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CARDIOMYOPATHY OF RUMINANTS INDUCED BY THE LITTER OF POULTRY FED ON RATIONS CONTAINING THE IONOPHORE ANTIBIOTIC, MADURAMICIN. I. EPIDEMIOLOGY, CLINICAL SIGNS AND CLINICAL PATHOLOGY

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ABSTRACT

FOURIE, N., BASTIANELLO, S. S., PROZESKY, L., NEL, P. W. & KELLERMAN, T. S., 1991. Cardiomyopathy of ruminants induced by the litter of poultry fed on rations containing the ionophore antibiotic, maduramicin. I. Epidemiology, clinical signs and clinical pathology. *Onderstepoort Journal of Veterinary Research*, 58, 291–296 (1991).

The epidemiological, clinical and clinical pathological findings in 20 cattle and 4 sheep from 15 outbreaks of poultry litter toxicity in South Africa over the past 6 years are documented. In 6 outbreaks, the litter emanated from batteries where maduramicin had been incorporated into rations of broilers. According to circumstantial evidence the litter involved in the 9 other outbreaks was also derived from broilers which had been fed on rations containing an ionophore. The litter was fed *ad libitum* to the affected stock or constituted 30–80 % by volume of their rations. The principal sign manifested was sudden mortality of up to 70 % of the herd or flock, usually within 20–40 days of commencement of feeding of poultry litter. A few cattle developed signs of congestive heart failure, and stiffness was commonly seen in sheep.

In a dosing trial with poultry litter involving 1 steer and 6 sheep, the steer and a sheep died suddenly and a second sheep was destroyed *in extremis*. Tachycardia and/or cardiac arrythmia were recorded in 5 sheep, and the activity of aspartate transaminase (AST) and/or lactate dehydrogenase (LD) in the sera of 4 was elevated.

Since the cardiac lesions in field cases were similar to those of ionophore poisoning and broiler rations containing maduramicin was a common factor in several outbreaks, toxic litter from some of these outbreaks were tested for the presence of this compound. Analysis by high performance liquid chromatography of litter from 2 specimens of outbreaks revealed that they contained 2,5 ppm and 6,1 ppm maduramicin. Sheep in a trial fed rations incorporating *c* 2,5 ppm and 5 ppm maduramicin, developed clinical signs and lesions consistent with those of the field cases.

INTRODUCTION

Poultry litter is fed to cattle and sheep as a cheap source of protein particularly during the winter and in times of drought. This practice is confined to a few countries, including South Africa (Nel, Kellerman, Prozesky & Van der Pypekamp, 1987; Prozesky & Nel, 1988), Israel (Perl, Schlosberg, Hoida, Davidson, Yakobsen & Orgad, 1991) and some South American states (C. Cook, P.O. Box 58, Isando 1600., personal communication, 1990).

The health hazards most frequently associated with the feeding of poultry litter to livestock are caused by the residues of antibiotic (other than ionophore) medicated feed additives, microbial toxins such as botulinum, pathogenic bacteria such as *Salmonella* spp., and elements such as copper (Ogonowski, Barnard & Giesecke, 1984).

In the past few years, numerous outbreaks of mortality have been associated with the feeding of poultry litter to cattle and sheep in South Africa. Some of these outbreaks, however, could not be correlated with any of the above listed causes of poultry litter poisoning.

Initial investigations suggested that the toxic agent in these undiagnosed outbreaks of poultry litter toxicity was an ionophore antibiotic incorporated into broiler rations as a coccidiostatic agent. The possible role of a specific ionophore, namely maduramicin, came to light after the sudden death of 15 out of 55 lambs which had been given a home-made ration containing 8,81 ppm maduramicin to control coccidiosis (Joyce Pearson, Department of Pathology, Faculty of Veterinary Science, University of Pretoria, personal communication, 1990).

The objectives of the present study were firstly to establish whether poultry litter was indeed the toxic component in the rations and secondly whether the toxic principle in the poultry litter was an ionophore, in particular maduramicin.

This report deals with the epidemiology, clinical symptoms and clinical pathological findings of 15 field outbreaks of the cardiotoxicosis, and feeding trials with poultry litter and feed pellets containing maduramicin. The pathological findings will be published elsewhere.

HISTORY OF FIELD OUTBREAKS

Since May, 1986, 15 outbreaks of poultry litter cardiomyopathy, 12 in cattle and 3 in sheep, have been investigated. The litter from 6 of these outbreaks emanated from a single poultry farm, while the exact source of the litter of the remaining 9 could not be determined. In the case of the former 6 outbreaks induced by poultry litter from a single farm, maduramicin had been added to the ration of the broilers. Ionophore antibiotics are also suspected of being present in the rations of the chickens from which the toxic litter of the other 9 outbreaks was derived, but this could not be confirmed. In 4 outbreaks, poultry litter had been fed to the cattle without any ill effect for several years before the introduction of an ionophore into the poultry ration. In the majority of outbreaks, chicken litter was fed *ad libitum* together with hay or veld grazing, while in the others litter constituted 30–80 % of the total volume of the ration (i.e. every 10 bags of feed contained 3–8 bags litter). A remnant of maduramicin-containing litter from one of the 6 outbreaks was still toxic after being stored for 16 months. Fourteen out of 20 steers to which it was fed died within 28 days.

Mortality varied greatly. In the outbreaks where maduramicin was specifically implicated, mortalities ranged from 11–70 %. Animals succumbed 14–150

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TABLE 1 Dosing regimen, clinical signs and clinical pathology in animals fed poultry litter

Animal			Dosing regimen				Results		
Number	Species	Initial live mass (kg)	Dose g/kg × N (Days)	Period dosed (Days)	Total dose g/kg	Total dose (kg)	Duration of trial (Days)	Clinical signs and fate	Clinical pathology
25	Bovine	297		Fed *ad lib* for 43 days			43	Sudden death D43	Not determined
26	Ovine	55	5 × 15 10 × 11 15 × 9	35	320	17,6	35	Tachycardia D35. Died D35	AST activity elevated D35, LD activity elevated D31–35
27	Ovine	33	15 × 78	78	1 170	38,61	107	Cardiac arrythmia D49–96. Slaughtered D107	Na
28	Ovine	31	15 × 78	78	1 070	36,27	107	Na. Slaughtered D107	Na
29	Ovine	31	10 × 107	107	1 070	33,17	109	Tachycardia and gallop rhythm D78–109. Slaughtered D109	AST activity elevated D64–78, LD activity elevated D64–81
30	Ovine	48	15 × 23	23	345	16,56	34	Tachcardia and gallop rhythm D15–34, lethargy D30–34, recumbency D34. Slaughtered *in extremis* D34	AST activity elevated D22–34, LD activity elevated D34
31	Ovine	52	5 × 9 10 × 7 15 × 98	114	1 540	80,06	114	Weakness, tachycardia, lethargy D114. Slaughtered D114	AST activity elevated D113–114, LD activity elevated D86–114

Na = within normal limits

days after commencement of feeding, with most dying between 20 and 40 days. Deaths usually occurred suddenly, without warning, often when the animals were stressed by handling, herding, etc. Apart from dying suddenly, some cattle were lethargic and became recumbent 12–24 h before death. Others showed signs of congestive heart failure for periods lasting from a few days to 3 weeks. These signs included dyspnoea, hyperpnoea, grunting, anxiety and moderate to extensive subcutaneous oedema, especially of the submandibular region, neck and brisket (Fig. 1). Severe tachycardia and gallop rhythm was evident on auscultation. A few developed signs of skeletal muscle involvement such as a stiff gait and fine tremors of the back and hind quarters.

In 1 of the 3 outbreaks involving sheep, many developed signs of skeletal muscle damage such as reluctance to move, a stiff gait, knuckling over of the fetlock joints, posterior paresis and eventual recumbency.

FIG. 1 Congestive heart failure in a natural case of poultry litter cardiomyopathy: Note submandibular oedema

Mortalities of non-clinically affected animals generally ceased within 10–21 days of withdrawal of the toxic poultry litter from the ration, although occasionally a few clinically normal animals died suddenly weeks or months later.

MATERIALS AND METHODS

Field outbreaks

Toxicological analysis of poultry litter samples

Samples of chicken litter from 6 outbreaks were examined for ionophore content by thin layer chromatography (TLC) (Golab, Barton & Scroggs, 1973). Specimens from 2 of these outbreaks were also submitted to the Cyanamid laboratory in Scotland for determination of the maduramicin content using high performance liquid chromatography (HPLC) [C. Cook, SA Cyanamid (Pty) Ltd, personal communication, 1989]. No samples of litter from the other 9 outbreaks were available for chemical analysis.

Poultry litter feeding trials

Feeding regimen

In a preliminary trial, poultry litter from the first outbreak to come to our attention (not listed amongst the 15 outbreaks in this series) was fed *ad libitum* to a 297 kg steer (Animal 25; Table 1). Six sheep (Animals 26–31; Table 1) were then dosed per rumen fistula with poultry litter from 4 of the outbreaks. The sheep were given daily doses ranging from 5–15 g/kg for periods of 23 to 114 days (Table 1).

The sheep were housed individually in cement-floored pens equiped with individual food and water troughs and observed daily.

TABLE 2 Clinical signs and clinical pathological changes in sheep fed maduramicin-containing pellets

Animal Number	Breed	Sex	Ration fed	Duration of feeding trial (Days)	Average daily intake (kg/ sheep/day)	Feed refusal	Clinical signs induced by exercise and fate	Clinical pathology (AST activity)
32	Merino	Wether	Control ration	78	D0–78: 1,400	—	Slaughtered D78	Within normal limits
33	Merino	Wether	Control ration	81	D0–81: 1,650	—	Slaughtered D81	Within normal limits
34	Merino	Wether	Control ration	92	D0–92: 1,600	—	Slaughtered D92	Within normal limits
35	Dorper	Ewe	A	28	D0–7: nd D8–19: 0,364	— D19–28	Dyspnoea, stiff gait, collapsed and died D28	Markedly elevated D15–26
36	Merino	Wether	B Control ration B	57	D0–8: 0,967 D11–42: 1,000 D43–50: 1,025	D8 D50	Tired rapidly, stiff gait, reluctant to move, collapse. Slaughtered D57	Markedly elevated D15–25
37	Merino	Wether	B Control ration B	57	D0–11: 1,205 D11–42: 1,000 D43–50: 1,600	D11 D50	Tired rapidly, stiff gait, reluctant to move. Slaughtered D57	Elevated D15–25
38	Merino	Wether	B Control ration B	57	D0–8: 0,983 D11–42: 1,000 D43–50: 1,163	D8 — D50	Tired rapidly, stiff gait, reluctant to move. Slaughtered D57	Elevated D15–25
39	Merino	Wether	Ration C	78	D0–78: 1,850	—	Tired rapidly, stiff gait, collapsed after minimal exercise. Slaughtered D78	Markedly elevated D10
40	Merino	Wether	C	81	D0–81: 1,410	—	Tired, rapidly, stiff gait, collapsed after minimal exercise. Slaughtered D81	Elevated D10
41	Merino	Wether	C	92	D0–92: 1,620	—	Reluctant to move, stiff gait. Slaughtered D92	Within normal limits

nd = Not determined
D = Day
AST = Aspartate transaminase

Clinical pathology

Blood was collected from the 6 sheep for clinical pathological determinations on Day −4, Day 0 and twice weekly thereafter.

Haemoglobin was determined by the cyanmethaemoglobin method (Anon., 1974a); haematocrit by using capillary tubes in a Damon IEC micro haematocrit centrifuge; and erythrocyte sedimentation rate (ESR) in Wintrobe tubes for 1 h at 20 ± 3 °C.

Total plasma protein (TPP) was determined by the Biuret method (Anon., 1974b); plasma glucose by the GOD-Perid method (Boehringer Mannheim); and serum urea by the Berthelot method (Anon., 1974c).

The activities of the following enzymes were determined in the serum using Boehringer Mannheim test kits: lactate dehydrogenase (LD), aspartate transaminase (AST), and gamma-glutamyl-transferase (GGT) (Table 1).

Maduramicin feeding trials

Feeding regimen

To determine whether maduramicin could be toxic to sheep a Dorper ewe of *c* 12 months with a live mass of 21 kg (Sheep 35, Table 2) was fed a commercial broiler ration stated to contain 5 ppm maduramicin (Ration A).

The ewe was gradually accustomed to the ration by initially giving her 10 g/kg pellets for 2 days followed by 15 g/kg for 5 days. Thereafter she received 20 g/kg pellets daily and hay *ad libitum*.

On completion of the pilot trial, a further trial involving 9 Merino wethers was carried out. The wethers, ranging in live mass from 36 to 54 kg, were randomly divided into groups of 3 each. The first group (Sheep 32–34), received the Control Ration, the second group (Sheep 36–38), Ration B, and the third group (Sheep 39–41), Ration C (Table 2). The sheep were housed individually as described.

The Control Ration was a maintenance pellet [sheep drought pellets, Nola Industries (Pty.) Ltd., Randfontein]. Ration B consisted of the Conrol Ration into which 5 ppm maduramicin had been incorporated. The mean maduramicin content of 5 specimens of this specially formulated ration was determined by HPLC to be 5,2 ppm. Ration C was a 50:50 mixture of the control ration and Ration B having a maduramicin content of *c* 2,5 ppm.

Each wether was given 2 kg of pellets per day. Each day, before being discarded, the mass of un-

eaten pellets in the cribs was recorded so that the intake of individual sheep could be calculated. Both the experimental and control sheep had free access to hay.

Clinical signs

The sheep were observed daily and their temperatures, pulse and respiratory rates recorded.

The Dorper ewe (Animal 35, Table 2) which received Ration A, was chased about 50 m on Day 28 of the feeding trial. The locomotory ability of the 3 control and 6 experimental wethers was initially evaluated on Day 9 and at least twice weekly thereafter. This was done by chasing the sheep from their pens to an exercising ring *c* 10 m in diameter, situated within 50 m of the feeding pens. The animals were then driven around the ring until they became tired or developed clinical signs.

Clinical pathology

Blood was drawn for clinical pathological determinations, as described under the poultry litter feeding trials, on Day 0 of the feeding trial and twice weekly thereafter.

RESULTS

Toxicological analysis of poultry litter samples

No ionophores could be detected by TLC in poultry litter from the 6 outbreaks which were analysed. However, 2,5 ppm and 6,1 ppm maduramicin could be demonstrated by HPLC in samples from 2 of these outbreaks.

Poultry litter feeding trials

Clinical signs and clinical pathology

The blood haemoglobin, haematocrit and ESR were within normal limits as were the TPP, plasma glucose and serum urea levels. The clinical signs and clinical pathological results are summarized in Table 1.

The steer (Animal 25), and one sheep (Animal 26) died after exposure to poultry litter for 43 and 35 days respectively. A second sheep (Animal 30) was slaughtered *in extremis* on Day 34. Tachycardia and/or arrhythmia were noted in 5 sheep (Animals 26, 27, 29, 30 and 31). The activities of AST and LD were elevated in the sera of 4 sheep (Animals 26, 29, 30 and 31).

Maduramicin feeding trials

Feed intake, clinical signs and clinical pathology

The haemoglobin, haematocrit, ESR and TPP, plasma glucose and serum urea levels were within normal limits in both the control and experimental sheep.

Control ration: The average daily intake of the sheep in this group was 1,55 kg pellets/day. No feed refusal or clinical signs were observed and the AST levels remained within normal limits (Fig. 2, Table 2). The sheep were euthanased on Day 78, 81 and 92 respectively (Table 2).

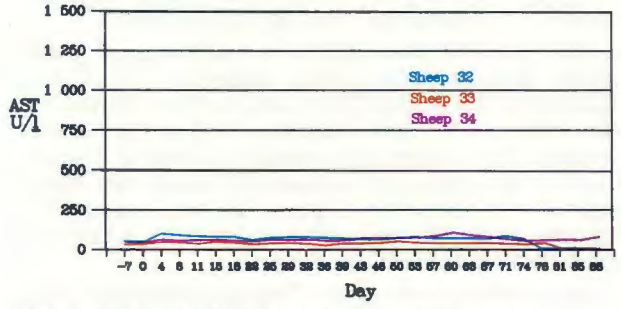

FIG. 2 Activity of AST in the sera of the control sheep

Ration A: Feed refusal was noticed on Day 19. On Day 20 the ewe was depressed and displayed abnormal and laboured abdominal breathing. On Day 28 the sheep was taken out of the pen and exercised. After being chased for approximately 50 m the ewe became tired, developed dyspnoea and a stiff gait, was extremely reluctant to move, collapsed, and died within minutes. The AST levels were markedly increased from *c.* Day 15 till death on Day 28 (Fig. 3).

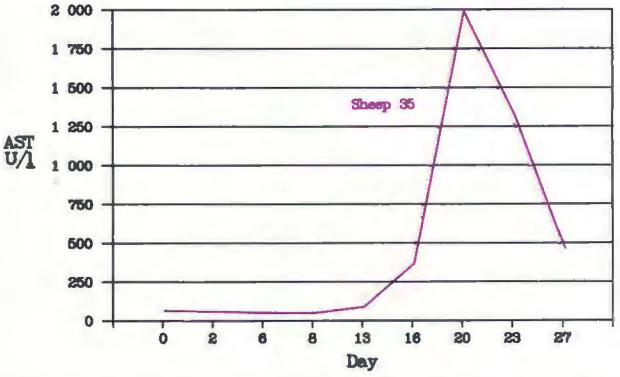

FIG. 3 Changes in the activity of AST in the serum of a sheep fed broiler ration containing maduramicin

Ration B: The average daily intake of the group was 1,1 kg/sheep/day. Two of the sheep (Numbers 36 and 38) stopped eating the pellets on Day 8, and the third (Number 37) on Day 11 (Table 2). Owing to this total refusal of feed, the 3 sheep were given access to 1 kg/sheep/day of the control pellets from Day 11 to Day 42. During this period the sheep readily consumed the control pellets but steadfastly rejected the experimental pellets when these were offered to them. From Day 43 the sheep were again supplied with 2 kg/day of Ration B and the control pellets were withdrawn. Intake averaged 1,2 kg/sheep/day for 8 days till Day 50, after which total feed refusal again developed. All three sheep were euthanased on Day 57.

From Day 9, marked locomotory disturbances were observed in the 3 sheep that received maduramicin in their rations and at all subsequent times when the sheep were chased around the exercise ring. The maduramicin sheep tired within minutes of being chased. They lagged behind the controls and were soon reduced to a walking pace while the controls still galloped around the ring. Within a further few minutes the affected sheep developed a stiff gait and were extremely reluctant to move at all. Sheep 36 collapsed into a sternal position, refused to get up

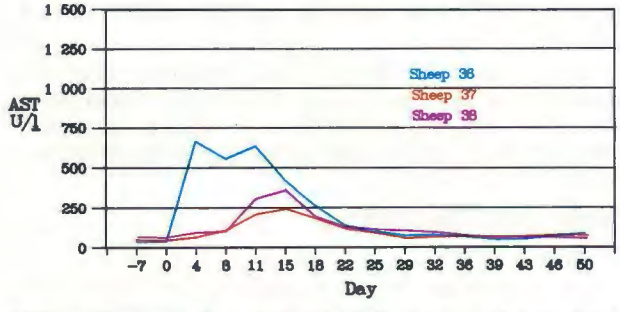

FIG. 4 Changes in the activity of AST in the sera of sheep fed a ration containing 5 ppm maduramicin

and had to be carried back to his pen. When at rest in the feeding pens, no clinical signs were observed.

Marked increases in the AST activity were observed in all 3 from *c.* Day 10 to *c.* Day 25 (Fig. 4).

Ration C: The average daily intake of these pellets for the group was 1,63 kg/sheep/day. No feed refusal was observed and the sheep ate the pellets readily throughout the trial.

Similar but more pronounced locomotory disturbances as previously described were evident after exercise. Sheep 39 and 40 collapsed into sternal recumbency following minimal exertion and were euthanased respectively on Days 36 and 39, while Sheep 41 developed only mild locomotory disturbance and was euthanased on Day 52 (Table 2). Sheep 40 displayed marked elevation of AST activity on Day 8, and Sheep 41 and 39 moderate elevations on *c.* Days 8 and 36, respectively (Fig 5).

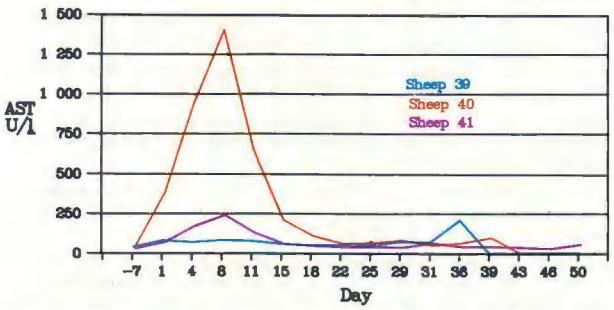

FIG. 5 Changes in the activity of AST in the sera of sheep fed a ration containing approximately 2,5 ppm maduramicin

DISCUSSION

In the 15 outbreaks of poultry litter toxicity reported in this series, toxicity occurred under 2 systems of management, i.e. when poultry litter was fed *ad libitum* to animals either grazing on the veld or receiving hay, or when the poultry litter was incorporated into the ration at levels above 30 % by volume.

In the majority of outbreaks involving cattle, the principle sign manifested was sudden mortality of up to 70 % of the herd. The interval between commencement of feeding of poultry litter and the first mortalities varied from 14 days to 5 months, with an average of about 20–40 days. Mortalities usually occurred without any clinical symptoms being noted, but a small proportion developed congestive heart failure, or became lethargic or recumbent 12–24 h prior to death. Some clinically affected cattle showed mild skeletal muscle involvement, evidenced by fine muscle tremors of the back and hindquarters. In many instances, mortality was triggered by stress, in particular by chasing or handling the animals. Similar epidemiological features and clinical symptoms have been reported in cattle fed poultry litter containing an unidentified ionophore in Israel (Perl *et al.*, 1991).

The epidemiology, clinical signs and pathological lesions (Bastianello, Prozesky, Fourie & Kellerman, unpublished data, 1991) pointed to heart failure being the cause of death both in the field outbreaks and feeding trials with poultry litter or maduramicin-containing feed pellets. In sheep, besides cardiac lesions, there was also clinical and pathological evidence of skeletal muscle damage. Since ionopores are known to affect myocardial and skeletal muscles (Van Vleet, Amstutz, Weirich, Rebar & Ferrans, 1983; Newsholme, Howerth, Bastianello, Prozesky & Minné, 1983), Nel *et al.*, (1987) speculated on the possibility of an ionophore being the toxic agent in poultry litter cardiomyopathy in South Africa. However, at that stage they were unable to prove involvement of an ionophore.

A common factor in all 15 outbreaks of mortality was that stock were fed with poultry litter at levels of 30 % or above. The first objective of the investigation, therefore, was to establish by means of dosing trials whether the litter was poisonous. The clinical signs (lethargy, tachycardia, gallop rhythm, recumbency and sudden death), clinical pathological changes (elevated activity of AST and LD in the serum), and lesions of the animals that had been dosed/fed with poultry litter at the laboratory, convincingly implicated the litter as the cause of cardiomyopathy of ruminants in the field outbreaks.

Several ionophores are registered in South Africa as coccidiostatic agents in broiler rations, namely, narasin, salinomycin, monensin, lasolacid and maduramicin. The first 4 are added at relatively high levels varying from 60–80 ppm for narasin to 75–125 ppm for lasolacid, whilst maduramicin is added at only 5 ppm (Immelman, 1991a). Some of these ionophores are also used in ruminant rations as growth promoters (Immelman, 1991b). Maduramicin, however, is registered for use in poultry only (Immelman, 1991a) and no published data are available on the toxicity of this particular ionophore for ruminants.

Monensin administered orally is readily absorbed and rapidly metabolised by poultry, with up to 99 % being excreted in the faeces via the bile (Hatch, 1982; Donoho, 1984). Only about 10 % is excreted as monensin, the remainder being disposed of as metabolites. These metabolites may be up to 20 times less active than the parent compound (Donoho, 1984). Monensin is usually incorporated at 100 ppm in poultry rations. Levels of *c.* 10–20 ppm monensin have been detected in poultry litter samples in our laboratory (N. Fourie, unpublished data, 1991), which is consistent with the findings of Hatch (1982) that only 10 % of monensin is excreted as such. Levels of 10–20 ppm monensin can be regarded as safe for ruminants, as this compound is registered for use in cattle at 10–30 ppm and sheep at 11–22 ppm (Immelman, 1991b).

Of the 5 ionophore antibiotics registered for use in poultry broiler rations, only maduramicin is added at a level as low as 5 ppm (*vide supra*). Unlike the other ionophore antibiotics, therefore, maduramicin (owing to its low concentration) could not be detected by TLC in our laboratory. The only reliable method for detecting maduramicin in poultry litter proved to be by HPLC.

Mortality associated with the feeding of poultry litter was first noticed in 1986, shortly after maduramicin was introduced as a coccidiostatic agent for broilers in South Africa. This fact, together with our failure to detect an ionophore antibiotic by means of TLC in the 6 poultry litter samples tested; evidence that lambs had been poisoned by a home-made ration containing 8,81 ppm maduramicin (J. Pearson, Faculty of Veterinary Science, University of Pretoria, personal communication, 1991); and the detection of maduramicin at 2,5 ppm and 6,1 ppm by means of HPLC in the poultry litter from 2 outbreaks, provided strong circumstantial evidence that maduramicin was the principal toxic agent in poisoning of stock with poultry litter in South Africa.

The feeding trials with maduramicin conclusively proved that maduramicin at levels as low as approximately 2,5 ppm and 5 ppm can be highly toxic for sheep, inducing mortality, clinical signs and pathological lesions (Bastianello *et al.*, unpublished data, 1991) indicative of cardiac and skeletal muscle involvement.

The clinical signs and pathological lesions (Bastianello *et al.* unpublished data, 1991) in the heart and skeletal muscles of the sheep in the maduramicin feeding trials were similar to those encountered in the field outbreaks and poultry litter feeding trials. AST activities, however, were markedly raised in those receiving poultry litter. This could be ascribed to the more severe locomotory disturbances and skeletal muscle damage observed in the sheep receiving maduramicin.

It is significant to note that while at rest, no clinical signs of locomotory abnormalities were noted in the sheep fed maduramicin. This implies that sheep may be able to tolerate toxic levels of maduramicin without apparent ill effects if they are kept quietly in pens. This could also explain the absence of locomotory disturbance in the sheep fed poultry litter, as they were not subjected to exercise. It follows that under field conditions, where sheep may have to walk long distances for food or water or where they are stressed by handling, locomotory disturbances and mortality are highly likely to occur.

The more severe locomotory disturbances observed in 2 of the sheep that received *c.* 2,5 ppm maduramicin compared to those that received 5 ppm, suggests that maduramicin is more toxic at lower than higher levels. This is an apparently unique feature of maduramicin, as the effects of toxicants generally become more pronounced at higher dosage levels. The phenomenon may have arisen from feed refusal. At *c.* 2,5 ppm feed refusal was not displayed by the sheep and the total intake of maduramicin was thus considerably higher than in those that received 5 ppm. At 5 ppm, pronounced feed refusal occurred within 8–11 days of commencement of feeding and persisted for 35 days.

The finding of 6,1 ppm maduramicin in one sample of poultry litter suggests that maduramicin may be excreted unmetabolised by the fowl or may even be concentrated in the gastro-intestinal tract of this species. The latter factor, as well as the extremely low levels (2,5 ppm and 5 ppm) at which maduramicin was toxic to sheep makes poultry litter containing maduramicin an extremely dangerous product to feed to ruminants.

As a result of this study, it is clear that poultry litter from broilers on maduramycin-containing rations cannot be fed with impunity to ruminants, particularly if the litter is supplied *ad libitum* or constitutes more than 20 % by volume of the total ration.

Litter derived from poultry fed rations containing one of the other ionophore antibiotics has never been implicated in an authenticated outbreak of cardiomyopathy of ruminants in South Africa. However, such litter must be used with caution and should not be fed in conjunction with a ruminant premix/ration containing an ionophore as growth promoter.

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