A Global Systematic Review of Lead (Pb) Exposure and its Health Effects in Wild Mammals

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ABSTRACT: Lead (Pb) is a toxic non-essential metal, known mainly for causing poisoning of humans and wild birds. However, little is known about Pb exposure and its associated health effects in wild mammals. We conducted a global systematic literature review to identify peer-reviewed studies published on Pb exposure in wild mammalian species and the health effects they identified. In total, 183 studies, conducted in 35 countries and published over 62 yr (1961-2022), were included in the review. Only 6% (11/183) of the studies were conducted in developing countries. Although 153 mammalian species were studied, most studies focused on species that are easy to access (i.e., hunted species and small mammals that are easy to trap). Therefore, carnivores and scavengers were less frequently studied than herbivores and omnivores. Despite all studies reporting Pb concentrations, only 45 (25%) studies investigated health effects and, of these 45 studies, only 28 (62%) found any health effect in 57 species. All health effects were negative, and ranged from subclinical effects to fatality. Methodologies of Pb sampling and quantification, and reporting of results, varied widely across the studies, making both Pb concentrations and health effects difficult to compare and evaluate. Thus, there is a need for more research on Pb exposure and its health effects on wild mammals, especially as carnivores and scavengers could be used as sentinels for ecosystem health.

Key words: Bioaccumulation, Mammalia, One Health, sentinel species, toxicology, wildlife population health

INTRODUCTION

Lead (Pb) is a toxic, non-essential metal that has no known biological function for living organisms, contaminates the environment, and causes negative health effects in humans and other animals (Ma 2011; European Chemicals Agency 2018; Lanphear et al. 2018; Pain et al. 2019). It occurs naturally in the Earth's crust, and has historically been used in many products, including water pipes, paints, gasoline, ammunition, aviation fuel, motor vehicle batteries, glassware and cosmetics (Bergdahl and Skerfving 2022). These anthropogenic activities have increased the amount of environmental Pb to around 1,000 times the natural levels (Renberg et al. 2001), thereby amplifying the potential environmental exposure of wildlife to Pb. Despite legislation banning or reducing the use of Pb, it is still present in many products. For example, very few countries, states or regions have banned all Pb-based ammunition (Sonne et al. 2022) and, according to the World Health Organization (WHO) as of June 2022, only 45% of countries had made legally-binding controls on the production, import, sale, and use, of Pb-based paints (WHO 2022a).

Children are generally more at risk of health effects from Pb exposure than adults, as children absorb more ingested Pb from their gastrointestinal system (WHO 2022b). Multiple organ systems, including the nervous, renal, cardiovascular, hematological, immune and reproductive systems, are negatively affected by Pb. The health effects of Pb exposure range from chronic and subclinical, to acute and fatal (Agency for Toxic Substances and Disease Registry 2020; Bergdahl and Skerfving 2022). Furthermore, there is no known safe level of Pb exposure in humans (WHO 2022b). Despite this, concentrations of concern vary between health authorities. For example, the Centers for Disease Control and Prevention (CDC) in the USA currently have a "blood lead reference value (BLRV)" of 35 µg/L, which is used to identify children with high blood Pb concentrations (the 2.5% with the highest concentration) that require additional actions to be taken by health care professionals (CDC 2022). The European Food Safety Authority (EFSA) uses a different system and has set lower confidence limits of 12, 15, and 36 μg/L as benchmark doses for developmental neurotoxicity, effects on the prevalence of chronic kidney disease, and effects on systolic blood pressure, respectively (EFSA Panel on Contaminants in the Food Chain (CONTAM) 2013). Furthermore, concentrations of concern set by different authorities may vary over time: Between 2012 and 2021, CDC's BLRV was 50 μg/L; prior to 2012, it was 100 μg/L and called the "level of concern in children" (CDC 2022). With this continuing lowering of the CDC's BLRV, it is clear that both health authorities agree that even very small concentrations of Pb can negatively affect human health, in alignment with the WHO's understanding of Pb exposure (WHO 2022b).

Research on Pb exposure and health effects in wildlife has often been undertaken on avian species, where the first poisonings were recognized nearly 150 yr ago (Calvert 1876). In birds, Pb exposure often leads to multisystemic clinical disease or even death, especially in waterfowl, scavenging birds and predatory birds (e.g., Pain et al. 2019). Consequently, Pb exposure has caused population declines, for example in the scavenging California condor (*Gymnogyps californianus*), a scavenging species (Green et al. 2008). Although toxicity thresholds in different avian species have previously been proposed (Franson and Pain 2011), scientists have recently suggested stopping this practice as it gives the impression that some levels of Pb are acceptable (Pain et al. 2019).

Previous reviews on Pb in mammals have focused primarily on animals in laboratory settings or on domestic species. For example, Ma (2011) showed that humans and laboratory mammals have similar susceptibility to Pb exposure (i.e, the same Pb dose-health effects relationship). In domestic mammals, young cattle appear most prone to Pb poisoning, probably due to their tendency to lick different items (Constable et al. 2017). However, young cattle may simply absorb Pb more efficiently than adults, as seen in humans (WHO 2022b).

There is a lack of a global systematic literature review focusing on Pb exposure and health effects in wild mammalian species. Synthesizing this scientific evidence is important to understand the breadth of wild mammalian species affected by Pb across the world, as there is no reason to expect wild mammals to be less at risk from Pb exposure than any other vertebrates, including humans.

Our article was designed to provide a global systematic review of the literature on environmental Pb exposure and health effects in wild mammals, including assessment of gaps and biases in the research, and suggestions on how to advance knowledge of the effects of Pb, particularly in identifying the types of species that may best indicate environmental Pb exposure. The outcomes of this review are important because they can be used to inform future studies, influence policymakers, and contribute towards relevant environmental legislation.

MATERIALS AND METHODS

Systematically identifying peer-review studies to include

This systematic review followed the workflow proposed by the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) 2020 statement (Page et al. 2021). A literature search for peer-reviewed scientific articles on Pb exposure in wild mammals was conducted using the database Scopus on 21 June 2022. Scopus was chosen over other well-known databases and online search engine, such as Web of Science, PubMed, or Google Scholar due to the ability of Scopus to allow the chemical lead (Pb) as a search term, an option not provided by other databases or online search engines. In addition, Scopus permitted the exclusion of articles containing the word “lead” when used as a verb in the absence of any occurrence of lead as a chemical in the source. Furthermore, Scopus only indexed peer-reviewed articles and did not have restrictions on the length of search queries.

In Scopus, different query combinations of the following searches were used: CASREGNUMBER (7439-92-1)/CHEMNAME (lead); wild/wildlife/free-living/"free living"/free-ranging/"free ranging"/semi-wild/"semi wild"/free-roaming/"free roaming"/street/feral; captive/zoo/domestic/domesticated/semi-captive/"semi captive"/semi-domestic/"semi domestic"/semi-domesticated/"semi domesticated"; exposure/expose/exposed/exposing/poisoning/poison/poisoned; keywords for mammals, and scientific nomenclature of all mammalian orders, families and genera taken from the International Union for the Conservation of Nature (IUCN) Red List of Threatened Species (IUCN 2021); details are given in the Supplementary Materials.

The first author conducted the assessment of all records and screening of studies. After identifying records via Scopus, records were checked for duplicates. Unique records were then screened by reading the title and abstract. The selected studies were thoroughly screened by reading the entire article. Articles on Pb exposure in wild mammals that were cited in the reference sections of the Scopus articles passing the full screening were also screened to identify additional publications not found by the original literature searches (i.e., snowball search). Inclusion criteria included the requirement that studies must be peer-reviewed original research studies reporting Pb concentrations in tissues or body fluids in a non-domestic mammal (called “wild mammals” in this review) species. Studies written in any language were included and language was not used as an exclusion criterion. Studies reporting Pb concentrations in captive wild mammals outside laboratory settings were included to illustrate the variety of wild mammalian species documented to be susceptible to Pb exposure from their environment. Exclusion criteria included articles not reporting Pb concentrations in wild mammalian tissues or blood, studies using purely experimental settings, and studies reporting Pb concentrations in free-ranging domestic mammalian species. Data from studies were excluded if the study reported Pb concentration in tissues or body fluids knowingly contaminated with Pb-based ammunition (i.e., from killing the animal). Some studies reported non-standard units (i.e., liquid concentrations for tissues or units unknown to the authors of this study). In these cases, or where there was a mismatch between data reported in text and tables, the corresponding author was contacted via the email provided in the publication and given a maximum of 30 d to respond. Without a response, either the data in question or the entire study was excluded.

Data extracted from the studies

For every study included, the following information was extracted where available: Taxonomy (order, family, common species name, scientific species name); continent and country where the study was conducted; description of known pollution sources nearby the study site; type of living condition (free-ranging, captive or semi-captive); year of sample collection; season; age; sex; tissue; sample size, Pb analysis method; reporting in wet weight or dry weight concentrations (where both were reported, dry weight concentration was preferred); and Pb concentration arithmetic mean (geometric means and arithmetic weighted means were excluded), standard deviation, standard error, median, minimum value and maximum value. The Pb concentrations were converted to μg/kg or μg/L where applicable, for comparison. Whether the study had investigated and identified any health effects of Pb was also recorded. To investigate in which part of the mammalian food web Pb exposure is most frequently reported, the feeding type of the mammalian species (i.e., herbivore, omnivore or carnivore), and whether or not the species scavenges on animal material, was determined by following species descriptions available in a recently published mammalian textbook (Wilson and Mittermeier 2009-2019). Articles from Russia were allocated to the European or Asia continent based on the geographical location of the sample collection. To investigate potential economic resource biases in the publications, the Organisation for Economic Co-operation and Development's designation of developed and developing countries was used (Organisation for Economic Co-operation and Development 2006).

Different parts of a tissue or body fluid (e.g., whole kidney versus kidney cortex or whole blood versus plasma) were considered separate tissues for the purpose of the review. Additionally, cortical bone and antler were differentiated, as cortical bone is permanent bone, whereas antler is deciduous bone (representing only short-term or annual exposure).

RESULTS

Characteristics of the studies

A total of 254 records were retrieved from Scopus (Fig. 1), with no duplicates identified. After the initial screening of the title and abstract, 125 studies remained for full screening, resulting in 69 studies from the Scopus search queries meeting the inclusion criteria. Additionally, 114 studies were identified for inclusion through a snowball search, giving a total of 183 studies for systematic review (see Supplementary Materials).

The studies were published over 62 yr (1961 to June 2022), with most of the studies (158/183, 86%) published in the second half of this period (1992 to 2022) (Fig. 2). The majority of studies (162/183, 89%) were conducted in Europe (108 studies, 59%) and North America (54 studies, 30%); some studies were conducted in multiple countries (but always within the same continent). The US was the country where most studies were conducted (38 studies), followed by

Canada (17 studies), Poland (16 studies), Germany (12 studies) and the UK (11 studies). Only 6% (11/183) of the studies were conducted in developing countries (Fig. 3).

Lead (Pb) exposure

Lead was present in all mammalian species studied, with concentrations reported in a total of 153 wild mammalian species belonging to 45 families and 11 orders. The most studied order, family and species, were *Cetartiodactyla*, *Cervidae* and red deer (*Cervus elaphus*), with 67, 46 and 20 studies, respectively (Table 1). In terms of feeding type, herbivores, omnivores and carnivores were researched in 92, 79 and 49 studies, respectively; 49 studies researched scavenging species.

A total of 33 different tissues and body fluids were tested. The five most studied tissues were the liver (123 studies), kidney (92 studies), skeletal muscle (54 studies), bone (32 studies) and blood (25 studies). At 1,506,000 μg/kg dry weight, the highest Pb concentration reported across all 11 mammalian orders studied was recorded in the kidney of a Northern short-tailed shrew (*Blarina brevicauda*; Table 2).

Health effects of lead (Pb)

A total of 45/183 (25%) studies investigated the health effects of Pb. Of these, 28 (62%) studies identified a negative health effect, in 57 species. No studies identified a positive health effect. Negative health effects were reported in 32 herbivores, 21 omnivores and four carnivores and ranged in severity from ‘interference with developing permanent teeth’ to ‘fatality’ (Table 3).

Variation in methodology

The 183 studies used a large variety of sampling approaches and Pb analysis techniques, and reported the results in different ways, making it hard to compare findings. For example, some studies only reported mean values, while others reported mean, standard deviation or standard error or both, median and range of Pb concentration. Full details on sex and age of the animals tested, and on whether the sampling was undertaken in an area with known Pb pollution, were not provided in 158 (86%), 134 (73%), and 101 (55%) studies, respectively.

DISCUSSION

Coverage of lead (Pb) exposure in wild mammals in the literature

The number of publications of Pb studies on wild mammalian species has increased over the last three decades. Nevertheless, the frequency of Pb publications on wild avian species still appears to be much higher, indicated by the large number of avian reviews published in recent years (e.g., Pain et al., 2019; Monclús et al., 2020; Ives et al., 2022).

Pb concentrations were reported in 153 wild mammalian species, highlighting that this Class of animals is exposed to Pb on a large scale. Despite this clear evidence of Pb exposure across many taxa, based on IUCN taxonomic classification, only 41% (11/27) of orders, 28% (45/162) of families and 3% (153/5,968) of species were studied, which evidences a large group of mammals with no information on Pb exposure (IUCN 2021). Understandably, there has been a tendency to study species that are easiest to acquire (i.e., hunted species and small species that are easy to trap without chemical immobilization). Consequently, the studies identified in this review are skewed towards herbivores and omnivores. It is not possible to determine whether tissues were selected due to easy access, or because the researcher hypothesized that the selected tissue would provide the most information in their study species. However, liver, kidney, skeletal muscle, bone and blood are commonly collected and stored for further investigations during wildlife necropsies (McAloose et al. 2018).

Health effects of lead (Pb) in wild mammals

Only 28 studies, 62% of those in which health effects were investigated, identified negative health effects of Pb in wild mammals. As expected, no positive effects were found. From the breadth of health effects identified and organ systems affected, it is clear that Pb affects many parts of the body in wild mammals, just like in other species (Pain et al. 2019; Bergdahl and Skerfving 2022). Many of the identified health effects would most likely be subclinical, so it is not possible to determine how exactly these impact wild mammalian populations.

It is expected that, due to their feeding behaviors, some mammal species are more likely than some bird species to be exposed to smaller amounts of Pb, relative to body mass, but over extended periods of time. For example, waterfowl are known to pick up large numbers of Pb-based shotgun pellets or fishing weights from the bottom of wetland areas when foraging (Pain et al. 2019), yet most wild mammals would not be exposed to such large amounts of Pb at once, as they forage using different methods (e.g., *Carnivora* species). This difference in feeding behavior would reduce the risk of acute poisonings, seen in many waterfowl, scavenging and predatory bird species, but may cause more chronic and often subclinical health effects (e.g., on the nervous and immune systems). Chronic effects tend to be much less apparent than acute effects in free-ranging wildlife, so may be overlooked unless investigated explicitly. Ecke et al. (2017) concluded that sublethal Pb exposure in golden eagles (*Aquila chrysaetos*) might impair flight performance and thus increase the risk of mortality from other causes. Yet, other eagle studies could not find evidence that subclinical Pb concentrations are linked to “increased risk of trauma” (Isomursu et al. 2018) or “other causes of mortality” (Franson and Russell 2014). These examples demonstrate the difficulty in investigating subclinical and chronic health effects in wildlife, especially when studies do not classify effects similarly. Furthermore, ethical permits to conduct Pb toxicological effect studies on wild mammals and other wildlife are, rightly, unlikely to be granted. Therefore, subclinical effects are difficult to confirm in wildlife.

Although the impacts of Pb exposure on human, laboratory mammalian, and wild avian health are well-documented, there is still much to learn about the impacts on wild mammal health. In contrast to important infectious diseases in animals, the World Organisation for Animal Health does not have any reference laboratories for any non-infectious diseases such as Pb poisoning, which could guide or help standardize how the diagnostic steps should be conducted (World Organisation for Animal Health 2022). Potential strategies to research the health effects of Pb on wild mammals include behavioral studies, reproductive success analyses, and immune system function assessments; these are all challenging to conduct in free-ranging animals. Research which would be easier to achieve in free-ranging settings includes correlations between blood Pb concentrations and hematological and biochemical parameters; investigations of blood and tissue Pb concentrations to understand the distribution of Pb in the body; and investigations of tissue pathologies in Pb-exposed populations. Ideally, studies should use the most sensitive techniques available for measuring Pb, such as inductively-coupled plasma mass spectrometry (Apostoli 2002) and report the results in dry weight for easier comparisons. Regardless of the approach taken by future studies to investigate Pb exposure and health effects in wild mammals, studies should report details of the study area, sex and age of animals, and analytical methods, as well as providing an appropriate range of descriptive statistics (e.g., sample sizes, standard deviation or standard error), which would facilitate future evidence-based policies.

Methodologies, kinetics and thresholds

Our systematic review found a lack of consistency in estimating Pb concentrations, health effects and how this is reported. The different Pb analytical methods used in the literature reviewed (e.g., atomic absorption spectroscopy and inductively coupled plasma mass spectrometry) vary in sensitivity and differ in susceptibility to matrix effects (Apostoli 2002). Therefore, some studies might have failed to detect Pb if present in low concentrations. In addition, some studies reported tissue concentrations by dry weight and others by wet weight, impeding direct comparison of such concentrations. Furthermore, Pb uptake and storage distribution potentially may differ between species: As there are no studies available on Pb kinetics in wild mammals, this remains unknown. Variations in methodologies and target species make it difficult to compare Pb concentrations between studies and between species. Consequently, it is not possible to establish toxicity thresholds for wild mammals based on the current body of literature. However, although thresholds may be a valuable tool for some professions (e.g., veterinarians in clinical practice), a pragmatic reason for not attempting to establish threshold values for different wild mammalian tissues or species is the risk of creating the false impression of acceptable or safe levels of Pb exposure in wild mammals. Therefore, we recommend ceasing the use of threshold values for Pb concentrations in wildlife research, as already suggested by Pain et al. (2019).

Designing future studies on lead (Pb) exposure and health effects

From a One Health perspective, human, animal and ecosystem health are interlinked. Whilst it would be beneficial to study Pb concentrations in species at differing trophic levels in the wild, the cost of periodic screening programs means that these are likely to be restricted to only a few selected species. Since Pb bioaccumulates in both plants and animals (Clemens 2006; Radomyski et al. 2018), testing for Pb in carnivorous and scavenging mammalian species might not only aid monitoring of environmental Pb exposure, but also indicate the potential exposure of humans to Pb, since species at these higher trophic levels often have long lifespans like humans (O'Brien et al. 1993). Using higher trophic-level species as sentinels is already being used in avian Pb research (e.g., Monclús et al. 2020), and in mammalian research on infectious diseases and antimicrobial resistance (e.g., Millán et al. 2014; Sacristán et al. 2020). Another benefit of studying top predatory and/or scavenging mammals, which are often iconic and charismatic (Albert et al. 2018), is that these mammals might attract more attention from stakeholders and policymakers involved in the regulation of Pb, a phenomenon already seen in conservation, with charismatic species receiving most attention (Sitas et al. 2009).

To assess or monitor short-term and recent Pb exposure using reduced sampling effort and non-invasive sampling, antlers or hairs might be suitable tissues to consider in the future. Antlers represent around 6 mo's worth of Pb exposure, spring to autumn, and have previously been used to assess Pb contamination (Ludolphy et al. 2022). Antlers do, however, introduce potential biases into a Pb monitoring program. For most cervid species, antlers are only available from adult and subadult males, thus detecting differences between age classes and sexes would not be possible using this tissue. Hair is often easily available even from museum specimens (i.e., on pelts), and it can be collected from free-ranging mammals non-invasively using hair traps. The period of Pb exposure can be estimated using laser ablation techniques provided that potential Pb surface contamination is removed, the particular species' hair growth cycle is known, and the sampling is carried out in a consistent manner (Sela et al. 2007).

To gain information on where Pb is storedin a particular wild mammalian species, researchers would have to analyze multiple tissues and blood all obtained from the same individual at the same time (Krone 2018; Bergdahl and Skerfving 2022). However, obtaining this quantity of samples would likely only be possible in freshly dead or mildly autolyzed individuals (McAloose et al. 2018). Additionally, extra expenses from analyzing multiple samples from each individual could be cost-prohibited. Therefore, more controlled studies on the storage and clinical pathology of Pb in captive individuals could help to understand the health effects of Pb in wild mammals.

With studies written in any language being included, this review highlights that few studies on Pb exposure in wild mammals have been conducted in developing countries. It is important to note that detection of studies in general always depends on how journals have indexed their articles in various databases, therefore it cannot be ruled out that studies written in other languages than English will have been missed. Moreover, it is important to consider that fewer studies published in developing countries does not mean the problem is less prevalent in these countries. Indeed, the lack of studies could be explained by lower access to research funding (Kpokiri et al. 2022). On the contrary, environmental exposure to Pb might be greater in developing countries due to fewer legislative controls on Pb use in products, as seen with Pb-based paints (WHO 2022a). Indeed, children in developing countries are more exposed to Pb than children in developed countries (Hwang et al. 2019; Bergdahl and Skerfving 2022). Therefore, more research on Pb exposure in wild mammals must be conducted and published in these countries to understand the levels of environmental exposure to Pb, the risk to human and animal health, and to study whether legislation on Pb in products affects the Pb present in the environment.

As all organisms are exposed to Pb, studies helping to determine the impacts of Pb on different species will add to current knowledge of this toxic metal. Collectively, this increase in knowledge will create stronger evidence to influence policymakers involved in the regulation of

Pb in products which continue to act as sources of environmental contamination and be a major One Health issue. Overall, Pb exposure in wild mammalian species must be recognized as an issue, as this systematic review demonstrates. Control and regulation of Pb need to take a One Health approach, not focus on single taxa groups when developing policies.

ACKNOWLEDGMENTS

We thank Victoria Boskett (Research Librarian at Nottingham Trent University) for her help with journal indexing and database search engines.

SUPPLEMENTARY MATERIAL

Supplementary material for this article is online at http://dx.doi.org/10.7589/JWD-D-23-00055.

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Table 1. Top 5 most studied mammalian orders, families and species by the number of studies published on lead (Pb) exposure in wild mammals between 1961 and June 2022.

Order	**No. of studies**
Cetartiodactyla	67
Carnivora	55
Rodentia	42
Lagomorpha	15
Eulipotyphla	14
Family	**No. of studies**
Cervidae	46
Muridae	23
Ursidae	19
Suidae	17
Cricetidae	16
Species	**No. of studies**
Red deer (*Cervus elaphus*)	20
European roe deer (*Capreolus capreolus*)	19
Wild boar (*Sus scrofa*)	17
Long-tailed field mouse (*Apodemus sylvaticus*)	12
Brown bear (*Ursus arctos*)	11

Table 2. Highest individual (where $n=1$) or mean lead (Pb) concentration (μg/kg or μg/L) reported in each wild mammalian order studied in studies published between 1961 and June 2022. Solid tissue concentrations are reported in either wet weight (w.w.) or dry weight (d.w.).

Order	**Concentration**	**Species**	**Sample size**	**Tissue**	**Location**[a]	**Country**[b]	**Reference**
Carnivora	861,900 μg/kg w.w.	Ringed seal (*Pusa hispida*)	1	Brain	F-R	Canada	(Chan et al. 1995)
Cetartiodactyla	97,300 μg/kg w.w.	Beluga whale (*Delphinapterus leucas*)	1	Blubber	F-R	Canada	(Chan et al. 1995)
Chiroptera	500,000 μg/kg w.w.	Grey-headed flying fox (*Pteropus poliocephalus*)	2	Liver	Captive	USA	(Zook et al. 1972)
Dasyuromorphia	62 μg/L	Tasmanian devil (*Sarcophilus harrisii*)	26	Blood	Captive	Australia	(Hivert et al. 2018)
Didelphimorphia	1,300 μg/kg w.w.	Virginia opossum (*Didelphis virginiana*)	4	Liver	F-R	USA	(Lewis et al. 2001)
Diprotodontia	2,950 μg/kg[c]	Common wombat (*Vombatus ursinus*)	4	Hair	F-R	Australia	(Penrose et al. 2022)
Eulipotyphla	1,506,000 μg/kg d.w.	Northern short-tailed shrew (*Blarina brevicauda*)	1	Kidney	F-R	USA	(Stansley and Roscoe 1996)
Lagomorpha	9,000 μg/kg w.w.	European hare (*Lepus europaeus*)	9	Muscle	F-R	Austria	(Ertl et al. 2016)
Primates	212,500 μg/kg w.w.	Stump-tailed macaque (*Macaca arctoides*)	2	Liver	Captive	USA	(Zook et al. 1972)
Rodentia	672,000 μg/kg d.w.	Long-tailed field mouse (*Apodemus sylvaticus*)	5	Bone	F-R	UK	(Johnson et al. 1978)
Sirenia	100 μg/L	American manatee (*Trichechus manatus*)	4	Blood	Captive	Brazil	(Anzolin et al. 2012)

[a] F-R: The wild mammal was from a free-ranging setting. Captive: The wild mammal was from a captive setting.

[b] Country in which the study was conducted.

[c] No indication of whether the concentration is reported in w.w. or d.w.

Table 3. Negative health effects associated with lead (Pb) exposure in wild mammals by organ system affected in studies published between 1961 and June 2022.

Organ or system affected	**Effects found**	**References**
Whole body	Fatality, DNA damage, oxidative stress	Sauer et al. 1970; Shlosberg et al. 1997; Skerratt et al. 1998: da Silva et al. 2000; Brumbaugh et al. 2010; Burco et al. 2012; North et al. 2015; Lazarus et al. 2020

Nervous system	Neurological clinical signs; demyelination of spinal cord and subcortical white matter of brain and optic tracts	Sauer et al. 1970; Zook et al. 1973; Diters and Nielsen 1978; Skerratt et al. 1998
Circulatory system	Decreased ALAD[a] activity; decreased haemoglobin; decreased haematocrit; increased MNEs[b]; increased total bilirubin; decreased calcium; decreased lactate dehydrogenase	Mouw et al. 1975; Ieradi et al. 1996; Stansley and Roscoe 1996; Rogival et al. 2006; Sánchez-Chardi et al. 2009; Chen et al. 2018
Reproductive system	Testicular structural and functional disruption; abnormal sperm cells; decreased proportion of live sperm	Ieradi et al. 1996; Parelho et al. 2016; Chen et al. 2018
Kidney	Decreased ALAD activity; necrosis and cell degeneration; INIBs[c] in proximal tubular epithelium; oedema; mitochondrial abnormalities; increased weight of kidneys; hyperplasia of tubules, atrophy of glomeruli, interstitial fibrosis; degenerate cells in the lumen of seminiferous tubules; mineralisation and degeneration of proximal tubules; karyocytomegaly; lymphocyte infiltrations; cell debris and change in glomerular aspect and size	Sauer et al. 1970; Zook et al. 1970, 1972; Mouw et al. 1975; Diters and Nielsen 1978; Roberts et al. 1978; Stansley and Roscoe 1996; Skerratt et al. 1998; Ceruti et al. 2002; Damek-Poprawa and Sawicka-Kapusta 2003; Brumbaugh et al. 2010; Tête et al. 2014
Liver	INIBs; necrosis; apoptosis; increased number of pyknotic nuclei; interstitial fibrosis, decreased glycogen content; increased liver-body ratio; steatosis; lymphocyte infiltrations	Sauer et al. 1970; Zook et al. 1970, 1972; Diters and Nielsen 1978; Damek-Poprawa and Sawicka-Kapusta 2003; Sánchez-Chardi et al. 2009; Tête et al. 2014
Teeth	Interference with developing permanent teeth	Rappaport et al. 1975; North et al. 2015

[a]ALAD: Aminolevulinic acid dehydratase.

[b]MNEs: Micronucleated erythrocytes.

[c]INIBs: Eosinophilic acid-fast Intranuclear inclusion bodies.

Figure 1. Modified PRISMA 2020 flow diagram for systematic reviews, indicating the number of studies that were included and excluded in the screening process for studies on lead (Pb) exposure in wild mammals.

Figure 2. The number of studies published per year on lead (Pb) exposure in wild mammals included in this systematic review (*n*=183). Studies were published in the period 1961-June 2022.

Figure 3. The number of studies (*n*=183) conducted on lead (Pb) exposure in wild mammals between 1961 and June 2022, per country. Studies were conducted in 35 countries across six continents. Darker color indicates a higher number of studies conducted. Created using Datawrapper (Datawrapper GmbH 2022).