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Review

Environment and Human Health: The Challenge of Uncertainty in Risk Assessment

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Abstract: High quality and accurate environmental investigations and analysis are essential to any assessment of contamination and to the decision-making process thereafter. Remediation decisions may be focused by health outcomes, whether already present or a predicted risk. The variability inherent in environmental media and analysis can be quantified statistically; uncertainty in models can be reduced by additional research; deep uncertainty exists when environmental or biomedical processes are not understood, or agreed upon, or remain uncharacterized. Deep uncertainty is common where health and environment interact. Determinants of health operate from the individual's genes to the international level; often several levels act synergistically. We show this in detail for lead (Pb). Pathways, exposure, dose and response also vary, modifying certainty. Multi-disciplinary approaches, built on high-quality environmental investigations, enable the management of complex and uncertain situations. High quality, accurate environmental investigations into pollution issues remain the cornerstone of understanding attributable health outcomes and developing appropriate responses and remediation. However, they are not sufficient on their own, needing careful integration with the wider contexts and stakeholder agendas, without which any response to the environmental assessment may very well founder. Such approaches may benefit more people than any other strategy.

Keywords: health; lead (Pb); response; management; investigation; source-pathway-receptor; environmental impact assessment; geochemistry; bioaccessibility; bioavailability

1. Introduction

The source-pathway-receptor approach to linking environmental chemicals, or other agents and factors, to identified receptors (human or animal health, or environmental states) has been very productive. Viable linkages between a potential source and appropriate receptors can be identified and quantified in such a way that remediation or other means of preventing adverse outcomes (e.g., disease or contamination) can be targeted. Suitable strategic, tactical and operational decisions and actions can be implemented in a way that ensures the breaking of any viable and identified linkages. Policy can then be adapted or developed to ensure the linkages remain broken and non-viable [1]. To fully characterize the source-pathway-receptor model needs coordinated input from a variety of environmental and health scientists and professionals.

There is an inherent variability in different environmental media—air > water > soil, depending on the sources over time and the residence time in the system [2]. The estimation of the true values of contaminant concentrations often plays a significant role in decision-making. In both contaminated land and air pollution investigations, regulatory limits are the guidance for costly decisions concerning

suitable action. It is important, therefore, that concentration estimates are determined with a specified level of confidence and methodological approach, so that they are understood to represent a proxy for the subsequent potential to affect the wider ecosystem, including direct exposure and consequential risk to human health. A sound methodology for the quantification of the uncertainties that exist in both concentration measurements and sampling strategy [3,4] has financial implications for any ensuing decisions around any response to the collection of that knowledge and possible remediation action.

However, finance is often only one contributing factor to the decision-making process. Uncertainties that contribute to decisions have been classed into three types as follows: (a) statistical variability and heterogeneity (also called aleatory or exogenous uncertainty), (b) model and parameter uncertainty (also called epistemic uncertainty) and (c) deep uncertainty (uncertainty about the fundamental processes or assumptions underlying a risk assessment) [5]. The following descriptions of these types of uncertainty are adapted from this document.

Variability and heterogeneity refer to the natural variations in the environment, exposure paths and susceptibility of subpopulations. They are inherent characteristics of any system. They cannot be controlled by decision makers, nor reduced by collecting more information. Variability can often be characterized and quantified with standard statistical techniques (e.g., variance, standard deviation and interquartile ranges reflect the variability within the data), although it may be necessary to collect additional data, for example in pollution transport [3] or the wider issues of exposure assessment [6].

Model and parameter uncertainty include uncertainty due to limited knowledge about the nature of the models used to link causes and effects of environmental risks with risk-reduction actions. It also includes uncertainty about the specifics of any model and how conclusions from other work are applicable to the current problem. In theory, model and parameter uncertainty can be reduced by additional research. For example, the development of models of indoor air exposure are refined by better chemical analysis [3,7].

Deep uncertainty is present in both environmental and health science. It can be found when underlying environmental processes or biomedical responses (e.g., to mixtures) are not understood, when there is fundamental disagreement among scientists about the nature of the environmental processes or the biomedical responses and when methods are not available to characterize the processes (such as the measurement and evaluation of chemical mixtures) or biomedical responses (e.g., to many endocrine disrupting chemicals at low concentrations). Deep uncertainty is unlikely to be reduced by additional research within the allotted time period; indeed, it is often unclear how such disagreements can be resolved. The task becomes the making of decisions despite deep uncertainty, using both available science and judgment, along with clear communication about the decision-making process. A commitment to revisit the decisions if further information becomes available is essential but not always obtainable.

Judgements in health situations with deep uncertainty include the making of diagnoses at individual and population levels, we can view a medical uncertainty "continuum" from the diagnosis through treatment and management across to practical and individual level responses [6]. An individual diagnosis may include much primary uncertainty around the biomedical response and disease mechanisms, while in a pollution incident the physical or social effect on the community may be hard to estimate or predict. This is particularly an issue when the health risk or the environmental situation is unclear or has wide confidence intervals—the environmental "mirror" of the medical situation exists in the continuum of obtaining suitable balance between knowledge of processes, parameters, modelled predictions and heterogeneity in the system [8,9]. In both situations, decisions may have to be made rapidly, based on incomplete data [10]. In the environmental world, this often results in a precautionary approach, while in health second opinions are sought and decisions made on likelihood (risk) and expected least long-term harm. Public health decisions are also often made with incomplete information particularly when responding to contamination, whether new or old [11,12].

The precision or uncertainty around the environmental sampling strategy, as well as inherent uncertainty in concentration measurements (as shown by variograms or statistical other methods),

may affect decision-making by the appropriate authority in other ways. However, the decision-making process is filled with numerous other factors. Besides the important decision whether or not to remediate, an understanding of the implications of the measurements for health is important, since many investigations do not arise from an already identified local health issue. Also, in formulating the appropriate response, consideration may need to be given to the interests and responses of a variety of concerned parties, both those who may be supportive of the investigation and any proposed remediation and those who are against some or all of such measures.

2. Causes of Ill Health

In order to understand how accurate analysis contributes to resolving pollution's effect on health, it is useful to understand some of the background to health issues. This will also show where non-environmental variation may be found in a source-pathway-receptor investigation. In general terms, children are often more at risk than adults, due to physical differences (closer to the ground, proportionally for their weight they have a larger surface area, faster breathing and greater ingestion of food and drink), critical time windows for organ development, immature and less efficient detoxifying and excreting mechanisms and different behavioural patterns (including hand-to-mouth exploration). Other vulnerable or high-risk groups include the foetus, pregnant and nursing women, the elderly and the socio-economically deprived [13].

The causes of ill-health are multifactorial and may operate at different scales, from the genome to international incidents and circumstances (see Figure 1). Very few diseases are mono-causal. Infections are often considered such but they need more than just the presence of the microbiological agent to produce active disease. This is seen best in conflict-affected populations, where the high excess mortality and morbidity from infectious diseases arises from the effects of population displacement, disturbed infrastructure and diet and the lack of basic health services. The microbiological agent (e.g., typhoid, dysentery, malaria, pneumonia) is a necessary but not sufficient cause [14]. But disease arising from a wide variety of influences is not restricted to conflict or infection.

Take, for example, lead (Pb) poisoning. The necessary cause is lead intake but a variety of factors can influence this:

Individual (genetic) inheritance: It is unlikely that a set of genes exist which give a molecular signature for Pb toxicity. Nevertheless, genetic diversity clearly modifies the body's response to developmental Pb exposure even if the evidence is not detailed [15–18]. Gender also plays a part, through epigenetics [19]. Children are more at risk from Pb exposure than adults because of their hand to mouth activity, higher respiratory rates and higher gastrointestinal absorption per unit body weight.

Personal and lifestyle choices: use of indigenous cosmetics, medicines and folk remedies containing Pb can give rise to toxicity, as can trace contamination of cosmetics [20–22]. Poor nutrition increases Pb absorption and toxicity [23].

Social support: the personal use of indigenous medicines and cosmetics is culturally determined [24,25] and has been for many centuries [26].

Living conditions: Pb water pipes and paint are still found in older houses, often in deprived communities [27,28], although it is paint, rather than water pipes, which is the more common source of exposure in children in high-income countries nowadays [29–33]. Nevertheless, residual contamination in the wider urban environment might still be an issue [34,35], particularly to the poorer member of a society, including migrant groups, who are over represented in the less developed and more deprived parts of the urban landscape [36,37].

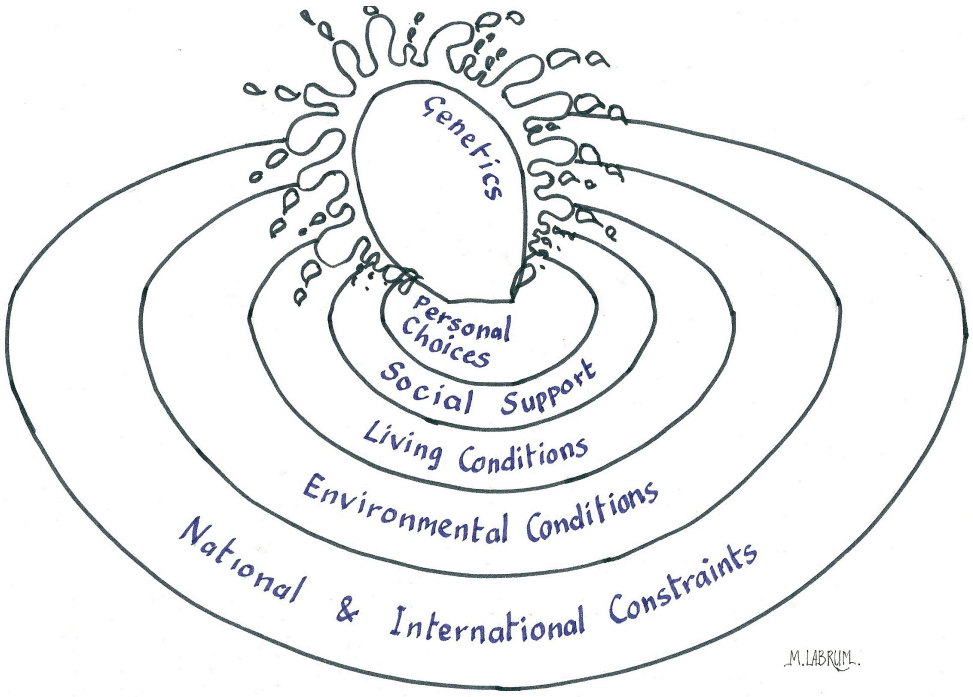

Figure 1. Causes of "ill-health". Note that some determinants of health and disease operate at more than one level. Examples in each layer include: Genetics—individual inheritance—sex, age, genetic makeup; Personal choices—diet, smoking, alcohol & illicit drugs, other lifestyle choices; Social support—family, friends, colleagues, local community; Living conditions—home, water supply, sewerage, employment, health care, peace/war; Environmental conditions—working environment, quality of food source and supply, schooling; National & international constraints—economy, religion & culture, trade, transport, natural world. (Figure drawn by Mike Labrum. The help of Professor Ewan Wilkinson, Chester University, UK is acknowledged in the development of this figure; Mrs Penny Watson, artist, drew the first version).

Environmental conditions: Pb is still used in many industries, including construction, mining and manufacturing, particularly in lower income countries [38]. Hotspots may be found around battery production and recycling plants, smelters, refineries, mines, hazardous waste sites and sites where waste is burned in the open [39–43]. Occupational exposure affects not just the worker [43] but the families as well, either by children accompanying workers or workers exposing their families at home [39,44]. Chronic, low-level exposure continues to be a risk, particularly in rapidly industrialising situations [45,46]. Children living on lead-contaminated land show evidence of exposure to Pb [35,47–49] while urban allotment contamination remains an important issue [50].

National and international: national transport policy has effects on Pb exposure. Tetraethyl lead was used globally in petrol (gasoline) from the 1920s until the 1980s to improve engine performance, before it was phased out due to increasing concern about childhood toxicity [51], although it is possible that a few countries still use leaded petrol for economic reasons [52]. The 2002 Basel convention on hazardous wastes stimulated international responses to reduce the hazards from the re-use of Pb from used batteries, including a ban on trade, not yet fully implemented [53].

High income countries export used Pb batteries to low and middle income countries for disposal and recycling, which is often undertaken by hand [54]. For example, while approximately 85% of all Pb used in the USA in 2016 went into batteries, with 69% being from recycled sources, the USA has become more reliant on imported refined lead recently owing to the closure of the last primary lead smelter in the USA in 2013 and also to an increase in exports of used lead-acid batteries, reducing the availability of scrap for secondary smelters [55]. Global lead battery production is steadily growing [45].

But international impacts from Pb on health are not limited to batteries. People movements have taken the culturally influenced, personal use of indigenous medicines and cosmetics and the associated Pb exposure to new homelands [24,56].

3. The Impact of Lead Poisoning

The acute dangers of Pb compounds were recognised in ancient times. Nicander of Colophon, a Greek poet and physician (flourished 2nd century BC), is generally credited with the first description of acute lead poisoning, in his poem about a disease caused by $PbCO_3$ (ceruse). In 70 AD, Pedanius Dioscorides (about 30–90 AD), a Greek physician employed in the Roman army, published his magisterial five volume pharmacopeia "Περί ὕλης ἰατρικῆς" ("Peri hules iatrikēs"/"De Materia Medica"/"Concerning medical matters"), in which he observed that "lead makes the mind give way". At the same time, he recommended PbO for the treatment of certain skin diseases and facial wrinkles. Pliny the Elder (Gaius Plinius Secundus, 23–79 AD), a Roman author and military commander, recognised the toxicity of Pb compounds, Pb fumes and 'sugar of Pb' (sapa) which was used to sweeten wine, in his "Historia Naturalis" ("Natural History"). Aulus Cornelius Celsus (about 25 BC–50 AD), a Roman encyclopaedist, refers to the poisonous nature of white lead in his "De Medicina" ("On medicine") [57].

The acute toxicity of water flowing through Pb pipes had also been noted [58,59]. Marcus Vitruvius Pollio (about 80–15 BC), a military engineer and architect with Julius Caesar's army, wrote in his multi-volume work "De architectura" ("About architecture") that,

> *"Water-supply by earthenware pipes has these advantages. First, if any fault occurs in the work, anybody can repair it. Again, water is much more wholesome from earthenware pipes than from lead pipes. For it seems to be made injurious by lead, because white lead is produced by it; and this is said to be harmful to the human body. Thus, if what is produced by anything is injurious, it is not doubtful but that the thing is not wholesome in itself. We can take example by the workers in lead who have complexions affected by pallor. For, when, in casting, the lead receives the current of air, the fumes from it occupy the members of the body and burning them thereupon, rob the limbs of the virtues of the blood. Therefore, it seems that water should not be brought in lead pipes if we desire to have it wholesome. Our daily table may show that the flavour from earthenware pipes is better, because everybody, even when they pile up their tables with silver vessels for all that, uses earthenware to preserve the flavour of water"*. [60]

However, the clinical picture of chronic Pb poisoning was not recognisably described in ancient times and Pb continued in pipes and the wine industry, amongst other uses. It was as true then as now, that " . . . *the path from sound science to sound environmental policy does not necessarily follow a straight line. Ignorance of the dangers posed by lead was not the primary impediment to addressing the problem*" [61].

The first clear description of chronic lead poisoning was made by Paul of Aegina, a 7th century AD Greek physician, in his "Επιτομής Ιατρικής βιβλία επτά, [Epitomes iatrikes biblia hepta]" ("Medical Compendium in Seven Books"), although he did not associate his epidemic of abdominal colic, paralysis, epilepsy and a high mortality rate with Pb [57].

During late Roman times, Pb concentrations in bone were 41–47% of present-day European levels. After 500 AD, bone levels dropped to 13% of modern levels but during the Middle Ages they increased again to approximately the same levels as those of ancient Rome. Pb levels in the inhabitants of Rome were not significantly higher than in residents of European cities manned by the Roman army, such as Augusta Vindelicorum (present-day Augsburg in Bavaria, Germany). Pb poisoning did not destroy the Roman empire, although, in contrast to today, it was a particular problem of the aristocracy [57].

The history of environmental Pb pollution has been explored and the 5000 year history of industrial production of lead [62] matches the atmospheric deposition pattern found in sediments and peats [63]. Interestingly, there was a dip in production and pollution in the Middle Ages, which matches the course of the Black Death (1346–1353), which killed up to 60% of Europeans [64,65].

Until the beginning of the 20th century, lead poisoning was viewed largely as an occupational disease of adults; however, lead paint poisoning in children was recognized in the 1890s [66]. It has been estimated that about 240 million people globally show exposure to Pb (2001 figures), with 97% of affected children being in low and middle income countries [67]. Despite a serious underestimate of the scale of the issue, Pb battery recycling range put almost 1.9 million people at risk (2016 figures).

Lead battery recycling is the number one polluting industry globally, contributing 2 M–4.8 M (27–29%) DALYs of the top 10 polluting industries' 6.9 M–17.8 M. DALYs (Disability Adjusted Life Years) are a measure of the overall burden of disease, expressed as the total number of years lost due to ill-health, disability or early death. They are seen as a better measure of the impact of disease than mortality (number dead from a specific disorder) or morbidity (number unwell from a specific disorder) (Table 1). Overall, these 10 industries put >32 M people at risk globally in low to middle income countries [68]. Other recent estimates [69] suggest 494,550 deaths and loss of 9.3 million DALYs world-wide due to lead exposure. Clearly, despite some variability in source and methodology of data analysis, the magnitude of the problem is still a major global burden.

Table 1. Worst polluting industries in 2016, ranked by Disability Adjusted Life Years (DALYs).

Rank	Industry	DALYs (Number)	DALYs (%)
1	Used Lead-Acid Battery Recycling	2,000,000–4,800,000	27–29
2	Mining and Ore Processing	450,000–2,600,000	7–15
3	Lead Smelting	1,000,000–2,500,000	14
4	Tanneries	1,200,000–2,000,000	11–17
5	Artisanal Small-Scale Gold Mining	600,000–1,600,000	9
6	Industrial Dumpsites	370,000–1,200,000	5–7
7	Industrial Estates	370,000–1,200,000	5–7
8	Chemical Manufacturing	300,000–750,000	4
9	Product Manufacturing	400,000–700,000	4–6
10	Dye Industry	220,000–430,000	2–3

Source: adapted from [59].

Lead affects virtually every system in the body (including cardiovascular, hepatic, immunological, renal, haematological) as well as having deleterious behavioural effects. More than 90% of the Pb body burden is localized in bone with an average half-life of more than 20 years. Bone releases Pb during periods of increased bone turnover, including pregnancy and lactation and thus has great potential to harm the growing child (e.g., intrauterine death, premature delivery, low birth weight), as well as leading to neuro-behavioural issues (Figure 2). There is no safe level of exposure to Pb [40].

One of the more intriguing associations with Pb is the correlation within the USA between mean blood Pb levels and the murder rate 21 years later, including a sharp fall in the murder rate following the removal of Pb from petrol (gasoline) [70] and more recent studies of the association of youth crime with atmospheric metal exposure (Mn and Pb) in a US county-wide study [71,72]. This is consistent with the notion that exposure to lead in early life is a powerful determinant of behaviour decades later in adult life [40], although there may be other explanations. Proving a causal link can be very difficult in such situations but before additional analysis can be further refined, improved understanding of exposure models will be necessary [72].

The multifactorial causes of ill-health (Figure 1) do not just operate at different scales but can be found operating concurrently, compounding each other. Batteries absorb 78% of Pb production, now largely concentrated in low income countries. The reasons for Pb poisoning there include poor nutrition, large numbers of children (in some countries, over 50% of the population is under 15 years of age), the movement of manufacturing and smelting to low cost centres leading to increased opportunities for exposure, a lack of infrastructure to collect and safely dispose of, or reuse, Pb-containing batteries and insufficient health services for screening and treatment. Sometimes the surprise is not that so many people suffer toxicity but that large numbers escape the ill effects!

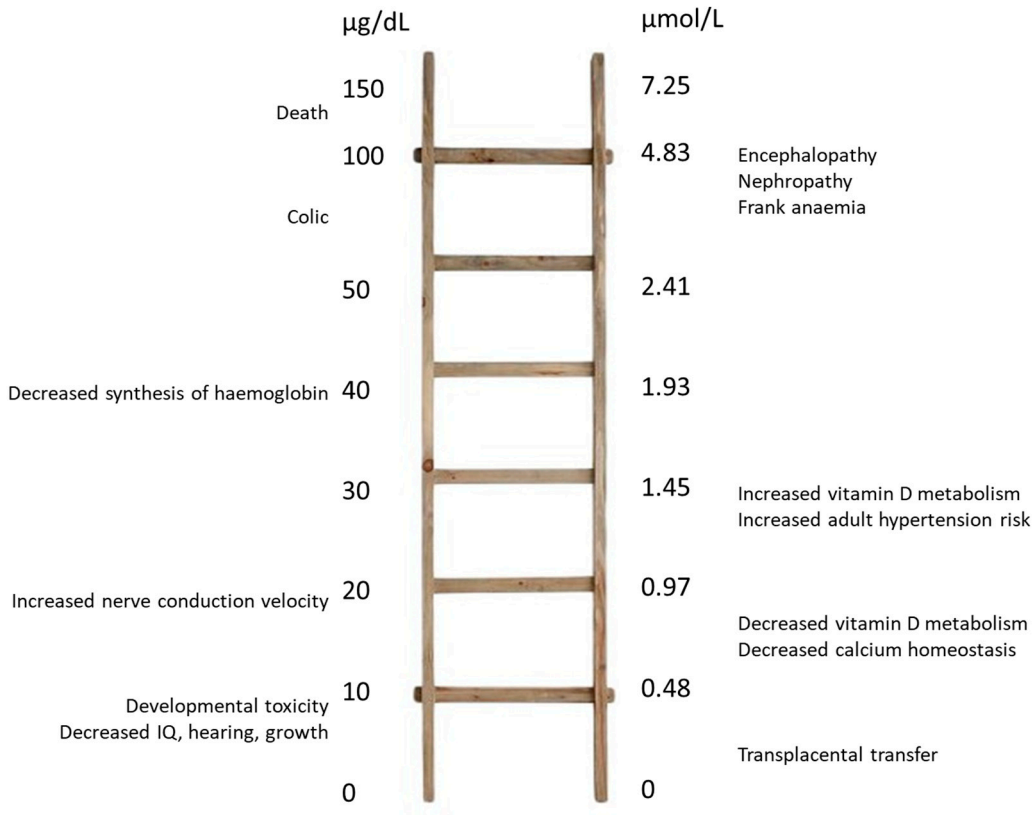

Figure 2. Health effects of Pb contamination at various blood Pb concentrations (adapted from [40]).

4. Receptors: Measurement of Disease and Risk

At a community or population level, disease is measured by rates: incidence and prevalence are the commonest. Incidence is the number of new cases within a specified time-scale (e.g., one year) divided by a standard denominator, such as 100,000 population. Prevalence is the number of existing cases at a point in time, again with a similar standard denominator. Rates allow comparison that numbers and totals do not. High incidence (many new cases) but low prevalence (few at any one time) diseases are those frequent diseases with short timespans, e.g., the common cold. Low incidence (few new cases) but high prevalence (many cases, each one usually lasting a long time) diseases include chronic disorders such as asthma. Incidence and prevalence allow comparison between different populations and times; they also form the basis for further estimates around the disease or its determinants. They may be further sub-divided by age, sex or other factors of interest.

Numbers can be useful. Like any illness, there is a decrease in numbers from the many exposed to a toxin, or microbiological agent, to the smaller number who die (Figure 3). The width of the pyramid varies from agent to agent, with narrower shapes (fewer differences between layers) arising from the more toxic agents, indicating a higher proportion of exposed individuals becoming ill or dying. The width of the pyramid will also vary according to which of the various layers are under consideration, or are known, as causes or influences.

One of the major issues in public health is that it is usually easier to identify and count those who die, than any of the layers beneath that. There may be many in the community who are symptomatic but not attending health care facilities; they are not easily identifiable.

It is even harder to identify those exposed who have some biochemical or physiological response (biomarker detectable—a biomarker is a molecule, gene, or characteristic by which a particular pathological or physiological process or disease is identifiable), since a suitable marker needs to be known and readily detectable, preferably without invasive techniques such as taking a blood, e.g., other less invasive bio-monitoring sampling methods such as hair, nail, urine, saliva for biomarker

determination [73,74]. In environmental situations, an estimate of the larger numbers potentially exposed (at risk) may be possible. However, such a risk estimate tells us little about the numbers of cases that can be expected to arise: only a few diseases, usually infections, have known estimates of some of the different layers of the pyramid [75]. Nevertheless, the relative, if not absolute, risk between different exposures and different clinical outcomes are known for an increasing number of diseases, e.g., smoking-induced heart disease or lung cancer [76,77].

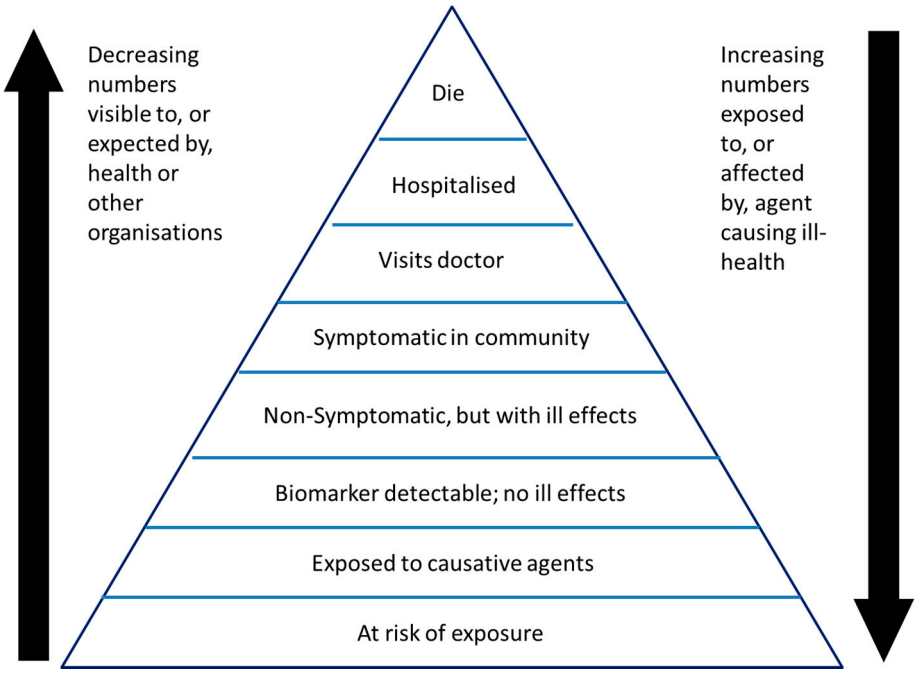

Figure 3. The disease pyramid (the help of Professor Ewan Wilkinson, Chester University, UK is acknowledged in the development of this figure).

The burden of disease concept was developed to quantify the burden of premature mortality and disability for major diseases or disease groups and uses the DALY (defined in Section 3) to combine estimates of the years of life lost prematurely with the years lived with disabilities arising from the same disorder [78]. DALYs are a way of measuring the impact a disease has and is a summary measure of population health: early death or disability lead to more DALYs than death or disability at an older age. Losing younger people is more incapacitating to a community than the early death of older people. Measuring the burden of disease allows comparisons between different conditions and outcomes, across geographies and time. It can help identify where government, community and professional action should be concentrated.

A review of the burden of disease from chemical exposures has been published [79], most likely a serious underestimate. Globally, from the few chemicals with available data ~5 M deaths occur annually, with >50% being in children <15years of age. Overall, acute poisonings account for 11% of the total DALYs, long term effects from occupational exposures 8%, long term effects from single chemicals 11% and air pollution mixtures 70%. Table 2 gives some examples of diseases and chemicals considered.

Table 2. Some diseases linked to chemicals exposure (suspected/confirmed).

Disease	Exposure	Outcome
Respiratory	Occupational chemicals; traffic exhausts	Chronic obstructive airways disease, asthma, silicosis
Peri-natal	Maternal (pesticides et al.)	Low birth weight
Congenital abnormalities	Maternal (pesticides, PCBs, PCDFs, Pb, Hg, endocrines)	Various birth defects
Cancers	Aflatoxins, smoking, PAH, As, asbestos, benzene, pesticides, dioxins	Many sites e.g., lung, skin, liver, brain, kidney, prostate, bladder, etc.
Neuro-psychiatric	Pb, methyl-Hg, PCBs, As, toluene, etc.	Cognitive delay, Parkinsonism, Minimata disease
Cardiovascular	PM2.5, Pb, As, Cd, Hg, solvents, pesticides, smoking	Ischaemic heart & cerebrovascular disease
Diabetes mellitus	As, *N*-3-pyridylmethyl-*N*′-p-nitrophenyl urea (rodenticide), 2,3,7,8-Tetrachlorodibenzo-p-dioxin	Type II diabetes

Source: adapted from [79].

The global burden of disease from Pb-induced mental retardation is 9.8 M DALYs and from Pb-induced cardiovascular diseases from raised blood pressure 250,000 premature deaths and 3.5 M DALYs. The full burden of disease due to environmental Pb exposure is probably underestimated because of a lack of data, the exclusion of geographical "hotspots" (outliers), conservative assumptions and the inability to quantify a number of health outcomes and social consequences of Pb exposure due to insufficient evidence (e.g., increased risk of criminality and drug abuse) [72,80].

Often in the interface between environment and health, what is needed is a measure of risk, the probability of something happening. Both incidence and prevalence can be used as such a measure. Other measures of risk include relative risk (risk ratio) and odds ratio. Relative risk is the ratio of the probability of an event occurring (e.g., developing a disease) in an exposed group to the probability of the event occurring in a similar but non-exposed group. Odds ratio is a measure of association between an exposure and an outcome. There are, of course, many other measures [81]. Good quality measurements of environmental concentrations of chemicals contribute to relevant risk assessments in responding to polluted situations [82].

5. Pathways: Exposure, Dose and Response

The measurement of environmental concentrations of chemicals is vital to an understanding of the relevant source-pathway-receptor model in any contamination situation. While information on the source relies on environmental scientists including environmental geochemists and information on the human receptor (Figure 4) is the domain of health professionals, both groups contribute to understanding the pathways linking sources to receptors. In health terms, all pathways, no matter how intricate or convoluted, reduce to inhalation, ingestion and touch (skin but including eye exposure).

Figure 4. Receptors: Usually, the <6 year old girl is considered the most vulnerable (see for example [83]) as she carries eggs which will become her children (and may thus give rise to exposure of grandchildren) but depending on the situation and the chemical under consideration, the vulnerable receptor may be the elderly, pregnant women or other particularly exposed person (image: MS Office).

The main pathway for most Pb compounds is ingestion, although inhalation in and near industrial sites is important. Tetra-ethyl lead, like all organic Pb compounds, is toxic by all three exposure routes (ingestion, inhalation, skin contact) [40,84,85].

Exposure can be thought of as a measurement of the level at which a person meets any substance; it is external to the body. The dose taken in by inhalation, ingestion and touch may not be the same as that retained within the body. Any individual's response to that chemical are dependent upon several factors: level of exposure, frequency of exposure, route of exposure, duration of exposure, dose (a variable fraction of exposure) absorbed by whatever route, dose retained and individual sensitivities [13]. Such factors can be influenced by the various factors in the seven levels in Figure 1.

The concepts of bioaccessibility (fraction which can be released from the carrier medium in the gastrointestinal tract and becomes available for absorption) and bioavailability (fraction of ingested chemical that reaches the systemic circulation and is used by the body) are very useful and well discussed in environmental circles [86]. It should be noted that bioavailability includes gastrointestinal digestion, absorption, metabolism, tissue distribution and bioactivity. While useful, the concepts have been hard to model or estimate accurately in a way that is meaningful for health professionals, although this is now changing [87].

Dose is often described simply, as the most important determining factor for whether a chemical will cause a harmful reaction; it is internal to the body and is a measure of the amount of an agent deposited therein. Paracelsus (1496–1531), a Swiss physician, is frequently quoted: "*Poison is in everything and no thing is without poison. The dosage makes it either a poison or a remedy*". Would that it were as simple. It has become clear recently that the relationship between increasing dose and increasing response is not necessarily linear, nor even mono-phasic. The endocrine disrupting chemicals are a case in point, where low doses may elicit a different toxic response from higher doses, with a very different dose-response curve [88].

While good exposure measurements are possible, it can be difficult to estimate dose. Good information on toxicity, sources, doses and health effects on common or important chemicals can be found in a number of places, including [89,90]. Sometimes an estimate of dose or exposure can be back calculated from health effects when such relationships are clearly quantified.

6. Sources

Lead ores comprise 0.002% of the earth's crust. The minerals include anglesite ($PbSO_4$), cerussite ($PbCO_3$), galena (PbS), mimetite ($Pb_5(AsO_4)_3Cl$) and pyromorphite ($Pb_5(PO_4)_3Cl$) [91]. However, the sources of Pb that give rise to health issues are mines, contaminated land from industrial heritage, leaded paint and pipes, incinerators, ceramics, indigenous medicines and cosmetics, tins, solder, electronics and leaded ($Pb(CH_3CH_2)_4$) petrol [40]). Environmental scientists may be asked to determine concentrations and bioavailability of Pb in many of these but the commonest situations where a health assessment is concerned involve assessment of contaminated land, acid mine drainage sites and leaded paint and incinerator residues [92,93].

7. Putting It All Together: Risk Assessment

Good quality environmental sampling and analysis are key to the health risk assessment. However, there is more to risk assessment than simply the steps often cited:

1. *Hazard identification*—recognition and characterisation of the toxin(s) present
2. *Exposure assessment*—measurement or estimation of the intensity, frequency and duration of human exposure to the agent
3. *Dose-response assessment*—characterisation of the relationships between varying doses and adverse effects in exposed populations
4. *Risk characterisation*—estimation of the incidence of health effects under the various actual conditions of human exposure
5. *Risk communication*—informing those affected or responding to the issue of the size of the risk and appropriate responses

By concentrating solely on risks to physical health, professionals from both public health and regulatory bodies fail to understand and take into account the wider determinants of public health and wellbeing [82] (Figure 1).

An understanding of the context within which the contaminated site or Pb source sits is important (Figure 5 and below). The history of the site, the locality, the presence or absence of community around and many other aspects (including previous environmental investigations and remediation efforts), can change the meaning of the risk and the appropriate response. The natural environment (air, land water) interacts with the built environment (commercial and industrial, residential, mobile); both are affected and affect the social environment (people, culture, human relationships) as well as the geography and epidemiology (both examine time, person, place: geography looking at relationships, epidemiology looking at disease patterns and causes). Without a consideration of such interactions, it is possible to put the wrong responses into place, unwittingly and with undesirable negative consequences.

Furthermore, mental health issues need to be considered [94]. Although some pollutants such as Pb and Hg can give rise directly to mental health issues, the fear of toxins can be enough to cause stress, anxiety and worry. The feared consequences of exposure to toxins give greater public reaction than any likelihood of such exposure. Such emotions measurably affect people's health and can give rise to strained relationships within families and communities and may even lead to community conflict and breakdown [82,95,96]. The concept of "total pain" (a complex of physical, emotional, social and spiritual elements), so useful in palliative care [97], should be applied and developed within environmental public health and pollution issues.

"Mental models" have been suggested as a means to integrate community and professional perspectives into an effective communication strategy [98]. But there is no reason why this approach should be limited to communication only. Developing and comparing two conceptual models, one expert and one lay, allows the identification of important discrepancies which can be measured with a structured survey instrument. This provides a rigorous baseline measure of the gaps in public

understanding, enabling full community involvement and participation in addressing the issues around the perception and management the specific environmental hazard under consideration [82] (Figure 5). It provides the underpinning rationalisation of decision-making and should provide a fair and equitable environment, moving closer to a more sustainable use of developed space.

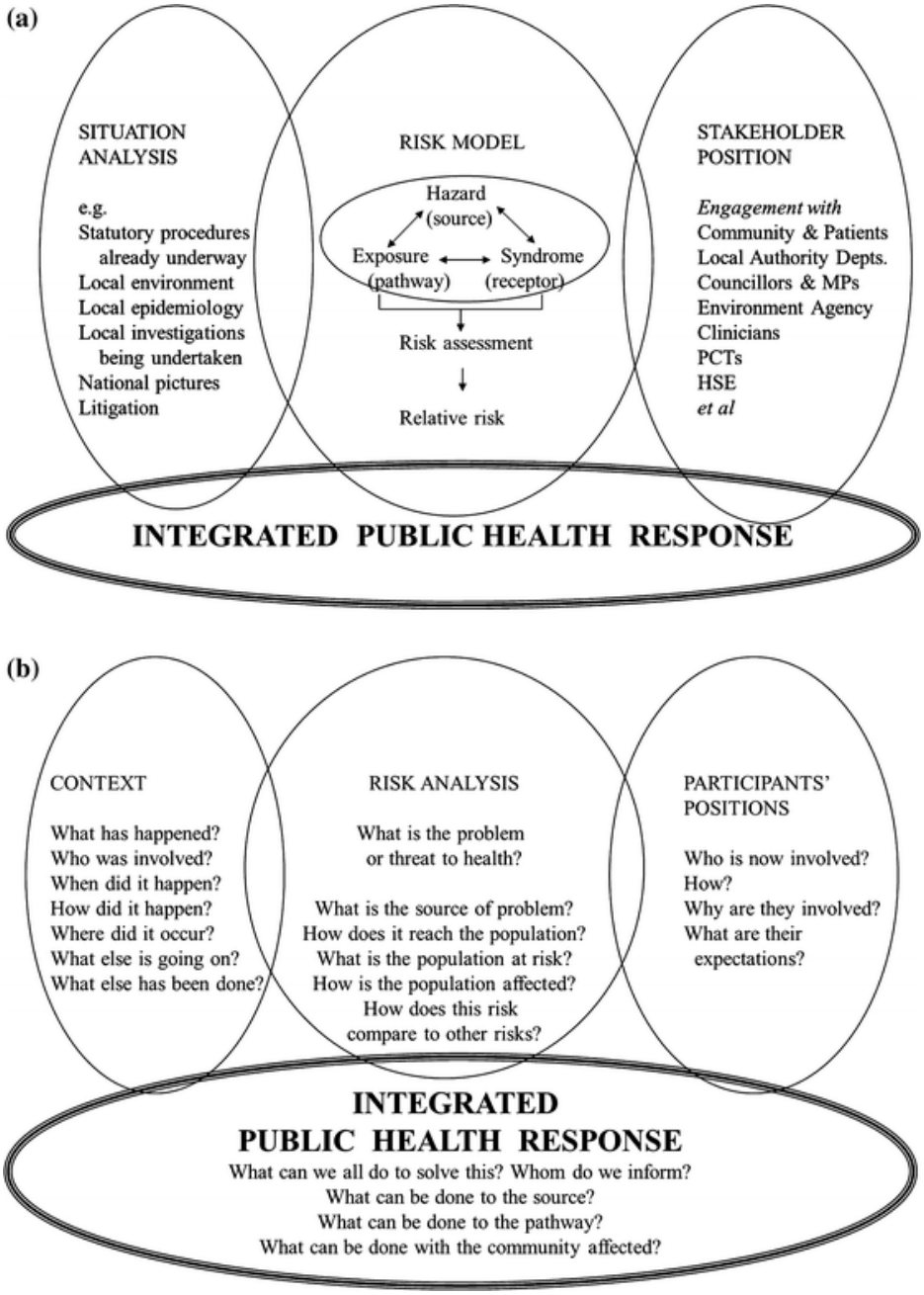

Figure 5. Public Health Risk Assessment. (**a**) Outline of the risk assessment; (**b**) application: some questions to be asked to make the risk assessment work. (Source: [12]; used with permission).

8. Putting It All Together: Preventing Adverse Health Outcomes

In evaluating the risk associated with a high-quality environmental investigation, an assessment of any relationship between exposure or environmental risk and reported disease needs to be undertaken. Association between raised environmental concentrations and ill-health of nearby residents or workers does not necessarily indicate a causal link. Such associations may be (a) real, or due to (b) chance,

(c) bias in the setting up of the study or measurement of the disease or the toxin or other bias, or (d) confounding, where the real link is due to something else and one of the measured factors is acting as a proxy for the unknown or unmeasured factor [81].

A large number of people at a small risk may give rise to more cases of disease, even if less severe, than the small number who are at a high risk. Much effort is often concentrated on dealing with the small number at high risk. This has only limited effect on the health of the wider population, leaving many at risk of disease. Deaths from common killers, such as heart attacks, occur frequently in those without risk factors for cardiovascular disease, although usually at a later age.

Accordingly, "*A preventive measure which brings much benefit to the population offers little to each participating individual*" [99], known as the prevention paradox ("Rose's paradox"). We all wear seat belts in cars to prevent the death of one or two of us. The challenge is to find preventive measures which do not adversely affect the majority while improving the health of the minority.

However, applying prevention measures across a population should also be an attempt to remove the underlying causes that make the disease common. This is in distinction to the individualistic approach of clinicians, who are concerned with response to a disease (management or cure). Such a community-wide approach has large potential, often larger than expected, for the population as a whole and can make substantial reduction in risk and disease (prevalence and incidence). Prevention applied at the high risk individual level does nothing to reduce underlying causes, seeking instead to interpose some new, supposedly protective intervention (e.g., immunization, drugs, jogging) [100].

A similar situation exists in environmental pollution. Targeting the largest polluters may remove an important source of contamination and be politically important but in many situations in the Pure Earth and Green Cross reports [68], including but not limited to Pb and Hg pollution, the largest health issues arise from the accumulation of disease across the small and artisanal industrial sites. Environmental investigations, response and prevention relating to these smaller but more frequent sites need different approaches from those targeting the largest sites.

Part of the answer is modifying the behaviour of individuals. Education is vital in improving understanding of risk assessment as applied to these sites and the products arising from them (on which we all depend, e.g., batteries, mobile phones). Shifting the socio-economic factors that drive these artisanal industries is harder but in the long term more effective from a health perspective (Figure 6) [101]. Artisanal industrial sites are likely to become increasingly problematic as populations increase in urban environments and re-use these contaminated environments. Accordingly, we have added an extra layer (environmental factors) to Figure 6 over the five posited by Frieden [101] in his extension of the original description.

Interventions targeted at environmental pollution can have a wider impact on a community's health than any other action. Nevertheless, long-term, community-wide improvements in respiratory health [102] arising from the Clean Air Acts (UK 1956 onward; USA 1963 onward), which enhanced not only the health of the vulnerable, socio-economically deprived but also the richer members of the relevant societies, are poorly documented. Further examination of mortality data for the 14 London winters, 1958/59–1971/72 shows a decreasing mortality trend (R^2 = 0.54 for 3-year rolling average number of deaths) consistent with the then decreasing atmospheric particulate matter [103]. Current concerns about air pollution, down even to local authority level, indicates the wide potential for improving health from improving the environment [104].

The response to contamination will be affected by interests and agendas of all concerned parties, whether officially part of the investigation or not. Pressure groups abound and voices need to be heard and opinion considered if sustainable decisions can be made but constraints of budgets and resources influence official agencies and political slants may override all inclusion principles [105], with the public health professional often negotiator for all parties.

The specifics of the interlinking of the knowledge from the scientific investigation with all the different concerns and interactions can be achieved through a small multi-agency team which can identify and evaluate the different aspects of the technical risk assessment, the context and the

stakeholder interests (Figure 5). Such a multi-agency approach needs quality environmental analyses as well as the soft intelligence around context and stakeholder agendas: (See [12] for worked examples and [1], pages 14–21, 163–173, 204–215 for practical support).

The sciences that may need integrating in such a public health risk assessment and response can be numerous (Table 3 lists those which we think are important, based on our experience). Skill is needed to enable quality cooperation of all the related professionals. One of the core competencies of Public Health professionals focuses on leading teams and individuals, building alliances, developing capacity and capability, working in partnership with other practitioners and agencies and using the media effectively to improve health and well-being [106]. Public Health professionals can thus make an important contribution, both from their understanding of health and disease, as well as through facilitation of the integration of hard and soft evidence from different stakeholders. The skills needed in our professional circles include the necessary high quality subject specialism as well as the ability to integrate across disciplines [107]. This is an effective and powerful way to address complex human-environment relationships but is fraught with many challenges, none the least in learning the language of contributing disciplines. There must always be a measured approach to guard against too superficial consideration of individual contributions by the discrete groups within the decision-making arena.

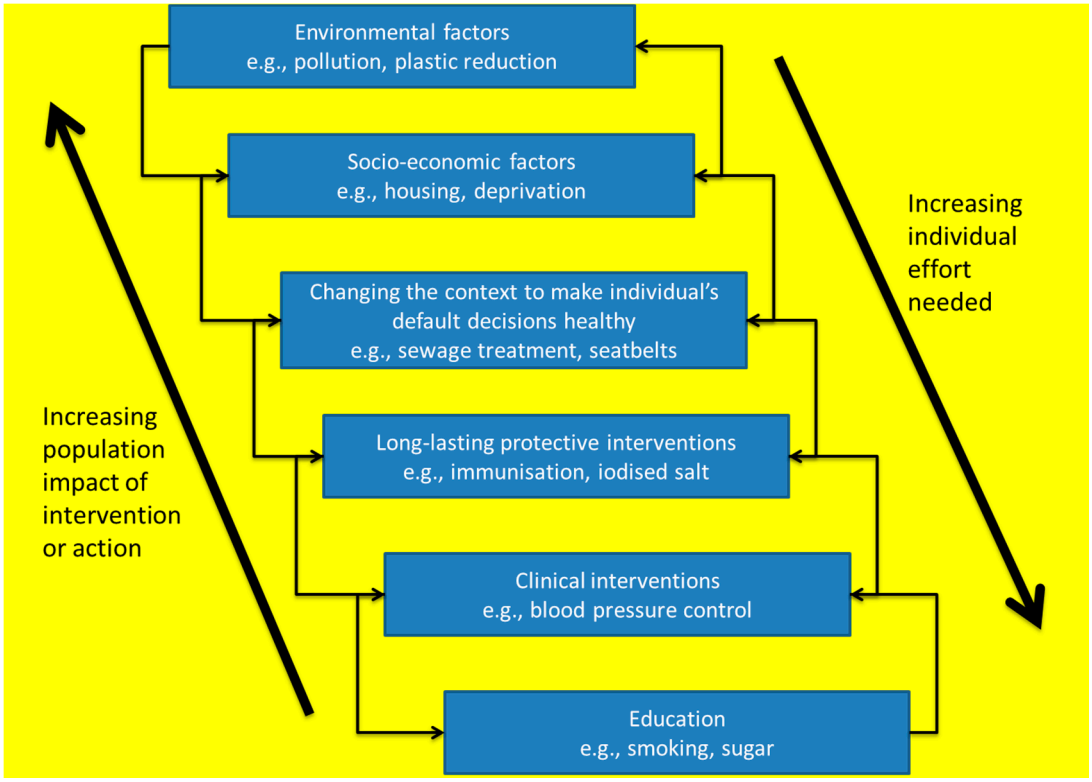

Figure 6. The health impact pyramid, showing the impact and effort of different types of public health interventions (redrawn from [101]).

Table 3. Some sciences that contribute to public health risk assessment and management of acute and chronic pollution situations.

Medicine
Environmental geochemistry
Geography
Toxicology
Genomics
Politics
Social Science
Epidemiology
Management
Statistics
Behavioural science

9. Conclusions

High quality, accurate environmental investigations into pollution issues remain the cornerstone of understanding attributable health outcomes and developing appropriate responses and remediation. However, they are not sufficient on their own, needing careful integration with the wider contexts and stakeholder agendas. Without these essentials, any response to the environmental assessment may very well founder.

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