Treating post calving dairy infections

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Reproductive performance of a dairy herd is an important factor influencing the financial success of the farm. Effects on average days in milk and average life time production of the cows are significant.

However, management of reproductive performance in dairy herds is a constant challenge due to its complex nature. This has mainly three reasons. Firstly, a timeline of approximately 140 days has to be managed (50 days dry period, 50 days voluntary waiting period, lag time of 40 days until pregnancy diagnosis). Secondly, events, disorders and activities are not independent from each other.

There are important dependencies and relationships, for example poor hygiene in the calving pen causes metritis which, in turn, leads to longer days open. Thirdly, there is a multitude of variables and risk factors in varying combinations that may influence reproductive performance.

On the occasion of a disappointing pregnancy examination it is usually not reflected that events that occurred a long time ago might have affected the outcome. In particular, fat body condition in late lactation, inadequate feeding in the dry period, poor calving hygiene or obstetrical procedures and post partum disorders are important.

Post partum health of the cow and the uterus are fundamental to ensure a good subsequent fertility. After parturition the uterine lumen is contaminated with pathogenic bacteria. Physiologically, many cows eliminate these bacteria within the first weeks after calving. The persistence of pathogenic bacteria causes inflammation and lesions of the endometrium and delays involution of the uterus. The inflammation can occur at different times and in varying degrees.

● **Puerperal or acute metritis.** Abnormally enlarged uterus, fetid watery red-brown discharge, signs of systemic illness and fever 39.5°C, within 21 days after calving.

● **Clinical endometritis.** Purulent or mucopurulent discharge, more than 21 days after calving, no signs of systemic illness, no fever.

● **Subclinical endometritis.** No clinical signs of endometritis, no purulent or mucopurulent discharge, can be determined only by cytology or ultrasound.

● **Pyometra.** Accumulation of pus in the uterus, enlarged uterus, corpus luteum present.

Predisposing factors post calving infections are dystocia, retained foetal membranes, as well as deficiencies in hygiene and metabolic imbalances around parturition. Associated bacteria are mainly arcanobacterium (actinomyces) pyogenes, coliform bacteria, and Gram negative anaerobic species such as Fusobacterium necrophorum and Bacteroides spp.

Retained membranes

Traditionally the treatment of choice for retained foetal membranes and puerperal metritis has been the infusion of antibiotics into the uterus. In cases with retained placentas an attempt is usually made to manually remove the foetal membranes.

However, the efficacy of a local antibiotic treatment as well as the removal of the placenta has been a controversial issue for many years. Negative interactions between antibiotic drugs and the uterine environment, the inhibition of the uterine defence mechanism by manipulations and by irritating drugs (for example oxytetracycline), as well as a questionable efficacy of antibiotics locally administered are some reasons to reconsider local manipulations and/or treatments. Also, variation in the duration of milk residues is huge and critical for milk producers to ensure high food safety standards.

In the last few years several large field studies have demonstrated the advantages of a systemic treatment for both retained foetal membranes and acute metritis in dairy cows. Therefore, the objective of this article is to summarise the meanwhile overwhelming evidence for a systemic treatment.

Since a cow with retained foetal membranes has a high risk of becoming sick with acute metritis the treatment of both diseases are combined. Veterinarians, milk producers and other dairy professionals usually raise five questions:

● **Does a systemic treatment lead to concentrations in the uterus that are high enough to eliminate the relevant bacteria?** Two studies were conducted to determine the concentrations of active ceftiofur metabolites in blood serum, endometrium, caruncles, cotyledons, and lochia. The first study examined healthy cows after calving, while the second study used cows that had a case of retained foetal membranes.

The goal was to examine whether the concentrations would be high enough to kill those bacteria that are most frequently associated with postpartum disorders such as E. coli, F. necrophorum, and A. pyogenes. The results from both studies were consistent.

Within four to 12 hours after subcutaneous administration of ceftiofur at the dose of 1mg/kg body weight concentration of active ceftiofur metabolites exceeded the minimum inhibitory concentrations (MIC's) for the common pathogens.

Fig. 1 shows the mean concentrations of ceftiofur metabolites in blood serum, endometrial and caruncular tissue after three subcutaneous administrations of 1mg of ceftiofur/kg body weight.

● Is a systemic treatment alone efficacious or is it better to remove the foetal membranes and infuse antibiotics into the uterus on top of a systemic treatment?

Several previous field trials had shown that a systemic intervention was equally effective to treat retained foetal membranes as the traditional approach. This was true not only for important clinical parameters such as incidence of endometritis one month after calving but also for reproductive performance parameters such as days open, first service conception rate, % of cows pregnant by 200 days in milk.

Therefore it was plausible to raise the question whether an attempt to remove the foetal membranes and infuse antibiotics into the uterus on top of a systemic treatment would result in additional benefits.

The Clinic of Animal Reproduction at the Free University of Berlin (www.tiergyn.de) conducted one of the largest field trials ever on retained foetal membranes to answer this question.

In this field trial, a standard protocol for the treatment of retained foetal membranes without any intrauterine therapy was compared to three protocols based on the intrauterine use of antibiotic pills, the manual removal of the foetal membranes, or the combination of both. The study was conducted on five commercial dairy farms in Germany. In total 501 cows with retained foetal membranes were enrolled.

Cows of all groups with a rectal temperature ≥ 39.5°C received a systemic antibiotic treatment with ceftiofur (1mg/kg body weight per day) for 3- 5 consecutive days. In the reference group, (n=131) cows did not receive any additional treatment. In the second group cows (n=119) were treated intrauterinely with antibiotic pills (1g of ampicillin and 1g of cloxacillin) for three days. In the third group (n=121) an attempt was made to remove the foetal membranes manually, but uterine pills were not administered. In the last group (n=130) an attempt was made to remove the foetal membranes manually and all cows received a local antibiotic treatment as in the second group.

All cows received two doses of PGF2_ (18-24 and 32-38 days post partum). Occurrence of fever within 10 days post partum was significantly lower in the two groups that received antibiotic pills intrauterinely compared to the reference group. Risk of a treatment failure in case of fever after five treatments with ceftiofur did not differ among groups. Also reproductive performance measures did not differ significantly between the reference group receiving only the systemic treatment and any of the comparison groups (Table 1).

This large scale field trial demonstrated that neither local antibiotic treatment nor manual removal of the retained placenta or the combination of both resulted in an improved clinical efficacy or reproductive performance compared to an exclusive systemic antibiotic treatment of cows having fever. Only the incidence of fever within 10 days post partum was reduced by local antibiotics. Clinical and reproductive performance variables were influenced by herd and parity but not by an additional intrauterine manipulation or treatments. Systemic treatment alone based on elevated rectal temperature was effective and reduced use of antibiotics compared to therapies that included intrauterine antibiotics.

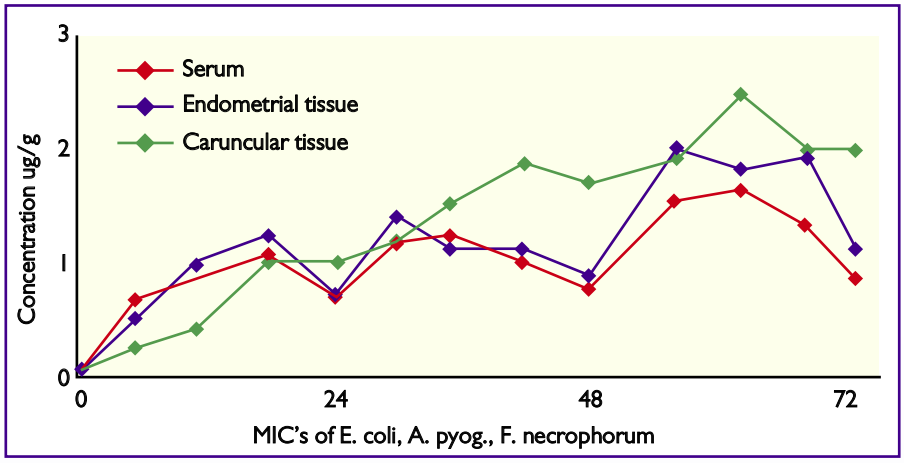

Fig. 1. Mean concentrations of ceftiofur metabolites in blood serum, endometrial and caruncular tissue after three subcutaneous administrations of 1mg of ceftiofur per kg body weight at 0, 24, and 48 h. The concentration necessary to kill relevant bacteria is marked in red (MIC= minimum inhibitory concentration).

● Does a systemic treatment also work on small farms?

Most of the trials presenting hard scientific evidence are conducted on large dairy farms because enrolment of cows and the strict implementation of a study protocol can be monitored more easily. Not necessarily the results obtained can be transferred to small farms.

Therefore it is valid to ask the question whether those results are also true for smaller farms which differ in housing and management practices. To address this question another study was performed on 32 farms ranging in herd size from 28 to 166 cows. A total of 264 cows could be analysed at the end of the trial.

Again a reference protocol for the treatment of retained foetal membranes without any intrauterine therapy or manipulation (group 1) was compared to a treatment protocol including the attempt to manually remove the foetal membranes and the intrauterine use of antibiotic pills (6g of tetracyclin). In case of fever (≥ 39.5°C) cows in group 1 received a systemic antibiotic treatment with ceftiofur (1 mg/kg body weight) for 3-5 consecutive days while cows of group 2 were treated with Amoxicillin (10mg/kg body weight) for 3-5 days.

Treatments of group 2 were chosen since they represented the typical intervention strategy for retained foetal membranes on the participating farms. The results were very interesting.

The incidence of fever within the first 10 days after calving was 76.9% in group 1, while only 21.1% of the cows in group 2 experienced fever. However, the prevalence of signs of endometritis in the fifth week post partum was almost identical (group 1: 33.9%, group 2: 37.1%).

Furthermore, reproductive performance of the two groups was comparable (Table 2). Therefore, we concluded that only the growth of the bacteria was reduced by the intrauterine antibiotics but no carry over effect existed in respect to the prevalence of endometritis nor to reproductive performance. Overall, there was no benefit in the traditional approach – removal of placenta and intrauterine antibiotics.

● Since a lot of cows get fever is a systemic treatment for all cows with retained foetal membranes advantageous?

It is well known that a significant proportion

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Table 1. Clinical and reproductive performance in the reference and three treatment groups.

Variable	Systemic treatment	Antibiotic pills	Manual removal	Manual removal and antibiotic pills
Number of cows	131	119	121	130
Incidence of fever (%)	85.5	78.2	84.3	71.5
Cows inseminated (%)	84.0	82.4	80.2	80.0
Days to first service (%)	77.0	74.0	75.0	75.0
1st service conception rate (%)	32.7	32.7	36.1	25.0
Days to pregnancy	97.5	104.0	93.0	99.5
Cows pregnant by 200 DIM (%)	61.1	64.7	58.7	52.3
Cows culled by 200 DIM (%)	16.0	21.0	19.0	20.8

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of cows with retained foetal membranes has an elevated body temperature post partum (35 to 95%) and requires special attention and treatment.

After having used and appreciated the systemic approach for a while veterinarians and dairymen raised the question of the efficacy of a blanket treatment for all cows with retained foetal membranes. Because that approach has the potential to jeopardise a prudent use of antibiotics a field study was conducted to provide good evidence.

The special hypothesis was whether a blanket or preventive treatment of cows with retained foetal membranes with ceftiofur on day 1 after calving, regardless of an elevated body temperature would reduce the occurrence of fever and improve reproductive performance compared to the selective treatment with ceftiofur only in case of fever.

Cows that retained their foetal membranes for at least 24 hours after calving were allocated to two groups. Rectal temperature was measured daily for 10 days post partum. In group 'blanket treatment' (n = 60) all cows with retained foetal membranes (regardless of fever) received a daily antibiotic treatment with ceftiofur (1.0mg/kg bw), administered on the first three days after diagnosis. In group 'selective treatment' (n = 53) the systemic therapy with ceftiofur was restricted only to cows with retained foetal membranes and fever within 10 days post partum. Treatment was conducted for 3-5 consecutive days beginning at the first day of fever. In both groups manual removal of the placenta was not attempted and antibiotic drugs were not administered into the uterus.

Surprisingly, the blanket antibiotic treatment did not reduce the proportion of cows experiencing fever within 10 days post partum compared to cows treated selectively (71.7 vs. 69.8%). While the service rate within 42 to 62 days post partum was significantly higher for the cows receiving the blanket treatment (41.2 vs. 20.8%), total conception rate was significantly lower compared to the selective treatment, respectively (25.0 vs. 36.8). Further clinical findings (proportion of cows with endometritis and reproductive performance parameters) did not differ between the groups.

Variable	Systemic treatment	Manual removal and antibiotic pills
Number of cows	117	147
Incidence of fever (%)	76.9	21.1
Cows inseminated (%)	73.5	70.7
Days to first service	97.1	95.6
1st service conception rate (%)	48.8	51.9
Days to pregnancy	113.1	110.9
Cows pregnant by 200 DIM (%)	59.0	56.5
Cows culled by 200 DIM (%)	15.4	11.6

Table 2. Clinical and reproductive performance in the reference and three treatment groups.

In summary, a blanket systemic antibiotic treatment of all cows with retained foetal membranes does not have advantages compared to a selective antibiotic treatment of cows only in case of fever. Very importantly the use of antibiotics can be reduced and is restricted to a clear diagnosis. Thus monitoring body temperature and treating only cows with fever ensures a prudent use of antibiotics and is cheaper.

● What is the best treatment for cows with acute metritis?

Acute postpartum metritis (APM) can be characterised by pyrexia up to 10 days post partum with a fetid purulent vulval discharge. These findings are associated with delayed involution of the uterus and subsequent lower fertility.

A severe case of acute metritis can be potentially life-threatening. Often the disease is preceded by a case of retention of the foetal membranes, hypocalcaemia and usually poor hygiene in the maternity area. Metritis causes severe economic losses due to costs for treatment, milk withdrawal, reduced reproductive performance, and premature culling. The economic losses due to milk withdrawal depend on milk yield, milk price, and length of withdrawal period.

A common treatment of acute puerperal metritis unfortunately is still the infusion of antibiotics into the uterus. However, the efficacy of a local antibiotic treatment is a controversial issue. Reasons to reject a local treatment include negative interactions between antibiotic drugs and the uterine environment, the impairment of the uterine defence mechanism and a questionable efficacy of antibiotics within the inflamed uterine and tubal wall.

To provide better information for decision makers a field trial on a commercial dairy was initiated to evaluate the efficacy and financial viability of a systemic treatment of APM in cattle with ceftiofur. Cure rates six days after treatment and subsequent reproductive performance were compared with two control groups treated with intrauterine and systemic application of antibiotic drugs.

Bacteria involved were determined and their antibiotic susceptibilities to the used antibiotic drugs were tested. Finally, a financial analysis with different cost scenarios was performed, including costs for veterinary treatments, milk withdrawal, reproductive performance and premature culling.

Cows with abnormal vaginal discharge at a postpartum examination (day 4-6 after calving) and a rectal temperature ≥39.5°C were assigned to three treatment groups. Cows in group 1 (n = 70) received 600mg of ceftiofur intramuscularly (i.m.) on three consecutive days. Cows in group 2 (n = 79) received an intrauterine treatment with antibiotic pills consisting of 2500mg of ampicillin and 250mg of cloxacillin and an additional 6000mg (i.m.) of ampicillin. This treatment was performed on three consecutive days. Cows in group 3 (n = 78) received the same intrauterine treatment as in group 2. In addition, 600mg of ceftiofur was administered i.m. on three consecutive days. Body temperature was recorded daily for six days after first treatment.

There were no major differences among the groups regarding clinical efficacy at day 6 after first treatment. The cure rates based on rectal temperatures declining to below 39.5°C on day six after treatment were comparable (82.9, 84.8, and 84.6% for groups 1, 2, and 3). Reproductive performance did not differ significantly between group 1 and groups 2 and 3 for any of the parameters tested. A financial analysis with different cost scenarios demonstrated that a systemic treatment of acute puerperal metritis in cattle with ceftiofur was advantageous in many scenarios. ■

- A systemic treatment with ceftiofur (1mg/kg bw) leads to concentrations in the uterus that are high enough to kill the relevant bacteria
- The infusion of antibiotics into the uterus and/or the attempt to remove the foetal membranes on top of a systemic treatment do not improve cure rate or reproductive performance
- A systemic treatment also works on smaller farms
- A blanket treatment for all cows with retained foetal membranes is not advantageous
- The systemic treatment of toxic puerperal metritis in cattle with ceftiofur is an effective alternative to protocols based on combined intrauterine and systemic antibiotic treatment