Article

Retrospective case study of fetal mummification in cows that did not respond to prostaglandin F2α treatment

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Abstract — Mummification of bovine fetuses is an uncommon condition, and cows do not always respond to treatment with prostaglandin F2α. The objective of the present retrospective and descriptive case study was to determine the conception rate and survival time of nonresponsive, prostaglandin F2α (PGF2α)-treated cows (*n* = 14), following hysterotomy or medical treatment and manual removal. Animal records from 1990 to 2005 from the Centre Hospitalier Universitaire Vétérinaire (CHUV) of the Université de Montréal were studied. Inclusion criteria were the nonexpulsion of the mummified fetus following PF2α treatment and absence of concomitant conditions upon physical examination. Of the animals included in the study, 36% (*n* = 5) became pregnant after extraction of the mummified fetus by hysterotomy and 0% conceived after medical treatment and manual extraction. In this study, hysterotomy represented an effective approach for extracting mummified fetuses from cows that did not respond to PF2α treatment.

Résumé — Étude rétrospective de cas de fœtus momifiés chez des vaches qui n'ont pas répondu à un traitement aux prostaglandines. La momification fœtale bovine est une condition rare et la vache ne réussit pas toujours à expulser le fœtus après un traitement aux prostaglandines F2α (PGF2α). L'objectif de l'étude rétrospective et descriptive était de déterminer le taux de conception et le temps de survie des vaches (*n* = 14) qui n'avaient pas répondu à un premier traitement de PGF2α, après une hystérotomie, ou un traitement médical avec une expulsion manuelle. Les dossiers médicaux du Centre hospitalier universitaire vétérinaire (CHUV) de l'Université de Montréal entre 1990 et 2005 ont été étudiés. Les critères d'inclusion pour l'étude étaient : 1) l'absence d'expulsion du fœtus momifié après un traitement de PGF2α, 2) l'absence d'une condition médicale secondaire détectée à l'examen physique de l'animal. Trente-six pour cent (*n* = 5) des vaches sont devenus gravides après l'extraction du fœtus par hystérotomie, alors qu'aucune vache n'a conçu après le traitement médical et l'extraction manuelle du fœtus. Dans la présente étude, l'hystérotomie représente une approche efficace pour extraire un fœtus momifié lorsque le traitement aux PGF2α s'est avéré inefficace.

(Traduit par Docteur André Blouin)

Can Vet J 2009;50:71–76

Introduction

Mummification of bovine fetuses is an uncommon condition with an incidence of less than 2% (1). Fetal mummification has been reported in several species, including the sheep (2), goat (3), horse (4), pig (5), and dog and cat (6), but it is more common in cattle (7). Breed and previous occurrence seem to be risk factors with a higher incidence of fetal mummification in Guernsey and Jersey cattle, and a higher risk (30%) of recurrence in cows that experienced a similar event in a previous gestation (7). In cattle, fetal mummification occurs after formation of the placenta and fetal ossification (70 d gestation). Most often, mummification occurs between the 3rd and 8th months of gestation, without concomitant luteolysis of the corpus luteum (CL) and opening of the cervix. Fetal mummification associated with a persistent CL is observed mainly in cattle and goats, both species being dependent on progesterone (P4) produced by the CL for the maintenance of pregnancy (8). In cattle, however, the placenta is capable of producing sufficient P4 to maintain pregnancy between days 150 and 200 of gestation (9). After fetal death, the amniotic and allantoic fluids are resorbed, dehydrating the fetal tissues and annex membranes. The immature, unkeratinized skin of the fetus may contribute to the mummification process by allowing a faster loss of body water (10).

Several potential causes for this condition have been proposed: bovine viral diarrhea (BVD), leptospirosis, and molds (11); mechanical factors, such as compression or torsion of the

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umbilical cord, or both (12); uterine torsion (13); defective placentation (14); genetic anomalies (11,15); abnormal hormonal profiles; and chromosomal abnormalities (7). However, a definitive etiology is rarely determined because of tissue degeneration and autolysis. The mummification process usually renders worthless the analysis of bacteria, viruses, biopsies, and chromosomes (16). In 1 study, DNA from mummified fetuses was extracted and 2 out of 10 were carriers (heterozygous) of the autosomal recessive gene for deficiency of uridine monophosphate synthase (DUMPS) (17), known to contribute to embryonic and fetal mortality in cattle (18).

Diagnosis is generally uncomplicated. Transrectal palpation and ultrasonographic examination determine that the mummified fetus has the appearance of a compact, firm, and immobile mass without placental fluid or placentomes. The general physical examination of the dam appears normal, except for some rare cases in which a decrease in milk production and a loss of weight have been observed (19).

The treatment of choice for fetal mummification is lysis of the CL by injection of prostaglandin (PG) F2α, which usually results in the satisfactory and safe expulsion of the fetus within 2 to 4 d of treatment (1). Surgical removal of mummified fetuses via colpotomy (15) or laparotomy (7) remains an option when medical treatment fails. There is currently no information on the fertility of the cow following expulsion of the fetus (1).

The objective of the present retrospective and descriptive case study was to determine the conception rate and survival time of nonresponsive, PGF2α-treated cows, following hysterotomy or medical treatment and manual removal.

Materials and methods

Criteria for selection of cases

The Veterinary Medical Data Base (VMDB) of the Centre Hospitalier Universitaire Vétérinaire (CHUV) of the Université de Montréal was searched and information from the records of all cows diagnosed with fetal mummification from January 1990 to July 2005 was compiled. Each record included date of admission, identification number, age and breed of the animal, history, preliminary diagnosis and treatment of the referring veterinarian, findings on physical examination, results from diagnostic tests, and treatments. As part of the study, a telephone survey was performed in 2005 to obtain information about the hospitalization recovery, reproductive status, and survival time of the animal in the herd. The mummification cases (n = 14) were included in the study if there was no fluid in the uterus, the fetus was firm and easy to feel on transrectal palpation, and there was no history of systemic disease prior to presentation or evidence of it on physical examination. The animal had to have received at least 1 treatment of PGF2α in the 2 wk preceding the referral that did not result in the expulsion of the fetus.

Procedures

General examination

A complete general examination had been performed on arrival for each animal. Blood samples had also been collected and submitted for a serum biochemical profile and a complete blood (cell) count (CBC).

Genital examination

The conformation of the vulva and perineal region of the animal had been assessed. Transrectal palpation and ultrasonography examination (Aloka 120V or 900; ISM, Montreal) had been performed to confirm the presence of a mass without fluid in the uterus. A vaginal examination had been carried out to confirm the presence of discharge and to estimate the degree of cervical dilation.

Surgical approach

Surgical extraction of the mummified fetus was performed on 11 cows. Following hair clipping, initial preparation and scrubbing was performed as described by Desrochers (20). A flank laparotomy in a standing cow was performed by opening the abdominal wall on the ipsilateral side to the pregnant horn and in the caudal area of the lumbar fossa. This incision site allowed the closest approach to the pregnant horn. However, the thickness of the internal and external abdominal oblique muscles hindered the manipulation of the horn. After opening the abdominal cavity, a tocolytic agent, was administered, as needed, before the pregnant horn was located and exteriorized to allow repositioning of the fetus and a good view of the incision site on the large curvature of the uterine horn (21). After extraction of the mummified fetus, the uterus was flushed with saline and cleansed. The exposed uterus was meticulously inspected for any anomalies or placental fragments, and an oxytocin injection in the coccygeal vein followed (Oxytocin; Vetoquinol, Lavaltrie, Québec), 15 IU, IV. The uterus was closed in 2 layers, using a Cushing pattern with USP 2 (Dexon II; Norwalk, Connecticut, USA). The abdominal wall and skin were closed, as described by Fubini (22). Procaine penicillin (Depocillin; Intervet, Whitby, Ontario), 22 000 IU/kg BW, IM q12h, was administered for 5 d. In the case of an uneventful recovery, the cow was discharged 2 d after surgery. Three cows (No 1, 9, and 13) from the surgically treated group received PGF2α prior to surgery.

Medical treatment

Three cows received medical treatment only (Table 1) consisting of estradiol 17ß (E17ß), oxytocin, and PGF2α injections. Cow No. 5 received E17ß, 25 mg, SC, q24h for 2 d for a total of 50 mg before the administration of oxytocin, 20 IU, IM, q6h, was initiated. The cow was examined vaginally q24h to perform manual dilation of the cervix. The mummified fetus was extracted on the 3rd d and the oxytocin treatment was discontinued. A uterine lavage with saline was performed before the animal was discharged. Cow No. 4 received E17ß, 50 mg, SC, q24h for 3 d for a total of 150 mg and oxytocin, 20 IU, IM q6h for 2 d. Following daily manual cervical dilation, the mummified fetus was extracted on the 4th d, 1 d after the completion of the E17ß treatment. Cow No. 6 received E17ß, 50 mg, SC, q12h for 3 d for a total of 300 mg, followed by oxytocin, 5 IU, IM, q8h for 1 additional day. Vaginal examination and manual cervical dilation were performed q24h. The fetus was expelled 1 d after the last oxytocin treatment. In this case, the cow was later diagnosed with and treated for a severe metritis caused by *Clostridum perfrigens*. All 3 cows had received PGF2α (Lutalyse,

Table 1. Summary of the 14 cases of fetal mummification diagnosed from January 1990 to July 2005 in cattle

Case number	Pregnant horn	Age (months)	Number of previous calving	Cervical status (cm)	Days in hospital	Months of pregnancy	Survival in the herd (months)	Gestation status	Treatment	Fetus length (cm)
1	Left	24	0	Closed	4	4	30	Pregnant	Laparo PGF2α	40
2	Left	70	3	Closed	2	9	36	Pregnant	Laparo	25
3	Right	117	5	Closed	3	6	36	Pregnant	Laparo	30
4	Right	27	0	Opened (5 cm)	4	9	X	Not pregnant	Manual PGF2α + E17β	50
5	Right	48	1	Opened (10 cm)	9	5	X	Not pregnant	Manual PGF2α + E17β	—
6	Left	31	0	Closed	9	9	X	Not pregnant	Manual PGF2α + E17β + O_X	—
7	Right	59	3	Closed	2	8.5	6	Not pregnant	Laparo	60
8	Right	47	0	Closed	2	12	3	Not pregnant	Laparo	10
9	Left	25	0	Closed	8	10	2	Not pregnant	Laparo PGF2α	40
10	Right	54	2	Closed	8	X	X	Not pregnant	Laparo	20
11	Left	29	0	Closed	5	11	24	Pregnant	Laparo	40
12	Left	71	4	Closed	4	5	2	Not pregnant	Laparo	18
13	Right	63	2	Closed	5	9	12	Not pregnant	Laparo PGF2α	25
14	Left	29	2	Closed	1	9	24	Pregnant	Laparo	20
Mean		52.8	1.5	Opened 2/14 14.3%	4.7	8.1	16.8	Pregnant 5/14 35.7%	Laparo: 11/14 = 78.6% Manual: 3/14 = 21.4%	31.5

X — missing data, Laparo — extraction of the fetus by laparotomy, PGF2α — prostaglandine F2α, manual — manual extraction of the mummified fetus.

UpJohn, Orangeville, Ontario), 25 mg, IM, at the beginning of the treatment.

Results

Fourteen cows with mummified fetuses were identified in the database as nonresponsive to at least 1 injection of PGF2α prior to presentation. The age of the cows ranged from 24 to 117 mo, with a mean and median age of 49.6 and 47.5 mo. Cows were presented between the 4th and 12th mo of gestation with a mean and median gestational age of 8.2 and 8.5 mo. Four cows (29%) reached the 9th mo gestation and 3 (21.4%) went beyond the normal parturition time (10, 11, and 12 mo gestation) before the diagnosis was made. One of the cows was diagnosed with a mummified fetus at 4 mo gestation, but only admitted to the hospital 4 mo later. Of all the cows, 43% (6 out 14) were carrying in their 1st pregnancy and 36% had completed more than 2 parturitions (Table 1).

On presentation, 2 cows (14%) had an open cervix (5- and 10-cm diameter cervical dilation for cow No. 4 and cow No. 5, respectively) with a small amount of odorless discharge in the cranial vagina. Eleven cows (79%) had their fetuses extracted by hysterotomy the day following their arrival and 3 (21%) had their fetuses extracted after manual cervical dilation and hormonal treatment. The average length of the extracted mummified fetus was 31.5 cm, with maximum and minimum lengths of 60 and 10 cm, respectively. Two out of 3 medically treated cows received PGF2α, based on the presumption of a functional CL, which was later confirmed by measuring the blood progesterone level (8.4 and 6.7 ng/mL for cows No. 5 and 6, respectively). On average, the medically and surgically treated cows were hospitalized for 7.3 and 3.8 d, respectively.

Of all the referred cows, 36% (5 out of 14) became pregnant shortly after being released from the hospital. None of the cows conceived when the fetus had been manually extracted

following medical treatment (n = 3). The 5 cows that became pregnant were 24, 70, 117, 29, and 29 mo old and had been 4, 6, 9, 9, and 11 mo pregnant on admission, with a mummified fetus size of 40, 25, 30, 20, and 40 cm in length, respectively. On average, these cows remained in the herd for 31.5 mo after the hysterotomy. Two cows (40%) gave birth twice more after removal of the mummified fetus.

Bacteria were isolated in only 1 case when bacteriologic culture had been performed on the uterine content (n = 4). In the case of cow No. 6, in which a severe metritis was diagnosed and treated, *C. perfinges Type C* was found a few days after extraction of the fetus.

Discussion

The main goal when treating an abnormal pregnancy is to propose a treatment that will either save the fetus, or expel the abnormal fetus, as is most often the case, in order to have the cow pregnant again within the shortest possible time. Although spontaneous abortion of mummified fetuses can occur (23), expulsion of the fetuses usually requires veterinary medical intervention. The treatment of choice in cases of fetal mummification is induction of luteolysis by injection of PGF2α, which is followed by the expulsion of the fetus within 2 to 4 d (24–28). In spite of having received PGF2α treatment, a certain percentage of animals do not expel the dead fetus. Vandeplassche et al (28) reported a spontaneous parturition rate of 60% (3 out of 5 cows) for cows carrying mummified fetuses.

Estrogens [estradiol, stilbestrol, and respositol diethylstilbestrol (DES)] are effective at provoking the regression of the CL and inducing contraction of uterine muscles, relaxation of the cervix, and expulsion of the mummified fetus in the cow (7): the administration of DES for a period of 2 to 6 d at doses ranging from 60 to 800 mg, IM, was 100% effective in causing expulsion of mummified fetuses diagnosed between 4 and 14 mo post-breeding (28). Estrogens can also induce abortion between 7 d and 5 mo gestation (29). Roberts (7) reported an 80% success rate within 3 d with a single injection of estrogens (80 mg of stilbestrol or 5 mg of estradiol 17ß). Even though estrogens are effective for expelling a uterine mummified fetus, their mechanism of action is still debated. One could assume that estrogens stimulate PGF2α production from the endometrium (28). In the present study, the medical treatment had allowed sufficient cervical dilation for the manual extraction of the fetus in all 3 treated cows within a relatively short period of time (< 5 d). Although estrogen is very effective in terms of expulsion of the mummified fetus, very little information is available regarding the future fertility of the dam. The present study reports no pregnancies following the medical treatment. It is not known whether or not this infertility is associated with the estrogen and oxytocin treatment, or if it is due to damage to the endometrium and cervical mucosa caused by the manual extraction of the fetus. However, no macroscopic lesions were observed during the vaginal examination following extraction of the fetus. Similar observations have been reported in previous studies where, in addition, histological assessment showed an intact epithelium and preserved uterine glands without signs of inflammation (28). In the case of cow No. 6, the clostridial metritis may have been secondary to lesions caused by uterine and vaginal manipulations. The total dose of estrogens administered to the animals in this study is exceedingly high, since it had been shown that a 4.0-mg dose of oestradiol cypionate could achieve serum estradiol concentrations similar to those associated with estrus (30). It is uncertain whether high concentrations of, or long-term treatment with, estrogens could be associated with low fertility. However, it is known that E17ß regulates uterine function by influencing PGF2α synthesis via endometrial oxytocin receptors (31,32). In addition to cervical relaxation, pelvic ligament relaxation was also observed under estrogenic medication, changing the conformation of the cows (33,34). Even though no statistical analysis was performed, the time of hospitalization (in this study) appeared longer in the group treated with estrogens (7.3 d) compared with the animals treated by hysterotomy (3.8 d). The potential risk of using estrogens in dairy cattle raises questions about food and environmental safety, as well as consumer acceptance (35).

In 1 study, a low parturition rate was reported with a single dose of PGF2α, even though relaxation of the birth canal was satisfactory, suggesting a uterine contractility defect (28). In situations where PGF2α did not lead to the expulsion of the mummified fetus, Hirsbrunner and Kaufmann (36) opted for a different medical approach. All mummified fetuses (6/6) were expelled manually after a combined treatment of PGF2α, 600 mg d-cloprosténol, IM, and prostaglandin E2 (PGE2), 2.5 dinoprotone, IV, Enducur, for a period of 3 to 6 d. In addition to their luteolytic properties (37), PGF2α and PGE2 have a direct effect on contractility of the myometrium (38–40). For cows in good condition, combined administration of PGF2α and PGE2 resulted in more effective uterine contractions than the injection of PGF2α alone (41). The synergistic effect of both prostaglandins could explain the increased success rate relative to the use of PGF2α alone. However, the high cost of the treatment (> $250) and the difficulty in obtaining the drug may limit the use of this protocol. To reach the most economically sound decision, the effect of surgical verses medical treatment on milk production has also to be taken into account.

Different surgical treatments are available for removing mummified fetuses that cannot be expelled by PGF2α injection. Hysterotomy, by a colpotomy approach (15,42), or by laparotomy using a caudal flank approach (43), has been used as a last resort. In both approaches, access to the pregnant horn is difficult. In the case of colpotomy, it is due to a lack of space for manipulation of the uterine horn containing the mummified fetus within in the vagina. With the caudal flank approach, the distance from the uterine horn to the caudal abdominal wall and the thickness of the abdominal wall may limit the surgeon's ability to exteriorize the uterus. The colpotomy approach is not recommended for large mummified fetuses (15). In the present study, access to the pregnant horn was improved by using a tocolytic agent (ritrodine), facilitating the exteriorization of the mummy by relaxing the uterine tract (21). Fifty percent of the surgeries (5/10) required the use of the tocolytic agent.

The present study is the first to report a 36% (5 out of 14) pregnancy rate within a few months after extraction of the mummified fetus by hysterotomy, using the flank approach.

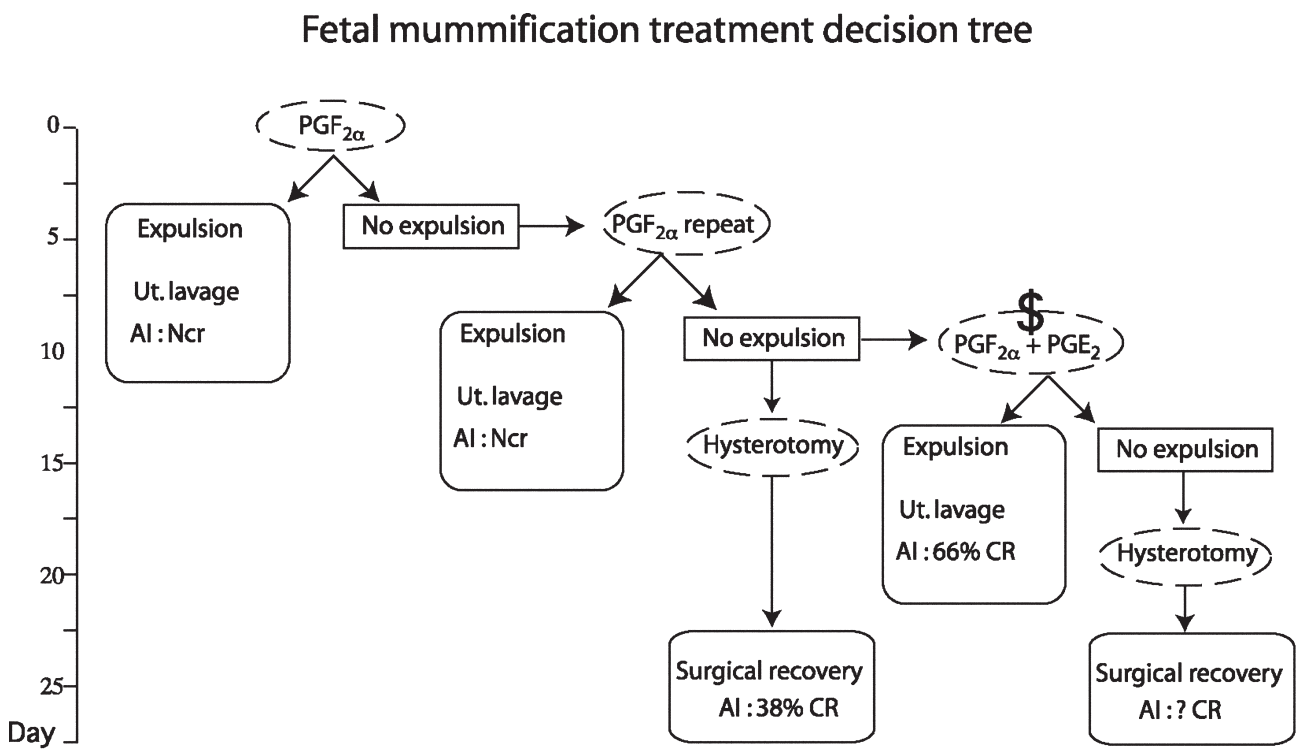

Figure 1. Decision tree for the clinical approach in cases of fetal mummification in cows. AI – artificial insemination, Ut. lavage – uterine lavage, N – normal, CR – conception rate, ? – unknown, PGF2α – prostaglandin F2α, PGE2 – prostaglandin E2, $ – expensive.

This pregnancy rate is comparable with the pregnancy rate (35%) in herds monitored by the veterinary school's ambulatory service [Dossier Santé Animal Health Records (DSA@HR) 2007, University of Montreal, Montreal]. Erb and Morrison (23) reported a pregnancy rate of 52% (15 out of 29) after natural expulsion of mummified fetuses. Within the limitations of the present study, it is difficult to assume that the method of delivery is the only factor affecting the conception rate. Although the potential bias in the selection of cases could not be controlled, all cases were assessed the same way and had to meet the inclusive criteria of the study.

In the present study, most of the diagnoses (63%) had been established by the veterinarian after the farmer had noticed the unusually small size of the cow's abdomen at a stage in the pregnancy when it should have been significantly larger. This is in agreement with the experience of Wenkoff and Manns (26), who reported that mummified fetuses stay in utero until they are removed following the presenting state of being several days past the calving date. However, Erbs and Morrison (23) reported a shorter mean period of gestation with mummified fetuses, with an average of 7.2 mo. This is in agreement with Davidson and Roberts (44). The mummification rate does not seem to be affected by the uterine horn in which the pregnancy is occurring, with 54% of the mummified fetuses being found in the right horn.

Based on the findings of the present study and those of previous reports, the authors propose a systematic approach to the treatment of pregnant cows diagnosed with a mummified fetus (Figure 1). In the case of a confirmed fetal mummification, administration of PGF2α is the primary and most effective treatment. In most cases, the mummified fetus will be expelled from the uterus. All treated cows should be assessed for 5 d after the 1st injection of PGF2α by transrectal and vaginal examination to verify the presence of a CL, dilation of the cervix, and the presence of the fetus in the vagina. After expulsion of the fetus, the uterus should be lavaged to remove fetal and placental debris, and the cow should be induced into estrus and inseminated. In the absence of a response to treatment, a 2nd injection of PGF2α should be administered, considering its cost effectiveness, followed by the same procedure as for the 1st treatment. In cases where the cow does not respond to the 2nd injection of PGF2α (after 5 d), a decision has to be made whether to proceed to hystorotomy (laparotomy or colpotomy) or pursue medical treatment with a combination of PGF2α and PGE2, based on the cost and on-farm feasibility. Depending on the circumstances, hysterotomy could result in a pregnancy rate comparable with that for the rest of the herd. Of course, in the situation where the combined treatment of prostaglandins (PGF2α and PGE2) is not effective, the veterinarian must proceed with the hysterotomy.

Authors' contributions

Drs. Francoz, Babkine, and Lefebvre participated in the cases, the analysis of the data, and the writing of the manuscript. Dr. Couto participated in the analysis and the writing of the manuscript. Drs. Saint-Hilaire and Morin participated in the review of the files and the writing of the manuscript.

Acknowledgment

The authors gratefully acknowledge the assistance of Mr. Guy Beauchamp for the data analysis. CVJ

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