# Livestock Poisoning Diagnostic Manual Online Version

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**This part translated the Livestock Poisoning Diagnostic Manual Online Version drew by Safety Research Team of National Institute Animal Health, with their permission.**

# Introduction

**What is Poisoning?**

“Poisoning (toxicosis) is the impact on health as manifests as specific pathology when a toxic chemical substance enters a living organism. Studies of toxic substances belong to Toxicology, while studies of pathology and treatment belong to Clinical Toxicology. However in a wider context, these studies also come within the realms of Internal Medicine, Microbiology and Pathophysiology. On the other hand, its relation to Pharmacology may be said a double edged razor, because if the changes are deemed caused by a medicine, it is handled by Pharmacology, while changes are deemed caused by a poison, it is studied carefully by Clinical Toxicology. In this case poison is medicine and medicine is poison.” (Tokutaro Okawa “Clinical Toxicology in Livestock”)

Substances causing poisoning (toxins) are defined as those exert harm at relatively small quantity and, are toxigenic when taken in via a normal course of intake (oral, respiratory, trans-dermal) ; and do not have organs, structure, or life functions as bacteria, etc, do.

In any case whether a chemical substance causes poisoning or not depends on the quantity of intake.

“Dosis sola facit venenum (Dosage alone makes the poison)” (The maxim by Paracelsus)

# ●Fundamentals of Diagnosis of Poisoning

**Disease diagnosis, let alone diagnosis of poisoning, must be comprehensively conducted based on a variety of data.**

**○Accurate understanding of clinical conditions**

**○Detailed investigation of situations leading to outbreak**

Unlike the infectious diseases, systematic differential diagnosis of poisoning is difficult. Therefore possible causes need to be narrowed down based on clinical conditions and the situations leading to outbreak. Consequently not only the understanding of characteristic pathological signs, but also detailed investigation to determine the type and position of livestock barn, existence of weeds and trees, the source of feeds given, timing of change of feeds if it was done, state of feed storage, feed contamination, existence of spoilage, use of agricultural chemicals or not, etc

**○Adequate sampling of specimens for diagnostic purposes**

Usually the first course of diagnostic actions of livestock illness is to suspect an infectious disease. This practice often leads to inadequate material collection for diagnosis of poisoning. In the cases in which the nature of incident is poisoning or not is unclear, it is important to collect and store necessary materials. Important matters when collecting and storing, is to store the specimens in clean containers, avoid use of preservative, immediately freeze live material immediately after collection, and so forth.

Feed: Collect and store the feed given at time of the outbreak. Refrigerate or freeze about 2 kg or more. Make sure to freeze the ones with higher moisture content.

Blood: Collect specimens for toxin analysis separate to those for the biochemistry studies. If in a case such as forensic killing in which it is possible to collect a large amount of blood, take as much as possible and cryopreserve

Urine: For some toxins, urine analyses are effective method. Cryopreserve

Various organs: Aside from the specimens for pathology and histology studies, collect liver, kidney and other major organs and organs with lesions should be collected and cryopreserved.

Stomach content: Collect as much as possible (500 g or more) and cryopreserve

Feces: Cryopreserve

Vitreous humor: Cryopreserve

**○Collection should be carried out as soon as the outbreak is confirmed**

(feed, blood, etc from the animals showing signs as well as the normal animals in the same housing)

**○Materials collected after the outbreak was controlled are also important**

**○Table of material to be collected**

Quantity, method of storage; for blood, also include the information about anticoagulant, etc,

## ＜ Pathological diagnostic ＞

In cases of acutely progressed poisoning, often characteristic morphological changes are not seen, but still may provide important data helpful in speculating site of toxic action and character of the toxin. At autopsy, stomach and intestines it is need to be examined for foreign object and residue of poisonous plant in stomach and intestines.

## ＜ Physicochemical diagnostic ＞

In cases of acutely progressed poisoning, characteristic results are often not obtained from biochemistry studies of blood. However, depending on the cause of poisoning, the results of blood biochemistry studies may provide an important clue. Therefore the general blood biochemistry studies are important items in the diagnostic studies.

Final diagnosis of poisoning is reached by detection and identification of the toxin. However various limitations often prove detection and identification of the toxin to be impossible.

How to conduct analyses of agricultural chemicals, heavy metal, mycotoxin, etc, in the feeds are stipulated by “Feed Analyses Standards” (Notice by Director General of Food Safety and Consumer Affairs Bureau, Ministry of Agriculture, Forestry and Fisheries). In cases such analyses are needed to diagnose poisoning, it is desirable to conduct analyses according to the Standards. With regard to other known toxic substances, refer to “Methods of Analysis in Health Science” (Kanehara-shuppan), “Chemical Analyses of Drugs and Toxins” (Nanzando), “Official Methods of Analysis of AOAC INTERNATIONAL”, and others. Other than those, there are rapid testing kits available for some toxins.

**Examples of rapid testing kits**

Nitrate Nitrogen: RQ Flex and “*Merukokuanto*” testing paper (from Kanto Chemical)

Major Mycotoxins: ELISA kit (AZmax, Air Brown, etc)

Cyanic ion: Wako (Cyan testWako)

Glufosinate: Qualitative kit (Aventis Crop Science Japan)

Organic phosphate based agricultural products: Organic phosphate product detection kit (Kanto Chemical); Kit Safe AT-10 (AZmax)

In cases where identification of the toxin is very difficult, it may be effective to see existence of toxicity by inoculating the collected feed or digestive tract content (or extract of it) to laboratory animals such as mice.

# ● Fundamentals of Toxicology

**○Absorption, distribution, metabolism and elimination of substance**

As most toxins are foreign to the living organism, they are often absorbed by passive diffusion.

**○Cell membrane consists of two layers of lipids**

The speed of passing across the membrane is determined by the concentration gradient of toxin in and outside of the membrane and by the partition coefficient of the toxin against the membrane lipids and water.

Non-polar lipid soluble substances easily pass across the cell membrane, while highly polar water soluble substances do not pass easily.

Generally non-dissociated molecules are highly lipid soluble, therefore with regard to weak acid or base molecules, ion types do not easily pass through while the non-dissociated do.

Weak acids in the acidic side and weak base in the alkaline side both have a higher proportion of non-dissociated molecule

Weak acids are mainly absorbed in stomach, while weak bases are absorbed in the small intestines.

Toxins absorbed from the digestive tract pass the liver, where they are detoxified or, in some cases, activated in the process of metabolism.

Distribution of absorbed toxins inside body is not uniform

Tissue distribution of toxin is determined by permeability of membranes that divide blood and tissue, degree of bonding with the components (proteins, nucleonic acids, etc) in blood and/or tissue, and existence of barriers between blood and tissues (blood – brain barrier; blood – testis barrier, blood – fetus barrier, etc)

When toxins are metabolized in the liver, they become water soluble so that can be eliminated to outside body.

Numerous enzymes are involved in metabolism of toxin, and, generally called drug metabolism enzymes

Toxins are metabolized through the phase I and phase II reactions

Phase I reactions may occur by oxidation, reduction and/or hydrolysis, involving enzymes such as the cytochrome P450 enzyme

Following Phase I, Phase II reactions involve conjugation reactions with glutathione, glucuronic acid, sulfonates, etc, which increase water solubility further

Generally herbivores have higher capacity to metabolize drugs (toxins) than carnivores

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