THE ADVERSE EFFECTS OF LEAD

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This article considers the problem of widespread environmental lead contamination. Aspects of its epidemiology and toxicology are presented, with emphasis on the effects of low-level lead exposure on people planning parenthood, on the fetus and on young children. Methods of screening for sub-clinical lead poisoning and dietary treatment and prevention are discussed. Remedial measures for containing and curtailing environmental lead pollution are recommended. Keywords: lead, lead poisoning, environmental pollution, fertility, prenatal influences, nutrition, nutritional status.

INTRODUCTION

Lead is naturally present in the earth's crust in small concentrations, but for centuries it has been mined and disseminated throughout the environment, from where it has gradually become incorporated into the structural tissue of plants, animals and humans. Evidence of the use of lead goes back almost 6000 years, and symptoms of plumbism were recognized by Egyptian, Greek and Roman physicians. For example, in 370 BC Hippocrates described a severe attack of colic in a man extracting metals, and Pliny reported cases of lead poisoning between AD 23 and 79 [I]. Even the fall of the Roman Empire has been attributed to chronic lead poisoning [2]. In more recent history, Thackrah in 1831 directly associated lead poisoning with the 'miners' sickness', first described by Paracelsus in the sixteenth century and supported later by a contemporary study of the ill-health of miners in Derbyshire in 1857 [1]. While cases of direct industrial poisoning have now been largely controlled, the extent of worldwide lead contamination has increased tremendously over the past 60 years or so. Worldwide, approximately 4.5 million tons of refined lead are consumed annually, about 300,000 in Britain alone [3]. Urban air has now been found to contain 20,000 times more lead since the beginning of modern technology [4]. Lead pollution is not confined to the urban environment; studies have shown that the lead contamination of polar ice and remote oceanic waters has also increased more than 400-fold. The degree of lead contamination is now so high that the average Westerner has been found to have a total body lead burden some 500-1000 times greater than the 'natural' background levels encountered by pretechnological man [4]. It should be noted, however, that one study has concluded that environmental (and human) lead levels have declined since the late 1960s [5].

EPIDEMIOLOGY

Sources of Lead. This unnaturally high exposure of humans today is almost entirely the direct result of the extensive technological uses of lead, primarily in petrol, but also in the paint, battery and pottery industries, and its contamination of food and water. In fact, it has been estimated that during recent years lead content in food has increased 100-fold and in tap water 750-fold [6].

Petrol. In recent years, the most contentious area of the environmental lead issue has been the vexed question of lead in petrol used as an anti-knock additive in the form of tetraethyl lead (TEL) and tetramethyl lead (TML) [7-14]. In the US, where catalytic converters were made obligatory in 1975, some studies have shown reduced lead contamination levels in children. The situation is different in the UK, however. Catalytic converters became obligatory on new registrations only in January 1993. A recent Royal Automobile Club (RAC) study, conducted on 60,000 car exhausts, found that 12% of cars caused 55% of the overall pollution. The conclusion of the researchers was that a single old and badly maintained car emits as much toxic gas as 40 cleaner cars [15]. There has been a phased reduction over some years in the lead content of petrol. However, according to one report only 52.6% of all petrol sold in 1993 was lead-free [16]. Furthermore, the number of vehicles on the road and the distances traveled by car, have increased considerably between 1975 and 1976 and 1988 and 1990 [17]. Thus, while newer vehicles may be cleaner, it is a moot point as to whether there is in fact any overall reduction in levels of pollution from petrol emissions. This presents an extremely serious problem because the air-borne particles derived from petrol emissions, because of their chemical composition and tiny particle size, ensure efficient pulmonary penetration and absorption [7]. Children are particularly affected by air-borne pollution because, at rest, pulmonary ventilation and oxygen consumption per kg body weight in children are about twice that in adults. Furthermore, the general activity level of children is usually higher than that of adults. In fact, it has been calculated that the absorption rate of children at play may be about 30% higher than that of adults [18]. In addition, an excessive lead absorption and accumulation in both children and adults has been directly linked to urban traffic densities [19-22]. The minute particles of air-borne lead are also dispersed into city and urban houses. Air lead levels in these houses can be up to four times higher than in houses away from heavy traffic [23].

Food. Besides inhalation, lead can also enter the body through ingestion. It should be noted, however, that the effective toxicity of lead entering via the gut is not considered to be quite as high as that of lead entering via the lungs [24]. The highly unnatural lead levels in the modem diet result from the use of lead in food technology e.g. from the rims of food cans as well as to some extent from lead-glazed pottery, particularly if the glaze is chipped, cracked or improperly applied [25]. However, most lead pollution found in foods is caused directly by the fall-out of air-borne lead particles originating from petrol emissions. Nature has provided natural barriers in the roots of food crops, grass etc. which largely prevent the uptake of lead found in soil. However, air-borne lead fall-out is especially dangerous because it bypasses these natural barriers. Consequently, agricultural crops grown near heavily used roads with heavy traffic, or near stationary sources of lead, have significantly higher concentrations of lead deposited on them, as lead appears to have a particular affinity for plant surface tissue and is only partially removed by rain or washing. Consuming such contaminated fruit or vegetables, as well as meat from farm animals grazed on polluted grass, can result in a considerable body burden of lead [1, 7]. Yet again, young children are particularly vulnerable because children absorb up to half the amount of ingested lead, whereas adults only absorb 5-10% [26-29]. In addition, as most young children are notorious for exploring their environment with their mouths, peeling lead-based paint, which may still be found in old houses, could considerably add to the child's overall lead contamination [30-34].

Drinking water. Normally only about 10% of dietary lead intake comes from drinking water. However, the concentration of lead in water, when it comes out of the tap, may be very different from when it leaves the pumping station. The reason for the high lead content found in some water supplies is that many houses still have old lead pipes, which release lead into the drinking water, particularly in areas where the water is soft, slightly acidic, or contains high concentrations of peaty organic acids [35]. For example, in a retrospective study in Glasgow, Scotland, where the water had been officially reported to contain abnormally high levels of lead, Beatty et al. [36] found that mentally retarded children were significantly more likely than other children, not only to have had high lead levels in their drinking water in their first year of life, but also to have had mothers who had been exposed to such high concentrations in pregnancy.

TOXICOLOGY

One action of lead, whether inhaled or ingested, is to inhibit enzymes concerned with haem synthesis [27, 29, 35]. Inhibition of delta-aminolaevulinic acid dehydrase begins at a blood lead level of 5-1Og [37]. Inhibition of ferrochelatase, resulting in elevation of erythrocyteprotoporphyrin, becomes detectable in children at blood lead concentrations of 15g. Renal toxicity in subclinical lead poisoning involves enzyme inhibition in the proximal tubular lining cells [38]. In these cells, even at blood lead levels below 25g, lead inhibits activation of vitamin D [39]. Lead metabolism can also closely mimic that of calcium, particularly at the receptor site of membranes, where it can in fact replace calcium and thus adversely affect both neuromuscular and synaptic transmissions. This parallelism with calcium metabolism also explains why lead can progressively accumulate in bone during the major part of our lives [35]. Maybe the most serious effect of a low-level lead exposure is as a potent neurotoxin. This explains why it’s most profound neurological effects seem to occur at times in the life-cycle when the human central nervous system is at its most vulnerable and still in the process of development, i.e. during intra-uterine life and during childhood [7, 40-

42]. While cases of classical lead poisoning, where blood lead concentration is above 8Og, are now hardly ever seen, the current debate centres on whether the current Department of Health (DoH) safety level of lead of 35g can cause, particularly in children, serious neurological and behavioural changes [6]. The argument still continues, even though research has indicated that in some children levels of 40 were associated with a risk of clinical poisoning. In addition, other children appear to be especially sensitive to the effects of lead and can display serious symptoms even below 20. Since average levels of 30 and more, are now frequently reported for groups of some inner city children, the problem is clearly very serious indeed [35] Fig. 1. Distribution of negative ratings by teachers on 11 classroom behaviours in relation to dentine lead concentration. The group boundaries were chosen to obtain symmetrical cell sizes for the median (Groups 1 and 6 = 6.8%, Groups 2 and 5 = 17.6% and Groups 3 and 4 = 25.6%). "Effect of Low Levels of Lead on Cognitive Functioning in Children". Numerous studies have reported a clear correlation between low-level lead exposure and childhood learning disabilities and disorders [7, 35, 42-64]. The effect of lead on learning ability appears to result from one or both of two phenomena: Firstly, lead-induced delays or deficits in maturation and inter-neuronal connectivity of the central nervous system, and secondly, lead-induced disturbances in brain biochemistry [7]. Young children are particularly vulnerable because the blood-brain barrier which largely, though not completely, protects the mature brain from lead, is not fully developed until some time after birth. Probably one of the best studies so far to prove how a low-level lead exposure in children can affect their school performance has been conducted by Needleman and associates [47]. Dentine lead levels were used as an indicator of long-term lead exposure rather than blood-lead, which only reflects a very recent exposure. Teachers' ratings were obtained for 2146 children. These covered such behavioural aspects as distractibility, lack of persistence, disorganization, hyperactivity, impulsive behaviour, a high level of frustration, day-dreaming, an inability to follow a sequence of directions and low overall functioning. Children were also compared for physical, medical, socio-economic and family variables. The results of teachers' evaluations, which were conducted in a blind trial, showed that every parameter of non-adaptive classroom behaviour and functioning of each of the 2146 children increased progressively in a dose-related manner as the dentine lead levels increased (Fig. 1). IQ scores were also found to be on average four points lower in children with sub clinical lead intoxication. Similar results of lead-induced IQ deficits in children have been confirmed by other researchers [65-67]. One study of children in London found lead-induced IQ deficits to be as high as seven points [68].Lead is a broad-spectrum toxin that can disturb almost every metabolic function in the body chemistry. Therefore, the different patterns of lead intoxication found in different individuals tend to be the result of a complex network of its several antagonistic interactions between genetics, age, dietary factors and other parameters of individual biological function. Thus, low-level lead exposure can manifest in some children as a general dulling of intelligence and as hyperactivity in others [7, 69-71]. The term hyperactivity describes a syndrome of behavioural rather than intellectual disorder, and is in a physiological sense characterized by an abnormally high level of excitable activity of the motor nervous system and an abnormally low threshold of stimuli. Thus, the hyperactive child tends to be emotionally labile, abnormally excitable, restless, distractible and to have poor impulse control. Research has shown that up to 40% of children in some city areas exhibit hyperactivity disorder [35].FIG. 2. Male fertility status and hair lead content. Furthermore, research indicates that children originally diagnosed as hyperactive, in comparison with controls, usually suffer from a higher drop-out and expulsion rate from schools, a higher rate of involvement in motor vehicle accidents and a greater tendency towards juvenile delinquency and criminality [35, 44, 69, 72, 73]. Some experts in behavioural toxicology have already suggested that subclinical lead intoxication is a significant contributing factor in promoting juvenile delinquency and criminal behaviour [35, 44, 74].Preconceptional and Antenatal Influences of Lead, historical evidence about the reproductive effects of lead exposure is generally based on much higher lead levels than are commonly found today, when lead was found to affect adversely both male and female reproduction. Studies around the turn of the century revealed an increased number of sterile marriages among those working in lead-exposed surroundings [75-79]. In females, a high lead concentration was associated with menstrual disorders, sterility, spontaneous abortions and still-births [75]. A textbook on lead poisoning published during the World War II included the following. "It is generally agreed that if pregnancy does occur, it is frequently characterised by miscarriage, intra-uterine death of fetus, premature birth, and if living children are born, they are usually smaller, weaker, slower in development and have a higher infant mortality" [80]. Recent studies, evaluating the effects of much lower lead exposure than those existing at the time of earlier studies, provide additional evidence of the damage lead can cause to the reproductive processes. Recent available data from both human and animal studies indicate that harmful effects in sperm can occur at “blood lead levels of around 3Og". This includes malformed sperm, low sperm count, decreased sperm motility and altered spermatogenesis [81]. A recent survey on semen quality, collected systematically from reports published world-wide between 1939 and 1990, gives a clear indication that sperm density and quality have declined appreciably over the past 50 years, reflecting an overall reduction in male fertility [82]. The report also suggests that such a remarkable decline in semen quality over such a relatively short time is more likely the result of environmental rather than genetic factors. Ward and associates at Guildford University in Surrey, England, conducted a study among 367 couples suffering from fertility problems and found significantly higher hair lead concentrations in men with low sperm count, malformed sperm and poor sperm motility compared with fertile men (Fig. 2). Pregnant women constitute a special at-risk group, as lead can easily cross the placental barrier and enter the fetus, causing the blood lead levels in the fetus to be at least comparable with that of the mother [83-88]. By studying stillborn and malformed infants, as well as infants dying during the first 28 days of life, researchers have found lead level concentrations in the bones of the infants 5-10 times higher than those of apparently normal infants in accident and cot-death cases [89]. Similar findings were subsequently confirmed by other researchers [90], indicating that lead exposure in utero could be one of the major factors in promoting birth defects and stillbirth [89-92].FIG. 3. Lead content of human placenta: birth defects (study awaiting publication). Bryce-Smith and Ward conducted a survey on placental samples of social terminations, stillbirths, spina bifida and hydrocephalus pregnancies from South Wales. The results showed a clear rise of lead concentration in placental samples in cases of spina bifida and hydrocephalus and an amazingly high lead concentration in cases of stillbirths (Fig. 3). These findings are hardly surprising when one remembers that lead has been used in the past as an effective abortifacient [35, 75]. Ward and his team also studied 37 placental element levels from obstetrically normal births and consistently found a highly significant negative dose-related relationship between placental lead and cadmium levels and birth weight, head circumference and placental weight [93]. Other studies have shown how neonatal head circumference can relate to the future growth of the central nervous system and total brain DNA, indicating that a small head circumference at birth may subsequently relate to slow mental development [93-96]. Low birth weight in humans has been established as an important clinical indicator of possible post-natal mortality and handicap [97-99]. It has also been linked to high blood pressure later in life [100], increased mortality rates from cardiovascular disease [101-102], and impaired glucose tolerance [103]. A number of other studies have also found a direct correlation between low-level foetal lead exposure in infants and subsequent physical disorders and negative mental development [7, 35, 42, 104, 111]. Low level lead exposure in utero has also been directly connected with mental retardation [36, 112-116]. Subclinical Lead Poisoning in adults and children, and adults at the time of reproduction, are not, of course, the only at-risk groups affected by cumulative lead exposure. There is already a great deal of epidemiological and laboratory evidence to link low-level lead exposure in adults with the aetiology of ischaemic heart disease [117-120], cancer [121-123] and with an impairment of renal function [124]. Although adults only absorb 5-10% of ingested lead, slightly more is retained than excreted, leading over the years to a progressive accumulation of body lead, mostly in the skeleton [35]. Bone wasting is universal in later life. It is now believed that bone lead, instead of being immobile and therefore toxicologically unimportant, is in fact gradually released from the bone into the soft tissue. This being the case, it is suggested that lead could also be a contributing factor in the development of motor neuron disease, bone fractures and wasting bone disease [35, 125]. Chronic low-level lead exposure has also been linked to an early development of pre-senile dementia of Alzheimer's type [126-127]. It has also been shown, using several animal studies, that chronic low-level lead exposure can greatly depress immune system function and thereby greatly increase susceptibility to all manner of infections [128-136]. The adult brain can also be vulnerable to the neurotoxic effect of lead exposure. The symptoms include restlessness, talkativeness, illusions, mania, over anxiety, aggression, suicidal tendencies and even some forms of schizophrenia [137]. Subclinical lead poisoning in adults has also been linked directly with excessive violence and criminal behaviour [44, 74].

DIAGNOSIS AND TREATMENT

Need for Detection of Subclinical Lead Poisoning. It has been shown that subclinical lead poisoning, in both children and adults, can be reduced by using dietary methods [7]. Screening for possible subclinical lead poisoning should therefore be available for all children suffering from various educational deficiencies and for children exhibiting anti-social behaviour and criminal tendencies, particularly if these children live in cities or areas with heavy traffic. These children are further compromised in soft water areas where lead pipes are still in situ. Furthermore, screening for subclinical lead intoxication should also be available preconceptionally for men and women, as low-level lead exposure of both prospective parents has been found to affect adversely both reproductivity and pregnancy outcome. This is particularly important, because if a living infant is born, the neurological consequences of low-level lead exposure in utero are permanent and irreversible, and linked with slow mental development, or at worst with a mental handicap.

Methods of Screening. A systematic study of the effect of lead on development in humans has been hindered, until recently, by the lack of an accurate retrospective measure of absorption. The use of blood for diagnosis of long-term lead exposure is ineffective, as blood lead levels are transient and therefore reflect only a very recent exposure of some days, thus giving no indication of a possible lead retention [14, 146, 147]. Since lead accumulates in the skeleton, estimates of lead in teeth can provide a good index of the body burden [138-145]. However, as teeth are not readily available, hair tissue has been found to provide an excellent alternative, as hair fixes easily elements such as lead, and thus provides an accurate and permanent record of exposure of some months duration. Furthermore, the results seem to indicate a good correlation between trace element concentrations found in hair and the intestinal organs [147]. Hair analysis techniques have been developed which use standard measures and sample preparations, so that hair mineral analysis by neutron activation or electrothermal atomic absorption is recognized to be a reliable diagnostic tool [146, 147]. Hair analysis should be conducted with proximal rather than distal hair in order to minimise contamination from air-borne lead fall-out. With hair sample collecting one must take into account that some hair-darkening cosmetics, e.g. Grecian 2000, "Morgan's Pomade, contain lead as the active ingredient, which could give misleading results.

Dietary Recommendation for Prevention and Treatment of Subclinical Lead Poisoning. The proportion of lead retained in the body varies widely between individuals, as both absorption and retention are clearly affected by diet [7]. For example, diets deficient in calcium enhance the gastrointestinal absorption of lead; or an optimum calcium intake can help to minimise lead absorption [7, 148]. Similar effects have been found with iron and phosphorus [7, 149]. Zinc is also antagonistic to the toxic effects of lead [7, 150, 151], and magnesium has been found to be a competitive lead inhibitor [152]. In addition, ascorbic acid has been used successfully in reducing the body lead burden [151, 153], and vitamin B has been found to protect against lead damage [154]. On the other hand, the main dietary factors found to promote lead toxicity are diets high in fat and low in protein [7]. Dietary recommendations for preventing or reducing chronic lead accumulation are as follows: the diet should be low in fat and high in protein, calcium, magnesium, zinc and ascorbic acid, and adequate in iron, phosphorus, B-vitamins and other essential nutrients. As most modem diets are notoriously low in both zinc and ascorbic acid, it is recommended that anyone affected by low-level lead contamination should take additional zinc and vitamin C supplements. Additional calcium, magnesium and B-vitamin complex supplementation can also be beneficial.

CONCLUDING REMARKS

Current medical practice, if it is to be effective, must consider and evaluate certain factors that are presently rather neglected, such as the impact of our rapidly changing environment as a cause for today's disease production. In recent years chronic lead exposure has indeed become one of the most pernicious factors in environmental pollution. Furthermore, there is now a wealth of evidence to indicate that this low-level lead pollution is seriously affecting the health and behaviour of both children and adults. In children this low-level lead exposure has been directly linked with educational underachievement, impairment of intellectual function, lowered IQ scores, hyperactivity, anti-social behaviour, juvenile delinquency and criminal behaviour. It is now also clearly established that a low-level lead exposure in utero can lead to spontaneous abortion, stillborn and malformed infants, low birth weight and subsequent impairment of both physical and mental development including mental retardation. In adults low-level lead exposure has been linked with infertility, ischaemic heart disease, cancers, impairment of renal function, ineffective immunity, motor neurone disease, bone wasting and fractures as well as early senility. In addition, in both children and adults, haem biosynthesis is affected and brain enzyme activity becomes inhibited at a far lower level than the level which is currently considered 'safe'. It is remarkable that humanity is still prepared to deposit such a dangerous and indestructible toxin as lead into the environment world-wide. The plain fact is that lead is pure poison, which to date has already accumulated in such vast amounts that there is no longer a corner left free from lead pollution. The following remedial actions are recommended. Although, contrary to the impression fostered by the oil industry, it is now established that all cars can run perfectly well on properly formulated lead-free petrol, the Society of Motor Manufacturers and Traders predicts that it will not be until the year 2002 that 90% of cars will be 'clean' [18]. The fitting of catalytic converters to all petrol-engine vehicles, and the use of lead-free petrol, must be made compulsory sooner than this.(2) Lead should be banned as a component of any item liable to come into direct contact with food or drink.

(3) All old lead water pipes should be removed and replaced using lead-free materials.(4) All paints should be produced completely lead-free, including those imported from abroad. Social costs of not controlling lead pollution now include special educational facilities and residential centres for backward and retarded children, the enormous costs now resulting from juvenile crime, violence and vandalism, medical treatment for infertility, and after-care for women experiencing miscarriage or giving birth to malformed children. Finally, the diminished capacity of individuals now suffering from heart disease, cancers, dementias etc. which may well be linked to lead poisoning, as well as medical treatment needed for these individuals, further adds to society's financial burden. The financial cost of controlling lead pollution may be high, but the cost in human terms, if remedial measures are not taken, is incalculable.

ACKNOWLEDGEMENTS

This study was supported by a grant from Foresight, The Association for the Promotion of Pre-conceptual Care. A special recognition is given to Professor Derek Bryce-Smith and Dr. Neil Ward and to other workers who have fought tirelessly to draw attention to the dangers of environmental lead pollution.

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