CHEMICAL POISONINGS

Aetiology Prevention and Control
Potential Impacts of Disease Agent Beyond Clinical Illness
ANTICOAGULANT RODENTICIDES - HEAVY METALS - PESTICIDES
References

AETIOLOGY

Classification of the causative agent

Because the term “chemical poisonings” encompasses a significant number of toxic agents, this technical card will focus on specific categories of toxins most relevant to wildlife species. Each group of toxicants will receive its own dedicated section; this preface serves to deliver information that pertains to chemical toxins as a whole, and these points should be considered in all cases of suspected chemical toxicosis.

Chemical agents to be discussed in this technical card include: anticoagulant rodenticides, heavy metals, and pesticides.

PREVENTION AND CONTROL

Sanitary prophylaxis

- When die-offs due to poisonings are suspected, animals should be removed and deterred from using the area as much as feasible.
    - Consider weather conditions such as wind patterns and aerosol dispersion, watersheds and runoff flow, industrial point-sources, et cetera, when investigating the source.
    - If the mortality event involves a migratory species, also consider more disparate locations as potential sources (e.g., nesting or breeding grounds).
- Some countries have banned the sale and use of specific chemical compounds, and control therefore relies on disposal of remaining products.
    - For cases regarding poisonings in migratory wildlife, identifying the source of toxic compounds may be difficult.
- Remove sources of additional toxin, such as treated plant material, packaging waste, and suspicious carrion (e.g., carcasses containing ammunition, carcasses suspected to contain toxicant in tissue, etc.). Preventing environmental contamination via thoughtful treatment and diversion of wastewater, including sewage, is also indicated.

Medical prophylaxis

- See individual sections for more specific information regarding medical prophylaxis.

POTENTIAL IMPACTS OF DISEASE AGENT BEYOND CLINICAL ILLNESS

Risks to public health

- Human health risks vary significantly by the toxin’s nature and the relevant environmental considerations. Exposures may occur via inhalation, transdermal absorption, ingestion, et cetera.
    - Individuals who hunt and kill animals for consumption should be aware of the activities present in the surrounding environment and thoroughly inspect carcasses for indicators of toxicity and foreign materials prior to preparation and consumption.
- Individuals responding to mortality and/or contamination events in the field should be cognisant of risks and wear appropriate personal protective equipment such as dedicated boots, nonpermeable gloves and clothing, and respirators as appropriate.

- Clinical signs of intoxication may be delayed days to weeks; individuals working with/near toxic compounds or contaminants should be aware of occupational hazards and know when to seek medical attention. Relevant parties should be educated about what constitutes an exposure, clinical manifestations associated with intoxication, et cetera.

Risks to agriculture

- Certain compounds can persist as residues in products intended for sale. Not only can this endanger consumers, but producers may suffer from economic implications and burdens secondary to prolonged withholding times, product adulteration, and any required decontamination.
- Many compounds have significant off-target effects on wildlife species and can therefore disrupt a population or niche within an ecosystem. Direct, long-term ramifications are a concern for the agricultural industry due to the potential for ecosystem destabilisation.

AETIOLOGY

Classification of the causative agent

When discussing wildlife toxins, the term “heavy metals” most commonly refers to a specific handful of elements: arsenic, copper, lead, mercury, selenium, and zinc. Cadmium, chromium, and thallium are sometimes included, but these will not be discussed in this technical card. Some heavy metals are essential minerals and are present in the environment naturally, but levels may vary dramatically across landscapes and soil types. Additionally, toxic doses may not be well established in a species or may be variable based on a metal’s relationships with other nutrients and metabolic compounds.

EPIDEMIOLOGY

Affected Species

Because heavy metals are capable of affecting numerous species, the term “affected species” as used in this technical card will refer to species for which these compounds are currently an appreciable danger. It should be noted that there may be variability in species’ relevance due to inherent differences in species sensitivity, environmental differences, anthropogenic factors, route of exposure, et cetera.

- Arsenic (As) - most living tissues contain a low concentration of arsenic
    - Marine animals are able to tolerate higher tissue concentrations, sometimes up to 100x that of terrestrial species
    - Freshwater and saltwater fish species are important sources of bioaccumulation
- Copper (Cu) - sheep are particularly susceptible; swine are relatively tolerant
- Lead (Pb) - waterfowl, raptors, and scavengers are commonly affected
    - Lead is a significant concern for conservationists particularly for endangered species such as the California condor (*Gymnogyps californianus*)
- Mercury (Hg) - species susceptibility is based on behaviour and proximity to point-sources
    - Seabirds appear more tolerant of mercury, but more research is needed to verify this
    - Freshwater and saltwater fish species are important sources of bioaccumulation
    - Fish-eating mammalian species and apex predators are considered high-risk species
- Selenium (Se) - herbivorous species are most at-risk by foraging selenium-accumulating plants
- Zinc (Zn) - populations that live in close proximity to humans are at increased risk

Routes of Exposure

- Arsenic - ingestion, inhalation (gas species or aerosols), skin or mucous membrane permeation; can cross placenta
- Copper - ingestion
- Lead - ingestion
- Mercury - ingestion, inhalation (gas species or aerosols)
- Selenium - ingestion
- Zinc - ingestion

Sources

- Arsenic
    - Naturally occurring element in the soil and water
        - Pyrite sources and related soils contain high concentrations of inorganic arsenic
    - Bioconcentration
    - Manufactured agricultural products such as growth stimulants, wood preservatives, defoliants, and pesticides
        - Often used to debark trees
    - Emissions from smelters and refineries
    - Byproduct of glass manufacturing

    - Component of arsenical drugs (including some chemotherapeutics, antiprotozoals, and antifilarials)
- Copper
    - Naturally occurring element in soil, but the amount is variable
    - Copper-accumulating plants
    - Agricultural products such as feed additives
- Lead
    - Ammunition, bait, and fishing tackle
    - Mine waste and smelter emissions
    - Paint pigment
    - Batteries
- Mercury
    - Naturally occurring element in the soil and water
    - Bioconcentration
    - Mercury-based fungicides
    - Industrial and mining waste
    - Fossil fuel combustion; incineration inputs and emissions
        - Can exist as a gas and travel distances before being deposited
- Selenium
    - Naturally occurring element in soil, but the amount is variable
    - Selenium-accumulating plants
        - Ability to accumulate depends on plant species (non-, obligate, or facultative accumulators), soil pH, and soil moisture content
    - Smelter emissions
    - Sewage sludge
- Zinc
    - Naturally occurring element in the soil and water
    - Paint
    - Batteries
    - Medicinals and cosmetic products
    - Agricultural products such as fertilisers and feed additives
    - Commonly used in human-made metallic items
- Human-made petroleum products and artificial metallic items can contain varied concentrations of multiple heavy metals and their chemical species

Occurrence

Arsenic

Arsenic is common in the environment in numerous forms; its chemical species can be organic or inorganic, and it can exist in four different oxidation states. As such, arsenic bioavailability and toxicity varies by chemical species, route of exposure, and exposure dose. Cycling in the environment is extremely complex due to constant reduction and oxidation, methylation and demethylation, and other chemical processes. Inorganic arsenic is typically more toxic than organic arsenic, and trivalent species are more toxic than pentavalent species.

Copper

Copper metabolism is altered by the relative levels of other compounds such as molybdenum or sulphur in the body; decreased formation of cuprous complexes limits copper excretion. Haemolysis typically develops approximately 3 days post-ingestion. Chronic toxicity may be mediated by a sudden release of accumulated copper from the liver or by ingestion of other compounds that cause excessive copper storage.

Lead

After ingestion, lead readily redistributes from the bloodstream into soft tissues and bone. Metabolically active cells and tissues are most severely affected due to lead's ability to interfere with antioxidant and mitochondrial activities. Calcium and iron levels affect the rate of tissue absorption and retention.

Mercury

Mercury poisoning is generally associated with industrial point-sources. Mercury cycling in the environment is complex due to the chemical nature of the element; it can exist in organic (ex: methylmercury, MeHg) and inorganic forms (ex: elemental mercury, Hg^0, and divalent mercury, Hg^{2+}). Toxicity also varies by chemical species - organic mercury is more toxic and more easily bioconcentrated than inorganic forms. Organic mercury species are able to be methylated and demethylated via numerous biotic and abiotic processes.

Selenium

Selenium is an essential element and plays a critical role in the function of glutathione peroxidase enzymes, which are significant metabolic antioxidants. However, the threshold for toxicity is very low. Acute, subchronic, and chronic toxicities are possible.

Zinc

Zinc is an essential element involved in numerous metabolic processes. It is an extremely common component of human-made metallic objects, which are often consumed by a curious animal. Free zinc is liberated by the low pH of the stomach and subsequently associates with other ions to create soluble and caustic zinc salts. These are extremely irritating compounds due to their corrosive nature, and they distribute readily to various tissues.

For more recent, detailed information on the occurrence of these diseases worldwide, see the OIE World Animal Health Information System - Wild (WAHIS-Wild) Interface [http://www.oie.int/wahis_2/public/wahidwild.php/Index].

DIAGNOSIS

Arsenic

Arsenic toxicosis is generally acute and dose-dependent; humans are the only species in which chronic toxicity is of significant concern. Arsenicals are readily absorbed by the body and are excreted via the kidneys within a week of exposure. It is believed that selenium and arsenic have an antagonistic relationship. Animals may become more tolerant of additional exposures by upregulating enzymes necessary for methylation. Recovery from acute toxicity is possible if the source of arsenic is quickly removed and adequate supportive care is provided.

Copper

Chronic toxicity typically manifests as a haemolytic crisis upon the sudden release of copper *en masse* from the liver. Stressful events are often believed to be the inciting cause. It is believed that low dietary molybdenum and sulphur increases an animal's risk of such a release.

Lead

Clinical signs of lead poisoning in waterfowl may not manifest for 7 days after acute toxicity, and mortality may be prolonged until 2-3 weeks post-ingestion. Chronic lead toxicity is also possible and occurs over a much longer timeframe. Ruminants develop gastrointestinal and central nervous system signs within days of ingestion.

Mercury & Selenium

Diagnostic determination of selenium and/or mercury toxicity is complicated by the elements' relationship with each other and with other metals and compounds in the body. These interactions can exacerbate or attenuate toxicity. For example, mercury is known to attenuate toxicity of selenium, and vice versa.

Organic mercury species are lipid soluble and therefore readily accumulate in tissues. Animals are typically exposed to inorganic mercury, which is poorly absorbed across skin, by inhaling vapors of elemental species. Elemental species are highly corrosive and cytotoxic.

Excess selenium readily replaces sulphur in amino acids and therefore alters protein structure and enzyme activity. Oral doses as low as 1-10 mg/kg can cause death within 48 hours. Younger animals are more susceptible to toxic effects.

Zinc

The molecular mechanisms of zinc toxicity are not entirely understood, but zinc is known to interfere with metabolic processes that involve copper and other ions.

Clinical diagnosis

Arsenic

Organic arsenic species interfere with oxidative processes and cellular metabolism. Its effects are highly variable due to the different metabolic pathways utilised by various animal species. As such, affected organs and therefore clinical signs depend on the host and arsenic species. Arsenic is known to predispose humans to developing skin neoplasia, but this has not been consistently replicable in animal models. It is, however, an appreciable teratogen across multiple taxonomic groups.

Affected birds are often unkempt and ataxic. Mammals also develop ataxia and incoordination, but are also often weak despite being alert and maintaining a good appetite. Other signs of toxicity include abdominal pain, vomiting and diarrhoea, salivation, blindness, and collapse. Inorganic arsenic species can induce hypovolaemic shock by damaging capillaries. Animals may develop posterior paralysis or quadriplegia. Rare instances of chronic arsenic toxicosis in animals have been associated with optic and sciatic nerve demyelination, immunosuppression, and stunted growth. In these cases, arsenic accumulates in keratinized tissues.

Copper

Acute toxicity often manifests as colic, diarrhoea, anorexia, and dehydration associated with gastroenteritis. Within days, there is progression to haemolysis. Chronic toxicity often appears suddenly and may be mistaken for an acute disease process. The presentation is similar to acute toxicity in that there is marked haemolysis. Animals develop dyspnoea, pale mucous membranes, haemoglobinuria, icterus, and weakness that may progress to recumbency secondary to this haemolytic crisis. Animals may succumb to renal or hepatic failure and can develop photosensitisation due to hepatotoxicity. More than half of affected animals die.

Lead

Lead poisoning in waterfowl often manifests as ataxia, weakness, and reluctance to fly when approached or disturbed. Green, bile-stained faeces and feathers near the vent strongly suggest lead toxicity. Eventually, birds become dull and display abnormal wing positioning that ranges from "roof-shaped" posturing to a complete wing droop. Canada geese (*Branta canadensis*) exhibit abnormal head and neck carriage during flight, and they may vocalise abnormally. Birds are easily captured if severely intoxicated. A study on free-ranging golden eagles (*Aquila chrysaetos*) in Sweden found that birds with a blood lead concentration of 25

parts per billion (wet-weight) exhibit a 10% reduction in flight altitude, and at approximately 43 parts per billion (wet-weight), flight altitude is reduced by 20%. The most common causes of mortality in the study cohort included starvation, trauma, and electrocution.

In ruminants, muscle twitching and tremoring, ataxia, blindness, hypersalivation, ruminal stasis, colic, constipation and/or diarrhoea, hyperaesthesia, bruxism and jaw clamping, convulsions, and head-pressing are common. Both central nervous system excitation and depression are possible, and manifestation often varies by species. Chronic exposure may cause laryngeal or pharyngeal paralysis and dysphagia with secondary aspiration pneumonia. Mammals may abort if lead accumulates in the placenta and/or foetus.

Radiographs can be extremely helpful in determining if the gastrointestinal tract contains metallic materials. Signs of wear indicate the object(s) may have been present in the gastrointestinal tract for an extended period of time. Lead is not magnetic, which may be useful when trying to ascertain the composition of a metallic object.

Mercury

Increased blood mercury concentrations have been correlated with skipped breeding and abnormal hormone activity as well as decreased fledgeling success in marine birds. Eggs are more frequently thin-shelled and laid outside the nest. MeHg is neurotoxic and can cause birds and mammals alike to become anorectic, ataxic, blind, hypermetric, or paralysed; multiple receptors and enzymes in the nervous system become dysregulated in the context of brain mercury accumulation, and both the central and peripheral nervous systems can be affected. MeHg and $HgCl_2$ are embryotoxic to vertebrates. They can also cause disrupted endocrine signaling and liver and kidney dysfunction. Fish and invertebrates suffering from mercury toxicosis experience movement dysfunction, difficulty feeding, delayed metamorphosis, and defective embryo development. Studies in reptiles and amphibians demonstrated negative effects on gene regulation as well as impaired embryonic development and generally decreased reproductive success.

Inorganic mercury species are corrosive and can cause significant irritation to the gastrointestinal tract, which may manifest as colic, anorexia, vomiting, or diarrhoea. If inhaled, there may be damage to the pharynx and upper airways resulting in dyspnoea.

Selenium

Selenium toxicity in mammals is often referred to as “blind staggers” or “alkali poisoning.” Keratinized tissues, such as hooves and hair, become significantly weakened and very susceptible to damage; animals may look unthrifty or alopecic due to a damaged haircoat, and ungulates may become lame or founder. Animals may develop a short-lived foul odour on their breath due to the production of volatile methylated selenium compounds. Some species may suffer from ataxia, paresis, and decreased reproductive success. Selenium toxicity in birds causes embryonic malformations and death as well as emaciation and death of adults.

Acute toxicity causes dyspnoea and tachypnoea, tachycardia, depression, anorexia and colic, ataxia, and frothy nasal discharge. Cyanosis, postural abnormalities, and sudden death are also common.

Zinc

The severity of clinical signs depends on the magnitude and duration of exposure. Animals may initially become anorectic and lethargic. Vomiting and diarrhoea are common early signs of toxicity. More severe toxicity can cause intravascular haemolysis and icterus, haemoglobinuria, decreased weight gain, decreased milk production, cardiac arrhythmias, and seizures.

Bloodwork may indicate significant changes in red blood cell count and morphology, leukogram abnormalities, renal and hepatic enzyme abnormalities, and impaired coagulation. Animals may develop azotaemia secondary to renal damage.

Radiographs can be extremely helpful in determining if the gastrointestinal tract contains metallic materials. Signs of wear indicate the object(s) may have been present for an extended period of time in the gastrointestinal tract. Zinc is not magnetic, which may be useful when trying to ascertain the composition of a metallic object.

Lesions

- Arsenic (lesions may vary by chemical species)
    - Foetal neural tube defects, skeletal anomalies
    - Demyelination and gliosis of peripheral nerves and the optic nerves/tracts
    - Fluid in pericardial sac
    - Reddened gastric and intestinal mucosa and submucosa
        - Oedema, sloughing, and necrosis of epithelium
        - Necrosis can progress to cause complete perforation
    - Soft, yellow liver
        - Fatty changes and necrosis apparent histologically
        - Endoplasmic reticulum swelling and subsequent hepatocyte damage
    - Red, oedematous lungs
    - Diffuse visceral inflammation
    - Capillary degeneration
    - Renal tubular damage
- Copper
    - Altered tissue pigmentation
        - Blue-green gastrointestinal content
        - Wine-red urine
        - Swollen, gunmetal-blue kidneys
        - Brown to black splenic parenchyma
    - Icterus
    - Gastroenteritis with erosions and ulcerations
    - Splenomegaly, hepatomegaly
    - Centrilobular hepatic necrosis
    - Renal tubular necrosis
- Lead
    - Presence of lead-containing materials in the gastrointestinal tract
    - Haematologic abnormalities such as anaemia, anisocytosis, and poikilocytosis
    - Birds
        - Green faecal staining of feathers near the vent and base of tail
        - Reduced to absent visceral and subcutaneous fat with pectoral muscle atrophy
        - Pale and “flabby” heart; pale viscera and muscle
        - “Puffy,” oedematous appearance of head and face due to fluid accumulation (common in Canada geese)
        - Oesophageal or proventricular impactions
        - Distended gallbladder with dark or bright green bile; ingesta may be bile-stained
    - Cerebellar haemorrhage and oedema
    - Renal tubular necrosis and degeneration
    - Osteoporosis
    - Placentits
- Mercury (lesions may vary by chemical species)
    - Neuronal demyelination and apoptosis
    - Astrocyte, microglia, monocyte, and lymphocyte apoptosis
    - Vacuolar change in hepatocytes
    - Perivascular cuffing
    - Upper airway damage (stomatitis, pharyngitis), corrosive bronchitis, and interstitial pneumonia
    - Gastrointestinal inflammation, ulceration, and necrosis
    - Renal tubular necrosis and interstitial nephritis
        - Kidneys are pale and oedematous
- Selenium

    - Embryonic deformities, especially limbs and beaks
    - Fluid accumulation in embryo skulls
    - Ascites
    - Emaciation
    - Articular cartilage degeneration
    - Hoof deformities or fractures
    - Hepatic cirrhosis and/or necrosis
    - Myocardial necrosis and/or fibrosis
    - Poliomyelomalacia
    - Pulmonary oedema, congestion, and/or haemorrhage
    - Renal necrosis
- Zinc
    - Presence of zinc-containing items in the gastrointestinal tract
    - Icterus
    - Renal tubular necrosis and haemoglobin casts
    - Pancreatic duct necrosis with interlobular fat fibrosis
    - Hepatocellular necrosis, vacuolar degeneration, and haemosiderosis

Differential diagnoses

- Arsenic
    - Salt poisoning
    - Pseudorabies
    - Bovine viral diarrhoea
    - Other teratogenic and reproductive toxins
    - Other heavy metal toxicoses
    - Insecticide toxicoses
- Copper
    - Plant-induced photosensitisation
    - Chronic active hepatitis
    - Immune-mediated haemolytic anaemia
    - Zinc toxicity
- Lead
    - Polioencephalomalacia
    - Tetanus
    - Rabies
    - Listeriosis
    - Canine distemper virus
    - Nervous coccidiosis
    - Hypovitaminosis A
    - Other heavy metal toxicoses
    - Organochlorine toxicosis
- Mercury
    - Primary gastrointestinal disease
        - Hog cholera
    - Renal or hepatic encephalopathy
    - Erysipelas
    - Feline panleukopoenia
    - Other heavy metal toxicoses
    - Organochlorine toxicosis
    - Mycotoxicosis
- Selenium
    - Hypovolaemic shock
    - Degenerative joint disease
    - Heart failure (left- or right-sided)
    - Primary pulmonary disease
    - Other teratogenic and reproductive toxins
    - Other heavy metal toxicoses

    - Other renal toxins (Mercury, ethylene glycol)
    - Ionophore toxicosis
- Zinc
    - Immune-mediated haemolytic anaemia
    - Copper toxicity
    - Other causes of acute kidney injury

Laboratory diagnosis

Samples

For identification of toxicant

- Arsenic
    - Liver, kidney
    - Stomach contents
        - Preferred sample for cases presenting 24-48 hours after ingestion
    - Urine
        - Preferred sample for cases presenting >48 hours after ingestion
        - Contains mostly inorganic and methylated arsenic species
- Copper
    - Gastrointestinal contents, faeces
    - Liver, kidney
    - Whole blood
- Lead
    - Liver (kidney may be substituted), fresh or frozen
    - 2-5 mL whole blood in lead-free tubes containing sodium citrate, heparin, or EDTA; can be frozen for preservation
- Mercury
    - Kidney (liver may be substituted)
        - Preferred samples for organic species detection
    - Brain
        - Preferred sample for organic species detection
    - Axial musculature (fish)
    - Whole blood (identifies MeHg only)
    - Urine
        - Preferred sample for inorganic species detection
- Selenium
    - Serum (whole blood may be substituted, but is less accurate)
    - Liver, kidney
- Zinc
    - Serum
        - Collect blood samples in glass or all-plastic heparinised tubes, trace element tubes, or EDTA tubes; rubber stoppers may artificially increase zinc levels
    - Liver, kidney
- Hair from the dorsal midline and feathers from the pectoral region are commonly used to detect many heavy metals
    - Heavy metal concentrations within feathers are variable based on type of metal, animal species, feather pigmentation, and part of feather used for analysis. It is recommended that diagnostic facilities are contacted before analysing samples to ensure proper collection, handling, and submission.Further research is still needed to establish applicable reference ranges for the metal and animal species of interest.
    - Hair best correlates with brain, liver, and kidney lead levels and is a poor indicator of tissue copper and zinc.

Serological tests

- Serology is not used to detect heavy metal toxicity.

Procedures

Identification of toxicant

- Arsenic
    - Mass spectrometry
        - Tissue concentrations >0.1 ppm (wet weight) are atypical in healthy animals; concentrations of >3 ppm (wet weight) strongly suggest toxicity
        - Stomach contents can be analyzed to estimate ingested dose
        - Feathers (reference ranges vary)
- Copper
    - Normal blood levels are approximately 1 mcg/mL and may rise to 5-20 mcg/mL during a haemolytic crisis
    - Mass spectrometry
        - Gastrointestinal content or faecal concentrations >8,000-10,000 ppm
        - Kidney concentrations >15 ppm (wet weight)
        - Feathers (reference ranges vary)
    - It is recommended to concurrently test for molybdenum concentrations and evaluate if toxicity is primary or secondary
- Lead
    - Blood concentrations >0.35 ppm
    - Blood δ-aminolevulinic acid dehydratase (ALAD) enzyme levels are often used as a biomarker that, when depressed, indicates sublethal lead toxicosis
    - Measurement of protoporphyrin IX in red blood cells is a sensitive screening tool, but elevated levels are only correlated with increased blood lead
    - Mass spectrometry
        - Wet weight liver or kidney concentrations of ≥6-10 ppm (≥20-30 ppm if dry weight)
        - Hair or feathers (reference ranges vary)
- Mercury
    - Whole blood MeHg concentrations >6 ppm suggest toxicity
    - Mass spectrometry
        - Feathers (reference ranges vary)
        - Wet weight mercury concentrations of ≥10-20 ppm in kidney or liver, ≥0.5 ppm in brain
            - Not solely diagnostic and must be interpreted in the context of the entire clinical picture
    - Determining the Hg:Se ratio in tissues may inform the impact of mercury in the animal
        - Ratios <1 suggest protective levels of selenium relative to mercury
- Selenium
    - Serum concentrations >3-4 ppm in acute toxicity, >1-2 ppm in chronic toxicity
    - Mass spectrometry
        - Liver concentrations >3-5 ppm in acute toxicity, >1.5 ppm in chronic toxicity
        - Kidney concentrations >1-5 ppm
        - Keratinized tissue (e.g., feathers) concentrations >1.5-5 ppm in chronic toxicity
- Zinc
    - The toxic thresholds of zinc concentrations appear to be variable by species
    - Blood zinc concentrations
    - Feather, liver and/or kidney mass spectrometry

Serological tests

- Serology is not used to detect heavy metal toxicity.

PREVENTION AND CONTROL

Sanitary prophylaxis

- Habitat modification may be appropriate in some circumstances, such as altering water levels to prevent certain species from ingesting settled lead shot. However, this can create a favourable habitat for other at-risk species. Broad consideration of local species diversity and behavior is indicated before instituting such changes.
    - Environmental alterations may increase the bioavailability of certain toxicants. For example, mercury is more easily accumulated in plant and animal tissue when terrestrial habitats are flooded for the production of wetlands.
- Routine tillage of agricultural fields can reduce the availability of certain materials (such as lead shot) to animals

Medical prophylaxis

- If an animal in a captive setting (e.g., rehabilitation clinic, captured for research) is observed with increased heavy metal concentrations in the blood, chelation therapy and induced emesis/catharsis (if indicated) can be initiated even before clinical signs of toxicosis develop.

POTENTIAL IMPACTS OF DISEASE AGENT BEYOND CLINICAL ILLNESS

Risks to public health

- Many heavy metals are appreciable human carcinogens and teratogens.
- It is known that fish are significant bioaccumulators of mercury and serve as a potential source of the metal for human consumption. Even low levels of mercury exposure have been shown to have negative effects on the neural development of infants and children.
    - Lead is known to have similar effects on child development.

Risks to agriculture

- Low levels of arsenic and zinc are often added to feed mixes for livestock and poultry; calculation and mixing errors may provide animals with an excess and induce toxicity.
- Sheep are extremely susceptible to copper toxicity, and feed contamination or mixing errors can have devastating effects in a herd. Additionally, low dietary sulphur and molybdenum can cause secondary copper toxicity.
- Because lead has a significantly prolonged half-life in blood, livestock with confirmed lead toxicosis may be subject to withdrawal periods ≥1 year. Asymptomatic animals may still have tissue levels that surpass food safety standards, and cattle can excrete lead in milk.

ANTICOAGULANT RODENTICIDES

Aetiology Epidemiology Diagnosis Prevention and Control
Potential Impacts of Disease Agent Beyond Clinical Illness

AETIOLOGY

Classification of the causative agent

The term “anticoagulant rodenticide” emcompasses many commercially available compounds and is further classified into generations; first generation compounds (e.g., warfarin) require multiple feedings or doses to cause death, whereas second generation compounds (e.g., brodifacoum) are highly lethal and require only one feeding. There are also intermediate compounds (e.g., diphacinone, chlorophacinone) that require fewer, but more than one, feedings. These chemicals act to disturb mechanisms of hemostasis by inhibiting clotting factors and/or vitamin K reactivation. Poisoned animals typically succumb to haemorrhage, trauma, or predation.

Other rodenticides such as zinc phosphide and cholecalciferol, while still toxic to wildlife species, will not be covered in this section.

EPIDEMIOLOGY

Affected Species

Because anticoagulant rodenticides are capable of affecting numerous species, the term “affected species” as used in this technical card will refer to species for which these compounds are currently an appreciable danger. It should be noted that there may be variability in species’ relevance due to inherent differences in species sensitivity, environmental differences, anthropogenic factors, route of exposure, et cetera.

- Risk of exposure increases with proximity to urban areas
- Rodents (order *Rodentia*), namely rats, mice, and voles
- Scavengers and non-herbivorous animals are at risk of secondary (non-target) toxicity
    - Birds of prey (e.g., *Accipitriformes, Strigiformes, Falconiformes,* and others)
    - Terrestrial carnivores and omnivores (commonly *Canidae*, *Felidae, Mustelidae*)
    - Insectivores (mammalian and avian)
- Recent data suggest reptiles across trophic levels with different prey preferences are susceptible, but there is appreciable variation across species
- There is evidence to suggest that aquatic species are susceptible, but further research is required to ascertain individual species susceptibility and necessary water concentrations for toxicity

Routes of Exposure

- Ingestion of bait or contaminated feed, including prey and carrion
- Consumption of faeces excreted by intoxicated animals
- Runoff from contaminated sources
- *In utero* exposure from maternal bloodstream

Sources

- Human application
- Contaminated or intoxicated feed, prey, or carrion
    - Second-generation compounds accumulate and persist in tissues, namely the liver, and therefore have high potential for bioaccumulation in prey
- Faeces excreted from intoxicated animals
    - Invertebrates feeding on these faeces are also considered a source
- Contaminated water

Occurrence

Rodenticides are commonly used by people to eliminate rodents that are perceived as pests. Wildlife species become vulnerable to toxicity after consuming bait directly or after consumption of prey or carrion contaminated with these compounds. Products may also be stored outside or in easily-accessible areas such as barns where non-target species may inadvertently ingest the pellets or blocks. There have been attempts to limit accessibility to non-target species by creating bait-stations, but these efforts do not address the presence of toxic compounds in the food web.

Secondary or non-target toxicity remains a significant cause of morbidity and mortality due to bioaccumulation and biomagnification across trophic levels and taxonomic groups. Second generation compounds have significant half-lives in rodent tissues, with some beyond 300 days. Reptiles are believed to metabolise these compounds more slowly and are more tolerant to their effects; therefore, they may pose a greater risk to predators.

Invertebrates are a recognised but understudied source of toxin; some slugs are known to ingest bait directly, and other invertebrates accumulate anticoagulant rodenticides by ingesting faeces excreted from intoxicated individuals.

For more recent, detailed information on the occurrence of these diseases worldwide, see the OIE World Animal Health Information System - Wild (WAHIS-Wild) Interface [http://www.oie.int/wahis_2/public/wahidwild.php/Index].

DIAGNOSIS

There is a latent period after ingestion during which viable clotting factors are consumed, however, this period is variable based on species, individual compound, and ingested dose. On average, clinical signs of acute toxicity arise within a week of ingestion, but a particularly large dose may manifest within days. Chronic, low-level exposure is of concern in wildlife species as internal haemorrhages associated with this type of exposure may not be outwardly observable.

Additionally, each compound has a different half-life in plasma, which can range from hours to days or months. Even after plasma concentrations decline, there may be rodenticide detectable in liver or faeces. There is evidence to suggest anticoagulant rodenticides act synergistically rather than cumulatively, especially in the context of chronic exposure.

Clinical diagnosis

Toxicosis secondary to anticoagulant rodenticides is characterised primarily by haemorrhage. This may manifest clinically as anaemia, pale mucous membranes, melaena, epistaxis, haematuria, haemoptysis, and subcutaneous haemorrhage/haematomas. Initially, clinical signs are vague - depression, anorexia, dyspnoea, and lethargy are common. Articular haemorrhage may manifest as limping, and retrobulbar haemorrhage may induce exophthalmos or buphthalmia. Once platelets are consumed, petechiae may develop. Animals may pass abnormal, brightly colored faeces because of the dyes added to these compounds; blues and greens are particularly common. Chronically intoxicated animals are more susceptible to predation and trauma, namely vehicular collisions.

Lesions

- Haemorrhage may manifest as petechiae, ecchymoses, and/or free serosanguinous fluid in body cavities
- Brightly colored bait or ingesta in the gastrointestinal tract

Differential diagnoses

- Disseminated intravascular coagulation or other consumptive coagulopathy
- Other causes of anaemia (e.g., haemolysis)
- Clotting factor deficiencies (e.g., Von Willebrand disease, vitamin K deficiency, thrombocytopoenia)
- Haemoparasitism
- Trauma
- Heavy metal toxicoses

Laboratory diagnosis

Samples

For identification of toxicant

- Stomach contents
- Faeces
- Liver or kidney
- Whole blood, plasma, or serum
- For coagulation assays: plasma (whole blood is acceptable but less stable)
    - Sodium citrate is the only acceptable anticoagulant for coagulation assays; ratio of 1 part citrate to 9 parts blood is critical
    - Atraumatic venipuncture technique is necessary to prevent activation or depletion of clotting factors during sample collection
    - Refrigerate and test as soon as possible

Serological tests

- Serology is not used to detect anticoagulant rodenticides.

Procedures

Identification of toxicant

- Various mass spectrometry and chromatography methods are suitable for identification (e.g., LC-MS, HPLC)
- Delayed prothrombin (PT) and activated partial thromboplastin (aPTT) times in the context of normal fibrinogen, fibrin degradation products (FDPs), and platelet counts

Serological tests

- Serology is not used to detect anticoagulant rodenticides.

PREVENTION AND CONTROL

Sanitary prophylaxis

- If anticoagulant rodenticides are present on a property, ensure they are properly stored in a manner that is unable to be tampered with by wildlife.

- Specific and targeted use of these compounds in conjunction with prompt carcass removal is recommended over diffuse application on a property. Alternative methods of pest control, such as live-trapping for release elsewhere, are preferred.
- If spreading bait over an area, ensure pellets and other particulates do not enter bodies of water.

Medical prophylaxis

- If ingestion of anticoagulant rodenticides was observed or is suspected and the animal has not yet developed clinical signs of toxicity, inducing emesis and initiating aggressive therapy with vitamin K_1 can prevent haemorrhage.
    - Administer 3-5 mg/kg/day of vitamin K_1 orally for 3-4 weeks followed by assessment of clotting times 72 hours after last dose
    - Administration of vitamin K_3 as a supplement or feed additive is ineffective in this context

POTENTIAL IMPACTS OF DISEASE AGENT BEYOND CLINICAL ILLNESS

Risks to public health

- Anticoagulant rodenticide toxicity poses a threat to any individual that consumes meat from wild animals, including mammals, birds, and reptiles.

Risks to agriculture

- Anticoagulant rodenticides are toxic to livestock and any exposure is considered hazardous.

AETIOLOGY

Classification of the causative agent

Pesticides are chemicals used to specifically repel or kill a group of undesired organisms. Insecticides such as carbamates and organophosphates (OPs) are among the most recognized. Acaricides, avicides, fungicides, algaecides, molluscicides, nematocides, piscicides, and herbicides are typical categories used for classifying the use of a compound. Rodenticides are also considered pesticides; anticoagulant rodenticides are discussed individually elsewhere in this technical card.

EPIDEMIOLOGY

Affected Species

Because pesticides are capable of affecting numerous species, the term “affected species” as used in this technical card will refer to species for which these compounds are currently an appreciable danger. It should be noted that there may be variability in species’ relevance due to inherent differences in species sensitivity, environmental differences, anthropogenic factors, route of exposure, et cetera.

- Birds are believed to be more sensitive to organophosphates (OP), chlorinated hydrocarbons, and carbamates than other vertebrates
    - Waterfowl, passerines, and raptors are commonly intoxicated
    - Individuals are more vulnerable if young, ill, in poor nutritional status, migrating, or otherwise expending large amounts of energy
- Pollinating birds, bees, and other nectivores are at particular risk of exposure to neonicotinoid, butenolide, and OP pesticides
- Fish and aquatic invertebrates are vulnerable to compounds routinely used in agriculture, including neonicotinoids, due to water runoff
- Insectivores are at risk of secondary toxicity

Routes of Exposure

- Ingestion of seeds, plant material, water, prey, or carrion with chemical residue, or intentionally contaminated bait
- Inhalation of aerosolised chemicals
- Transdermal absorption or absorption via gills

Sources

- Human application
    - Aerosols
    - Contamination of surfaces or ingesta
- Water contamination, especially from runoff

Occurrence

Persistence in the environment is influenced by compound mobility (ability to be aerosolized, compatibility with substrate), bio- and photochemical degradability, and solubility. Additionally, biomagnification and bioconcentration in food items (prey, plant material) are important methods by which animals are exposed to toxicant. For example, neonicotinoids accumulate in soil and, because they are highly soluble, easily leach into waterways.

Pesticide use is often associated with agricultural land, especially during the growing season (herbicides and insecticides), and livestock receiving pour-on acaricide treatment. Additionally, residential areas and urban greenspaces such as golf courses or parks can be significant sources of herbicidal, insecticidal, and avicidal

compounds. Intoxication may occur in the context of malicious human use, such as baiting wildlife for intentional poisoning. Intoxication that manifests in the reproductive system, such as that due to DDT, is most apparent during the breeding season.

Some species may be exposed seasonally due to changing behavioral and foraging patterns. Additionally, exposure may vary across age groups and sexes due to differences in behaviour.

For more recent, detailed information on the occurrence of these diseases worldwide, see the OIE World Animal Health Information System - Wild (WAHIS-Wild) Interface [http://www.oie.int/wahis_2/public/wahidwild.php/Index].

DIAGNOSIS

The time between ingestion of toxicant and the onset of clinical signs is variable and dependent upon the compound itself, ingested dose, and the species in question. Animals may suffer from acute toxicity by ingesting a large amount of toxicant over a short period of time, or from chronic toxicity by ingesting low concentrations of toxicant over a prolonged period of time. Manifestations of chronic toxicity tend to be more subtle and vague than acute toxicity. Many pesticides are highly lipophilic and are stored in adipose tissue; weight loss, which is common in cases of chronic toxicity, can exacerbate illness by liberating additional toxicant from tissue.

Clinical diagnosis

Mortality may be the first indication of pesticide intoxication, and animals may be found dead in clusters if death was acute. Surrounding vegetation may be disrupted if moribund animals were thrashing or otherwise struggling. Raptors exposed to OPs or carbamates will commonly have plant material clutched in their talons.

Animals can develop a wide array of clinical signs, such as lethargy, paralysis or paresis, tremors, convulsions, opisthotonus, vomiting, diarrhoea, dyspnoea, miosis or mydriasis, epistaxis, ataxia, hyporexia, inability to regulate body temperature, weight loss, decreased reproductive success, and behavioural changes. Sublethal exposures can predispose animals to physical trauma and other physiologic disturbances. Collapsed or broken eggshells may be seen in nests of birds exposed to chlorinated hydrocarbons, and viable offspring may have noticeable delays in normal development. Wild white-crowned sparrows (*Zonotrichia leucophrys*) experimentally exposed to neonicotinoids during migratory stopover exhibited decreased food consumption, decreased mass and fat stores, and increased migratory delays.

Lesions

- Granular or dyed material in the gastrointestinal tract
- Presence of fresh ingesta in the gastrointestinal tract is a strong indicator of acute death, and the nature of the ingesta may indicate the source of the toxin (e.g., carrion and other animal tissues indicate secondary poisoning, whereas grains and plant materials indicate primary poisoning)
- Reddening or haemorrhage of the intestinal wall
- Reddening of the lungs +/- excess fluid in airways
- Emaciation may be consistent with chronic exposure
- Signs of trauma may be apparent
- Secondary disease due to immunosuppression may be present

Differential diagnoses

- Trauma
- Heavy metal toxicoses
- Central or peripheral nervous system disease
- Endocrine disease
- Reproductive disease

Laboratory diagnosis

Samples

For identification of toxicant

- Brain
- Crop and/or stomach contents
- Liver
- Blood
- Feathers
- Cloacal fluid
- Bee honey or nectar
- Water and sediment samples
- If samples are being collected for chlorinated hydrocarbon insecticide analysis, take care to follow specific precautions to avoid contamination:
    - Instruments and containers should be treated with solvents such as hexane or acetone to remove residues
    - Tissue samples should be wrapped in aluminium foil produced without the use of oils or animal fats, especially before placing in plastic containers.

Serological tests

- Serology is not used to identify pesticides.

Procedures

Identification of toxicant

- Multiple gas or liquid mass spectrometry or chromatography assays are available to identify chemical residues (e.g., LC-MS, HPLC)
- Brain cholinesterase (ChE) expression assays
    - Significant variation exists between individual assays; compare results with controls and references from the same laboratory and method only
    - A decrease in brain ChE ≥25% from normal (in conspecifics) suggests exposure to a ChE-inhibiting compound, and a decrease of ≥50% indicates lethal exposure
    - If ChE enzyme activity reactivates or returns to normal (reference) levels of activity after incubating the sample at 37-40°C, carbamate intoxication is suspected. This method may be confounded if the carcass has been exposed to warm temperatures for extended periods; chill carcasses immediately for diagnostic testing within 48 hours, otherwise freeze as soon as possible.
    - Reactivation of ChE activity in the presence of 2-PAM, a cholinesterase regenerating agent, indicates presence of OPs rather than carbamates
    - Blood may be used antemortem, but interpretation of results is challenging

Serological tests

- Serology is not used to identify pesticides.

PREVENTION AND CONTROL

Sanitary prophylaxis

- The Food and Agriculture Organisation of the United Nations (FAO) has outlined steps for integrated pest management (IPM) approaches to minimise the use of chemical pesticides in agriculture. Suggestions include:

- Thoughtful cultivation utilising methods such as crop rotation and intercropping as well as various sowing techniques
- Selection of plant cultivars suitable for specific needs, i.e., pest resistance/tolerance
- Assessing and monitoring the presence of pests and various intervention points/methods; priority should be given to biological, physical, and non-chemical control methods
- Applying chemical pesticides as minimally and specifically as possible to minimise off-target effects; consider time of day, location of application (e.g., plant leaf versus flower), et cetera.

Medical prophylaxis

- Prophylaxis for pesticides is typically not medical in nature and relies primarily upon sanitation and judicious use.

POTENTIAL IMPACTS OF DISEASE AGENT BEYOND CLINICAL ILLNESS

Risks to public health

- Many pesticides are easily aerosolised, which poses a hazard to individuals working near application sites. Additionally, many compounds persist in the environment for prolonged periods, and residues may be detected in soil, water, and agricultural products.

Risks to agriculture

- Apiculture facilities are particularly vulnerable to the effects of pesticides due to the nature of the compounds used. Fipronil, organophosphates, neonicotinoids, and pyrethrins are known hazards to bees and other pollinating insects. Exposure is commonly via contaminated pollen, nectar, and water, and is commonly characterised by abnormal foraging behaviours, disorientation, prolonged excursion times, immunosuppression, impaired communication and memory, and general weakening of colony health. Individuals that have been exposed are often not recognized by the colony and are shunned or killed. Many pesticides can be identified in the wax and honey produced by exposed colonies, which compromises the integrity and safety of products intended for sale.

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The OIE will periodically update the OIE Technical Disease Cards. Please send relevant new references and proposed modifications to the OIE Science Department (scientific.dept@oie.int). Last updated 2020. Written by Samantha Gieger and Erin Furmaga with assistance from the USGS National Wildlife Health Center.