/day (two tablets or 40 drops once a day). Severe renal impairment- dose is 10 mg/day. Mild-moderate hepatic impairment- no dose adjustment. Severe hepatic impairment- no data available. Children & Adolescents: Not recommended. **Contraindications:** Hypersensitivity to the active substance or any of the excipients. **Pregnancy and Lactation:** **Pregnancy:** Memantine should not be used in pregnant women unless clearly necessary. **Lactation:** Memantine should not be used in women who are breastfeeding. **Special Warnings and Precautions for use:** Caution is recommended in patients with epilepsy. Caution is advised in patients with raised urine pH as this may elevate plasma levels. Clinical trial data are limited on patients with myocardial infarction, uncompensated congestive heart failure and uncontrolled hypertension and patients with these conditions should be closely supervised. Avoid concomitant use of NMDA antagonists (see also interactions). Patients with sugar intolerance should not take Ebixa. Patients should be warned to take special care if driving and using machines as Ebixa has minor to moderate influence on these tasks. **Interactions:** Effects of L-Dopa, dopaminergic agonists and anticholinergics may be enhanced. Effects of barbiturates and neuroleptics may be reduced. Effect of concomitant treatment with antispasmodic agents e.g. dantrolene and baclofen may be modified. Plasma levels of cimetidine, ranitidine, procainamide, quinidine, quinine and nicotine may be increased. Co-administration with hydrochlorothiazide (HCT) may lead to a reduced serum level of HCT. Concomitant use of NMDA antagonist- amantadine, ketamine, dextromethorphan or phentoin should be avoided. Close monitoring of prothrombin time or INR is advisable for patients treated concomitantly with oral anticoagulants. **Adverse reactions:** Common (≥1/100 and <1/10) headache, somnolence, hypertension, constipation, dizziness and dyspnoea. Uncommon reactions (≥1/1000 and <1/100): cardiac failure, fatigue, fungal infections, confusion, hallucinations (mainly in severe Alzheimer's disease), venous thrombosis/thromboembolism, vomiting, gait abnormal. Very rare (<1/10,000): seizures. Not known: Isolated cases of pancreatitis and psychotic reactions have been reported post-marketing. Alzheimer's disease has been associated with depression, suicidal ideation and suicide. In post-marketing experience these events have been reported in patients treated with memantine. **Overdose:** Symptomatic treatment. **Elimination:** Mainly in unchanged form via the kidneys. **Legal Category:** POM. **Marketing Authorisation Holder:** H.Lundbeck A/S, 9 Otrikavej, DK-2500, Valby, Denmark. **Marketing Authorisation Numbers:** EU/1/02/219/005 Ebixa 10mg/g Oral drops solution-50g bottle. EU/1/02/219/006 Ebixa 10mg/g Oral drops solution-100g bottle. EU/1/02/219/007 Ebixa Tablets 10mg, 28 pack size. EU/1/02/219/008 Ebixa Tablets 10mg, 56 pack size. Further information may be obtained from: Lundbeck (Ireland) Ltd., 7 Riverwalk, Citywest Business Campus, Citywest, Dublin 24. **Date of Preparation:** July 2009. References 1. Wilkinson et al. Dement Geriatr Cogn Disord 2007; 24:138-145 2. Reisberg et al. 2006. Arch Neurol. 63:49-54 3. Claxton et al. Clinical Therapeutics 2001; 23:1296-1310. 4. Summary of Product Characteristics (SmPC).



It should be noted that early studies exploring the links between Pb and IQ often failed to control adequately for relevant covariates such as socio-economic and familial factors.¹²⁻¹³ In addition the validity of such studies has also been questioned on a number of grounds, including the lack of quality control in measuring children's IQ, the inclusion of groups with extreme Pb levels, and the failure to correct for multiple comparisons.¹²⁻¹⁴

However despite some methodological issues, the detrimental effects of 'early exposure to lead are credible and persistent'.¹⁰ Contemporary research continues to identify the heightened susceptibility of the foetal nervous system to low level Pb exposure.¹⁵ Fewtrell et al have estimated that mild mental retardation and cardiovascular outcomes resulting from Pb exposure amount to almost 1% of the world's total burden of disease.¹⁶

Children are particularly susceptible to the toxic effects of Pb due to increased absorption and increased hand to mouth contact. Pb poisoning is usually asymptomatic with the result that most cases go undiagnosed and untreated. The adverse neurological, behavioural, and growth effects of Pb exposure are well documented in infants and young children.¹⁷⁻²¹

The public health implications of low Pb exposure in children will continue to provoke widespread concern in many countries worldwide. The overall evidence suggests a small but potentially important deficit in full scale IQ among children with elevated body Pb burdens. The most recent and compelling evidence on the relationship between low level Pb exposure found that children who had a BPb lower than 10 µg/dL suffered intellectual impairment from the exposure. It was found that the amount of impairment attributed to Pb was most pronounced at lower levels providing further support for the goal of primary prevention of Pb exposure.⁸ Based on this new evidence, preventing elevations in BPb by decreasing environmental exposure is warranted.

Despite the progressive medical and scientific understanding of the effects of Pb, there remain limitations in clarity of diagnosis of Pb toxicity at low exposure levels. Effects are variable and do not have a consistent behavioural signature. As Bellinger notes:

'There currently is no particular constellation of neuropsychological findings that can be used in the diagnostic sense. Some studies indicate that verbal abilities are most impacted by Pb, while others indicate that the visual and spatial abilities are most affected. The most consistent finding is that of the reduction in the ability to sustain attention'.²²

It should be noted that unlike other metals, Pb serves no useful purpose in the human body, and its presence in the body can result in toxic effects, regardless of exposure pathway. It has been stated that there is no naturally occurring level of Pb in the human body.²³ Pb toxicity causes haematological, gastrointestinal, and neurological dysfunction in adults and children. Symptoms are usually noted with BPb greater than 40 µg/dL (1.93 µmol/L).

Severe or prolonged exposure may also cause chronic nephropathy, hypertension, and reproductive impairment. Pb inhibits enzymes; alters cellular calcium metabolism; stimulates synthesis of binding proteins in kidney, brain, and bone; and slows nerve conduction. Less severe exposure to Pb, designated by BPb of 10 µg/dL to 20 µg/dL has been implicated in poor pregnancy outcome, impaired neurobehavioural

development, reduced stature in young children, and higher blood pressure in adults.²⁴

Future issues

Despite improved protection measures Pb remains a threat in human environments. Recent alarms over water quality and the numerous recalls of children's toys continue to highlight the need for strict surveillance, communication and action on the issue of Pb exposure. Particular attention must continue to be exercised around the issue of Pb via occupational exposure, individuals with associated hobbies, polluted industrial and extraction sites, and older industrial and residential premises (where Pb pipes and peeling Pb paint may be an issue). One of the major threats caused by Pb may result from complacency about the issue in an era of tighter environmental controls, and a lack of familiarity with exposure sources and their potential impacts. As the broad threat of Pb diminishes its chronic impact may go unnoticed. In terms of surveillance for Pb as a constant threat to neurobehavioural development it is important to note the provocative statement about Pb from the US Centre for Disease Control:

'Pb is ubiquitous in the human environment as a result of industrialisation. It has no known physiologic value. Children are particularly susceptible to Pb toxic effects. Pb poisoning, for the most part, is silent: most poisoned children have no symptoms. The vast majority of cases, therefore, go undiagnosed and untreated. Pb poisoning is widespread. No socio-economic group, geographic area, or racial or ethnic population is spared'.²⁵

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Book Reviews

Handbook of evidence-based psychodynamic psychotherapy: bridging the gap between science and practice

Levy R, Albon J eds. Humana Press: New York, 2008.

This is a superb book. It does what it says on the cover. It is the best current summary of scientific research in this area. The research in the book is mostly describing hypothesis-driven research using the best available measurement instruments. There are imperfections in this kind of work as the science is crude compared to the physical sciences. This book is written with the backdrop where psychoanalysis is "knocked flat on the ground" with almost zero influence as a power broker in the medical psychological and political worlds.

In my view the key element in psychoanalytic psychotherapy and indeed any psychotherapy, including behaviour therapy, is the human relationship. How this is managed is critical for the outcome of treatment no matter what form of psychotherapy is used. This is highlighted in this book.

To the huge credit of Freud and his followers they studied this relationship in great detail and what they found is still relevant today in what is called the permanent contribution of psychoanalysis. Many of the specific psychoanalytic theories were found to be time-bound and have disappeared except for a few 'die-hard' psychoanalysts and their disciples. No one form or theory of psychoanalysis or any other psychotherapy has been found to be the 'greatest of them all'. The Dodo bird was largely right.

Unfortunately psychoanalysts gradually began to see psychoanalysis as a theory of all mental phenomena and a treatment of almost all psychiatric and psychological conditions. There is always the danger with a theory of everything

The changing face of ADHD

Dear Editor – It is now accepted that there are three valid types of ADHD:

1. Full ADHD^{1,2} meeting DSM-IV criteria.
2. Late onset ADHD.
3. Sub-threshold ADHD which is a milder form of the disorder.

ADHD Questionnaires are screening instruments, the diagnosis is a clinical diagnosis.

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that you have a theory of nothing. Psychoanalysis was grossly overambitious as usual. Pride comes before the fall of psychoanalysis to its current state. This book shows that psychoanalysis is well worth resuscitating by the 'emergency medical services'.

Indeed Levy and Ablon are so successful that by the end of the book they have psychoanalytic theory and therapy 'sitting up'. This is a more modest position but the correct position for psychoanalysis. Psychoanalysis and psychoanalytic therapy will never die and will have a modest 'healthy' future after its grandiose past during the so called golden age.

Any psychiatric team that has a trained psychotherapist of any persuasion is very well endowed and very lucky. Never more so than now when the biological treatments possess the unbalanced grandiose position that psychoanalysis had in the first 60-70 years of the 20th century. Human beings including psychiatrists abhor a balanced approach. They like extremes and the treatment now bares a great deal of resemblance to the opposite extreme in much of the 20th century. The psychoanalytic 'wars' and the wars between psychoanalysts and behaviourists must be confined to the dustbin of history. They were due to the narcissism of small differences anyhow. They share more commonalities than differences and the massive commonality is the therapeutic relationship. These kinds of relationships have existed for the past 120,000 years of Homo sapiens and indeed probably in the Neanderthals, Homo erectus, etc. and can be easily seen in the non-human world.

This book provides unequivocal evidence that psychodynamic psychotherapy has an evidence base but of course the same is true of cognitive behaviour therapy. It is of vital importance that all mainstream psychotherapies are valued, encouraged, and cherished.

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