https://doi.org/10.5281/zenodo.19917557

Question raised by requestor

How does lead poisoning of cattle affect the animal welfare in an acute/sub-acute/chronic way? What is the current background level of lead in blood from cattle today? What is the half-time of lead in blood? What is the connection between blood level of lead and the level of lead in muscle tissue?

Answer

EURCAW *Ruminants & Equines* is responding to a query resulting from an accidental exposure of cattle to lead (***Pb***) through their silage.

Executive summary

How does lead poisoning of cattle affect the animal welfare in an acute/sub-acute/chronic way?
See Table 1 for an overview.

What is the current background level of lead in blood from cattle today?
Although Pb is generally poorly absorbed in adult ruminants, blood levels may rise to 2000–4000 µg/L within 12 hours after ingestion of toxic doses (100 mg/kg body weight) and decline to 1 µg/L within 72 h. However, the blood levels remain above controls for a period of 2 months, indicating a slow elimination rate of blood Pb.

What is the half-time of lead in blood?
The half-life in blood of cattle is reported at 5–9 days, its half-life in soft tissues is approximately 28–36 days.

What is the connection between blood level of lead and the level of lead in muscle tissue?
Blood Pb concentrations correlate with liver, kidney and bone concentrations but not skeletal muscle concentrations. During long-term exposure, Pb accumulates also in the bones by co-precipitation with calcium. It is deposited predominantly in physiologically inactive cortical bones, where it may persist for decades without substantially influencing the concentrations of Pb in blood and other tissues. However, accumulated Pb may be released when bone re-composition occurs (for example due to severe calcium deficiency or osteoporosis in humans). Body clearance of Pb is incomplete and slow, resulting in bioaccumulation in target tissues, especially after long-term exposure. The half-life of elimination (body clearance) is between 95 and 760 days in cattle.

Legal framework

Pb as undesirable substance in animal feed
The maximum permitted content of Pb in feed materials is 10 mg/kg, except for 'forage' for which the maximum is 30 mg/kg relative to a feed with a moisture content of 12 %, laid down in Directive 2002/32/EC on undesirable substances in animal feed [1].

Maximum levels for certain contaminants in food
Meat, offal, and milk (i.e. raw milk, heat-treated milk and milk for the manufacture of milk-based products) of bovine animals shall not be placed on the market and shall not be used as a raw material in food or as an ingredient in food where it contains Pb exceeding levels of 0.10, 0.20, and 0.02 mg/kg wet weight, respectively, as laid down in Commission Regulation (EU) 2023/915 on maximum levels for certain contaminants in food [2].

Occurrence, toxicity, elimination and tissue accumulation of Pb

Pb is a persistent environmental contaminant, and its occurrence, toxic effects, limited elimination, and tendency to accumulate in tissues – particularly bone, liver, and kidney – are well described by EFSA (2004) Opinion of the Scientific Panel on contaminants in the food chain related to lead as undesirable substance in animal feed [3] and Bates and Payne (2017) Lead poisoning in cattle [4] highlighting its relevance for animal health and food safety. Excerpts thereof are provided in the following subparagraphs:

- Average concentration of Pb in most commercial feed materials is below the permitted level, and typically < 1.50 mg/kg dry matter. Values in excess of maximum permitted limits are only encountered where contamination has occurred.
- Concentrations of Pb in forage crops are generally higher than in concentrate feed materials. Since concentration in forages grown on non-contaminated soils are generally low, the elevated levels may reflect crops that have been grown on contaminated soils, or that contain higher amounts of contaminated soil. The main sources of exogenous Pb are mining activity and the application of sewage sludge to farmland. Concentrations in excess of 600 mg/kg dry matter have been reported in herbage grown on soil subjected to mining activity or to which sewage sludge has been applied. In addition, the processes of harvesting herbage for conservation as hay or silage often result in soil being picked up with the crops, and therefore elevated levels of Pb may reflect soil contamination of the material being analysed.
- Dietary concentrations for ruminant livestock are most likely to exceed maximum levels in cases where the diet consists entirely of forage, and where the forage has been contaminated.
- Accidental exposure of animals may result from Pb shots (e.g. ball traps ingested by cattle), disposed linoleum, and from Pb containing ornaments, toys and pigments. Particularly, intoxications of cattle resulting from ingestion of disposed batteries have been regularly reported.
- The toxicity of Pb depends on the chemical form, e.g. the solubility of individual Pb salts and their absorption from the gastrointestinal tract. It is generally recognised that following oral exposure, the toxicity of Pb decreases in the following order: Pb acetate > chloride > lactate > carbonate > sulfite > sulfate > phosphate. A reliable estimate of dose-dependent effects, however, is impossible as the relevant information is lacking and clinical reports are often based on accidental exposure of which the exact dose/concentration remains unknown.
- In animals, prominent toxic effects of Pb have been related to its ability to bind to proteins, including binding to haemoglobin, binding to and inhibition of δ-aminolaevulinic acid dehydratase (***ALAD***), or dihydrobiopterin reductase. Clinically, diagnostic signs of Pb poisoning include elevated levels of δ-aminolaevulinic acid (***ALA***) in serum and urine, elevated coproporphyrinogen levels in red blood cells and urine, and the presence of immature erythrocytes with basophilic stippling.
- Cattle are considered one of the most sensitive animal species for Pb intoxication. Clinical signs (see Table 1) comprise neurotoxicity, including blindness, muscle twitching, hyperirritability, depression, convulsions (mainly in young animals), grinding teeth, ataxia, circling, and head pressing (manifestation of cerebral oedema). It is worthwhile to mention that those signs may resemble other neurological diseases such as hypomagnesemic tetany, BSE and listeriosis or other intoxications e.g. organochlorine insecticide, arsenic or mercury poisoning. Additional signs are gastrointestinal symptoms including excessive salivation, anorexia, tucked abdomen and rumen stasis, and diarrhoea alternating with constipation. Lethal single doses are reported to vary between 400–600 mg/kg body weight in calves and 600–800 mg/kg body weight in adult cattle.
- Sub-acute toxicity occurred following ingestion of silage containing Pb at a dose of 140 mg/kg feed, and herbage grown on Pb contaminated soil containing 200–900 mg/kg, induced clinical intoxications. Ingestion of Pb containing paint (22–24 mg Pb per animal per day) did not induce any clinical signs in heifers. The maximum tolerable level was estimated to be 100 mg/kg feed (total diet).
- Although Pb is generally poorly absorbed in adult ruminants, blood levels may rise to 2000–4000 µg/L within 12 hours after ingestion of toxic doses (100 mg/kg body weight) and decline to 1 µg/L within 72h. However, the blood levels remain above control animals for a period of 2 months, due to the slow elimination rate of Pb. The half-life in blood of cattle is reported at 5–9 days, its half-life in soft tissues is approximately 28–36 days.
- Blood Pb concentrations correlate with liver, kidney and bone concentrations but not skeletal muscle concentrations.
- Following binding to metallothionein, a protein that binds and regulates essential and toxic metal ions, Pb accumulates in the liver and in the kidney (particularly in the cortical zone). During long-term exposure, Pb accumulates also in the bones by co-precipitation with calcium. It is deposited predominantly in physiologically inactive cortical bones, where it may persist for decades without substantially influencing the concentrations of Pb in blood and other tissues. However, accumulated Pb may be released when bone re-composition occurs (for example due to severe calcium deficiency or osteoporosis in humans).
- Body clearance of Pb is incomplete and slow, resulting in bioaccumulation in target tissues, especially after long-term exposure. The half-life of elimination (body clearance) is between 95 and 760 days in cattle.

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- The major route of elimination of ingested Pb is by faeces. Faecal excretion contains unabsorbed Pb with a variable proportion of Pb excreted with bile. Urinary excretion is usually < 2 % of the ingested dose in ruminant species.
- Excretion in milk may occur following high-doses exposure, but the amount excreted is relatively low. In ewes receiving Pb chloride at a dose of 2.3 mg/kg body weight/day throughout a 52-day lactation period, the Pb concentration in milk ranged from 97–205 µg/L, and the milk to blood concentration ratio slightly exceeded 1. In contrast, the ratio is 0.1–0.2 in lactating cows. The apparent species difference may be explained by the curvilinear relationship between Pb in milk and blood, because higher milk to blood ratios occurs at higher blood Pb levels. Excretion in milk may however increase in diseased animals, suffering from sub-clinical or clinical mastitis. In cattle, Pb deposited in bones is normally not mobilised during pregnancy and lactation, which explains the very limited amounts found in dairy milk.
- Experimental studies in cattle, sheep, and swine that were fed diets containing levels of Pb varying between 15–25 mg/kg dry matter indicate that although residues in the liver, and especially in the kidney, were generally higher than in the control animals, they remained below the maximum permissible levels for animal products. In muscle tissues, Pb residues were low and not significantly different from those in the control animals.
- At higher levels of Pb dietary exposure (100 mg/kg dry matter) no significant changes in the tissue residues were found in the liver, kidney or muscle of sheep, although tissue levels significantly increased when dietary levels of Pb were 500 or 1000 mg/kg dry matter. Similar results were obtained for calves fed 100 mg/kg dry matter for 100 days; liver and kidney contained 2.3 and 4.7 mg/kg fresh weight, but Pb concentration in muscle tissue remained below the limit of detection.

Table 1: Welfare implications in relation to Pb intoxication levels [3,4].

Intoxication level	Animal health and welfare implications
Sub-acute Pb poisoning (usually seen in older cattle or sheep)	Anorexia, rumen stasis, colic, dullness, and transient constipation, frequently followed by diarrhoea, blindness, head pressing, grinding teeth (bruxism), hyperesthesia, incoordination, nephrosis
Acute Pb poisoning (more common in young animals due to higher absorption rates compared to adult animals)	Blindness, muscle twitching/spastic twitching of eyelids, muscle tremors, hypersalivation, hyperirritability, depression, convulsions (mainly in young animals), bruxism or jaw champing, ataxia, circling, and head pressing (manifestation of cerebral oedema)
Chronic Pb poisoning	May produce a syndrome that has many features in common with acute or subacute Pb poisoning. Impairment of the swallowing reflexes frequently contributes to development of aspiration pneumonia. Embryotoxicity and poor semen quality may contribute to infertility.

Pb intoxication during gestation

Only little information is available on Pb poisoning during gestation, however, Pb crosses the placenta and therefore is potentially harmful to the foetus. In a case study on accidental Pb poisoning 9 heifers showed toxic (n=5, 4 pregnant) or high–normal (n=4, all pregnant) Pb levels in the blood. While none of the 8 heifers confirmed pregnant aborted before calving, 1 heifer lost her calf at birth and the size and consistency of the uterus of the nonpregnant heifer suggested that she might have aborted recently. None of the 7 surviving calves from these heifers died between birth and weaning. Blood samples collected from the calves around the time of birth showed low concentrations of Pb in the blood of the calves exposed *in utero* (0.010–0.095 ppm) [5]. Another case study of accidental Pb poisoning included 4 pregnant cows in the first or second month of gestation at the time of exposure. Two of these cows were slaughtered 20 weeks after exposure (showing elevated levels of Pb in kidney and liver) where the foetuses (6^{th} month of gestation) were found normal in size and development, however, 10-fold higher levels of Pb were found in the liver (elevated) compared to the kidney (not elevated). Blood Pb levels of the foetuses were low. The two other cows delivered their calves which had low blood Pb levels [6]. Still, abortion may occur as a consequence of Pb poisoning at mid to late gestations [3,4].

Treatment and prognosis of Pb poisoning

Prevention of Pb exposure is crucial as treatment is mainly supportive (securing hydration and nutrition). Chelation therapy (e.g. sodium calcium edetate) may be given but is costly and may be impractical if numerous animals are affected as extensive supportive care is required. Anorexia, permanent tissue damage, the lack of approved chelation products, and significant tissue residues create significant economic and public health concerns, which is why treatment in food-producing animals is not recommended. Response to treatment and prognosis are both poor for acutely poisoned animals due to the rapid onset of life-threatening symptoms [4,7].

Conclusion

Pb is a highly toxic, persistent environmental contaminant. Preventing exposure to Pb is of the utmost importance since treatment is not recommended for food-producing animals, as significant tissue residues could pose a threat to public health. Blood Pb concentration is a poor biomarker for Pb skeletal muscle concentrations due to lacking correlation. Furthermore, animal welfare may be severely compromised due to a poor response to treatment, which is associated with a poor prognosis and a considerable economic burden for the producer. Nevertheless, foods of animal origin generally contain levels well below the statutory maximum, thus they are not a major source of human exposure to Pb.

References

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