Defining, Preventing, and Treating Anoestrus Condition in Cattle
ReprodAction meeting:
Defining, Preventing, and Treating Anoestrus Condition in Cattle

Ceva Animal Health organised the first reprodAction Scientific Meeting with a renowned group of researchers on the field of cattle reproduction. The meeting was held on May 3rd and 4th 2012 at the Grand Hôtel de Bordeaux (France).

The main objective of the meeting was to create an environment for open exchange of ideas and science-based discussion among experts on a specific reproductive topic: “Defining, Preventing, and Treating Anoestrus Condition in Cattle”.

Data from different countries and management conditions were presented by participating experts. The proposal was to have a broad understanding of the anoestrus issue in different production systems.

The contents of this short review do not represent the opinion of a single expert, but rather includes a summary of opinions from different experts participating in the meeting. We encourage the reader to communicate directly with the expert of its interest for further details on their particular line of research and individual points of view regarding the topics that will be covered in this manuscript.
The group attending the scientific meeting

From left to right:

Front row, Pedro Rodríguez (Ceva Corporate Product Manager), Maykin Englebienne (Ceva Product Manager/Benelux), Prof. Hilary Dobson (University Liverpool/UK), Gamze Alpun (Ceva Product Manager/Turkey), Anouck Lagarde (Ceva Project Manager), Prof. Nicole Hagen-Picard (Veterinary School of Toulouse/France). Mid row, Antonio Jimenez (Ceva Product Manager/Spain), Giorgio Valla (Ceva Marketing Manager/Italy), Tatjana Andres (Ceva Technical Manager/Germany), Clare Turnbull (Ceva Veterinary Advisor/UK), Prof. Geert Opsomer (University of Ghent/Belgium), Alex Souza (Ceva Corporate Reproduction Manager), Prof. Ahmet Gumen (University of Uludag/Turkey), Prof. Jose Santos (University of Florida/USA). Rear row, Rafal Trukan (Ceva Product Manager/Poland), Prof. Tomasz Janowski (University of Warmia and Mazury/Poland), Dr. Giovanni Gnemmi (Bovinet/Italy), Martin Gough (Ceva Ruminant Business Unit Manager/UK), Stephane Floch (Ceva Product Manager/France), Prof. Heinrich Bollwein (University of Zurich/Switzerland), Prof. Fernando Lopez-Gatius (University of Lleida/Spain).
DEFINING
Anoestrus Condition in Cattle

During the reprodAction meeting, the group of specialists agreed that the term “anoestrus” refers to cows either not showing or simply not been detected in oestrus due to management constraints (Roelofs, López-Gatius et al. 2010). The specialists and vets in the meeting were also in agreement that, from a veterinarian standpoint, the term “non-cyclic” rather than “anoestrus” seems to better describe and define the problem of having cows failing to ovulate and initiate regular oestrous cycles of nearly 21 days. Most experts agreed that the use of ultrasound significantly improves the accuracy of detection of ovarian/uterine disorders. Therefore, since expression of oestrus appears to be highly variable from herd to herd, obviously dependent on the farmer’s performance in detecting cows showing behavioural oestrus, and affected by several other environmental factors such as heat stress, feet problems, etc, a more simple definition based mainly on characteristics of the ovary and uterus was proposed to help field veterinarians and producers as follows:

- **Non-cyclic Type 1**: Cows or heifers presenting small (smaller than deviation size) ovarian follicles and absence of a Corpus Luteum (CL) structure for at least 7 to 10 days and normally not showing oestrus behaviour.

![Ultrasound images of ovaries of cows presenting non-cyclic Type 1 (left – presence of small follicles <10 mm), Type 2 (centre and right pictures, presence of follicles greater than 10 mm -centre- or even greater than 25 mm -right – classical follicular cyst).](image-url)

*Pictures presented by Dr. Fernando Lopez-Gatius during the meeting.*
Non-cyclic Type 2: Cows or heifers presenting larger follicles (greater than deviation size including classical large cystic condition) and absence of CL structures for 7 to 10 days with or without demonstration of oestrus behaviour.

Non-cyclic Type 3: A third classification of non-cyclicity due to abnormally prolonged ovulatory intervals was proposed as caused by persistent CL structures (Opsomer, Gröhn et al. 2000), a problem commonly associated to uterine infection and/or inflammation. The CL structure seems to persist in these animals longer than their normal lifespan due to alterations in the normal mechanism related to luteolysis. The definite diagnosis of this reproductive abnormality in field conditions is rather complex and would require multiple and frequent ultrasound examinations or a complete profile of circulating progesterone throughout several weeks. Thus, under field conditions, cows in the postpartum period having uterine disorders such as presence of muco-purulent or purulent uterine contents and a mature CL might be likely to have a persistent CL.

Figure 2. Ultrasound images of ovaries of cows classified as Non-cyclic Type 3. Presence of a persistent CL (far-left) normally associated with uterine disorders such as muco-purulent (middle) and purulent (far right) contents.
The ovulatory process in cattle encompasses a complex sequence of events during the later stages of the oestrous cycle that involve a rise in circulating oestradiol due to high steroidogenic activity of pre-ovulatory follicles. This causes behavioural oestradiol, positive feed-back of oestrogen on the hypothalamus and anterior pituitary to release LH/FSH,
and ultimately ovulation of the oocyte followed by luteinisation of remaining cells in the follicle to form the new CL. The normal sequence of these events as well as the underlying proposed physiology of animals undergoing non-cyclicity Types 1 and 2 are represented in the following working models below:

**Figure 4** Representation of main reproductive hormone cascade and ovarian structures during the oestrous cycle in non-cycling cows. On the left, *Non-cyclic Type 1*, follicles are unable to grow to pre-ovulatory size due to limited supply of GnRH/LH pulses. The ovulatory cascade is then interrupted before or near deviation time. On the right, *Non-cyclic Type 2*, low amounts of LH pulses do not seem to be a problem and dominant follicles seem to be able to grow after deviation size threshold and produce enough oestrogen, however the hypothalamus is unable to respond with a GnRH/LH surge after the pre-ovulatory oestrogen increase and ovulation does not occur. Follicles eventually may grow enough (>25 mm) to be called follicular cysts. Source (Wiltbank, Gümen et al. 2002) with permission from authors.

FSH: follicle-stimulating hormone
LH: Luteinising hormone
GnRH: Gonadotropin-releasing hormone
**PREVALENCE of the Anoestrus condition in cattle**

Prevalence of non-cyclicity postpartum in dairy herds is around 30% at 50 to 60 days in milk (DIM), but varies a lot from herd to herd from 5% to as high as 50% according to management conditions (Opsomer, Gröhn et al. 2000; Wiltbank, Gümen et al. 2002; Santos, Rutigliano et al. 2009). This incidence can be even higher for beef herds due to suckling-induced anoestrus.

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**Prevalence of Anovular Cows in High-Producing Canadian Dairy Herds**


**Prevalence of Anovular Cows in Grazing dairy Herds in New Zealand**


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*Figure 5.* Non-cyclicity is highly variable both in confined and pasture dairy herds – slides above were presented by Dr. José Santos at the ReprodAction Scientific Meeting.
Modern-confined dairy herds seem to have a lot more non-cyclic cows in category **Type 2** (Gümen, Sartori et al. 2002; Wiltbank, Gümen et al. 2002; Gümen and Wiltbank 2005). In this regard, a new working model on possible reasons for non-cyclic condition **Type 2** was presented by Dr. Ahmet Gümen during the reprodAction Scientific Meeting. The model developed during Dr. Gümen’s PhD work with Dr. Wiltbank proposes that lactating cows need to be exposed to progesterone before ovulation in order to present normal oestrogen-induced ovulation and formation of a CL (Corpus Luteum) with normal life-span. Apparently, cows not exposed to progesterone have fewer oestrogen receptors in the hypothalamus, making these animals problematic in terms of responding to a GnRH/LH peak to increasing oestradiol levels that happen near oestrus. For instance, in an elegant manipulative experiment using cystic cows, Dr. Gümen has proven that non-cyclic **Type 2** cows failed to respond with LH peaks to exogenous oestrogen treatments. Interestingly, barely all cystic cows in his trials that were previously treated with progesterone through intravaginal devices had normal LH peaks and ovulation after being challenged with exogenous oestrogen compounds. It seems that progesterone can increase the number of oestrogen receptors in the mediobasal area in the hypothalamus and normalise the disrupted ovulatory pathways in cows undergoing non-cyclic **Type 2**.

![Figure 5](image-url) Working-model on non-cyclicity Type-2 presented by Dr. Ahmet Gümen during the reprodAction meeting. This work was developed during his PhD and more details can be found at: (Gümen, Sartori et al. 2002; Wiltbank, Gümen et al. 2002).
PREVENTING
Anoestrus Condition in Cattle

The incidence of non-cyclicity in cattle seems to be affected by many variables, as follows:

- **Parity:** agreed by most specialists as an important risk factor, in which first lactation or primiparous cows (beef or dairy) seem to undergo longer periods of non-cyclicity in the postpartum period as compared to multiparous cows.

<table>
<thead>
<tr>
<th>Study</th>
<th>Percentage of anovular cows</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opsomer et al., 2000 (n=334)</td>
<td>27% 20%</td>
<td>at 50 DIM by P4</td>
</tr>
<tr>
<td>Moreira et al., 2001 (n=499)</td>
<td>37% 16%</td>
<td>at 63 DIM by P4</td>
</tr>
<tr>
<td>Gumen et al., 2003 (n=316)</td>
<td>28% 15%</td>
<td>at 57 DIM by US &amp; P4</td>
</tr>
<tr>
<td>Lopez et al., 2005 (n=267)</td>
<td>29% 28%</td>
<td>at 71 DIM by US &amp; P4</td>
</tr>
<tr>
<td>Chebel et al., 2006 (n=968)</td>
<td>54% 32%</td>
<td>at 49 DIM by P4</td>
</tr>
</tbody>
</table>


**Figure 7** Incidence of non-cyclicity postpartum by parity number in dairy cows (Opsomer, Gröhn et al. 2000; Moreira, Orlandi et al. 2001; Gumen, Guenther et al. 2003; Lopez, Caraviello et al. 2005; Chebel, Santos et al. 2006).

- **Postpartum diseases:** Different specialists including Dr. Dobson, Dr. Opsomer, Dr. Santos and others during the meeting showed plenty of evidence relating postpartum diseases as playing a major role on non-cyclicity in cattle. Improved transition cow management was agreed to be an important preventive measurement for herds with excessive problems with postpartum diseases (Opsomer, Gröhn et al. 2000; Nordlund and Cook 2004; Caraviello, Weigel et al. 2006).
Body weight loss and uterine infections after calving: also identified as a major factor for anovulation and strategies to increase dry matter intake including increased feed trough space (>70 cm/cow), separating older cows from 1st lactation cows, avoiding heat stress, more frequent feeding, and use of a balanced ration and Total Mixed Ration (TMR) were mentioned as important factors that may help improve dry matter intake and reduce problems with non-cyclicity.

Figure 8. Herds with limited feed-bunk space seem to have more problems with sick cows in the postpartum period, including uterine infections which increase the risk of delayed postpartum ovulation (Non-cyclic Type 2) and problems related with persistent CL structures (Non-cyclic Type 3).
**Herd type (pasture vs. confined herds):** in which cows in confined herds receiving high energy diets to match greater milk production seem to have less problems with cyclicity; and the vast majority of confined cows under high feeding planes seem to present non-cyclic Type 2 (larger follicles in the ovary) as proposed above. In contrast, cows kept at pasture and receiving no or limited feed supplementation were described to have more problems to return to cyclicity postpartum with most cows being non-cyclic Type 1 (smaller follicles in the ovary).

**Dry period length:** Data from two studies were shown describing the need for avoiding longer than 60-70 days of dry period. Cows with shorter dry periods (ideal 40 to 60 days) have less metabolic problems and therefore start cycling earlier postpartum (Opsomer, Gröhn et al. 2000; Gümen, Rastani et al. 2005; Pezeshki, Mehrzad et al. 2007).

**Season:** Winter was argued to be a risk factor for non-cyclicity (Santos, Rutigliano et al. 2009) in US herds. However, that may not necessarily apply to other areas of the world as mentioned by Dr. Lopez-Gatius during the meeting. Dr. Lopez-Gatius highlighted the greater proportion of cyclicity problems during summer months due to heat stress. The inconsistent effects of season might likely be related to the level of stress experienced by the cows (i.e. extreme heat stress or even lack of good quality forages in some seasons).

**Mycotoxins:** Data presented by Dr. Janowski during the meeting showed the important role of some mycotoxins on nutrition-induced delayed postpartum ovulation. Thus, management to ensure high feed quality and frequent evaluation of feed ingredients are highly recommended practices.
TREATING
Anoestrus Condition in Cattle

Treatment approaches based on general recommendations from experts:

- **Non-cyclic Type 1**: Cows having smaller ovarian structures do not respond well to LH-inducing hormones such as GnRH or human chorionic gonadotropin (hCG). Thus, most effective hormonal treatment for these animals is thought to be exogenous progesterone supplementation that will result in increased LH pulse activity and follicular growth. Equine chorionic gonadotropin (eCG, formerly known as PMSG) at the final stages of progesterone treatment was agreed by most specialists to be very beneficial to improve ovulation rates and conception rates when associated with progesterone-based synchronisation protocols. Physiologically, both pharmacological compounds increase circulating LH, which in turn will allow for greater follicle growth, ovulation rates, and ultimately improved conception rates compared to untreated cows. Obviously, if the herd is continuously exposed to high amounts of anti-nutritional factors such as oestrogen-active mycotoxins, preventive measures are paramount.

- **Non-cyclic Type 2**: Non-cycling cows with ovarian follicles capable of responding to GnRH (threshold approximately >10mm) can be treated if non-cyclic either with exogenous progesterone supplementation or by pre-synchronising cows using LH-inducing hormones. Apparently, progesterone supplementation will increase the number of oestadiol receptors in the hypothalamus of the cow. As a result, in most cases, cows will start having regular endogenous oestrogen-induced LH peaks and re-establishment of normal cyclicity (Wiltbank, Gümen et al. 2002). Strategies that maximize circulating progesterone during the use of synchronisation hormones tend to improve conception rates in both non-cyclic and cyclic cows. There are advantages and disadvantages related to each strategy that will need to be thoroughly discussed by consultants and/or the herd veterinarian taking into account specific farm management level and costs-per-pregnancy achieved with each hormonal therapy. Equine gonadotropin might be beneficial by improving ovulation rates and fertility, but mostly recommended in cows with lower (<2.75) body condition scores (BCS).

- **Non-cyclic Type 3**: Preventive measures to avoid uterine disorders are extremely important when trying to reduce incidence of persistent CL structures. Fortunately, simple prostaglandin treatments should be fairly effective on inducing luteolysis in attempt to bring cows to normal inter-ovulatory intervals.
Non-cyclicity is a major problem for cattle producers world-wide. Its incidence varies considerably across herds, and the condition normally affects ~30% of dairy cows at breeding time. “Non-cyclicity”, based on ovarian & uterine features (defined as lack of ovulation and CL formation in two consecutive ovarian examinations 7 to 10 days apart or presence of persistent CLs and altered uterine contents) rather than simply referring to cows as in “anoestrus” due to lack of oestrus expression seem to be a preferred term as pointed out by most attending specialists. In addition, non-cyclic cows can be classified into three categories as non-cyclic Type 1 (presence of small follicles in the ovary and absence of CL 7 to 10 days apart), Type 2 (presence of follicles past deviation size including follicles >25 mm and absence of CL 7 to 10 days apart), and Type 3 (persistent CL structures most likely accompanied by altered uterine contents). An important preventive measure to avoid delayed cyclicity postpartum definitely includes optimising fresh cow management to minimise negative energy balance. Avoiding BCS loss postpartum is paramount to increase proportion of cycling cows at breeding time. Progesterone supplementation is thought to be one of the most effective approaches to increase ovulation rates and conception results for cows undergoing non-cyclicity Types 1 and 2. Non-cyclicity Type 3 is largely underestimated in field conditions due to its laborious identification, but non-pregnant cows presenting mature CL structures and altered uterine contents should be treated with prostaglandins in attempt to bring cows to normal inter-ovulatory activity (López-Gatius, Santolaria et al. 2001).
References


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