THE INDUSTRIAL INJURIES ADVISORY COUNCIL

POSITION PAPER 28

Lead and a) Fertility or b) Cancer

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LEAD AND FERTILITY OR CANCER

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Summary

1. In November 2009 concerns were expressed in sections of the media that a number of conditions, thought to be associated with occupational exposure to lead, were not included in the terms of current prescription. In particular, a special report in the magazine ‘Hazards’ highlighted concerns relating to hypertension and heart disease, kidney disease, cancer and reproductive disorders. The current prescription (PD C1) is limited to anaemia, peripheral neuropathy and toxicity of the central nervous system associated with lead or lead compounds.

2. In response, the Industrial Injuries Advisory Council (IIAC) undertook to re-examine the evidence relating to the health effects of lead exposure and to consider whether the prescription should be amended to include other health outcomes. In accordance with the requirements for prescription, the Council sought robust epidemiological evidence of a doubling of risk in relation to various putative health outcomes. This position paper summarises IIAC’s consideration of the evidence and sets out its conclusions.

3. The Council undertook a preliminary literature search to determine whether there was sufficient evidence in any of these areas to merit further consideration. The results of this search indicated that in two areas (i) reproductive effects and (ii) cancer, there existed a sufficiently large body of literature to justify more detailed review.
4. In considering reproductive effects the Council focussed its attention on the risk of adverse effects on male and female fertility, since other reproductive health outcomes, such as foetal toxicity and the risk of spontaneous abortion, would not fall within the terms of the Industrial Injuries Scheme.

5. Research into reduced fertility presents a number of methodological difficulties. These include the method of assessment of fertility, the measurement of lead exposure and the control of personal confounders. Studies identified in this review assessed fertility in terms of time to pregnancy or absence of pregnancy. In most studies lead exposure was measured in terms of current blood lead levels although this is representative only of very recent, rather than longer term exposure. While most studies included control for age, control for other potential confounders and effect modifiers was variable.

6. Collectively, the studies identified suggested that there may be a slight reduction in fertility in lead-exposed workers when average blood lead levels are greater than 40 microgram/dl. However, no evidence was found of a doubling of risk of reduced fertility (which is equivalent to a halving of fertility) in lead-exposed workers.

7. A substantial literature on the potential association between lead exposure and the risk of different cancers was identified. However, many cancer sites have been investigated and the evidence base relating to any one cancer site proved small. For most cancer sites there were inadequate data on which to assess associations with lead exposure.

8. For lung cancer the evidence base was more substantial than for other cancers. However, findings were inconsistent when gauged against the usual threshold of a more than doubling of risk.
9. Most studies of lung cancer lacked data on smoking and so could not take account of this important confounder. In addition, many of the studies identified were set in workplaces where there were co-exposures to other known carcinogens, such that the separate effects of lead exposure could not be differentiated.

10. The Council has concluded that the current evidence does not support the amendment of the prescription for lead exposure to include either reproductive effects or any specific type of cancer. However, the Council will keep the evidence in respect of both these health outcomes under review.

This report contains some technical terms, the meanings of which are explained in a concluding glossary.

Background

11. IIAC is an independent statutory body set up in 1946 to advise the Secretary of State for Work and Pensions in Great Britain and the Department for Social Development in Northern Ireland on matters relating to the Industrial Injuries Disablement Benefit Scheme (IIDB). This scheme provides a benefit that can be paid to an employed earner because of an industrial accident or prescribed disease. The major part of the Council’s time is spent considering whether the list of prescribed diseases for which benefit is paid should be enlarged or amended.

12. In November 2009 concerns were expressed in sections of the media that a number of conditions thought to be associated with occupational exposure to lead were absent from the prescription schedule. In particular, a special report¹ highlighted concerns relating to

hypertension and heart disease, kidney disease, cancer and reproductive disorders. The current prescription (PD C1)\textsuperscript{2} relating to exposure to lead or compounds of lead, is limited to anaemia, peripheral neuropathy and central nervous system toxicity. The Council therefore undertook to re-examine the evidence relating to the health effects of lead exposure and to consider whether the prescription should be amended to include other health outcomes. This position paper summarises IIAC’s consideration of this evidence and sets out its conclusions.

**The legal requirements for prescription**

13. The Social Security Contributions and Benefits Act 1992 states that the Secretary of State may prescribe a disease where he is satisfied that the disease:

i. ought to be treated, having regard to its causes and incidence and any other relevant considerations, as a risk of the occupation and not as a risk common to all persons; and

ii. is such that, in the absence of special circumstances, the attribution of particular cases to the nature of the employment can be established or presumed with reasonable certainty.

14. In other words, a disease may only be prescribed if there is a recognised risk to workers in an occupation, and the link between disease and occupation can be established or reasonably presumed in individual cases.

15. In seeking to address the question of prescription for any particular condition, the Council first looks for a workable definition of the disease. It then searches for a practical way to

\textsuperscript{2} Prescribed Disease. C =Conditions due to chemical agents. No. 1.
demonstrate in the individual case that the disease can be attributed to occupational exposure with reasonable confidence. For this purpose, reasonable confidence is interpreted as being based on the balance of probabilities according to available scientific evidence.

16. Within the legal requirements of prescription it may be possible to ascribe a disease to a particular occupational exposure in two ways – from specific clinical features of the disease or from epidemiological evidence that the risk of disease is at least doubled by the relevant occupational exposure.

Clinical features

17. For some diseases attribution to occupation may be possible from specific clinical features of the individual case. For example, the proof that an individual's dermatitis is caused by his/her occupation may lie in its improvement when s/he is on holiday and regression when s/he returns to work, and in the demonstration that s/he is allergic to a specific substance with which s/he comes into contact only at work. It can be that the disease only occurs as a result of an occupational hazard (e.g. coal workers' pneumoconiosis).

Doubling of risk

18. Other diseases are not uniquely occupational, and when caused by occupation, are indistinguishable from the same disease occurring in someone who has not been exposed to a hazard at work. In these circumstances, attribution to occupation on the balance of probabilities depends on epidemiological evidence that work in the prescribed
job, or with the prescribed occupational exposure, increases the risk of developing the disease by a factor of two or more.

19. The requirement for, at least a doubling of risk is not arbitrary. It follows from the fact that if a hazardous exposure doubles risk, for every 50 cases that would normally occur in an unexposed population, an additional 50 would be expected if the population were exposed to the hazard. Thus, out of every 100 cases that occurred in an exposed population, 50 would do so only as a consequence of their exposure while the other 50 would have been expected to develop the disease, even in the absence of the exposure. Therefore, for any individual case occurring in the exposed population, there would be a 50% chance that the disease resulted from exposure to the hazard, and a 50% chance that it would have occurred even without the exposure. Below the threshold of a doubling of risk only a minority of cases in an exposed population would be caused by the hazard and individual cases therefore could not be attributed to exposure on the balance of probabilities.

20. The epidemiological evidence required should ideally be drawn from several independent studies, and be sufficiently robust that further research at a later date would be unlikely to overturn it.

21. In the context of this report it should be noted that an increased risk of an unwanted trait (e.g. infertility) may equivalently be expressed as reduced likelihood of a positive trait (e.g. fertility). Thus a relative risk of two for the former (the normal threshold applied by the Council as seen in paragraphs 18-19) may correspond to a “fertility ratio” of 0.5, when expressed in the latter terms.
Health outcomes selected for consideration

22. The Council conducted an initial search of the literature relating to lead exposure to determine whether there might be sufficient epidemiological evidence to merit a more detailed review of any specific health outcomes not included in the current prescription. The results of this search indicated that in two areas (i) reproductive effects and (ii) cancer, there existed a sufficiently large body of literature to justify further consideration. The Council has examined this evidence and its conclusions are summarised below.

Reproductive effects

23. Certain reproductive effects of high levels of lead exposure, notably foetal toxicity and the increased risk of spontaneous abortion have been extensively studied. However, effects on the unborn child would not fall within the terms of the Industrial Injuries scheme. The Council has therefore focussed its attention on the risk of adverse effects on male and female fertility, a health outcome which would fall within the scheme. In keeping with the framework within which IIAC assesses the case for prescription, (as described above), the Council looked for consistent evidence of a doubling of risk of reduced fertility (or equivalently a halving of the risk of fertility) in those occupationally exposed to lead.

24. Epidemiological studies in the field of occupational infertility have tended to focus primarily on men. A number of studies have suggested that exposure to high levels of lead may adversely affect semen quality and sperm concentration. In addition, the majority of workers employed in industries involving exposure to lead are male. With one exception, therefore, those studies identified in the current literature search were concerned only with male workers.
25. Research into reduced fertility presents a number of methodological difficulties. These include the control of personal and social confounders, the assessment of fertility and the measurement of lead exposure. While most studies have included control for age, control for other variables is often limited. It may be imagined, for example, that accurate measurements of certain determinants of infertility, such as frequency of sexual intercourse and partners’ fertility, are often lacking. The measurement of fertility has been addressed in a variety of ways, notably in terms of the time to pregnancy or the lack of pregnancy of spouse/partner or the number of children fathered by exposed compared with non-exposed workers. The involvement of self-report in some of these measures presents problems of reliability. Lead exposure is usually measured in terms of current blood lead levels, although this is representative only of very recent, rather than longer term exposure.

26. Studies which have considered increased time to pregnancy or absence of pregnancy have generally failed to find effects of lead exposure or have found only small differences between exposed and non-exposed workers. In one study the partners of lead-exposed workers in fact showed a shorter time to pregnancy than those of non-exposed controls. In this study average blood lead levels in the highest exposure group were >40 micrograms/dl.3

27. Similarly, no effects on time to pregnancy were observed in partners of lead-exposed workers in a European study of 6553 workers carried out in four countries, including the UK. Here data on blood lead levels over several years were available, the average for most workers falling below 50 micrograms/dl.4

28. In Finland, a study based on birth registers identified a slightly increased risk of infertility (defined as non-occurrence of marital pregnancy) in workers in the highest blood lead category, defined as blood lead levels higher than 2.5 micromols/L, (52 micrograms/dl).\(^5\) Relative Risk (RR) was 1.90, 95% Confidence Interval (95% CI) 1.30-2.59. Lead exposure was not associated with delayed pregnancy in couples with at least one pregnancy prior to the study.\(^6\)

29. Finally, a case-control study in the United States found no association between male infertility and lead exposure in 650 infertile males whose partners were medically ascertained to be fertile.\(^7\)

30. Studies which have considered the number of children born to lead-exposed workers have similarly failed to identify a consistent effect of lead. A French cohort study involving 229 lead exposed battery workers (886 person-years) and 125 non-exposed workers (598 person-years) found no association between exposure and subsequent numbers of pregnancies.\(^8\)

31. A Danish study, in which blood lead levels averaged 35.9 micrograms/dl, showed no reduction in birth rate amongst battery plant workers compared with non-exposed employees, (Odds Ratio (OR) 0.99, 95% CI 0.88-1.13).\(^9\)

\(^5\) To assist comparison between studies, where lead levels have been expressed in micromols/L the equivalent in micrograms/dl has been added in following brackets.

\(^6\) Sallmén M, Lindbohm ML, Nurminen M. Paternal exposure to lead and infertility. Epidemiology. 2000 Mar;11(2):148-52


32. A study based on birth certificates in the United States, which considered the number of children born to lead exposed workers, compared to non-exposed controls, found a slightly reduced rate of fertility in those with more than 5 years exposure (RR 0.38, 95% CI 0.23-0.61).  

33. A Finnish study, based on questionnaire data, showed that in men routinely monitored for lead exposure, the so-called “fecundity density ratio” decreased in a dose-related manner with increases in current blood lead levels. However, this decrease was small, from 0.92 (95% CI 0.73-1.16) in those with blood levels of 0.5-0.9 micromols/L (10 - 19 micrograms/dl) to 0.83 (95% CI 0.50-1.32) in those with blood lead levels >1.9 micromols/L (> 39 micrograms/dl).  

34. A study of Belgian battery workers, with an average blood lead level of 46.3 micrograms/dl, and average duration of exposure of 10.7 years, also showed a decrease in fertility compared to non-exposed workers which only occurred following onset of exposure, (OR 0.65, 95% CI 0.43-0.98). This figure approached a doubling of risk (as represented by an OR of 0.5 (see paragraph 21).  

35. A single Finnish study has considered fertility in female lead-exposed workers by documenting incidence rates of clinically recognised pregnancies by blood lead level in women workers routinely monitored for lead exposure. Pregnancy incidence was not associated with blood lead levels up to 1 micromols/L (21 micrograms/dl). However in a


group of eight women with blood lead levels between 1.4 and 2.4 micromols/L, (29 and 50 micrograms/dl) pregnancy incidence was significantly reduced compared to that of non-exposed controls. Numbers in this study were small, however, and require verification in a larger cohort of workers. 

Conclusions

36. Evidence suggests that there may be a slight effect on male fertility in lead-exposed workers where average blood lead levels are greater than 40 microgram/dl. However, these effects appear to be relatively small and there is currently no evidence of a more than doubling of risk of reduced fertility in male lead-exposed workers. Information on infertility in female lead-exposed workers is limited to a single small study and the data are therefore insufficient on which to base conclusions.

37. The Council has concluded, therefore, that reductions in fertility should not be included in the prescription for lead exposure.

Cancer

38. There is a substantial literature on the potential association between lead exposure and the risk of different cancers. However, a large number of cancer sites have been investigated and, while the total body of literature is large, the evidence base relating to any given cancer site is small. In a meta analysis carried out in 1995 Fu & Boffetta reported slightly increased RRs of 1.10 (95% CI 1.05-1.17) for all cancers and 1.33 (95% CI 1.18-1.49), 1.29 (95% CI 1.10-1.50) and 1.41 (95% CI 1.61-1.71), for stomach, lung

and bladder cancer respectively. However, the authors noted that, in most studies, little account was taken of potential confounders such as smoking and dietary habits.\textsuperscript{14}

39. Several mortality studies and a smaller number of morbidity studies have been carried out during the last 30 years, together with a number of case control studies which have focussed on specific cancer sites. Those cancers which have been referred to in the literature include leukaemia and cancer of the stomach, breast, pancreas, oesophagus, brain, lung, kidney and renal system. The evidence for each of these cancers was considered separately and this is summarised below.

40. For a number of cancer sites the evidence of an association with lead exposure was limited to a solitary case-control study, unsupported by evidence from other mortality or morbidity studies. Case-control studies usually rely on patient report to determine previous exposures. Although this enables the collection of data relating to potential confounders, which may be unavailable in cohort studies, case-control studies are subject to recall bias and are usually considered to provide less compelling evidence of causality than that derived from cohort studies.

41. Case-control studies have identified an association between lead exposure and increased risk of acute myeloid leukaemia (OR 3.7),\textsuperscript{15} squamous cell carcinoma of the oesophagus (OR 5.30),\textsuperscript{16} stomach cancer (OR 3.0),\textsuperscript{17} and cancer of the pancreas (OR>3).\textsuperscript{18} In addition, a case-control study identified an OR of 1.3 for cancer of the

gastric cardia in those whose last occupation involved exposure to lead.\textsuperscript{19} The results of these isolated studies, however, were not supported by those of other cohort studies which investigated multiple cancer sites.

42. No studies were identified which focussed specifically on breast cancer in lead-exposed workers. However, a population-based study which explored the relationship between urinary lead concentrations and breast cancer found no association.\textsuperscript{20}

43. Data on renal cancer is also limited. However, in a study of 4519 lead battery plant workers and 2300 lead smelter workers, followed between 1947 and 1980, renal cancer deaths were fewer than expected, yielding Standardised Mortality Ratios, (SMRs) of 0.41 and 0.74 for the two groups respectively.\textsuperscript{21}

44. Several studies have investigated a possible association between brain cancer and lead exposure. However, brain cancer is not a single disease entity, which limits the comparability of results from different studies.

45. A mortality study in the United States found a higher risk of brain cancer in subjects with a higher intensity occupational lead exposure (medium/high, SMR 1.9, 95% CI 1.0-3.4; as opposed to low, SMR 1.2, 95% CI 0.7-2.1).\textsuperscript{22} Similarly a very large study in Italy involving 27,060 cases and 108,240 controls, which created job-exposure matrices from death certificate information, reported an OR of 2.1 (95% CI 1.1-4.0) for men with a high

\textsuperscript{22} van Wijngaarden E, Dosemeci M. Brain cancer mortality and potential occupational exposure to lead: findings from the National Longitudinal Mortality Study, 1979-1989. Int J Cancer. 2006 Sep 1;119(5):1136-44.
probability of occupational exposure to lead. In both studies, however, types of brain tumour were not differentiated, and in those studies where this was attempted numbers were small. Thus, a Finnish case-control study involving only 26 male cases, of whom 16 were specifically diagnosed with gliomas, found a twofold increase in this sub-group, where lifetime lead exposure had exceeded an average of 1.4 micromols/L (29 micrograms/dl).

A larger hospital-based study in China involving 183 cases investigated risk factors specifically for brain meningioma and reported an association with exposure to a number of metals, including lead, but here it was not possible to differentiate the separate effects of lead.

Lung cancer has been studied in a number of mortality and morbidity studies, largely carried out in lead battery or smelter works. The data are somewhat inconsistent. For example, a mortality study in an Italian lead smelting works reported that lung cancer rates were lower than expected, while an incidence study in a lead smelter in Sweden reported a Standardised Incidence Rate (SIR) of 2.8 (95% CI 2.1-3.8).

Most studies have found a moderately increased risk. For example, a study among 4518 lead battery workers and 2300 lead smelter workers reported an SMR of 1.16 (95% CI

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However, the majority of studies failed to account for smoking as a potential confounder and, importantly, where studies were carried out in these settings, interpretation of the data is complicated by co-exposure to other known carcinogens. Thus in a mortality study of tin smelter workers which identified an excess of lung cancer, there was co-exposure to arsenic and antimony.\(^{29}\) Similarly a mortality study in an Italian lead smelter identified an SMR of 1.96 (95% CI 1.02-3.68) in the highest exposure group\(^{30}\) and an incidence study in a Swedish smelter reported an SIR of 3.6 (95% CI 1.2-8.3) amongst lead workers.\(^{31}\) In both cases workers also experienced exposure to arsenic and the authors noted the difficulty of attributing risk to any specific exposure.

This difficulty also affects interpretation of the limited data relating to cancer of the kidney. Thus in a mortality study of 1,990 lead smelter workers an SMR of 1.93 (95% CI 0.88-3.67) for kidney cancer was reported for those working in the highest exposure areas, but these involved exposure to arsenic.\(^{32}\)

### Conclusions

As noted above, in considering the case for prescription, the Council normally looks for consistent evidence of a doubling of risk for a particular exposure-outcome combination, derived from several independent high quality studies. For most cancer sites, it is clear that there are inadequate data on which to assess an association with lead exposure. In the case of lung cancer the evidence base is more substantial. However, the results have

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been inconsistent in terms of indicating a doubling of risk. In addition, most studies have been unable to take account of smoking as an important confounder or to differentiate between the effects of lead exposure and exposure to other known carcinogens.

51. The Council has concluded, therefore, that the prescription for PD C1 should not be amended to include any specific type of cancer.

Prevention

52. Occupational exposure to lead is regulated by the Control of Lead at Work (CLAW) Regulations 2002 which are supported by an Approved Code of Practice and guidance. The Regulations require employers to assess the risks of employees’ exposures to lead and implement control measures to prevent or control such exposures. If exposure to lead is significant, employers are required to provide employees with protective clothing and carry out air monitoring and medical surveillance (biological monitoring) of employees.

53. Employees likely to be significantly exposed to lead at work must be made subject to a blood lead concentration ‘action level’. There are different action levels for different groups of employees, namely women of reproductive capacity, young people (16 and 17 years) and all other employees. If action levels are reached the employer must investigate why this has happened and try to reduce exposure to below that level by reviewing the control measures and checking they are working properly, making sure proper hygiene procedures are followed and consulting relevant health professionals
about any additional protective measures. These groups of employees are also subject to a blood lead concentration 'suspension level', a level at which a doctor has decided that an employee should no longer be exposed to lead.

Diversity and equality

54. IIAC is aware of issues of equality and diversity and seeks to promote them as part of its values. The Council has resolved to seek to avoid unjustified discrimination on equality grounds, including age, disability, gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion or belief, gender and sexual orientation. During the course of the review of lead and cancer no diversity and equality issues were apparent. However, during the course of the review on lead and fertility it was noted that there was a lack of data relating to infertility in female lead-exposed workers. Thus it was only possible to draw conclusions about the risk of infertility in male workers.
Glossary of terms used in this report

Types of study

Case-control study: A study which compares people who have a given disease (cases) with people who do not (controls) in terms of exposure to one or more risk factors of interest. Have cases been exposed more than non-cases? The outcome is expressed as an Odds Ratio, a form of Relative Risk.

Cohort study: A study which follows those with an exposure of interest (usually over a period of years), and compares their incidence of disease or mortality with a second group, who are unexposed or exposed at a lower level. Is the incidence rate higher in the exposed workers than the unexposed/less exposed group? Sometimes the cohort is followed forwards in time (‘prospective’ cohort study), but sometimes the experience of the cohort is reconstructed from historic records (‘retrospective’ or ‘historic’ cohort study). The ratio of risk in the exposed relative to the unexposed can be expressed in various ways, such as a Relative Risk or Standardised Incidence Ratio or Standardised Mortality Ratio.

Measures of association referred to in this paper

Relative Risk (RR): A measure of the strength of association between exposure and disease. RR is the ratio of the risk of disease in one group to that in another. Often the first group is exposed and the second unexposed or less exposed. A value greater than 1.0 indicates a positive association between exposure and disease. (This may be causal, or have other explanations, such as bias, chance or confounding.)

Odds Ratio (OR): A measure of the strength of association between exposure and disease. It is the odds of exposure in those with disease relative to the odds of exposure in those without disease, expressed as a ratio. For rare exposures, odds and risks are numerically very similar,
so the OR can be thought of as a **Relative Risk**. A *value greater than 1.0 indicates a positive association between exposure and disease*. (This may be causal, or have other explanations, such as bias, chance or **confounding**.)

**Standardised Mortality Ratio (SMR):** A measure of the strength of the association between exposure and mortality, a form of **Relative Risk (RR)** in which the outcome is death. The SMR is the ratio of the number of deaths (due to a given disease arising from exposure to a specific risk factor) that occurs within the study population to the number of deaths that would be expected if the study population had the same rate of mortality as the general population (the standard).

**Standardised Incidence Rate (SIR):** The ratio of the observed number of cases of disease to the expected number of cases.

By convention SMRs and SIRs are usually multiplied by 100. Thus an SMR of 200 corresponds to an RR of 2.0. For ease of understanding in this report, SMRs and SIRs as quoted as if RRs and not multiplied by 100. *Thus a value greater than 1.0 indicates a positive association between exposure and disease.*

**Fecundity ratio:** The term fecundity refers to a woman’s ability to become pregnant. In fertile couples seeking conception the probability that a woman will become pregnant during one menstrual cycle has been estimated to be between 20 and 25%. In studies of reproductive hazards, the fecundity ratio is the ratio of the observed incidence of pregnancies to the expected number of pregnancies within a given time frame. *A value lower than 1.0 indicates a negative association between exposure and outcome – i.e. a reduced fertility in those with exposure.*
Other epidemiological terms

Confidence Interval (CI): The Relative Risk reported in a study is only an estimate of the true value in the underlying population; a different sample may give a somewhat different estimate. The CI defines a plausible range in which the true population value lies, given the extent of statistical uncertainty in the data. The commonly chosen 95% CIs give a range in which there is a 95% chance that the true value will be found (in the absence of bias and confounding). Small studies generate much uncertainty and a wide range, whereas very large studies provide a narrower band of compatible values.

Confounding: Arises when the association between exposure and disease is explained in whole or part by a third factor (confounder), itself a cause of the disease, that occurs to a different extent in the groups being compared.

For example, smoking is a cause of lung cancer and tends to be more common in blue-collar jobs. An apparent association between work in the job and lung cancer could arise because of differences in smoking habit, rather than a noxious work agent. Studies often try to mitigate the effects of (‘control for’) confounding in various ways such as: restriction (e.g. only studying smokers); matching (analyzing groups with similar smoking habits); stratification (considering the findings separately for smokers and non-smokers); and mathematical modelling (statistical adjustment).

Meta-analysis: A method of synthesising results which uses statistical techniques to combine the results of several similar studies.

Other technical terms used in this report

Units: Micrograms/dl (micrograms per decilitre) = the number of micrograms of lead in each decilitre (100 millilitres) of blood. A microgram = 1/1,000,000 of a gram. A decilitre = 100 millilitres.
Micromols/L (micromols per litre) = the number of micromols of lead in one litre of blood. The mole is a unit based on the molecular weight of a substance and which is used in medicine to measure small amounts of the substance in the blood. A micromol is 1/1,000,000 of a mole.

1 micromol=207 micrograms. Thus 1 microgram/dl = 1*10/207.2 micromols/L

**Anaemia**: A condition where there is less than the normal number of red blood cells or less than the normal quantity of haemoglobin in the blood, decreasing the oxygen-carrying capacity of the blood.

**Acute myeloid leukaemia**: Cancer of the myeloid line of blood cells, where abnormal white cells grow rapidly, accumulate in the bone marrow and interfere with the production of normal white cells.

**Squamous cell carcinoma**: Cancer of squamous cells, which are flat, scale-like cells which form a layer/s to line cavities and surfaces of the body.

**Gastric cardia cancer**: Cancer of the uppermost part of the stomach (the cardia).

**Glioma**: A tumour arising in the neuroglia of the brain or spinal cord.

**Brain meningioma**: A tumour of the meninges part of the brain.

**Foetal toxicity**: The quality of being toxic, or poisonous, to the foetus.