

## Metritis and endometritis in high yielding dairy cows

### *Metritis en endometritis bij hoogproductief melkvee*

G. Opsomer, A. de Kruif

Department of Reproduction, Obstetrics and Herd Health,  
Faculty of Veterinary Medicine,  
Ghent University, Belgium

#### ABSTRACT

Since a few decades, dairy cows have shown a steep increase in milk production, which is unfortunately accompanied by a dramatic decline in reproductive performance.

In these high yielding cows there are more puerperal problems than in low yielding cows, such as retained placenta, acute metritis and abnormal vaginal discharge. Cows affected by retained placenta and/or acute metritis are furthermore at a significantly higher risk of other typical 'dairy cow diseases' as acetonemia, left displaced abomasum and cystic ovarian disease.

Therefore it is important that puerperal metritis is treated properly with broadspectrum antibiotics both parenterally and intra-uterine during 1 – 3 days depending on the severity of the symptoms. Cows with chronic endometritis need no treatment before 30 days post partum. From day 30 on they should be treated twice with prostaglandins at an interval of 14 days.

A challenge for the future is to clearly determine all risk factors for uterine disease. One of the major risk factors is a retained placenta. Correct nutrition during the dry off period and a normal calving process under hygienic conditions are the paramount factors in the prevention of this risk factor.

#### SAMENVATTING

De vruchtbaarheid van hoogproductieve melkkoeien is de laatste decennia sterk verminderd. Een van de redenen is dat hoogproductieve koeien meer problemen hebben in het puerperium, zoals retentio secundinarum, endometritis en witvuilen. Bovendien is gebleken dat koeien met retentio secundinarum of endometritis een veel hoger risico lopen op andere ziekten, zoals een linkse dislocatie van de lebmaag, acetonemie of cysteuze ovariële follikels. Het is daarom belangrijk dat koeien met een puerperale endometritis snel en doeltreffend worden behandeld met antibiotica gedurende 1 tot 3 dagen. Koeien met een chronische endometritis kunnen het beste 2 keer, met een interval van 14 dagen, worden behandeld met prostaglandinen vanaf 30 dagen post partum.

Omdat retentio secundinarum de belangrijkste risicofactor is voor tal van problemen bij pasafgekalfde koeien moet er alles aan gedaan worden om dit probleem te voorkomen. Een correcte droogstandvoeding, een normaal afkalfproces en een zeer goede hygiëne rond het afkalven zijn wat dit betreft uiterst belangrijk.

#### INTRODUCTION

Before milk production starts, cows have to calve and each calving is followed by a milk production peak. This standard 'cow knowledge' clearly illustrates why reproduction is still of paramount importance in the modern dairy industry.

Recent studies both in the US and in Europe indicated that during the last 35 years, the genetic potential for milk production in Holstein Friesian cows has increased by over 3000 kg per lactation, resulting in an actual genetic increase of about 100 kg/year. However, this is only a part of the (success) story. The genetic potential for milk production sets the upper limit which an individual cow can achieve. How close she actually comes to reaching that limit is determined by the management conditions under which she has to produce.

During the last decades these conditions have been improved tremendously. There have been improvements in feeding practices, in the control and prevention of diseases and in other management practices such as housing. All together these improvements have contributed to the actual level of milk production, which on many farms has gone above 9000 kg per lactation (of 305 days).

Clearly, the aggressive genetic selection together with the fine tuning of the management has proven to be very successful. However, this has not been without costs. When dairy farmers are currently asked what the principal health problems will be their business will be facing in the near future, they invariably mention subfertility, mastitis and lameness. These diseases are known to be multifactorial and are to a large extent dependent on management practices.

## HIGH YIELDING DAIRY COWS PRODUCE WELL BUT REPRODUCE BAD

The time period characterized by the steep increase in milk production, is unfortunately also characterized by a dramatic decline in reproductive performance. Both the average number of days open (interval from calving to the next conception) and the number of services per conception have increased substantially, whereas the conception rate has declined significantly (Lucy, 2001, Leroy and de Kruif, 2006).

Worldwide, calving rates to first service are reported to have declined from 60% to 30-40% over the past 25 years. If this trend continues at its current rate, in a further 20 years only 20% of the cows will conceive to first service. This conclusion has been confirmed independently in the UK (Royal *et al.*, 2000 a, b) and in the US (Butler, 2000), and subsequently in many other European countries.

Also in Flanders and The Netherlands, the increase in milk production per cow has been accompanied by a significant increase in the calving interval, from 395 days in 1987 to 419 days in 2007 while the 56 day non-return rate has remained relatively stable (Opsomer *et al.*, 2006 a,b; de Kruif *et al.*, 2008). Analyses of fertility data from local AI centres revealed that the prolongation of the calving interval was mainly due to a prolongation of the interval from parturition to first insemination, due to the inability of the farmers seeing their cows in heat at the moment they should inseminate them (Opsomer *et al.*, 2000b).

The main negative results of this decline in fertility are longer and hence 'inefficient' lactations and an increase in the number of cows that are culled for reproductive reasons. The significant waste of sperm and the retarded increase of young stock are also important contributors to a significant loss of income.

**Table 1. Average incidence of puerperal disturbances on 9 high-yielding dairy herds in Belgium (Opsomer *et al.*, 2000a).**

Puerperal disturbance	Incidence (n=463)
Abnormal calvings	16%
Retained placenta	18%
Acute (endo)metritis	15%
Abn vag discharge	20%
Perivaginitis	5%

So why has reproductive performance declined so precipitously? This has proven to be a very difficult question to answer (Vanholder *et al.*, 2006). However, a recurring theme is that for cows to reproduce successfully, a clean and healthy uterine environment is essential. Indeed, the uterus not only influences the resumption of normal ovarian cyclicity to a large extent, but also has to promote sperm transport and finally has to undergo considerable changes to support pregnancy.

## THE DILEMMA OF THE POSTPARTUM COW

A remarkable feature of cattle is the almost constant bacterial contamination of the uterine lumen within the first 2 weeks after parturition. However, cows have always been considered to be highly efficient in clearing this contamination, in contrast for example to horses. Present-day, high-yielding dairy cows obviously have more problems and do not quite live up to this reputation. As a result, we now see more cows with puerperal problems, such as retained placenta, acute metritis, abnormal vaginal discharge. (Table 1).

Although it is very difficult to compare these data with those from earlier studies because of possible (historical) differences in the use of the terms 'endometritis' and 'metritis', it is clear that the overall incidence of uterine diseases in high yielding dairy cows has increased over time (Table 2). Besides the recurrent discussion about the definition of the words 'endometritis' and 'metritis', this large variation is also due to the differences in the diagnostic methods used to classify uterine infections. The use of modern techniques such as ultrasonography and the examination of endometrial aspirates for the presence of inflammatory cells have obviously caused a steep increase in the reported incidence of endometritis (Figure 1).

Throughout the years however, authors always have agreed that the incidence of chronic endometritis (= localized infection of the superficial lining of the uterus occurring >3 weeks after calving), is significantly dependent on the incidence of acute metritis (= infection of the uterine cavity, and of the deeper layers of the uterus causing a sometimes life threatening disease shortly after calving). There is general agreement nowadays that up to 40% of animals have metritis within the first two weeks of calving and that in 10-15% of these animals infection

**Table 2. Evidence of an increasing trend in the incidence of (endo)metritis based on an extensive literature review.**

Endometritis incidence	Year of the study	Authors
11%	1968	Tennant and Peddicord
10%	1977	Bouters and Vandeplassche
38%	1983	Oltenu, <i>et al.</i>
37%	1984	Markusfeld
20%	1986	Whitmore and Anderson
17% (clin) + 37% (subclin)	2002	LeBlanc/Kasimanickam
53%	2005	Gilbert, <i>et al.</i>

persists for at least another three weeks causing the chronic uterine disease called endometritis (Sheldon and Dobson, 2004).

As uterine inflammation occurs in all cows during uterine involution, the factors responsible for the failure to resolve the endometrial inflammation at the start of the breeding period seem to be critical. The latter clearly emphasizes the need to detect and treat animals suffering from endometritis efficiently and as soon as possible to avoid problems later on. On the

average dairy farm however, disease detection is done by the veterinarian, but typically only during routine herd health checks. This means that in many cases, early warning signs of disease go unnoticed until such time that the disease is in its full clinical stage and becomes much more difficult to treat. As a result chronic endometritis may still be present at the moment cows should become pregnant.

Cows affected by retained placenta and/or acute metritis are furthermore at a significantly higher risk of

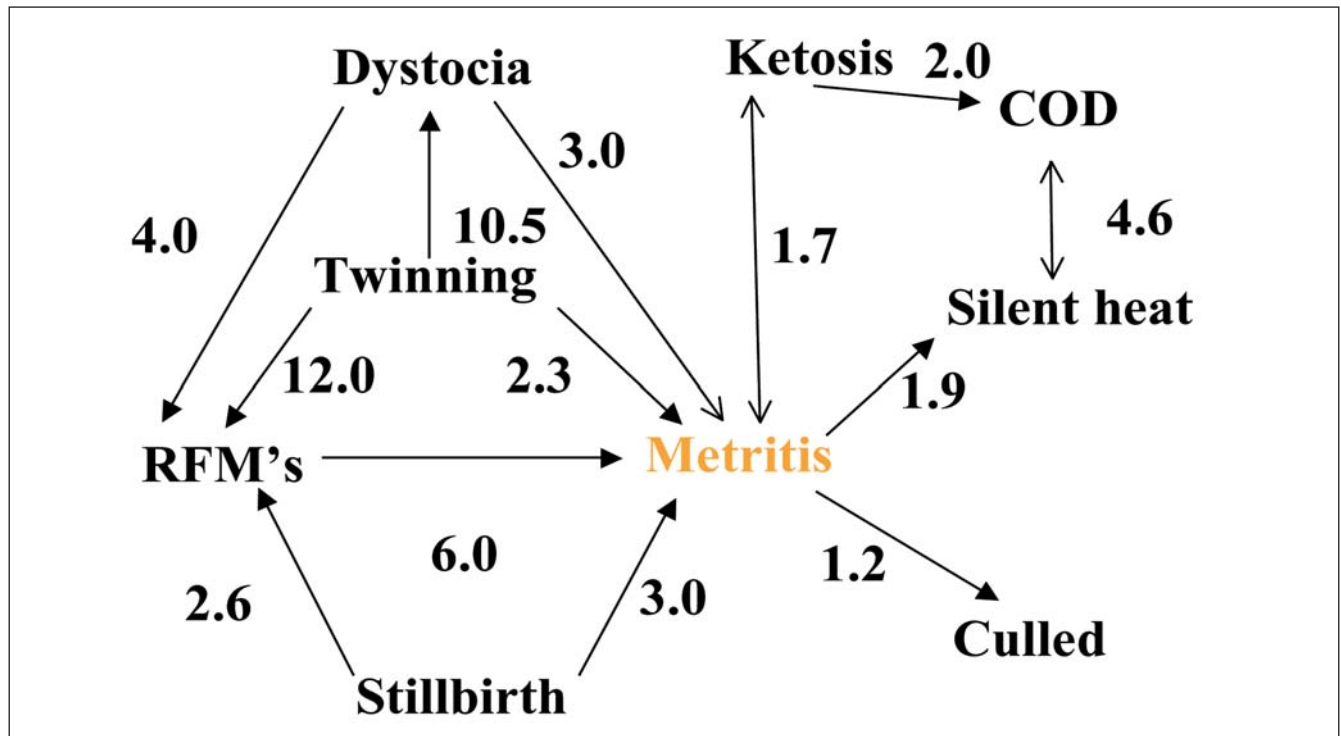


Figure 1. Results of risk factor analyses (odds ratios) for different postpartal diseases in high yielding dairy cows and underlying interactions. RFM= retained fetal membranes. COD= cystic ovarian disease.

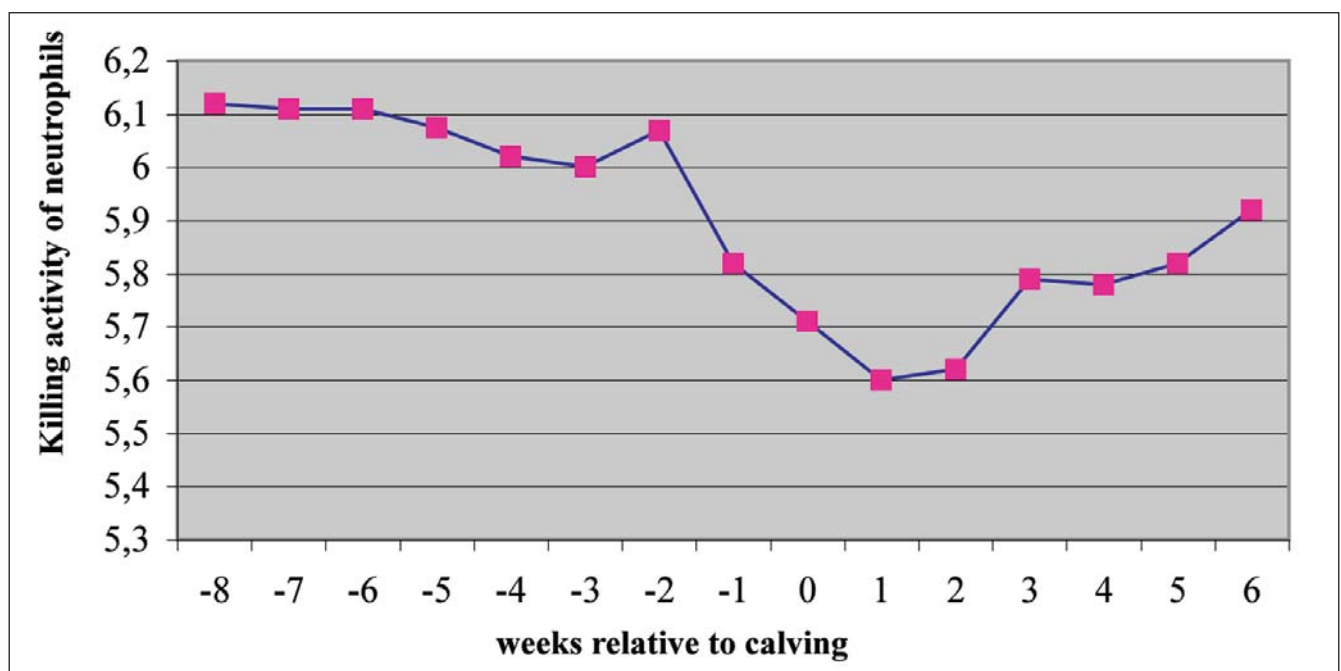


Figure 2. Killing activity of neutrophils around calving.

other typical 'dairy cow diseases' as acetonemia, left displaced abomasum and cystic ovarian disease. Large scale studies based on both American and European data showed, for example, that cows with retained placenta are 2.2 times more at risk of left displaced abomasum and 6.0 times more at risk of developing metritis. Metritis itself causes cows to be 2.0 times more at risk of ketosis; and ketosis makes cows significantly more sensitive to cystic ovarian disease and left displaced abomasum. Although there are some differences in the final numbers published among the different studies, there is an overall agreement that retained placenta and/or acute postpartum metritis is often, if not always, the key element in the disease history of recently calved high yielding dairy cows (Curtis *et al.*, 1985; Peeler *et al.*, 1994; Correa *et al.*, 1993).

Although these relationships are clearly proven in large scale epidemiological studies, the underlying pathogenesis has not yet been fully elucidated. In a number of studies it was demonstrated that the killing activity of neutrophils in high-yielding dairy cows is significantly reduced around the time of calving (Hoben *et al.*, 2000) (Figure 2). This was further confirmed by *in vitro* studies in which a decreased killing activity of these cells was demonstrated when elevated amounts of ketone bodies were added to the culture medium. This finding probably explains the close relationship between infectious diseases and ketosis seen on present-day dairy herds.

Furthermore it has recently been shown that cows going off feed, is one of the most important risk factors for a left displaced abomasum after calving (Van Winden *et al.*, 2003). In this case, the rumen is not able to act as a physical barrier against the gas filled enlarged abomasum which is hence able to change place in the abdomen. Cows suffering from acute metritis after calving have a distinct decrease in dry matter intake, which might explain the remarkably high incidence of left displaced abomasum in these patients.

#### A BAD START USUALLY ENDS UP IN A LOT OF COSTLY TROUBLES

Greater uterine bacterial contamination is associated with reduced ovarian follicular growth and function. Late resumption of regular ovarian cyclicity after

parturition has, of course, long-term consequences for subsequent fertility. A comparison of ovarian activity in moderate yielding (4000-5000 kg milk per lactation) Friesian cows fed mainly grass and grass silage in Ireland (Fagan and Roche, 1986), versus Belgian Holsteins producing 8000 to 9000 kg milk per lactation and fed high amounts of concentrates (Opsomer *et al.*, 1998), revealed interesting differences. The Belgian cows not only had an increased number of puerperal disorders, but also a significantly elevated incidence of postpartum anoestrus, abnormal ovarian cycles and prolonged luteal phases (high progesterone for >20 days before breeding) (Table 3).

Large scale progesterone monitoring projects carried out in the UK over the last 30 years, have confirmed these striking data. Furthermore, a high number of puerperal disorders is significantly associated with an elevated number of postpartum aberrations of ovarian cyclicity, leading to an increased number of cows not seen in heat at the moment farmers should inseminate them.

Overt infection of the uterus not only influences ovarian cyclicity (Sheldon *et al.*, 2002), but also disrupts the establishment of pregnancy, both by the physiological presence of pus, and by altered immune responses that are essential at the interface between the endometrium and the embryo. In this context, we can refer to cows discharging small amounts of pus in their mucus around the time of oestrus and insemination. While these cows are not clinically ill, they need veterinary attention because they may often end up as repeat breeders. Although it is quite obvious that pus reflects the presence of bacterial infection, in the majority of cases these small amounts of pus are just the remainders of the neutrophils which cleaned the uterus of bacterial contamination.

Based on the above it is clear that difficulties during calving (dystocia), and immediately after calving (e.g. retained placenta) predispose cows to endometritis and subfertility. Hence, all authors agree that the calculation of the total costs associated with uterine infections consists of a composition of both direct (such as treatment costs and the direct decrease in milk production) and indirect costs (such as the increased number of inseminations, prolongation of the calving interval and increased culling rate). That's why depending on the source, calculated losses caused by

**Table 3. A comparison of postpartum reproductive parameters based on measurement of progesterone in milk twice weekly in two different studies using moderate yielding Friesians (Fagan and Roche, 1986) or high-yielding Holsteins (Opsomer *et al.*, 1998).**

Results of studies based on prog analysis	Traditional herds (Fagan and Roche 1986)	High-yielding herds (Opsomer <i>et al.</i> 1998)
No. of cycles	448	463
Normal cyclical patterns (%)	78	53
Delayed cyclicity (%)	7	21
Temporary cessation of cyclicity (%)	3	3
Prolonged luteal phase (%)	3	20
Short cycles (%)	4	0.5
Other irregular patterns (%)	4	2.5



puerperal disorders and endometritis vary between 160 to 420 euro per case.

Although many authors mention that cows with puerperal disorders are at a significantly higher risk of other diseases, such as left displaced abomasum and ketosis, studies focusing on economic losses caused by endometritis often do not mention this. Therefore, it is clear that the figures mentioned are a serious underestimation of the real losses farmers have to face.

## TREATMENT

Puerperal metritis should be treated with broad-spectrum antibiotics both parenterally and intra-uterine during 1-3 days depending on the severity of the symptoms.

However, many veterinary surgeons treat animals suffering from chronic endometritis intra-uterine with antibacterials. One should ask why? One answer might be that farmers force practitioners to treat these animals although most practitioners do know that such a treatment is not very helpful. This is based on psychology and only reflects our own weakness in the sense of '...at least we do all we can to treat these patients...'. It should be realized that in a lot of cases these treatments are not only an example of off label use of antibiotics, but that the success of such a treatment is generally known to be poor and in some cases even has been demonstrated to be deleterious. Especially farmers who perform 'do it yourself insemination' are all too often guilty of this kind of uterine misuse of antibiotics and should be told that this is not the strategy to go for.

Cows with chronic endometritis need no treatment before 30 days post partum. From day 30 p.p. on they should be treated twice with prostaglandins at an interval of 14 days. This treatment leads to regression of the corpus luteum (if present), uterine contractions, discharge of pus, and oestrus, resulting in a clean uterus at the beginning of the insemination period.

## PREVENTION

A basic principle in veterinary medicine is that the earlier an abnormality is diagnosed and care is provided, the faster that animal will return to a normal state of health. In the past, cows with endometritis were often identified too late, leaving little chance for a successful outcome once care was administered. Cows with chronic endometritis displaying pus in their discharge at the time of insemination illustrate this reasoning well. In this context, it is absolutely without any doubt that the management of cows with uterine health problems should be based on a preventive approach rather than another disappointing curative one. This preventive approach definitely needs to include an early identification and treatment of cows with puerperal metritis in the postpartum period. Careful clinical examination of animals at risk is strictly needed in order to detect affected animals in time. This should then be followed by a prompt and effective treatment.

A further challenge for the future is to clearly identify all risk factors for metritis, and design prevention and control programs to reduce the disease's incidence.

One of the already well known risk factors is a retained placenta. The prevention of this problem is therefore very important in order to reduce endometritis postpartum. A correct nutrition during the dry off period (Opsomer *et al.*, 2004) and a normal calving process under hygienic conditions are the paramount factors in the prevention of placental retention.

## CONCLUSION

This article focuses on the importance of the immediate post-partum period in high-yielding dairy cows. To get through this period with minimal disease impact, it is highly advisable to follow a pre-established fresh cow program. It is clear that the greater the cow's genetic ability to produce milk, the greater the need for proper adjustment of the multiple factors that will allow her to better express her genetic potential. A pre-established fresh cow program is, however, not the only variable that will help to solve the equation! Reliable procedures that can identify problem cows as soon as possible in order to get them treated with efficacious drugs before serious harm has occurred, are at least as important!

## REFERENCES

- Bouters R., Vandeplassche M. (1977). Post partum infection in cattle: diagnosis and preventive and curative treatment. *Journal of the South African Veterinary Association* 48, 237-239.
- Butler W.R. (2000). Nutritional interactions with reproductive performance in dairy cattle. *Animal Reproduction Science* 60, 449-457.
- Correa M., Erb H., Scarlett J. (1993). Path analysis for seven postpartum disorders of Holstein cows. *Journal of Dairy Science* 76, 1305-1312.
- Curtis C., Erb H., Sniffen C., Smith R., Kronfeld D. (1985). Path analysis of dry period nutrition, postpartum metabolic and reproductive disorders, and mastitis in Holstein cows. *Journal of Dairy Science* 68, 2347-2360.
- De Kruif A., Leroy J., Opsomer G. (2008). Reproductive performance in high producing dairy cows: practical implications. *Tierärztliche Praxis* 36 (Suppl 1), S29-S33.
- Fagan J.G., Roche J.F. (1986). Reproductive activity in post partum dairy cows based on progesterone concentrations in milk or rectal examination. *Irish Veterinary Journal* 40, 124-131.
- Gilbert R., Shin S., Guard C., Erb H., Frajblat M. (2005). Prevalence of endometritis and its effects on reproductive performance of dairy cows. *Theriogenology* 64, 1879-1888.
- Hoeben D., Monfardini E., Opsomer G., Burvenich C., Dossogne H., de Kruif A., Beckers J.F. (2000). Chemiluminescence of bovine polymorphonuclear leucocytes during the periparturient period and relation with metabolic markers and bovine pregnancy-associated glycoprotein. *Journal of Dairy Research* 67, 249-259.
- Kasimanickam R., Duffield T., Foster R., Gartley C., Leslie K., Walton J. (2004). Endometrial cytology and ultraso-

- nography for the detection of subclinical endometritis in postpartum dairy cows. *Theriogenology* 62, 9-23.
- LeBlanc S.J., Duffield T.F., Leslie K.E., Bateman K.G., Keefe G.P., Walton J.S., Johnson W.H. (2002). Defining and diagnosing postpartum clinical endometritis and its impact on reproductive performance in dairy cows. *Journal of Dairy Science* 85, 2223-2236.
- Leroy J.L.M.R., de Kruif A. (2006). Reduced reproductive performance in high producing dairy cows: is there actually a problem? *Vlaams Diergeneeskundig Tijdschrift* 75, 55-60.
- Lucy M.C. (2001). Reproductive loss in high-producing dairy cattle: where will it end? *Journal of Dairy Science* 84, 1277-1293.
- Oltenucu P.A., Frick A., Lindhé B. (1990). Epidemiological study of several clinical diseases, reproductive performance and culling in primiparous Swedish cattle. *Preventive Veterinary Medicine* 9, 59-74.
- Opsomer G., Coryn M., Deluyker H., de Kruif A. (1998). An analysis of ovarian dysfunction in high yielding dairy cows after calving based on progesterone profiles. *Reproduction in Domestic Animals* 33, 193-204.
- Opsomer G., De Vlieghe S., de Kruif A. (2004). Droogstand en transitieperiode van hoogproductieve melkkoaien: wat met de voeding? *Vlaams Diergeneeskundig Tijdschrift* 73, 374-383.
- Opsomer G., Gröhn Y.T., Coryn M., Hertl J., Deluyker H., de Kruif A. (2000a). Risk factors for postpartum ovarian dysfunction in high producing dairy cows in Belgium. *Theriogenology* 53, 841-857.
- Opsomer G., Laevens H., Steegen N., de Kruif A. (2000b). A descriptive study of postpartal anoestrus in nine high-yielding dairy herds in Belgium. *Vlaams Diergeneeskundig Tijdschrift* 69, 31-37.
- Opsomer G., Leroy J., Vanholder T., Bossaert P., de Kruif A. (2006a). High milk production and good fertility in modern dairy cows: the results of some recent research items. *Slovenian Veterinary Research* 43, 31-39.
- Opsomer G., Leroy J., Vanholder T., Bossaert P., de Kruif A. (2006b). Subfertility in high yielding dairy cows: how to bring science into practice? *Vlaams Diergeneeskundig Tijdschrift* 75, 113-119.
- Peeler E.J., Otte M.J., Esslemont R.J. (1994). Interrelationships of periparturient diseases in dairy cows. *The Veterinary Record* 134, 129-132.
- Royal M.D., Darwash A.O., Flint A.P.F., Webb R., Williams J.A., Lammung G.E. (2000a). Declining fertility in dairy cattle: changes in traditional and endocrine parameters of fertility. *Animal Science* 70, 487-501.
- Royal M.D., Mann G.E., Flint A.P.F. (2000b). Strategies for reversing the trend towards subfertility in dairy cattle. *Veterinary Journal* 160, 53-60.
- Sheldon I.M., Dobson H. (2004). Postpartum uterine health in cattle. *Animal Reproduction Science* 64, 295-306.
- Sheldon I.M., Noakes D.E., Rycroft A.N., Pfeiffer D.U., Dobson H. (2002). Influence of uterine bacterial contamination after parturition on ovarian dominant follicle selection and follicle growth and function in cattle. *Reproduction* 123, 837-845.
- Tennant B., Peddicord R.G. (1968). The influence of delayed uterine involution and endometritis on bovine fertility. *Cornell Veterinarian* 58, 185-192.
- Van Winden S., Jorritsma R., Müller K., Noordhuizen J. (2003). Feed intake, milk yield and metabolic parameters prior to left displaced abomasum in dairy cows. *Journal of Dairy Science* 86, 1465-1471.
- Vanholder T., Leroy J.L.M.R., Opsomer G., de Kruif A. (2006). Interactions between energy balance and ovarian activity in high yielding dairy cows early postpartum: A review. *Vlaams Diergeneeskundig Tijdschrift* 75, 79-85.
- Whitmore H., Anderson K. (1986). Possible adverse effects of antimicrobial treatments of uterine infections. In: Morrow D.A. (editor). *Current Therapy in Theriogenology*. Vol 2. W.B. Saunders, Philadelphia, 42-44.