NITRITE INTOXICATION IN PIGS

Nitrietintoxicatie bij varkens

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ABSTRACT

Nitrite intoxication is known to be a cause of methemoglobinemia in several species. This article describes three cases of acute mortality caused by massive ingestion of nitrite by pigs raised on commercial farms. Bacterial contamination of drinking water with subsequent nitrite formation was identified as the cause of the methemoglobin formation. The present study indicates that still standing drinking water within the water systems of modern pig farms constitutes a risk for nitrite intoxication.

SAMENVATTING

Nitrietintoxicatie wordt bij verschillende diersoorten beschreven als oorzaak van methemoglobinemie. Dit artikel beschrijft drie gevallen van acute sterfte bij varkens tengevolge van massale nitrietopname. Een bacteriële verontreiniging van het drinkwater met vorming van nitriet was verantwoordelijk voor de methemoglobinemie. Deze studie belicht het risico op nitrietintoxicatie door stilstaand water in de leidingen, zelfs in de moderne varkenshouderij.

INTRODUCTION

Nitrate or nitrite ingestion is a cause of methemoglobinemia in animals and humans (Buck *et al.*, 1976; Fan and Steinberg, 1996). Nitrate, from which the toxic nitrite is formed, is commonly found in plants, fertilizers and animal wastes (Buck *et al.*, 1976). High nitrate levels in water can originate from heavy applications of nitrogenous fertilizers to land or from the contamination of runoff water by animal wastes (Wendt, 1985). Monogastric animals seem to be quite tolerant to nitrate, whereas ruminants are more susceptible because of the substantial transformation to the more toxic nitrite by the ruminal flora (Buck *et al.*, 1976). In pigs, Sørensen *et al.* (1994) concluded that weaned piglets and growing pigs could tolerate at least 2000 ppm nitrate in the drinking water. By contrast, single oral doses of nitrite above 20 mg/kg (Muirhead and Alexander, 1997) or 70mg/kg (Wendt, 1985) are considered to be lethal.

Methemoglobin is formed when nitrite oxidizes the Fe^{2+} ion within the hemoglobin molecule to Fe^{3+}, thus inhibiting the oxygen binding capacity (Wendt, 1985). The resulting degree of tissue anoxia correlates with the percentage of methemoglobin formation and accounts for the symptoms, which range from restlessness and dyspnea to coma and death (Wendt, 1985).

Most reports on nitrite intoxication in pigs mention the oral uptake of contaminated water originating from a source of still water used to feed or drench the pigs. Rain water, with excessive alga and decaying leaves in open troughs or reservoirs (Hoorens and Thoonen, 1961; Gibson, 1975), combined with a period of drought (Counter *et al.*, 1975) was identified as a source of nitrite. Even soaked ceiling material acted as a source of nitrite (McParland *et al.*, 1980) in methemoglobinemia in fattening pigs. These reports described small farms with manual water supply from an open well or reservoir to each pen. The present study

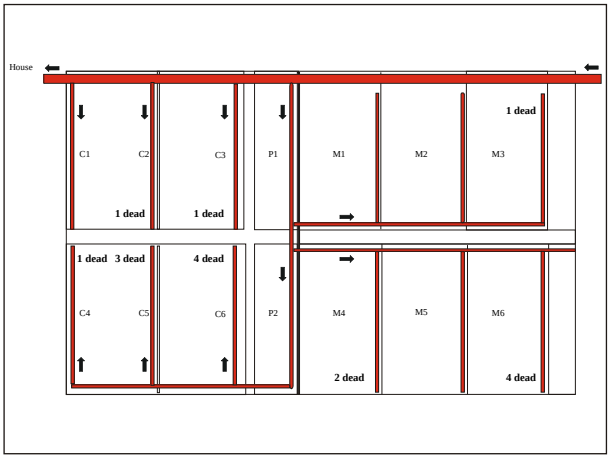

Figure 1. Water circuit and number of dead animals at each branch in case 1. The direction of the water flow is indicated with arrows. Four branches bring the water from the main pipe to the animals. C: row of individual cages; P: pens; M: farrowing unit.

Figure 2. Macroscopic necropsy findings of a growing pig that died from nitrite intoxication. Blood and tissues are characterized by a brown color due to the presence of methemoglobinemia. Notice the normal color of the pig that was not affected by nitrite intoxication (upper right).

describes three cases of nitrite poisoning in modern housing facilities, where nitrite was formed within the water distribution system of the farm itself.

CASE DESCRIPTION

Case 1

To enable the construction of a new building for a breeding herd, in November 2000 a pig producer moved 140 sows to another location, a sow facility that had been empty for 6 months and that was not cleaned prior to the arrival of the sows. The sows were housed in individual crates with individual trough and nipple. They were transported in two groups. The first group consisted of recently weaned sows and sows in early gestation; the second group consisted of sows in late gestation. Upon the arrival of the second group, 3 hours after the arrival of the first group, several sows, (most of them weaned) were found dead. Within 1.5 hours, several sows of the second group also died, mostly without clinical symptoms. One sow showed excitation before death and four sows were seen vomiting. Two hours after the arrival of the second group, mortality seemed to stop, but at feeding time, an hour later, another seven sows died. The veterinarian noticed that the conjunctivae and the mucosa of the vulva of all the dead sows, and of some of the others, were cyanotic. Due to the suspicion of nitrite intoxication, all troughs and water pipes were emptied.

Post-mortem examination of two of the sows two days after mortality, revealed no significant macroscopic lesions. Nitrite levels in the stomach of the sows were 570 and 1810 mg/L, respectively. In the troughs, nitrite levels ranged between 1610 mg/L and 2430 mg/L. A water sample taken when the mortality had stopped after the water system was emptied had a nitrite level of 0.03 mg/L.

Figure 1 illustrates the water circuit in the stable. Water from the public water supply entered the stable on one end and passed through the sow units. Four branches brought the water to the animals. Mortality was highest at the longest end pipes (C4, C5, C6, M4, M3 and M6), where the animals had access to the longest contaminated water column. Mortality after feeding was highest in the recently weaned sows (C5, C6), probably because they had not been fed in the morning before the move and because they were thirsty.

Case 2

In December 2001, a housing unit for 790 pigs in a fattening herd of 5000 pigs was filled in a two-day period with 22 to 25 kg growing pigs. On the second day, 185 pigs from the same origin arrived and were housed in rows 3 and 4. Within a few hours, 20 (11%) of them died, mostly without symptoms, sometimes with nervous signs such as paralysis, muscle weakness and lateral recumbency. At first, the mortality was related to the fact that the piglets originated from the same herd, but when mortality continued, the herd veterinarian was called. Brown discoloration of the nose and cyanosis of the conjunctivae were noted. Nitrite intoxication was suspected and diagnosed by examining the drinking water with urine strips containing a nitrite

test field (Combur 10 test, Roche Diagnostics, Vilvoorde, Belgium).

On post-mortem examination, brown discoloration of the blood, indicating severe methemoglobinemia, was the single, striking feature (Figure 2). The nitrite levels in the stomachs of 3 piglets were 49, 164 and 1420 mg/L, respectively.

Mortality occurred in several pens in rows 3 and 4, at the end of the water distribution system. Because of the quick diagnosis and the subsequent emptying of the water pipes, mortality stopped immediately. The observation of the black color of the water drained from the tubes in several pens was a confirmation to the owner that further mortality was prevented by emptying the pipes.

Case 3

A farm with 300 sows and 660 fattening pigs had sold piglets at 22 kg during a period of several months in an attempt to eradicate Aujezky's disease virus. In July 2003, a compartment was filled with 159 growing pigs of approximately 22 kg after it had stood empty for a period of two months. One and a half hours after feeding (dry feeding with a separate nipple away from the feeder), several piglets were found dead. They were immediately sent to the laboratory for necropsy and further analysis.

The brown color of the organs and the blood was prominent. The nitrite level in the stomach of one piglet was 800 mg/L, while the nitrate level was 700 mg/L. On the basis of the post-mortem findings, instructions were given to empty the water pipes immediately, after which mortality stopped.

In this compartment, the water passed through an open barrel equipped with a float. Neither the compartment nor the water system was cleaned before the entry of the piglets. Planning to clean the barrel when it was empty, the owner had closed the water valve to prevent filling with fresh water. Therefore the piglets were forced to drink the water that had stayed in the pipes and the barrel for more than two months, which led to mortality throughout the entire compartment. Water taken at a nipple during the mortality episode contained 570 mg/L nitrite and 270 mg/L nitrate, as well as a high level of bacteriological contamination (1.88×10^5 bacteria per mL at 37°C; >1000 fecal streptococci / 100 mL).

DISCUSSION

The three cases illustrate the possibility of nitrite intoxication in pigs in modern housing facilities. Still water within the water distribution system was identified as the source of the nitrite. The nitrite formation was likely due to a bacterial reduction of nitrate within the pipes.

Two sources of nitrite have been described in cases of nitrite intoxication: the direct intake of nitrite salts (Gowans, 1990) and nitrite originating from a reduction of nitrate outside the pig. A case of nitrate reduction by plants was described by Wiese and Joubert (2001) in pigs fed with Capsella bursa-pastoris, but the most important nitrate reduction is of bacterial origin. Different bacterial species (e.g. *Escherichia coli*, *Pseudomonas aeroginosa*, *Streptococcus* spp., *Staphylococcus* spp. and *Pasteurella* spp.) are able to transform nitrate to nitrite by means of the enzyme nitrate reductase (Carter *et al.*, 1995; Li *et al.*, 1997).

Ingestion of nitrate by pigs is known to have no adverse effects at a concentration of 2 g/L (Sørensen *et al.*, 1994). Transformation to nitrite after ingestion is due to gastro-intestinal bacteria (Duncan *et al.*, 1995) and is assumed to be about 10% in infants (Fan and Steinberg, 1996). Data on nitrate reduction within the pigs intestinal tract were not available. The presence of nitrate and the bacteriological contamination of the water in case 3, together with the normal nitrite levels after the emptying of the pipes, confirm that the stagnation of water in the presence of bacterial proliferation was the source of nitrite in these cases. Considering these arguments, the time needed to build up toxic nitrite levels within the water system depends on several factors: the presence or production of nitrate, the bacterial proliferation, the atmospheric conditions and the length of the stand-empty period of the stable. Since the stand-empty period in these cases was at least two months, the short period of sanitary vacancy between rounds as applied in modern management systems is very likely too short to build up toxic nitrite levels within the pipes. This was confirmed in a small experiment in which several water samples were examined after a stand-empty period of 10 to 14 days and compared with samples of adjacent compartments that were occupied. Only a slight increase in bacterial count and similar concentrations of nitrate and nitrite were found (Vyt, unpublished data).

Nitrate, the substrate from which nitrite is formed, can originate from nitrogen-fixing bacteria, plants and decaying organic matter (Buck *et al.*, 1976), or it can be washed out after the fertilization of farmland

(Wendt, 1985). This is an increasing problem in the EU and has been one of the reasons for implementing the Nitrate Directive (Monteny, 2001). The exact source of nitrate could not be established in the present cases. In case 1, water was used from the community water supply, whereas in cases 2 and 3 the water originated from a drilled well. In all three cases, the stand-empty periods with water stagnating in the pipes were very likely the key factors in the accumulation of nitrite.

When the animals consumed the drinking water, especially in association with thirst or feeding, they ingested high quantities of nitrite. Hoorens and Thoonen (1961) stressed the importance of a single ingestion of high doses (> 70 mg/kg) to provoke lethal effects. London *et al.* (1967) observed methemoglobinemia with subsequent recovery in pigs administered potassium nitrite in a single dose at 19.8 mg/kg bodyweight, but mortality at a dosage of 21.3 mg/kg. Taking into account the nitrite concentrations found in the water, the consumption of 2 to 8 liters was lethal for sows, and 1 to 3 liters was lethal for growing pigs weighing 25 kg at a dosage of 21 or 70mg/kg, respectively. These amounts are only part of the normal daily water intake of these animals (Henry and Ampley, 1999). Therefore, an ingestion of this quantity at feeding is considered to be likely and was confirmed by the levels of nitrite found within the stomachs.

After ingestion, nitrite is readily absorbed into the circulatory system, where it is scavenged by the erythrocytes. Uptake by erythrocytes is fast, as was demonstrated in vitro by May *et al.* (2000), who found a half-time of 11 min for an uptake of 0.08mM nitrite with subsequent methemoglobin formation. Methemoglobin concentrations higher than 75 % are associated with acute mortality (Wendt, 1985; Saito *et al.*, 2000). The methemoglobin concentration was not measured in the blood of these animals.

The characteristic brown color of the blood was not found in case 1. Since Sato *et al.* (1988) mention a rapid reduction of methemoglobin in whole blood at 3°C, a possible explanation in this case might be that the necropsy was performed after the weekend, which was two days after death.

Confirmation of nitrite intoxication can be done by determining nitrite levels in the drinking water or by determination of methemoglobin concentrations in blood samples taken in fully filled EDTA tubes that are not frozen. Drinking water samples should be transported under cold conditions to prevent further nitrite formation.

Treatment with methylene blue, which brings about a reduction of the methemoglobin to hemoglobin (Wendt, 1985), was not used in these cases. In cases of acute mortality, a rapid removal of the nitrite source is essential to prevent further mortality, as was demonstrated in cases 2 and 3.

The present cases, recorded between 2000 and 2003, stress the risk of still water within the pipes in empty stables. Since stables can stay empty for several reasons (e.g. economic or hygienic reasons, disease eradication), cleaning the water pipes or at least washing them through after a period of vacancy should be part of good management practices. This study demonstrates that even in modern swine facilities, nitrite intoxication should be incorporated into the differential diagnosis when facing problems with acute mortality in pigs housed in barns with a history of standing empty for several weeks.

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Uit het verleden

DE UITVINDING VAN HET GAREEL EN HET VERDWIJNEN VAN DE SLAVERNIJ UIT ONZE STREKEN

De slavernij is slechts zeer geleidelijk uit onze streken verdwenen. Slaven behoorden net als huisdieren helemaal toe aan hun meesters. Deze beschikten over alles, leven en dood incluis. Slaven bezaten geen enkel recht. Het was menselijk vee. In de vroege middeleeuwen werd dit systeem afgezwakt tot lijfeigenschap. Sporen daarvan, in het erfrecht bijvoorbeeld, bleven nog bestaan tot aan de Franse Revolutie.

De oorzaken die aan de basis van deze afzwakking lagen, zijn complex en moeilijk achterhaalbaar. De Franse militaire historicus Lefebvre des Noëttes liet in 1931 een werk verschijnen *L'attelage à travers les âges* (De bespanning van trekdieren doorheen de eeuwen) waarin hij vooropstelde dat de geniale uitvinding door onbekenden van het gareel een totale omwenteling in de menselijke werkcondities met zich meebracht. In de Oudheid werden trekdieren alleen ingespannen bij middel van een band omheen de hals. Vanaf de 10de eeuw werd het schoudergareel ingevoerd bij trekdieren allerhande: koeien, ossen, paarden, muilezels en muildieren. De trekkracht werd op relatief eenvoudige en goedkope wijze een veelvoud van vroeger. Op die wijze werd de menselijke trekkracht in de landbouw zo goed als overbodig … en juist de nood aan mensen voor dergelijk slafelijk werk was vermoedelijk een belangrijke reden geweest voor het ontstaan en het in stand houden van de slavernij.

L. Devriese