



ISSN NO. 2320-5407

Journal homepage: <http://www.journalijar.com>

INTERNATIONAL JOURNAL  
OF ADVANCED RESEARCH

## RESEARCH ARTICLE

## Cases of chronic intoxication with Poison Hemlock (*Conium maculatum*) in calves

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### Manuscript Info

#### Manuscript History:

Received: 10 February 2014  
Final Accepted: 12 March 2014  
Published Online: April 2014

#### Key words:

Hemlock (*Conium maculatum*),  
Multiple congenital contractures,  
calves.

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### Abstract

Clinical observations of 20-year duration (1993 to 2013) on chronic intoxication with Poison Hemlock (*Conium maculatum*) in newborn calves are described. This type of intoxication is manifested by birth of calves with multiple congenital contractures (MCC) of fore limbs during the autumn-winter period (most commonly in November and December). The effect of immobilization of limbs by splints is investigated, and the course of disease is monitored. The present survey was made on the basis of several sporadic cases (n=14) and one massive outbreaks (n=8).

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### Introduction:

The related malformations caused by poison hemlock have been described in calves, piglets, kits, and lambs: at birth they show multiple congenital contracture (MCC), scoliosis, torticollis, cleft palate, and excessive flexure of the carpal joints (Panter et al., 1990, 1992; López et al., 1999; Vetter, 2004). These injuries were reproduced experimentally to cows during the 55–75 days. The piperidine toxins from poison hemlock induce in livestock reduction of fetal movement and fetal malpositioning and produce a similar sedative and anesthetic effect on the fetus (Panter et al., 1992; López et al., 1999; Panter and Stegelmeier, 2011). Since the piperidines behave in a specific way and are teratogenic, they also fulfill specific criteria for teratogenesis (López et al., 1999; Vetter, 2004; Binev, 2008; Panter and Stegelmeier, 2011). The birth defects caused by *Conium maculatum* are the same, and their biological activities occur by a similar mechanism of action (López et al., 1999; Binev, 2013). As usual with biological active compounds one use to characterize the toxicity into acute and chronic forms. The peripheral actions of coniine are similar to those of nicotine, but it produces more pronounced paralysis of the central nervous system and of the skeletal muscle nerve (Panter et al., 1992; Binev, 2008, 2013).

### Case history

Clinical observations of 20-year duration (1993 to 2013) on chronic intoxication with Poison Hemlock (*Conium maculatum*) in newborn calves are described. This type of intoxication is manifested by birth of calves with multiple congenital contractures (MCC) of fore limbs during the autumn-winter period (most commonly in November and December). The effect of immobilization of limbs by splints is investigated, and the course of disease is monitored. The present survey was made on the basis of several sporadic cases (n=14) and one massive outbreaks (n=8).

We have observed birth of calves with multiple congenital contractures (MCC) of fore limbs during the autumn-winter period (most commonly in November and December) over 20 years (1993 to 2013). The clinical surveys were performed in cattle farms in the southern part of the country. Several sporadic cases (n=14) and one massive MCC outbreak (n=8) are described. The history showed that during the pregnancy, cows grazed on pastures, including at location with profuse growth of the toxic plant poison hemlock (*Conium maculatum*). In all cases, cows were in the second or third month of pregnancy.

In all instances, MCC symptoms appeared first immediately or up to 1–2 hours after the birth, during the first attempts for standing up and walking. Most frequently, the animals were able to stand up on their hind limbs, but not on fore limbs. A generalised tremor of the body was established. The animals did not respond to pinprick in the

interdigital cleft (lack of sensitivity). After repeated attempts, the animals staggered and fell on the ground. Newborn calves preferred to lie down with their fore limbs flexed under the trunk.

The clinical parameters were within the reference values, and the appetite – preserved. The suckling reflex in most calves with MCC was preserved. Until the 10<sup>th</sup> day after the birth, MCC signs became so strong that the normal position of metacarpal joints could not be assumed (ankylosis) (Fig. 1) despite of applied efforts (Fig. 2).

Until the 10<sup>th</sup> day after the birth, calves refused bear weight on claws, and instead walked on metacarpal or metatarsal joints, assuming a kneeling posture. Afterwards, due to increased muscle mass, the animals succeeded to maintain a standing position, bearing weight only on the toes of fore limbs (Fig. 3).

In the massive outbreak, calves were born with malformations over 3 to 4 weeks, in November, and after that time, no data for the teratogenic effect of poison hemlock alkaloids could be observed.

In some calves (n=5) joints were immobilized with wooden splints 2-3 days after the birth. These patients exhibited weight bearing while moving on toes of their feet on the next day, but the gait were still uncertain and stiffed.

Calves whose feet were not splinted, began to rose on fore limbs about the 10<sup>th</sup> day after the birth and managed to stand, bearing weight on the toes of their hooves and to make their first steps/ The status improved with each subsequent day and about 4 weeks of age, the animals could bear weight on the entire hoof surface. After 5-6 weeks of age, MMC signs have disappeared.

The calves with splints exhibited improvement as early as the next day, beginning to bear weight on the toe or the major part of fore limbs' hooves. The improvement, however, was only short-time and by the 3<sup>rd</sup> day after splinting, the animals refused again to stand up. In two calves, an unpleasant odour from the site of splinting was established, due to the developing moist gangrene. That is why, splints were removed which resulted in fast improvement of metacarpal joints posture. The complete recovery occurred only a week later as compared to calves, whose joints were not fixed.

## Discussion

We assume that the observed cases of MCC in newborn calves were due to the teratogenic effect of poison hemlock (*Conium maculatum*) alkaloids. This hypothesis was supported by the fact, that in Bulgarian lowlands the acute intoxication with poison hemlock is most commonly observed in March and April, while in mountainous and semi-mountainous regions – from April to June. The seasonal pattern is due to the prolific growth of the green toxic plant and the scanty grass vegetation on pastures by that time (Binev, 2001, 2008, 2013; Binev et al., 2007). Having in mind that embryos were most sensitive to the teratogenic effects of piperidine alkaloids about the 2<sup>nd</sup> and the 3<sup>rd</sup> foetal months (Panter et al., 1990, 1992, 1999, 2013) the observed cases of MCC could be attributed to chronic intoxication with poison hemlock (*Conium maculatum*).

The molecular structure determines the teratogenicity (chronic toxicity) of *Conium maculatum* alkaloids. The side chain must be a propyl group or larger. For instance, 2-ethylpiperidine has been shown to be nonteratogenic. Partial unsaturation seems to increase toxicity since coniceine is more toxic than coniine, while 2-propylpyridine is nonteratogenic, i.e., aromatization of the ring suppresses toxicity. The piperidine toxins from poison hemlock induce in livestock (Panter et al., 1992; James et al., 2004; Binev, 2013). The most distinctive action of the three other hemlock alkaloids (coniine,  $\gamma$ -coniceine, N-methylconiine) plus nicotine is their ability, provided the dose is small, to inhibit the crossed extensor reflex and the so-called knee-jerk by an action potential in the spinal cord. Since neurons in the spinal cord may both be inhibited and activated by the action of hemlock, the mechanisms involved are a bit complicated. If the alkaloids initially stimulate inhibitory neurons rather than blocking excitatory ones, the antagonistic relationship of the two substances may be explained. There is evidence that its central synapse is controlled by polysynaptic inhibitory pathways, although the patellar reflex is monosynaptic (López et al., 1999; Reynolds, 2005; Binev, 2013). It is possible that the *C. maculatum* piperidine alkaloids may act upon the mechanism that regulates the amniotic liquid, adding to the production of malformations. Lack of fetal movement, whatever its origin, can also cause limb malformations (Swinyard and Bleck, 1985; Panter and Stegelmeier, 2013). The MCC is caused by loss of muscle mass with imbalance of muscle power at the joints which provokes a collagenic response consisting of partial replacement of muscle volume and collagenous thickening of the joint capsules, the latter leading to joint fixation (López et al., 1999).

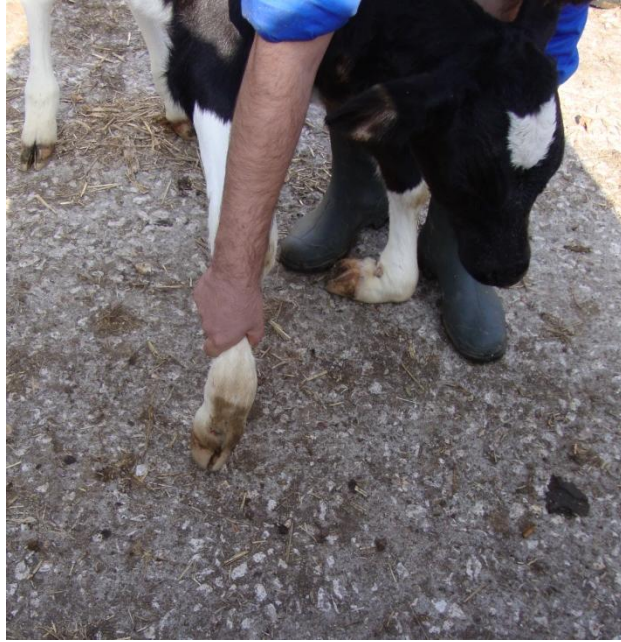
It should be noted that about the 10<sup>th</sup> day after the birth of calves, MCC signs became more pronounced, and afterwards they were followed by spontaneous remission lasting 3-4 weeks. On 6-7 weeks of age, the malformations disappeared on their own. Therefore, immobilization of joints by splints or plaster casts is not recommended, as they interfere with the spontaneous recovery.

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**Fig. 1. Multiple congenital contracture in calves. Chronic intoxication with Poison Hemlock (*Conium maculatum*).**



**Fig. 2. Inability to maintain normal metacarpal bones position in a 10-day-old calf with Multiple congenital contracture. Chronic intoxication with Poison Hemlock (*Conium maculatum*).**



**Fig. 3. Weight bearing on toes of fore limbs in a 10-day-old calf with Multiple congenital contracture. Chronic intoxication with Poison Hemlock (*Conium maculatum*).**