Anim. Reprod., v.11, n.2, p.63-73, Apr./Jun. 2014

# Ovarian cysts in dairy cows: old and new concepts for definition, diagnosis and therapy

**K. Jeengar, V. Chaudhary, A. Kumar, S. Raiya, M. Gaur, G.N. Purohit[1]**

Department of Veterinary Gynecology and Obstetrics, College of Veterinary and Animal Sciences,
Rajasthan University of Veterinary and Animal Sciences, Bikaner, Rajasthan, India.

## Abstract

Ovarian Cyst (OC) is an important ovarian dysfunction and a major cause of reproductive failure in dairy cattle. Previously defined as enlarged anovulatory follicle like structures (<2.5 cm) and persisting for 10 or more days OC in dairy cows are currently defined as cystic ovarian follicular structures of at least 17 mm that persist for more than 6 days in the absence of corpus luteum. However, clear cut definitions of this disorder are yet to be made. Past evaluations of OC using transrectal palpations have increased, and accurate diagnosis currently employs a combination of transrectal palpation, transrectal ultrasonography and plasma progesterone assay. However, the accurate diagnosis of the type of OC seems less important as therapies are similar for both the types of OC and clinicians often evaluate the OC again under conditions of pregnancy failures. During earlier times, the manual rupture of OC was advocated, yet during the past several years single or combination hCG, GnRH, progesterone and prostaglandins have been frequent in clinical practice. Other therapies include estrogen receptor blocker clomiphene citrate and trans-vaginal ultrasound guided cystic follicle aspiration. Among the various therapies suggested the OvSynch treatment appears to be the most logical approach, yet the pregnancy rates with timed inseminations following therapy with the OvSynch treatment are low, as with other hormonal treatments. The success of therapy is governed by many confounding variables such as persistence of the cystic follicles and initiation of therapy as pathological alterations that occur following OC persistence require some time for spontaneous recovery. It can be concluded that OC can be diagnosed easily yet in spite of many therapeutic options the establishment of pregnancy in cows with OC requires a longer time.

**Keywords:** cows, CL, follicles, GnRH, ovarian cyst, ovsynch, ultrasonography.

## Introduction

Over the past few decades milk yield per dairy cow has increased considerably due to continuing genetic selection and improvement of nutrition and herd management. Simultaneously with this selection for production characteristics, dairy cow fertility has declined significantly (Lucy, 2001; Butler, 2003). Economically, it is most beneficial if a cow calves each year (Dijkhuizen *et al*., 1997; Huirne *et al*., 2002). One of the most common ovarian dysfunctions during the postpartum period is formation of cyst following ovulation failure (Youngquist, 1986; Day, 1991b; López-Diaz and Bosu, 1992; Laporte *et al*., 1994; Opsomer *et al*., 1998). Ovarian Cyst (OC) is a common and economically significant condition of dairy cattle (Johnson and Coates, 2004) affecting fertility. The condition was first described in the early 1900's and has been recognized as an important cause of reproductive loss in cattle. McNutt was probably one of the first to use the term “cystic” in referring to persistent follicles >20 mm in diameter (McNutt, 1927). In this manuscript we review the old and new concepts of definition, diagnosis and therapy for bovine ovarian cysts.

## Definition

In the past OC were defined as fluid filled or hard structures of 2.5 cm or more in diameter persisting on the ovarian surface for 10 or more days (Roberts, 1971; Youngquist and Threlfall, 2007). The condition has been referred to by many names over the past century including adrenal virilism, nymphomania, cystic ovarian degeneration, cystic ovaries, and ovarian cysts (Garverick, 1997). Over time new definitions have been suggested, however, there is still lack of consensus and clearly defined definition. The condition is a consequence of a mature follicle that fails to ovulate at the appointed time of ovulation during the estrous cycle (Peter, 2004). Research using ovarian ultrasonography indicates that follicles typically ovulate at 13-17 mm in diameter (Ginther *et al*., 1989) so follicles that persist at that diameter or greater may be considered to be cystic (Hatler *et al*., 2003). Silvia *et al*. (2002) defined them as follicle like structures, with a minimum diameter of 17 mm and persisting for more than 6 days in the absence of a corpus luteum and clearly interfering with normal ovarian cyclicity. The diameter of the cyst may vary and reach up to 25 mm or larger (Roberts, 1971; Kesler and Garverick, 1982; Arbeiter *et al*., 1990; Cook *et al*., 1991; López-Diaz and Bosu, 1992; Boryczko *et al*., 1995; Fleischer *et al*., 2001; Silvia *et al*., 2002; Wiltbank *et al*., 2002; Youngquist and Threlfall, 2007). More recently, OC has been defined as anovulatory

[1]Corresponding author: gnpobs@gmail.com
Received: July 26, 2013
Accepted: April 1, 2014

follicles (<2 cm) on one or both ovaries that fail to regress yet maintain growth and steroidogenesis and interfere with normal ovarian cyclicity (Vanholder *et al*., 2006). The absence of a corpus luteum is an essential OC criterion (Arbeiter *et al*., 1990).

The cyst may be present for less than 10 days (Arbeiter *et al*., 1990). On average, cysts are maintained for 13 days (Hamilton *et al*., 1995). Follicular turnover in cows with ovarian cysts takes 13 (Hampton *et al*., 2003) to 19 (Todoroki *et al*., 2004) days, whereas in clinically normal cows, it occurs every 8.5 days (Sirois and Fortune, 1988).

Cysts are often diagnosed in the absence of clear clinical signs, therefore the term "Cystic Ovarian Disease" no longer seems appropriate and should be replaced by the term "Cystic Ovarian Follicle (COF)" which does not necessarily implicate a state of disease (Vanholder *et al*., 2006). Non-steroidogenic cysts which are hormonally inactive do not influence the normal estrous cycle, so they can occur together with a corpus luteum. Therefore, recent research articles define COF differently and perhaps more logically (Hamilton *et al*., 1995; Gümen *et al*., 2002; Zulu *et al*., 2002; Hatler *et al*., 2003). In this review the condition is referred to as Ovarian Cyst (OC).

In most cases (62-85%), cows with luteinized cysts remain anoestrous (Day, 1991a; Watson and Cliff, 1997) as a result of the production of progesterone by luteinized cysts. Ball and Peters (2004) refer to these cysts as luteinized cystic follicles, describing them as cysts with thicker walls that produce high levels of progesterone.

Many researchers showed that OC are actually dynamic structures, which can regress and be replaced by new cysts (Kesler *et al*., 1980; Cook *et al*., 1990; Hamilton *et al*., 1995; Yoshioka *et al*., 1996). The factors that determine whether a cyst will regress or not, continue to be poorly known (Wiltbank *et al*., 2002; Peter, 2004).

## Diagnosis

Diagnostic approaches for OC in cows include history and clinical signs, transrectal palpation, ultrasonography and plasma or milk progesterone assay. In the 1940's, the presence of cystic follicles on the ovaries was mainly associated with nymphomania and a bull-like appearance in cows (Casida *et al*., 1944; Garm, 1949). Williams and Williams (1923) documented some of the physical signs associated with OC which include: loss of tone throughout the female genital tract, relaxation or stretching of the sacrosciatic and sacroiliac ligaments giving the raised tail head appearance, behavioral changes (buller cow) which are characteristic of nymphomania (i.e., excessive mounting, standing, and bawling with noticeably deeper tone) and erratic milk production.

The clinical signs that accompany ovarian cysts are variable. Anoestrus is most common, especially during the postpartum period (Kesler and Garverick, 1982). Irregular estrus intervals and development of masculine physical traits are other signs which may be present especially later during lactation (Roberts, 1971; Youngquist, 1986). It has also been determined that follicular cysts are anovulatory structures so, as long as they persist, cows will remain infertile (Youngquist and Threlfall, 2007). Nymphomania and irregular cycles are common (Kasari *et al*., 1996). Watson and Cliff (1997) detected OC during investigations for anoestrus (58%) and irregular heat (12%), at a negative pregnancy diagnosis (12%), and at a pre-breeding examination (17%). A proportion of cows with follicular cysts can also evidence regular estrous cycles but a lowered fertility. When follicular cysts persist for prolonged periods in dairy cows, endometrial glands hypertrophy and pathologies in the uterus many times culminate in clinical mucometra with normal estrous cycle lengths (Purohit, 2008). The presence of such cysts leads to an increase in calving-to-conception and calving intervals, resulting in significant economic losses in the dairy industry (Silvia *et al*., 2002; Isobe, 2007).

Due to many exogenous and endogenous factors, perturbation of the hypothalamo-hypophyseal-ovarian (HHO) axis results in anovulation (Peter, 2004). When compared to follicular cysts, luteinized cysts are more likely to persist over long periods of time and can lead to nymphomania in some animals (Ball and Peters, 2004). Ovarian cysts diagnosed after the puerperium had a negative effect on fertility, whereas when cysts are diagnosed during the puerperium they do not affect reproduction (Gossen and Hoedemaker, 2006).

The most likely time of diagnosis is 30-60 day after parturition in high-yielding dairy cows (Gordon, 1996) but the detection of anovulatory follicles during the first weeks after calving should not be considered an ovarian impairment. From a practical point of view, an ovarian impairment may be suspected when anovulatory follicles are detected no earlier than 7 weeks after calving, a time when reproductive functions are thought to be restored (Gier and Marion, 1968; Sheldon and Dobson, 2004).

Ovarian cysts and normal preovulatory follicles are differentiated on the basis of number and size but mainly on the basis of uterine tonicity (Bierschwal, 1966; Zemjanis, 1970). During transrectal palpation, ovarian cysts are identified as multiple follicles that are typically larger than normal ovulatory follicles with an increased overall ovarian diameter (Purohit, 2008) along with a flaccid uterus in the absence of a corpus luteum while cows in proestrus have an erect, turgid uterus (Bierschwal, 1966; Zemjanis, 1970). Differentiating ovarian cysts from deep postpartum nutritional anestrus is not difficult because cows in deep anestrus have low FSH secretion and small ovaries with minimal follicular development (Roche *et al*., 1992). OC are differentiated from shallow anestrous on the basis of the number and

size of the follicles, occurrence of follicular waves, body condition score (BCS), and stage of lactation (Bartolome *et al*., 2005).

Although transrectal palpation has long been the diagnostic approach, follicular cysts cannot be differentiated from luteal cysts solely by palpation (McLeod and Williams, 1991). It is difficult to distinguish between follicular and luteinized cysts without using ultrasonography in anoestrous cows (Jeffcoate and Ayliffe, 1995). The accuracy of diagnosing ovarian cysts and differentiating follicular and luteal cysts can be increased by combining transrectal palpation of the genital tract to determine that a corpus luteum is absent and the uterus lacks tone; ultrasonography to confirm that a corpus luteum is absent, to determine the size of follicles that are present, and to check for luteinization; and measurement of plasma progesterone concentration to determine the degree of luteinization (Bartolome *et al*., 2005). The accuracy of diagnosis can be increased by obtaining information about the reproductive history of the animal, vaginal examination and progesterone determination (Hanzen *et al*., 2000). Some cows may evidence normal estrous cycle although they may have one or multiple cysts in one or both ovaries.

Kahn (2010) described a luteal cyst as being characterized by enlarged ovaries with one or more cysts with thicker walls than those of follicular cysts because of a lining of luteal tissue. Ultrasonography is effective in detecting follicular and luteal cysts with high accuracy (Farin *et al*., 1990). Color Doppler sonography is superior to B-mode sonography for differentiating follicular and luteal cysts and aids in the selection of treatment (Rauch *et al*., 2008). However, exact prediction of OCs destined to regress or persist and the response of OCs to treatment with a GnRH analogue were not possible using color Doppler sonography (Rauch *et al*., 2008).

According to Bartolome *et al.* (2005), two approaches can be considered in the diagnosis of OC. First, detection of multiple follicles approximately 18 to 20 mm in diameter and second, ovarian follicular waves during a period of 7 to 10 days in the absence of ovulation, absence of corpora lutea, and a lack of uterine tonicity. Determining the presence of ovarian follicular waves during a 7 to 10 day period with follicles that reach ovulatory size (12 mm) can be used to retrospectively differentiate ovarian cysts from shallow nutritional anestrus with low BCSs (Bartolome *et al*., 2005).

In general, luteal cysts are associated with relatively high concentrations of progesterone in the peripheral circulation while follicular cysts are associated with relatively low concentrations of progesterone (Dobson *et al*., 1977; Farin *et al*., 1990, 1992; Jeffcoate and Ayliffe, 1995). Many researchers have used a plasma P4 concentration greater than 1 ng/ml as the minimum P4 concentration for a cyst to be considered luteal (Nakao *et al*., 1983b; Ax *et al*., 1986; Dinsmore *et al*., 1989; Jou *et al*., 1999; Santos *et al*., 2000). However, P4 limits above 0 ng/ml (plasma), and up to 10 ng/ml (milk) have been used (Farin *et al*., 1990; Nanda *et al*., 1991; Chavatte *et al*., 1993; Ribadu *et al*., 1994; Kasari *et al*., 1996). It should not be confused with hollow corpora lutea, which are not pathological at all (Garverick, 1997).

Thus accurate diagnosis of the type of OC requires a combination of diagnostic approaches such as transrectal palpation, transrectal ultrasonography and plasma progesterone profiles.

## Therapy

The OC therapy appears to be simple however, regaining fertility, which often requires longer time due to perturbations in endocrinology and uterine pathology that follows in long standing cases (Purohit, 2008), seems to be more important. Treatments for OC are numerous and variable, and have changed considerably over the years (Roberts, 1986; Woolums and Peter, 1994; Peter, 2004; Purohit, 2008). Economically, the decision to treat an animal is influenced by the costs and the expected treatment benefits, the costs of replacement, and the breeding value of the animal (Bierschwal *et al*., 1975; Dinsmore *et al*., 1989; Scholl *et al*., 1992; Suriyasathaporn *et al*., 1998; Jou *et al*., 1999; Douthwaite and Dobson, 2000). Many endocrine based treatments for cysts have been evaluated including steroids (Johnson and Ulberg, 1967), gonadotropins (Casida *et al*., 1944; Bierschwal., 1966; Bierschwal *et al*., 1975; Nakao *et al*., 1978) and GnRH (Bierschwal *et al*., 1975; Seguin *et al*., 1976; Kesler *et al*., 1978; Nanda *et al*., 1988). Some of the earliest treatments include: manual rupture, ovariectomy, injection of ovarian extract, injection of CL extract, uterine infusions of antibiotics or antiseptics, and injections of adrenaline chloride and Pituitrin (Albrechtsen, 1917; Williams and Williams, 1923; Tutt, 1932; Casida *et al*., 1944). Roberts (1986) refuted ovariectomy as a treatment option suggesting that spaying will correct nymphomania but the removal of only one ovary if it is affected with cysts is useless, since the remaining ovary will promptly develop cysts. According to Bartolome *et al*. (2005) differentiation is not always necessary for understanding the type of cysts because treatments under both conditions are similar. The success of therapy in terms of disappearance of OC with different hormonal treatments is good, yet the establishment of pregnancy requires variable times due to formation of new OC and pathological alterations that occur in the uterus with long term persistence of OC (Purohit, 2008). Many variables such as OC time of diagnosis, OC persistence period, presence of mucometra and milk production determine the outcome of therapy (Purohit *et al*., 2001; Purohit, 2008).

*Spontaneous recovery*

The spontaneous recovery percentage of early cysts is 60-65% (Kesler and Garverick, 1982; Refsdal, 1982; Day, 1991b). Arbeiter *et al.* (1990) and Purohit *et al.* (2001) found a spontaneous recovery percentage of OC in 27.17 and 24% of cows, respectively. Steinbauer (1985) recommended treatment only after day 50 post partum, because of possible spontaneous regression of the cyst. Youngquist (1986) stated that spontaneous recovery might reach 60% if the condition is present before 30 days post partum. It would be profitable to treat multiparous cows having cysts very early in the postpartum period, while treatment of primiparous cows should be delayed, at least until the end of the preservice period, to provide the opportunity for spontaneous recovery (López-Gaitus *et al*., 2002). Dinsmore *et al.* (1989) did not find major differences between clinical response to treatments given before or after 35 days post partum.

*Manual rupture*

In the past, manual rupture of OC had been suggested (Roberts, 1971) however, recently it has been mentioned that this method should be weighed against the cost of hormone therapy (Kahn, 2010). Brito and Palmer (2004) did not recommend manual rupture of cysts because it may result in trauma and hemorrhage causing adhesions and contributing to fertility reduction. Currently manual rupture of OC is not suggested due to potential dangers of hemorrhages and adhesions that may follow manual rupture (Purohit, 2008).

*GnRH alone*

The distinction between follicular cyst and luteal cyst is not important in practice, because the response of both types of cysts to GnRH treatment is similar (Youngquist, 1986; Dinsmore *et al*., 1989; Day, 1991b) and usually results in luteinization of the cysts followed by estrous within 4 weeks of treatment (Dinsmore *et al*., 1990). Cows with ovarian cysts are capable of releasing LH in response to GnRH (Cantley *et al*., 1975). GnRH is most effective for returning cows with anovulatory follicular cysts to a normal cyclic ovarian condition (Brito and Palmer, 2004). GnRH induces the release of LH, with a maximum plasma LH concentration being reached 90 to 150 minutes after application which initiates the formation of active luteal tissue, as indicated by increased serum progesterone levels 7 days after treatment onwards (Seguin *et al*., 1976; Kruip *et al*., 1977). In response to treatment with GnRH, ovulation of the cyst does not occur, but other follicles present at the time of treatment may ovulate (Brito and Palmer, 2004). GnRH had no effect on intervals from treatment to CL detection or from treatment to cyst disappearance, and that CL detection and cyst disappearance are not correlated; also there is no association between the gonadotropin response to GnRH and the interval from treatment to CL detection (Jou *et al*., 1999).

Thus, a single GnRH treatment has been the standard treatment for cows with ovarian cysts (Bierschwal *et al*., 1975; Seguin *et al*., 1976; Nakao *et al*., 1992; Osawa *et al*., 1995). However, a large proportion (25-39%) of cows with ovarian cysts treated with GnRH did not respond (Cantley *et al*., 1975; Nakao *et al*., 1992; Osawa *et al*., 1995; Tebble *et al*., 2001), probably because other follicles capable of responding to GnRH were not present (Tebble *et al*., 2001). Etherington *et al.* (1985) concluded that treating normal cows with GnRH in the early postpartum period may increase the risk of pyometritis and OC. It has been reported that following treatment with GnRH, OC may luteinize, but they never ovulate (Garverick, 1999). There is presence of a CL approximately 7 days after treatment with GnRH (Bierschwal, 1966; Ambrose *et al*., 2004) indicating that the CL formed from ovulation of an ovarian follicle, and not the existing ovarian cyst.

After the GnRH treatment and subsequent luteinization, the cyst becomes responsive to prostaglandin-F2α (PGF2α) because the steroidogenic synthesis pathway has switched from estradiol to progesterone. The newly elevated levels of progesterone are responsible for a restoration of responsiveness to the positive feedback effect of estradiol, resulting in the resumption of normal cyclic ovarian activity after the release of endogenous PGF2α and cyst regression (Brito and Palmer, 2004).

*GnRH analogs*

The epidural administration of lecirelin (a GnRH analogue) promotes the remission of follicular cysts and an improvement of reproductive parameters (Annalisa *et al*., 2011). A single intramuscular injection of buserelin at a dose of 10 µg or higher is recommended for the treatment of ovarian follicular cysts in cows (Nakao *et al*., 1992). A single injection of 20 µg buserelin and 200 µg fertirelin have equal therapeutic effects in lactating cows having OC (Osawa *et al*., 1995). Buserelin, a nanopeptide GnRH analog, is 10 to 20 times more potent than fertirelin acetate in eliciting the release of LH and FSH (Dinsmore *et al*., 1987; Chenault *et al*., 1990). The effects of either fertirelin or buserelin on the luteinization of follicular cysts and on subsequent reproductive performance are fairly well known (Nakao *et al*., 1980, 1983a, 1992; Dinsmore *et al*., 1987). In comparative studies, buserelin (a more potent GnRH analogue) or human chorionic gonadotropin (hCG) produced similar effects (Brito and Palmer, 2004). A recent study found beneficial effects of a single IM administration of 0.1 mg lecirelin acetate in the therapy of cows suffering from OC (Silva *et al*., 2012).

*hCG*

Since the 1970s hCG and GnRH analogues have been used to treat ovarian cysts, and both appear to be equally effective with regards to treatment response and fertility (Peter, 2004) but the next estrus would occur 5-21 days after treatment (Kahn, 2010). GnRH and hCG elicit equivalent endocrine and clinical responses, but GnRH has an advantage over hCG in its minimal antigenicity (Drost and Thatcher, 1992).

The treatment of OC with hCG is somewhat more effective than a treatment with hCG + P4 (Alanko and Katila, 1980).

*PGF2α*

Prostaglandin F2α (PGF2α) has been used for the treatment of luteinized cyst because of its luteolytic activity, and estrous symptoms can be observed within 2 or 3 days of treatment (Kesler and Garverick, 1982). It is the most effective treatment for luteinized cysts, and in one study, 75% of the cows were in estrus within 7 days after treatment and pregnancy rates at first estrus were 66% (Brito and Palmer, 2004).

Kahn (2010) recommended luteolytic doses of PGF2α as the ideal treatment for luteal cyst, with estrus being evident within 3-5 days. Intervals from treatment to resumption of ovarian activity are affected by the characteristics of ovarian cysts, with a faster recovery for the luteal type (Probo *et al*., 2011).

*Progesterone and progesterone implants*

Treatment with progesterone may disrupt the endocrine environment needed to maintain ovarian follicular cysts and thus lead to their regression (Hatler *et al*., 2006). At high doses, it exerts a strong negative feedback on LH pulse frequency (Kinder *et al*., 1996) which reduces LH in cows with cysts, and this was followed by development of normal ovulatory follicles (Calder *et al*., 1999). Acute treatment as well as chronic treatment (9-14 days) with progesterone caused a rapid reduction in the size of persistent follicles and restored cyclic ovarian activity (Johnson and Ulberg, 1967; Anderson and Day, 1994; McDowell *et al*., 1998; Calder *et al*., 1999). Cows with persistent follicles can be successfully synchronized and time inseminated using progesterone, GnRH and PGF2α but show a limited response to treatment with GnRH plus PGF2α (López-Gatius *et al*., 2001).

Treatment with CIDR proved effective in restoring ovulation and reestablishing normal cyclicity in beef donor cows with cysts persistent for a long period (Douthwaite and Dobson, 2000). Insertion of a CIDR and GnRH injection in cows with follicular cysts can induce synchronous follicular wave emergence with the same pattern as observed in cows having normal estrous cycles (Kim *et al*., 2006). The CIDR reduces and maintains LH secretion at normal luteal levels, thereby, inducing atresia of estrogen-active cysts and preventing formation of cysts from the newly emerged follicles (Todoroki *et al*., 2001). Progesterone works against follicular cysts by restoring the responsiveness of the hypothalamus to the positive feedback of estradiol, resulting in normal estrus and ovulation within 7 days after the implant is removed (Brito and Palmer, 2004). Although the use of CIDR may eliminate the need for evaluation of the presence of a corpus luteum at the time of PGF2α treatment (Bartolome *et al*., 2005), the combination of both minimizes the risk of incorrect treatment and provides sufficient reproductive performance (Iwakuma *et al*., 2008). Progesterone and Estradiol Benzoate treatment administered using a PRID have a high rate of therapeutic effectiveness in cows with OC (Kim *et al*., 2004).

Moreover, when progesterone is used for estrus synchronization after embryo collection instead of PGF2α, the proportion of cows developing OC decreased from ~25% to <3% (Brito and Palmer, 2004).

*GnRH+CIDR*

Treatment of cows with OC with CIDR intra vaginal placement, GnRH followed by PGF2α 7 days later resulted in recruitment of new healthy follicles, synchronization of ovulation and resulted in a marked improvement in pregnancy rate (Amer and Badr, 2007). Treatments with progesterone releasing intravaginal devices (PRID) in combination with estradiol benzoate for 12 days evidenced therapeutic efficacy in resolving OC in post partum dairy cows (Kim *et al*., 2004). The effects with progesterone treatments were proposed to be mediated by restoration of the ability of hypothalamo-pituitary axis to generate an LH surge in response to an increasing estradiol (Todoroki and Kaneko, 2006).

*GnRH+ PGF2α combination*

Comparatively, ovarian cysts are less responsive to treatment with GnRH alone. GnRH plus Cloprostenol (CLP) 14 days later is effective in resolving cysts with significantly higher percentages of ovulation rates, returns to estrus, and pregnancy rates, and a much lower level of cystic persistence. It was previously suggested that more research be done on using different combinations of GnRH and CLP as treatments for OC in order to combat the problem to the fullest (López-Gaitus and López-Béjar, 2002). However, currently GnRH followed by PG 7-10 days later is a routinely used therapy for OC (Purohit, 2008).

*Ovsynch protocol*

Some recent protocols for synchronization of ovulation, commonly referred as Ovsynch, followed by

timed artificial insemination (AI) performed 16- 20 h after the 2nd GnRH injection, yields pregnancy rates of about 25% in cows suffering from OC (Fricke and Wiltbank, 1999; Bartolome *et al*., 2000; Meyer *et al*., 2007). Stevenson and Tiffany (2004) used ovsynch protocol as a treatment for OC and found it to be effective in curing the cystic condition and got the previously cystic animal pregnant after AI. During the warm period, the pregnancy rates of the cystic cows were similar whether they received GPG or GPH treatment, during the cool period, there is a beneficial effect in using hCG at day 9 of the ovsynch protocol compared to GnRH on cumulative pregnancy rate (De Rensis *et al*., 2008). It appears paradoxical that high milk production predisposes to the occurrence of ovarian cysts, but that high-producing cows respond better to treatment compared to low-producing cows. It is hypothesized that the level of milk production on the day of cyst diagnosis could be an additional potential predictor of success of treatment of lactating cows with ovarian cysts using the Ovsynch protocol (Crane *et al*., 2006). The addition of CIDR to the Ov-Synch protocol had no remarkable effects on circulating plasma steroids and conception rates following fixed time artificial insemination in cows (Kawate *et al*., 2011).

*Clomiphene citrate*

It is an antiestrogen and may exert direct action on the pituitary gland to augment estrogen-induced LH release (Terakawa *et al*., 1985) so a dose of 300 mg of clomiphene citrate administered to cows after a 1% copper sulphate drench has been suggested for the treatment of OCs (Thakur *et al*., 1983).

*Needle aspiration*

Single transvaginal-guided needle aspiration of ovarian follicular cysts is an easy and good method for the treatment of follicular cysts. Moreover, it is a safe and good alternative method against the manual, active rupturing of cysts during trans-rectal palpation (Lievaart *et al*., 2006) but there is a tendency of the cyst to reform, and the difficulty in such a clinical condition lies not in the resolving of the cyst but in the attainment of a successful pregnancy, which is extremely difficult when cows develop clinical mucometra (Purohit, 2008). Regimens suggested to resolve mucometra include oral (3-10 gm of potassium iodide for 5-10 days; Bugalia and Kohli, 1981, 1983; Rajan *et al*., 1991; Purohit *et al*., 2001) or injectable administration of elemental iodide (McDonald *et al*., 1961) or uterine lavage (Prasithiphol *et al*., 1999).

*Homeopathic drugs*

Homeopathic remedies like homeopathic *Apis* (for the right side OC) or homeopathic *Lachesis* (for the left side OC) twice daily for 5 days, with either one being immediately followed by homeopathic *Natrum mur*; twice daily for three days are effective treatments for OC (Karreman, 2007). *Apis mellifica* is a common homeopathic medicine made from the female honeybee, while *Lachesis* is prepared from the fresh venom of the South American bushmaster snake and *Natrum mur* is made simply from sodium chloride, or table salt. If this treatment doesn't work, Heat Seek, a botanical herb blend typically used to enhance the observable signs of estrus, may be given as 10 tablets orally every other day for twelve doses (24 day treatment; Karreman, 2007). According to Rautha Filho and Bison (2009) the use of homeopathic medicines can't be considered a source to study about homeopathic therapy due to its clinically and scientifically weak base.

## References

**Alanko M, Katila T**. 1980. Treatment of cystic ovaries in dairy cattle using human chorionic gonadotropin or a compound consisting of human chorionic gonadotropin with progesterone. *Nord Vet Med*, 32:122-127.

**Albrechtsen J**. 1917. Sterility of cattle and methods of treatment. *Cornell Vet*, 7:57-110.

**Ambrose DJ, Schmitt EJP, Lopes FL, Mattos RC, Thatcher WW**. 2004. Ovarian and endocrine responses associated with the treatment of cystic ovarian follicles in dairy cows with gonadotropin releasing hormone, and prostaglandin F2α, with or without exogenous progesterone. *Can Vet J*, 45: 931-937.

**Amer H, Badr A**. 2007. Hormonal profiles associated with treatment of cystic ovarian disease with GnRH and PGF2α with and without CIDR in dairy cows. *Int J Vet Med*, 2:51-56.

**Anderson L, Day M**. 1994. Acute progesterone administration regresses persistent dominant follicles and improves fertility of cattle in which estrus was synchronized with melengestrol acetate. *J Anim Sci*, 72:2955-2961.

**Annalisa R, Debora C, Maddalena M, Giuseppe M, Massimo S, Luigi SR**. 2011. Epidural vs intramuscular administration of lecirelin, a GnRH analogue, for the resolution of follicular cysts in dairy cows. *Anim Reprod Sci*, 126:19-22.

**Arbeiter K, Aslan S, Schwarzenberger F**. 1990. Untersuchungen über die Ovarzyste beim Rind œ Entstehung, Therapieerfolge, Fruchtbarkeit. *Dtsch Tierärtl Wschr*, 97:380-382.

**Ax RL, Bellin ME, Scheinder DK, and Haase-Hardie JA**. 1986. Reproductive performance of dairy cows with cystic ovaries following administration of procystin. *J Dairy Sci*, 69:542-545.

**Ball PJH, Peters AR**. 2004. Reproductive problems. *In*: Ball PJH, Peters AR. *Reproduction in Cattle*. Oxford, UK: Blackwell. pp. 172-175.

**Bartolome JA, Archbold LF, Morresey P**. 2000. Comparison of synchronization of ovulation and

induction of estrus as therapeutic strategies for bovine ovarian cysts in the dairy cow. *Theriogenology*, 53:815-825.

**Bartolome JA, Thatcher WW, Melendez P, Risco CA, Archbald LF**. 2005. Strategies for the diagnosis and treatment of ovarian cysts in dairy cattle. *J Am Vet Med Assoc*, 277:1409-1414.

**Bierschwal CJ**. 1966. A clinical study of cystic conditions of the bovine ovary. *J Am Vet Med Assoc*, 149:1591-1595.

**Bierschwal CJ, Garverick HA, Martin CE, Youngquist RS, Cantley TC, Brown MD**. 1975. Clinical response of dairy cows with ovarian cysts to GnRH. *J Anim Sci*, 41:1660-1665.

**Boryczko Z, Bostedt H, Hoffman B**. 1995. Comparison of the hormonal and chemical composition of the fluid from bovine ovarian follicles and cysts. *Reprod Domest Anim*, 30:36-38.

**Brito LFC, Palmer CW**. 2004. Cystic ovarian disease in cattle. *Large Anim Vet Roun*ds, 4:1-6.

**Bugalia NS, Kohli IS**. 1981. Comparative efficacy of proluton depot, gonadotropin-LH and potassium iodide in nymphomaniac Rathi cows. *Haryana Agric Univ J Res*, 11:575-577.

**Bugalia NS, Kohli IS**. 1983. Clinical studies on cystic ovarian degeneration in Rathi cows. *Indian J Anim Reprod*, 3:1-3.

**Butler WR**. 2003. Energy balance relationships with follicular development, ovulation and fertility in postpartum dairy cows. *Livest Prod Sci*, 83:211-218.

**Calder MD, Salfen BE, Bao B, Youngquist RS, Garverick HA**. 1999. Administration of progesterone to cows with ovarian follicular cysts result s in a reduction in mean LH and LH pulse frequency and initiates ovulatory follicullar growth. *J Anim Sci*, 77:3037-3042

**Cantley TC, Garverick HA, Bierschwal CJ, Martin CE, Youngquist RS**. 1975. Hormonal responses of dairy cows with ovarian cysts to GnRH. *J Anim Sci*, 41:1666-1673.

**Casida LE, McShan WH, Meyer RK**. 1944. Effects of an unfractionated pituitary extract upon cystic ovaries and nymphomania in cows. *J Anim Sci*, 3:273-282.

**Chavatte PM, Archbald LF, Risco C, Tran T, Sumrall D**. 1993. Effectiveness of prostaglandin F2α in the initial treatment of bovine ovarian cysts. *Theriogenology*, 40:745-755.

**Chenault JR, Kratzer DD, Rzepkowski RA, Goodwin** MC. 1990. LH and FSH response of Holstein heifers to fertirelin acetate, gonadorelin and buserelin. *Theriogenology*, 34:81-98.

**Cook DL, Smith CA, Parfet JR, Youngquist RS, Brown EM, Garverick HA**. 1990. Fate and turnover rate of ovarian follicular cysts in dairy cattle. *J Reprod Fertil*, 90:37-46.

**Cook DL, Parfet JR, Smith CA, Moss GE, Youngquist RS, Garverick HA**. 1991. Secretory patterns of LH and FSH during development and hypothalamic and hypophyseal characteristics following development of steroid induced ovarian follicular cysts in dairy cattle. *J Reprod Fertil*, 91:19-28.

**Crane MB, Melendez P, Bartolome J, de Vries A, Risco C, Archbald LF**. 2006. Association between milk production and treatment response of ovarian cysts in lactating dairy cows using the Ovsynch protocol. *Theriogenology*, 66:1243-1248.

**Day N**. 1991a. The diagnosis, differentiation and pathogenesis of COD. *Vet Med*, 41:753-760.

**Day N**. 1991b. The treatment and prevention of cystic ovarian disease. *Vet Med*, 86:761-766.

**De Rensis, Bottarelli F, Battioni E, Capelli F, Techakumphu T, García-Ispierto M, López-Gatius F**. 2008. Reproductive performance of dairy cows with ovarian cysts after synchronizing ovulation using GnRH or hCG during the warm or cool period of the year. *Theriogenology*, 69:481-484.

**Dijkhuizen AA, Huirne RBM, Jalvingh AW, Stelwagen J**. 1997. Economic impact of common health and fertility problems. *In*: Dijkhuizen AA, Morris RS (Ed). *Animal health economics, principles and applications*. Sydney: University of Sydney. pp 41-58.

**Dinsmore RP, White ME, Guard CL, Jasko DJ, Perdrizet JA, Powers PM, Smith MC**. 1987. A randomized double blind clinical trial of two GnRH analogs for the treatment of cystic ovaries in dairy cows. *Cornell Vet*, 77:235-243.

**Dinsmore RP, White ME, Guard CL, Jasko DJ, Perdrizet JA, Powers PM, Smith MC**. 1989. Effect of gonadotropin-releasing hormone on clinical response and fertility in cows with cystic ovaries, as related to milk progesterone concentration and days after parturition. *J Am Vet Med Assoc*, 195:327-330.

**Dinsmore RP, White ME, English PB**. 1990. An evaluation of simultaneous GnRH and cloprostenol treatment of dairy cattle with cystic ovaries. *Can Vet J*, 31:280-284.

**Dobson H, Rankin JE, Ward WR**. 1977. Bovine cystic ovarian disease: plasma hormone concentrations and treatment. *Vet Rec*, 101:459-461.

**Douthwaite R, Dobson H**. 2000. Comparison of different methods of diagnosis of cystic ovarian disease in cattle and an assessment of its treatment with a progesterone-releasing intravaginal device. *Vet Rec*, 147:355-359.

**Drost M, Thatcher WW**. 1992. Application of gonadotrophin releasing hormone as therapeutic agent in animal reproduction. *Anim Reprod Sci*, 28:11-19.

**Etherington WG, Martin SW, Dohoo IR, Bosu WTK**. 1985. Interrelationships between postpartum events, hormonal therapy, reproductive abnormalities and reproductive performance in dairy cows: a path analysis. *Can J Comp Med*, 49:261-267.

**Farin PW, Youngquist RS, Parfet JR, Garverick HA**. 1990. Diagnosis of luteal and follicular ovarian cysts in dairy cows by sector scan ultrasonography. *Theriogenology*, 34:633-642.

**Farin PW, Youngquist RS, Parfet JR, Garverick HA**. 1992. Diagnosis of luteal and follicular ovarian cysts by palpation per rectum and linear-array ultrasonography in dairy cows. *J Am Vet Med Assoc*, 200:1085-1089.

**Fleischer P, Metzner M, Beyerbach M, Hodemaker M, Klee W**. 2001. The relationship between milk yield and the incidence of some diseases in dairy cows. *J Dairy Sci*, 84:2025-2035.

**Fricke PM, Wiltbank MC**. 1999. Effect of milk production on the incidence of double ovulation in dairy cows. *Theriogenology*, 52:1133-1143

**Garm O**. 1949. A study of bovine nymphomania. *Acta Endocrinol Suppl*, 3:1-144.

**Garverick HA**. 1997. Ovarian follicular cysts in dairy cows. *J Dairy Sci*, 80:995-1004.

**Garverick HA**. 1999. Ovarian follicular dynamics and endocrine profiles in cows with ovarian follicular cysts. *In*: Howard JL, Smith RA (Ed.). *Current Veterinary Therapy, Food Animal Practice*. Philadelphia: WB Saunders. pp. 577-580.

**Gier HT, Marion GB**. 1968. Factors affecting bovine ovarian activity after parturition. *J Anim Sci*, 27:1621-1626

**Ginther OJ, Knopf L, Kastelic JP**. 1989. Temporal associations among ovarian events in cattle during estrous cycles with two and three follicular waves. *J Reprod Fertil*, 87:223-230.

**Gordon I**. 1996. The cow's oestrous Cycle. *In*: Gordon I. *Controlled Reproduction in Cattle and Buffaloes*. Wallingford: CAB International., 123-125.

**Gossen N, Hoedemaker M**. 2006. Reproductive performance of dairy cows with relation to time of ovarian cyst formation. *Bull Vet Inst Pulawy*, 50:159-160.

**Gümen A, Sartori R, Costa FMJ, Wiltbank MC**. 2002. A GnRH surge without subsequent progesterone exposure can induce development of follicular cysts. *J Dairy Sci*, 85:43-50.

**Hamilton SA, Garverick HA, Keisler DH, Xu ZZ, Loos K, Youngquist RS, Salfenet BE**. 1995. Characterization of ovarian follicular cysts and associated endocrine profiles in dairy cows. *Biol Reprod*, 53:890-898.

**Hampton JH, Salfen BE, Bader JF, Keisler DH, Garverick HA**. 2003. Ovarian follicular response to high doses of pulsatile luteinizing hormone in lactating dairy cattle. *J Dairy Sci*, 86:1963-1969.

**Hanzen C, Pieterse M, Scenzi O, Drost M**. 2000. Relative accuracy of the identification of ovarian structures in the cow by ultrasonography and palpation per rectum. *Vet J*, 159:161-170.

**Hatler TB, Hayes SH, Fonseca LFL, Silvia WJ**. 2003. Relationship between endogenous progesterone and follicular dynamics in lactating dairy cows with ovarian follicular cysts. *Biol Reprod*, 69:218-223.

**Hatler TB, Hayes SH, Anderson LH, Silvia WJ**. 2006. Effect of a single injection of progesterone on ovarian follicular cysts in lactating dairy cows. *Vet J*, 172:329-333

**Huirne RBM, Saatkamp HW, Bergevoet RHM**. 2002. Economic analysis of common health problems in dairy cattle. *In*: Kaske M, Scholz H, Höltershinken M (Ed). *Recent Developments and Perspectives in Bovine Medicine: Keynote Lectures of the XXII World Buiatrics Congress, 2002, Hannover*. Hannover: Tierärztliche Hochschule, 2002. pp. 18-23.

**Isobe N**. 2007. Follicular cysts in dairy cows. *Anim Sci J*, 78:1-6.

**Iwakuma A, Suzuki Y, Haneishi T, Kajisa M, Kamimura S**. 2008. Efficacy of intravaginal progesterone administration combined with prostaglandin F(2alpha) for cystic ovarian disease in Japanese Black cows. *J Vet Med Sci*, 70:1077-1083.

**Jeffcoate IA, Ayliffe TR**. 1995. An ultrasonographic study of bovine cystic ovarian disease and its treatment. *Vet Rec*, 136:406-410.

**Johnson A, Ulberg L**. 1967. Influence of exogenous progesterone on follicular cysts in dairy cattle. *J Dairy Sci*, 50:758-761.

**Johnson WH, Coates AE**. 2004. An update on cystic ovarian disease. *In*: Proceedings of the 15th International Congress on Animal Reproduction, Porto Seguro, Brazil, Porto Seguro, BA: ICAR. pp. 60-65.

**Jou P, Buckrell BC, Liptrap RM, Summerlee AJS**. 1999. Evaluation of the effect of GnRH on follicular ovarian cysts in dairy cows using transrectal ultrasonography. *Theriogenology*, 52:923-937.

**Kahn CM**. 2010. Cystic ovary disease. *In*: Kahn CM, Line S (Ed.). *The Merck Veterinary Manual*. 10th ed. Whitehouse Station, NJ: Merck. pp. 1243-1247.

**Karreman HJ**. 2007. Ovarian cysts. *In*: Karreman HJ. *Treating Dairy Cows Naturally: Thoughts and Strategies*. Austin, TX: Paradise Publications. pp. 291-292.

**Kasari R, Fuller DT, Wideman D, Jaques JT, Slay L, Lee J**. 1996. Bovine COD and the role norgestomet can play in its treatment. *Vet Med*, 91:156-162.

**Kawate N, Watanabe K, Uenaka K, Takahashi M, Inaba T, Tamada H**. 2011. Comparison of plasma concentrations of estradiol 17β and progesterone, and conception in dairy cows with cystic ovarian diseases between Ovsynch and Ovsynch plus CIDR timed AI protocols. *J Reprod Dev*, 57:267-272.

**Kesler DJ, Garverick HA, Candle AB, Bierschwal CJ, Elmore RG, Youngquist RS**. 1978. Clinical and endocrine responses of dairy cows with ovarian cysts to GnRH and/or PGF2α. *J Anim Sci*, 46:719-725.

**Kesler DJ, Garverick HA, Caudle AB, Elmore RG, Youngquist RS, Bierschwal CJ**. 1980. Reproductive hormone and ovarian changes in cows with ovarian cysts. *J Dairy Sci*, 63:166-170.

**Kesler DJ, Garverick HA**. 1982. Ovarian cysts in dairy cattle: a review. *J Anim Sci*, 55:1147-1159.

**Kim IH, Suh GH, Kim UH, Kang HG**. 2006. A CIDR-based timed AI protocol can be effectively used for

dairy cows with follicular cysts. *Anim Reprod Sci*, 95:206-213

**Kim S, Kengaku K, Tanaka T, Kamomae H**. 2004. The therapeutic effects of Progesterone-Releasing Intravaginal Device (PRID) with attached esradiol capsule on ovarian quiescence and cystic ovarian disease in postpartum dairy cows. *J Reprod Dev*, 50:341-348.

**Kinder J, Kojima F, Bergfeld E, Wehrman M, Fike K**. 1996. Progestin and estrogen regulation of pulsatile LH release and development of persistent ovarian follicles in cattle. *J Anim Sci*, 74:1424-1440.

**Kruip TA, de Leeuw van Weenen A, Dieleman SJ**. 1977. Endocrine features in the treatment of cystic ovarian follicles in cattle with gonadotrophin-releasing hormone. *Tijdschr Diergeneeskd*, 102:1306-1311.

**Laporte HM, Hogeveen H, Schukken YH, Noordhuizen JPTM**. 1994. Cystic ovarian disease in Dutch dairy cattle, I. Incidence, risk-factors and consequences. *Livest Prod Sci*, 38:191-197.

**Lievaart JJ, Parlevliet JM, Dieleman SJ, Rientjes S, Bosman E, Vos PL**. 2006. Transvaginal aspiration as first treatment of ovarian follicular cysts in dairy cattle under field circumstances. *Tijdschr Diergeneeskd*, 131:438-442.

**López-Diaz MC, Bosu WTK**. 1992. A review and an update of cystic ovarian degeneration in ruminants. *Theriogenology*, 37:1163-1183.

**López-Gatius F, Santolaria P, Yaniz J, Ruthant J, López-Bejar M**. 2001. Persistent ovarian follicles in dairy cows: a therapeutic approach. *Theriogenology*, 56:649-659.

**López-Gatius F, López-Béjar M**. 2002. Reproductive performance of dairy cows with ovarian cysts after different GnRH and cloprostenol treatments. *Theriogenology*, 58:1337-1348.

**López-Gatius F, Santolaria P, Yániz J, Fenech M, López-Béjar M**. 2002. Risk factors for postpartum ovarian cysts and their spontaneous recovery or persistence in lactating dairy cows. *Theriogenology*, 58:1623-1632.

**Lucy MC**. 2001. Reproductive loss in high-producing dairy cattle: where will it end? *J Dairy Sci*, 84:1277-1293.

**McDonald RJ, McKay GW, Thomson JD**. 1961. The use of organic iodine in the treatment of repeat breeder cows. *In*: Proceedings of the IV International Congress on Animal Reproduction, The Hague, 1961. The Hague: ICAR. pp. 679-681.

**McDowell C, Anderson L, Kinder J, Day M**. 1998. Duration of treatment with progesterone and regression of persistent ovarian follicles in cattle. *J Anim Sci*, 76:850-855.

**McLeod BJ, Williams ME**. 1991. Incidence of ovarian dysfunction in post partum dairy cows and the effectiveness of its clinical diagnosis and treatment. *Vet Rec*, 128:121-124.

**McNutt GW**. 1927. The corpus luteum of pregnancy in the cow (*Bos taurus*) and a brief discussion of the clinical ovarian changes. *J Am Vet Med Assoc*, 72:286-299.

**Meyer JP, Radeliff RP, Rhoads ML, Bader JF, Murphy CN, Lucy MC**. 2007. Timed artificial insemination of two consecutive services in dairy cows using prostaglandin F2-alpha and gonadotropin-releasing hormone. *J Dairy Sci*, 90:691-698.

**Nakao T, Numata Y, Kubo M, Yamauchi S**. 1978. Treatment of cystic ovarian disease in dairy cattle. *Cornell Vet*, 68:161-178

**Nakao T, Kawata K, Numata Y**. 1980. Therapeutic effects of an analog of luteinizing hormone-releasing hormone (Des-Gly is-LH-RH-Ethylamide) on cows with cystic ovary. *Jpn J Vet Sci*, 42:459-462.

**Nakao T, Sugihashi A, Saga N, Tsunoda N, Kawata K**. 1983a. A further study on the dosage of an analog of luteinizing hormone-releasing hormone (fertirelin; Des-GlylO-LH-RH-ethylamide) for treatment of ovarian follicular cyst in cows. *Jpn J Vet Sci*, 45:269-273.

**Nakao T, Sugihashi A, Saga N, Tsunoda N, Kawata K**. 1983b. Use of milk progesterone enzyme immunoassay for differential diagnosis of follicular cyst, luteal cyst, and cystic corpus luteum in cows. *Am J Vet Res*, 44:888-890.

**Nakao T, Tomita M, Kanbayashi H, Takagi H, Abe T, Takeuchi Y, Ochiai H, Moriyoshi M, Kawata K**. 1992. Comparisons of several dosages of a GnRH analog with the standard dose of hCG in the treatment of follicular cysts in dairy cows. *Theriogenology*, 38:137-145.

**Nanda AS, Ward WR, Williams PCW, Dobson H**. 1988. Retrospective analysis of the efficacy of different hormone treatments of cystic ovarian disease in cattle. *Vet Rec*, 12:155-158.

**Nanda AS, Ward WR, Dobson H**. 1991. Lack of LH response to oestradiol treatment in cows with cystic ovarian disease and effect of progesterone treatment or manual rupture. *Res Vet Sci*, 51:180-184.

**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. *Reprod Domest Anim*, 33:193-204.

**Osawa T, Nakao T, Kimura M, Kaneko K, Takagi H, Moriyoshi M, Kawata K**. 1995. Fertirelin and buserelin compared by LH release, milk progesterone and subsequent reproductive performance in dairy cows treated for follicular cysts. *Theriogenology*, 44:835-847.

**Peter AT**. 2004. An update on cystic ovarian degeneration in cattle. *Reprod Domest Anim*, 39:1-7.

**Prasithiphol S, Virakul P, Suwimoltheerabutr J, Santi P, Prachin V, Junpen S**. 1999. Uterine flushing in repeat breeding dairy cows using normal saline and antibiotic solution. *Thai J Vet Med*, 29:33-43.

**Probo M, Comin A, Mollo A, Cairoli F, Stradaioli G, Veronesi MC**. 2011. Reproductive performance of dairy cows with luteal or follicular ovarian cysts after treatment with buserelin. *Anim Reprod Sci*, 127:135-139.

**Purohit GN, Joshi BK, Bishnoi BL, Gupta AK, Joshi RK, Vyas SK, Gupta KA, Pareek PK, Sharma SS**. 2001. Cystic ovarian disease in Rathi Cattle. *Ann Arid Zone*, 40:199-202.

**Purohit GN**. 2008. Recent developments in the diagnosis and therapy of repeat breeding cows and buffaloes. *CAB Rev: Perspect Agric Vet Sci, Nutr Nat Res*, 3(62):1-34.

**Rajan A, Sreekumaran T, Abraham MJ, Vijayakumar V**. 1991. Efficacy of iodine supplementation in cows with anoestrum and repeat breeding. *J Vet Anim Sci*, 22:119-121.

**Rauch A, Krüger L, Miyamoto A, Bollwein H**. 2008. Colour Doppler sonography of cystic ovarian follicles in cows. *J Reprod Dev*, 54:447-453.

**Rautha Filho MA, Bison L**. 2009. Homeopathic medicines for the treatment of dairy cows with cystic ovarian disease. *Braz Homeopathic J*, 11:8-13.

**Refsdal AO**. 1982. Ovariecyster hos melkekyr. *Norsk Veterinærtidsskr*, 94: 89-796.

**Ribadu AY, Ward WR, Dobson H**. 1994. Comparitive evaluation of ovarian structures in cattle by palpation per rectum, ultrasonography and plasma progesterone concentration. *Vet Rec*, 135:452-457.

**Roberts SJ**. 1971. *Veterinary Obstetrics and Genital Diseases (Theriogenology)*. 2nd ed. Ann Arbor, MI: Edward Brothers. pp. 421-435.

**Roberts SJ**. 1986. *Veterinary Obstetrics and Genital Disease*. Woodstock, VT: Published by the author. pp. 521-522.

**Roche JF, Crowe MA, Boland MP**. 1992. Postpartum anoestrus in dairy and beef cows. *Anim Reprod Sci*, 28:371-378.

**Santos JE, Huber JT, Theurer CB, Nussio CB, Nussio LG, Tarazon M, Fish D**. 2000. Effects of grain processing and bovine somatotropin on metabolism and ovarian activity of dairy cows during early lactation. *J Dairy Sci*, 83:1004-1015.

**Scholl DT, Carpenter TE, BonDurant RH**. 1992. Economic evaluation of not-treating cows with bovine cystic ovarian disease relative to gonadotropin releasing hormone therapy: a decision-tree analysis approach. *In*: Proceedings of the XXV World Association for Buiatrics Congress, St. Paul, MN, 1992. St. Paul, MN: WAB. v.1, pp. 304-309.

**Seguin BE, Convey EM, Oxender WD**. 1976. Effect of gonadotropin-releasing hormone and human chorionic gonadotropin on cows with ovarian follicular cysts. *Am J Vet Res*, 37:153-157.

**Sheldon IM, Dobson H**. 2004. Postpartum uterine health in cattle. *Anim Reprod Sci*, 82/83:295-306.

**Silva AM, Moreira RJC, Fernandes CAC, Palhao MP, Gioso MM, Neves JP**. 2012. Treatment of ovarian cysts in cattle with lecirelin acetate. *Anim Reprod*, 9:591. Abstract.

**Silvia WJ, Hatler TB, Nugent AM,** . 2002. Ovarian follicular cysts in dairy cows: an abnormality in folliculogenesis. *Domest Anim Endocrinol*, 23:167-177.

**Sirois J, Fortune JE**. 1988. Ovarian follicular dynamics during the estrous cycle in heifers monitored by real-time ultrasonography. *Biol Reprod*, 39:308-317.

**Steinbauer M**. 1985. *Occurence of ovarian cysts in cows after parturition*. München: Tierärtzliche Fakultät der Ludwig-Maximilians Universität. Inaugural Dissertation,

**Stevenson JS, Tiffany SM**. 2004. Resychronizing estrus and ovulation after not- pregnant diagnosis and various ovarian states including cysts. *J Dairy Sci*, 87:3658-3664.

**Suriyasathaporn W, Nielen M, Dieleman SJ, Brand A, Noordhuizen-Stassen EN, Schukken YH**. 1998. A cox proportional-hazards model with time-dependent covariates to evaluate the relationship between body-condition score and the risk of first insemination and pregnancy in a high-producing dairy herd. *Prev Vet Med*, 37:159-72.

**Tebble JE, O'Donnell MJ, Dobson H**. 2001. Ultrasound diagnosis and treatment outcome of cystic ovaries in cattle. *Vet Rec*, 148:411-3.

**Terakawa N, Shimizu I, Tsutsumi H, Aono T, Matsumoto K**. 1985. A possible role of clomiphene citrate in the control of preovulatory LH surge during induction of ovulation. *Acta Endocrinol (Copenhagen)*, 109:58-63.

**Thakur MS, Pandey SK, Shrivastava OP**. 1983. Efficacy of fertivet (clomiphene) on cystic ovaries in crossbred Holstein Friesian and Haryana cows. *Cheiron*, 12:263-264.

**Todoroki J, Yamakuchi H, Mizoshita K, Kubota N, Tabara N, Noguchi J, Kikuchi K, Watanabe G, Taya K, Kaneko H**. 2001. Restoring ovulation in beef donor cows with ovarian cysts by progesterone-releasing intravaginal silastic devices. *Theriogenology*, 55:1919-1932.

**Todoroki J, Noguchi J, Kikuchi K, Ohnuma K, Ozawa M, Kaneko H**. 2004. Plasma concentrations of inhibin A in cattle with follicular cysts: relationships with turnover of follicular waves and plasma levels of gonadotropins and steroid hormones. *Domest Anim Endocrinol*, 27:333-344.

**Todoroki J, Kaneko H**. 2006. Formation of follicular cysts in cattle and therapeutic effects of controlled internal drug release. *J Reprod Dev*, 52:1-11.

**Tutt JFD**. 1932. Nymphomania in the cow: observations on treatment by the injection of adrenalin chloride and by pituitary (posterior lobe) extract injections. *Vet Rec*, 12:521-523.

**Vanholder T, Opsomer G, de Kruif A**. 2006. Aetiology and pathogenesis of cystic ovarian follicles in dairy cattle: a review. *Reprod Nutr Dev*, 46:105-119.

**Watson CL, Cliff AJA**. 1997. Survey of cystic ovarian disease in practice. *Bov Pract*, 31:15-18.

**Williams WL, Williams WW**. 1923. Nymphomania of the cow. *North Am Vet*, 4:232-241.

**Wiltbank MC, Gümen A, Sartori R**. 2002. Physiological classification of anovulatory conditions in

cattle. *Theriogenology*, 57:21-52.

**Woolums AR, Peter AT**. 1994. Cystic ovarian condition. *In*: Cattle. 1. Folliculogenesis and ovulation. *Compend Contin Educ Pract Vet (Food Anim)*, 16:935-942.

**Yoshioka K, Iwamura S, Kamomae H**. 1996. Ultrasonic observations on the turnover of ovarian follicular cysts and associated changes of plasma LH, FSH, progesterone and oestradiol- 17β in cows. *Res Vet Sci*, 61:240-244.

**Youngquist RS**. 1986. Cystic follicular degeneration in the cow. *In*: Morrow DA (Ed.). *Current Therapy in Theriogenology*. 2nd ed. Philadelphia: WB Saunders. pp. 243-246

**Youngquist RS, Threlfall WR**. 2007. Ovarian follicular cysts. *In*: Youngquist RS, Threlfall WR (Ed.). *Current Therapy in Large Animal Theriogenology*. St. Louis, MO: Saunders Elsevier. pp. 379-383.

**Zemjanis R**. 1970. *Diagnostic and Therapeutic Techniques in Animal Reproduction*. 2nd ed. Baltimore: The Williams & Wilkins. 242 pp.

**Zulu VC, Sawamukai Y, Nakada K, Kida K, Moriyoshi M**. 2002. Relationship among insulin like growth factor-I, blood metabolites and post partum ovarian function in dairy cows. *J Vet Med Sci*, 64:879-885.