Organophosphate Poisoning in Cattle

Dr Rick Last – BVSc, M.Med.Vet (Pathology)
Specialist Veterinary Pathologist

Organophosphates are chemical compounds that are widely employed as herbicides, insecticides and pesticides in agriculture, with applications in cattle being as ectoparasiticides and anthelmintics. Organophosphate exposure in cattle can occur through inhalation, ingestion, or contact with skin. Although these compounds are readily absorbed systemically after inhalation and ingestion, systemic absorption following dermal exposure is more variable.

Following systemic absorption, organophosphates inhibit the enzyme acetylcholinesterase (AChE), resulting in over-accumulation of the neurotransmitter acetylcholine. An abundance of acetylcholine in the nervous system manifests with overstimulation of nicotinic and muscarinic receptors, as well as the central nervous system (CNS).

Organophosphate (OP) toxicity in cattle may occur under various circumstances including.

- Organophosphate contamination of bovine feed or water sources by chemical spills.
- Cattle breaking into chemical storage areas and directly accessing OP products.
- Accidental application of agricultural herbicide/pesticide/insecticide OP products on animals.
- Exposure of cattle to aerial crop spraying of agricultural OP or land spraying of these products during windy conditions leads to inhalation and conjunctival contamination.
- Grazing in recently sprayed land or on land contaminated with spray drift.
- Application or registered pour on OP ectoparasiticides at the incorrect concentration/dilution.
- Access of cattle to empty pesticide containers (poor container disposal or use of old insecticide containers as feed utensils).

Predisposing factors to OP toxicity in cattle.

- Age - Young animals are more susceptible.
- Tired or stressed animals.
- Dehydration.
- Hypothermia.
- Breed - Brahman cattle and their crosses are more susceptible to some compounds.

Mechanism of Action in Toxicity.

The neurotransmitter acetylcholine is present in skeletal neuromuscular junctions, parasympathetic and sympathetic ganglia and all postganglionic parasympathetic nerves. With the depolarization of axons, acetylcholine is released into the synaptic cleft, which activates the postsynaptic receptors, resulting in the propagation of an action potential and the progression of the nerve impulse. Carboxylic ester hydrolases metabolize acetylcholine into acetic acid and choline through hydrolysis. This process occurs rapidly, with choline being reabsorbed into the presynaptic nerve to be used for the synthesis of additional acetylcholine. The main enzyme involved in this metabolism is acetylcholinesterase (AChE), which is located in nervous and skeletal tissues.

The OPs inhibit acetylcholinesterase irreversibly by phosphorylation resulting in the accumulation of acetylcholine, which overstimulates both muscarinic and nicotinic acetylcholine receptors at nerve junctions, as well as having central effects (OP compounds cross the blood-brain barrier inhibiting nerve tissue cholinesterase).

OPs can also inhibit other cholinesterases in the body (erythrocyte, serum, liver and pancreas). Neurotransmission is continuous until the organophosphate is removed. Recovery of cholinesterase activity in cases of OP toxicity can only occur through the synthesis of new enzymes.

Organophosphate compounds result in cholinergic overstimulation with three phases of toxic effects namely acute cholinergic crisis, intermediate syndrome, and delayed neurotoxicity.

Acute cholinergic crisis (the most common syndrome in cattle).

- Muscarinic effects usually occur first with bronchospasm, bronchorrhea (voluminous mucous secretion) with dyspnea, miosis, increased gastrointestinal peristalsis (diarrhoea, colic), salivation, frequent urination, lacrimation, and bradycardia.

- Nicotinic effects involve skeletal muscle responses with muscle twitching, tremors, weakness and paralysis.

- Central nervous system effects include nervousness, ataxia, apprehension, and seizures. Cattle and sheep commonly show severe CNS depression.

Organophosphorus-induced intermediate syndrome (no reliable reports in cattle).

- Myopathy syndrome of unknown pathophysiology affecting muscles of respiration, cervical, proximal limbs, neck flexor and facial muscles. This syndrome follows severe OP toxicity and persistent inhibition of acetylcholinesterase. Intermediate syndrome (IMS) is a well-described and common syndrome in human OP toxicity, but poorly described in animals, although it has been reported in cats and dogs.

July 2024

- This syndrome does not appear to have been reported in cattle.

Organophosphorus-induced delayed neurotoxicity (uncommon in cattle).

- Delayed neurotoxicity is characterized by distal degeneration of axons of both the peripheral and central nervous systems and involves phosphorylation and then ageing of neuropathy target esterase (NTE) in peripheral nerves.

- This organophosphate induced delayed neuropathy (OPIDN) has been described with Triaryl phosphates, Chlorpyrifos, Dichlorvos, Ethyl 4-nitrophenyl phenylphosphonothioate (EPN), Haloxon, Isofenphos, Leptophos, Methamidophos, Mevinphos, Mipafox, Parathion, Diisopropylphosphorofluoridate, Tetraethyl pyrophosphate, Trichlorfon and Trichloronat. These OP most commonly used as defoliants and herbicides have low acute mammalian toxicity but may induce (OPIN).

Clinical Signs of Toxicity.

With acute toxicity (most common form in cattle) there is a rapid onset of clinical signs (minutes to hours depending on the toxicity of the particular OP), following ingestion or inhalation of high concentrations. Primary signs include severe respiratory distress with laboured breathing, frequent urination with straining, meiosis, salivation, cyanosis, muscle fasciculation, bradycardia, convulsions and collapse. A grunting dyspnoea is usually the most prominent sign reported and is frequently audible from some distance, particularly when multiple animals are involved.

Death usually results from respiratory failure and hypoxia due to bronchorrhea (excessive bronchial mucous production) and bronchospasm and is the leading cause of death in cases of organophosphate toxicity in cattle.

In cases of organophosphorus-induced delayed neurotoxicity (OPIDN) clinical symptoms usually take at least 8 days, but more frequently up to 2 weeks to develop, although some cases only present 4 weeks after exposure. Symptoms are characterised by muscle weakness and ataxia progressing to flaccid paralysis.

Pathology.

In acute OP toxicity, OP only induce biochemical changes, in the absence of any morphologically visible tissue injury. Diagnostic pathological lesions are only observed histologically in peripheral nerves (demyelination), from cases of OPIDN.

Diagnosis of Toxicity.

Diagnosis is based on the history of known exposure to an organophosphate, consistent clinical signs, decreased AChE activity in EDTA blood (erythrocyte, plasma) or brain tissue and detection with quantification of the implicated organophosphate in rumen content.

AChE activity should be determined in RBCs and/or plasma from EDTA whole blood (live animals), or brain cortex (dead animals). Enzyme activity that is substantially inhibited (>50%) is confirmatory. Screening rumen contents for OP by gas chromatography-mass spectrometry (GC-MS) is helpful in the identification, confirmation, and quantitation of a particular OP. Blood, brain and rumen content samples should be held at 4 to 8°C following collection and during transport to the laboratory. Samples are frozen at the laboratory on receipt if they cannot be immediately analysed. Repeated freeze-thaw cycles degrade cholinesterase within samples.

On arrival at the laboratory whole brain, whole blood, plasma and rumen contents should be tested within 24-36 hours, otherwise, they should be frozen at -18ºC in a standard freezer, until they can be analysed (or at -80 °C if to be held for longer than 1 month). Red blood cell cholinesterase analysis needs to be performed immediately, as freezing lyses erythrocytes.

Treatment and Control in Outbreaks

Specific treatments for OP toxicity include atropine and the antidote pralidoxime (also called 2PAM) to reverse signs of organophosphate poisoning. Removing the source of the OP where feasible, should also be attempted. If the OP exposure was by topical skin application, animals should be washed with water and detergent to remove any residue.

Atropine acts as a non-competitive antagonist by blocking the effect of the muscarinic receptors on target organs. Atropine sulphate (0.1 mg/kg injected slowly intravenously followed by 0.4 mg/kg injected subcutaneously) and this is repeated as required, if clinical signs return, every 4 to 5 hours. Atropine does not reverse the nicotinic effects (tremors, twitching) of increased acetylcholine, but does block the muscarinic effects.

Oximes such as pralidoxime (2-PAM), accelerate the hydrolysis of the phosphorylated enzyme to reverse inhibition but have no effect on an 'aged' phosphorylated enzyme. So, this treatment modality is more applicable for carbamate toxicity (acetylcholine inhibition reversible) rather than OP toxicity (acetylcholine inhibition irreversible). In addition, the use of 2-PAM in cattle is often cost-prohibitive.

Long-term effects of OP in cattle herds include a reduction in milk yield which may take months to recover, and semen production can be reduced in bulls.

Public health considerations.

Outbreaks of OP toxicity may have food safety implications for meat and milk. Food safety implications are compound dependent and assessment should always be carried out by the relevant authorities.

Further Reading.

1. Boermans H.J. et al. Terbufos Poisoning in a Dairy Herd. *Canadian Veterinary Journal*. 25: 335-338 (1984).
2. Gupta R.C. & Doss R.B. Delayed Neurotoxicity from Triaryl Phosphates and Other Organophosphates and Carbamates in

Animals. *MSD Veterinary Manual.* https://www.msdvetmanual.com/toxicology/insecticide-and-acaricide-organic-toxicity/delayed-neurotoxicity-from-triaryl-phosphates-and-other-organophosphates-and-carbamates-in-animals (2022).
3. Gupta R.C. & Doss R.B. Organophophate toxicosis in animals. *MSD Veterinary Manual.* Organophosphate Toxicosis in Animals - Toxicology - MSD Veterinary Manual (msdvetmanual.com). (2022).
4. Hamernick K.L. TERBUFOS 333–385. Joint Meeting Pesticide Resistance. *Office of Science Coordination and Policy, United States Environmental Protection Agency Washington DC, USA* (2003).
5. Khan O. Organophosphate poisoning in a group of replacement heifers and dry cows. *Canadian Veterinary Journal* 42: 561-3. (2001).
6. Mostrom M. Pesticides and rodenticides. *In:* Smith B P, Van Metre D C & Pusterla N (eds). *Large Animal Internal Medicine* 6th ed. Elsevier, St. Louis. (2020).
7. Sharpe R T, Livesey C T, Davies I H, Jones J R & Jones A. Diazinon toxicity in sheep and cattle arising from the misuse of unlicensed and out-of-date products. *Veterinary Record* 159: 16-19. (2006).
8. Vermunt J J, Malmo J & Parkinson T J. Causes of sudden death. *In*: Parkinson T J, Vermunt J J, Malmo J & Laven R (eds). *Disease of Cattle in Australasia* 2nd ed. Massey University Press, Auckland. (2019).

QUESTION 1

Which of the following statements about organophosphate poisoning in cattle is incorrect?

a. Organophosphates are more readily absorbed after cutaneous exposure, than with ingestion or inhalation
b. Acetylcholinesterase results in over accumulation of the neurotransmitter acetylcholine
c. Acetylcholine over-stimulates nicotinic receptors
d. Acetylcholine over-stimulates muscarinic receptors
e. Acetylcholine over-stimulates the central nervous system

QUESTION 2

Which of the following clinical signs of organophosphate poisoning is not a muscarinic effect?

a. Dyspnea
b. Miosis
c. Muscle tremors
d. Salivation
e. Frequent urination

QUESTION 3

Which of the following is not known to contain cholinesterase?

a. Erythrocyte
b. Plasma/serum
c. Liver
d. Pancreas
e. Kidney

QUESTION 4

Which of the following clinical signs would not be considered a central nervous system effect of organophosphates passing through the blood-brain barrier?

a. Ataxia
b. Flacid paralysis
c. Depression
d. Seizures
e. Apprehension

QUESTION 5

What is the most significant organ affected by the organophosphate-induced intermediate syndrome?

a. Neuropathy
b. Myopathy
c. Encephalopathy
d. Hepatopathy
e. Nephropathy

QUESTION 6

In cattle suffering from acute organophosphate poisoning, what is the most common cause of mortality in these animals?

a. Respiratory failure
b. Convulsions
c. Bradycardia
d. Paralysis
e. Heart failure

QUESTION 7

In organophosphate-induced delayed neuropathy, what is the most common delay period following exposure to the appearance of clinical signs?

a. One to 2 days
b. 3 to 5 days
c. 8 to 14 days
d. 2 months
e. 4 months

QUESTION 8

Which is the only diagnostic histopathology lesion that has been described in some cattle with organophosphate poisoning?

a. Pulmonary alveolar wall necrosis in acute toxicity
b. Retinopathy of the eye in acute toxicity
c. Polioencephalomalacia of the brain and acute toxicity
d. Myocardial necrosis in acute toxicity
e. Peripheral nerve demyelinization in organophosphate-induced delayed neuropathy

QUESTION 9

At what temperature should EDTA blood samples and fresh brain tissue samples, be transported to the laboratory for acetylcholine esterase analysis?

a. -80°C
b. -18°C
c. 0 to 2°C
d. 4 to 8°C
e. Room temperature

QUESTION 10

Which of the following statements about the treatment of organophosphate toxicity in cattle is incorrect?

a. Atropine blocks the effects of muscarinic receptors on target organs
b. Atropine therapy may be repeated every 4 to 5 hours if clinical symptoms return
c. Atropine does not reverse the nicotinic effects of increased acetylcholine
d. Oxime 2-PAM reverses the inhibition of aged, phosphorylated acetylcholinesterase
e. The use of 2-PAM in organophosphate poisoning in cattle is cost-prohibitive and ineffective

SAVC CPD Accreditation Code:
AC/1788/24
To answer the questions and obtain your CPD points for this article visit the Online On Demand Journals page on www.veted.online