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## **Accidental poisoning with the Lindane pesticide in a few rabbit**

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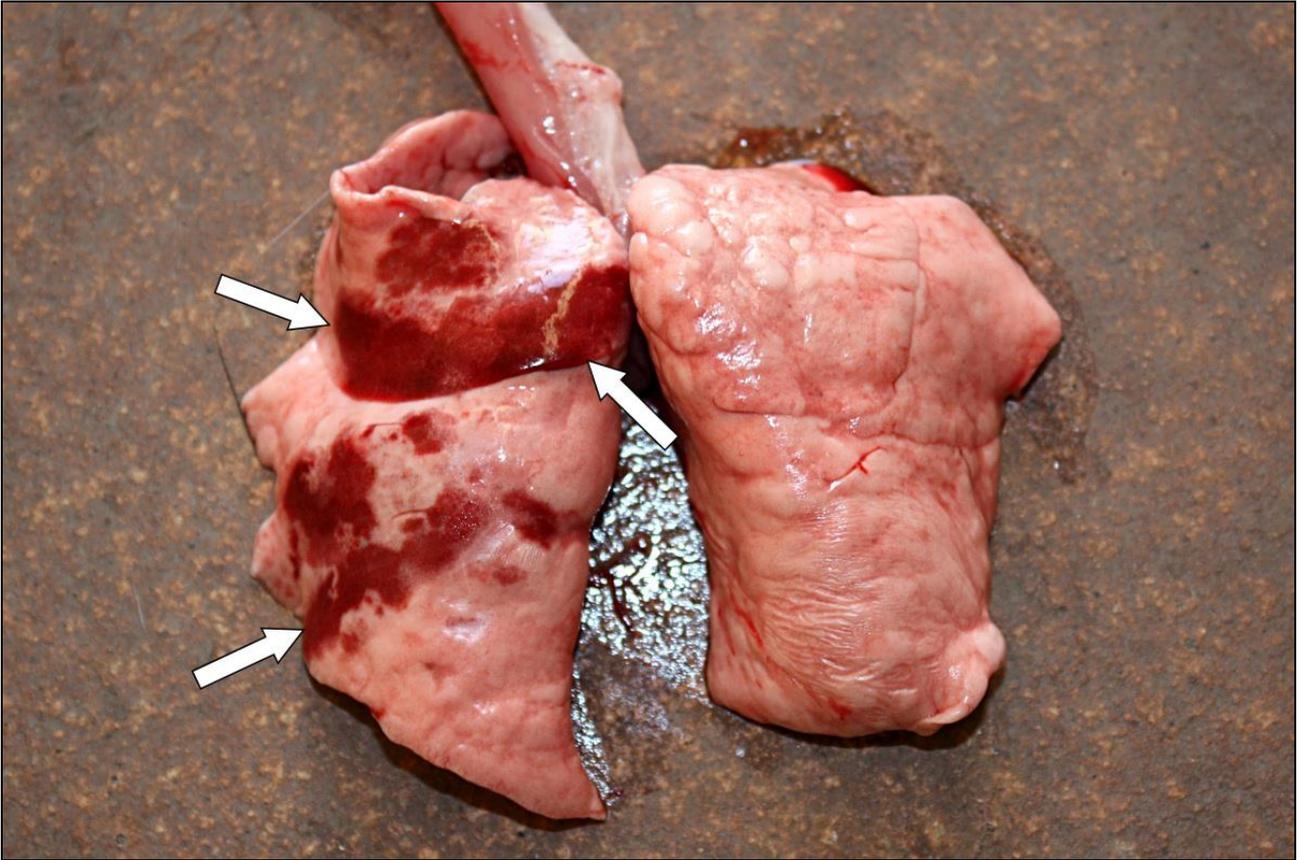
**Lindane is a pesticide, isomer of hexachlorocyclohexane, synthesized from benzene and chlorine. In spite of its toxicity on living organisms, it has been commercialized all over the world since 1938.**

Lindane possesses a broad insecticide spectrum; therefore it is used both in agriculture, to treat seeds, leaves of trees or

livestock, as well as in pharmaceutical products in order to treat mites responsible for scabies and lice. Today lindane has been



**Figure 1:** Paralysis of the hind limbs and swelling on the back in a rabbit after it accidentally ate apples treated with the lindane pesticide.



**Figure 2:** During the autopsy, lungs show multifocal hemorrhagic foci.

banned in more than 50 countries.

In animals and humans, the pesticide is quickly absorbed through the skin, is inhaled as particles or fumes, or is ingested with contaminated food or drinking water. Its elimination by the urine is relatively fast.

Since 1953, negative effects of lindane have been observed in mammals and man. The presence of different isomers of lindane in the blood leads to their distribution in the adipose tissue and, to a lesser extent, in muscles, the nervous system and brain, the mucous membranes of the respiratory airways and lungs, the cardiovascular system, digestive organs such as the liver and spleen, kidneys, and endocrine glands such as the pituitary and thyroid glands (Ejobi et al, 1996 Schoula et al., 1996; Siddiqui et al, 1981; Baumann et al., 1980).

Lindane can also cross the placenta and is found in breast milk (Saxena et al., 1981). Its effect on metabolism is extensive.

#### **Neurotoxic effects**

Lindane is a potent neurotoxin that interferes with  $\gamma$ -aminobutyric acid, GABA, a neurotransmitter of the central nervous system in mammals and man, which acts on the ionic channels of the GABA-A receptor in order to regulate the conduction of the chlorine, sodium and potassium fluxes (Abalis et al., 1985; Anand et al., 1998; Casida and Lawrence, 1985; Lawrence and Casida, 1984; Pomès et al., 1994). Exposure to high concentrations of lindane causes neurological disorders such as convulsions, dizziness, and seizures as well as changes the electrical activity of the brain (EEG abnormal rhythm).

Lindane has additional effects on other organs.

### **Hemato- et immunotoxic effects**

Lindane is hematotoxic. It acts on the bone marrow and inhibits the hematopoietic system. This can lead to modifications in the composition of the blood (blood dyscrasia): leukopenia, leukocytosis, granulocytopenia, hyper-eosinophilia, lymphopenia, thrombocytopenia. After an initial stimulation, lindane causes a suppression of the immune system, rendering people more susceptible to disease.

### **Endocrine anomalies**

Lindane induced endocrine abnormalities by interfering with the levels of hormones in human beings. Sperm count is reduced. It seems also to mimic the action of estrogen, the female sex hormone. In pregnant animals, lindane can induce resorption of fetuses and/or abortions.

### **Hepatotoxic effects**

Exposure of liver cells to lindane causes an increase in liver enzymes. Centrilobular liver hypertrophy is dose dependent. Various studies suggest that the hepatotoxic effects of lindane are more severe in humans than in animals.

### **Renal toxicity**

Exposure of renal cells to lindane does not cause toxic effects or impaired renal function, except in rats (Dietrich and Swenberg, 1990, 1991).

### **Carcinogenic effects**

A further detrimental effect of lindane seems to be the development of cancer, including Hodgkin's lymphoma, liver and breast cancer. Specific studies are, however, lacking and were unable to conclude that lindane is carcinogenic.

### **Toxic effects of lindane in rabbits**

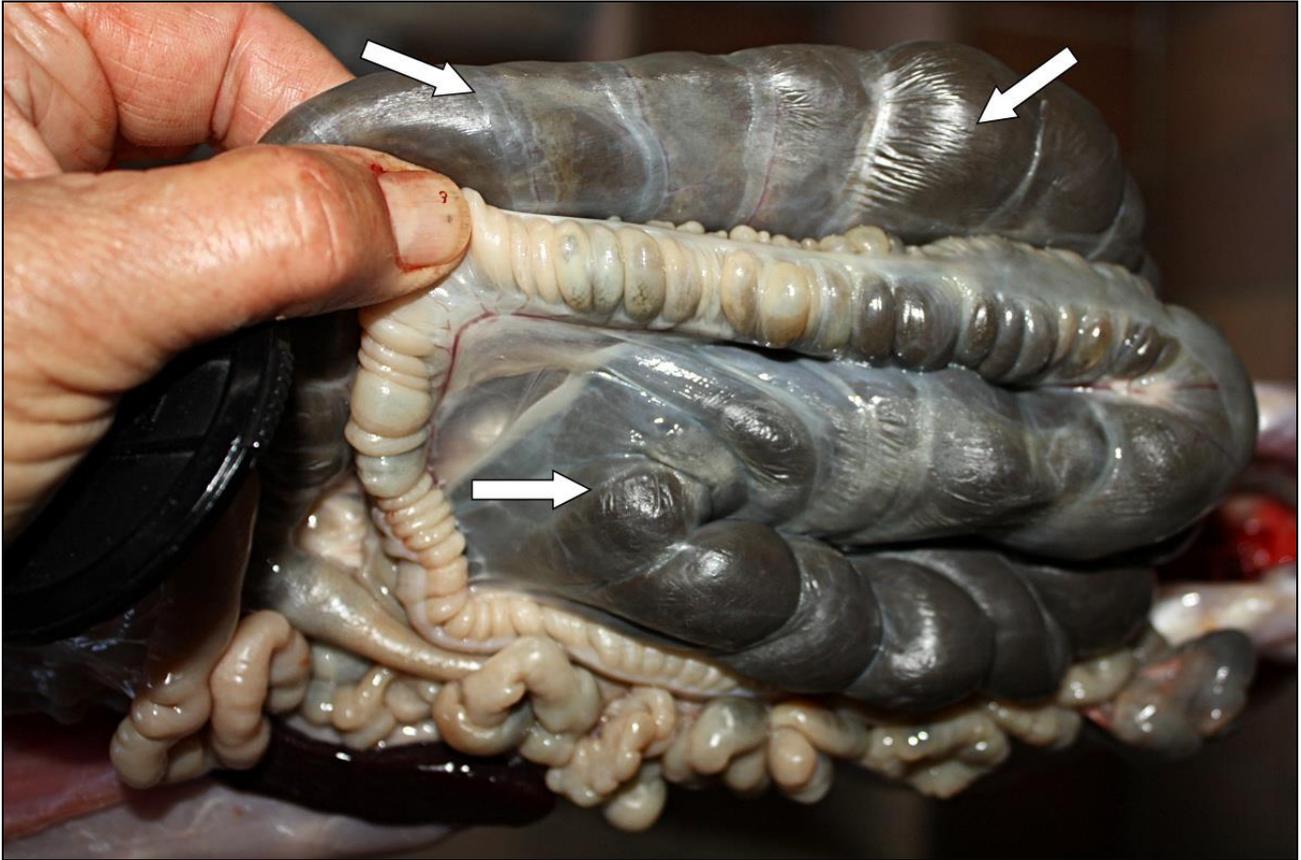
Effects of an acute poisoning depend on the age of the rabbit, young rabbits being

most affected, and the state of health and nutrition of the animal. The nervous system is mainly affected, with the appearance of neurological disorders that result in hyperactivity and hypersensitivity, tonic-clonic convulsions and paralysis of the hindquarters (Figure 1). These disorders precede a depression of the nervous system sometimes accompanied by coma or death of the animal. Other signs include difficult breathing, diarrhea, hypothermia and nasal bleeding (epistaxis). At necropsy, anomalies were observed in the lungs, liver (localized degeneration of hepatocytes, cellular hypertrophy, fatty degeneration) and kidneys (glomerulonephritis) (Grabarczyk et al., 1990-Szlezak Kopec et al. 1989) (Figs 2, 3).

When a rabbit is exposed to chronic poisoning of lindane, it becomes apathic and loses weight. In female rabbits, the anti-estrogen action of lindane causes a decrease in fertility and ovulation either by mimicking the action of estrogen on the hormone receptors, or by interfering with the progesterone receptor (Lindenau and al., 1994). In pregnant females, the risk of fetal resorption or miscarriage is increased. Some fetuses exposed to lindane have a supernumerary rib, but teratogenic effects of the pesticide have nonetheless been excluded (Palmer et al., 1978a).

When the chronic exposure to lindane is stopped, a significant but transient increase in liver enzymes (alkaline phosphatase (ALP), alanine aminotransferase (ALT) and aspartate aminotransferase (AST)) is noted. They return to normal values between 7 and 14 days after the end of exposure while pesticide residues are still measurable in the blood (Ceron et al., 1995).

The median lethal dose (LD50) of lindane in rabbits depend on the route by which it enters the body. The LD50 ranges between 40 and 200 mg/kg for an oral doses, while dermal exposure ranges from 50 mg/kg to



**Figure 3:** The caecum of a poisoned rabbit looks dried out, as in case of enterocolitis.

4000 mg/kg depending on the type of product applied on the skin.

### **Treatment**

Contaminated food should be removed. There is no treatment against lindane poisoning in rabbits. Nevertheless, the treatments applied in humans can be used.

Poisoning through the digestive tract are the most dangerous. The rabbit must be constantly monitored. The depression of the central nervous and respiratory systems prevents the immediate administration of activated charcoal or cholestyramine resin that helps neutralize the pesticide and promote its elimination from the digestive system. If no neurological disorder is observed after one hour, these products can be given to the rabbit.

A control of seizure may be attempted with the administration of antiepileptic drugs

such as benzodiazepines or second-line drugs such as barbiturates or propofol. Phenytoin is ineffective in the treatment of organochlorine pesticide poisoning.

If the rabbit suffers from ventricular dysrhythmia caused by lindane, it is imperative to administer beta-adrenergic agents and magnesium, but not adrenaline. This helps reduce the effect of endogenous catecholamines secreted by the adrenal glands on the heart muscle.

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