Benha University
Faculty of Vet. Medicine
Dept. of Theriogenology

Time allowed: Three Hours

4th Class Exam. Gynecology (Vet 643a, 2012/2013) *Total Marks: 50*

Answer the following questions:

1- Write briefly on the following and illustrate with examples whenever possible: (15 Marks)

a- Estrous cycle in a cow (3 Marks).

b- Methods of estrus synchronization in large ruminants (4 Marks).

c- Factors affecting age of puberty in a ewe.

d- Positive signs of pregnancy in a cow (3 Marks).

2- Mention the origin, functions, commercial preparations, Doses and practical uses of the following reproductive hormones in a cow: (15 marks)

1- Prostaglandin $F_{2\alpha}$ (5 Marks). 2- Gonadotrophic hormones (5 Marks).

3- Estrogen (5 Marks).

3- Compare clinically between the followings: (10 marks)

a- Cow in normal estrus and nymphomanic one (3 marks)

b- Graffian follicle and corpus luteum (3 marks)

c- Different types of corpus luteum. (2 marks)

d- True and false double cervix in a cow. (2 marks)

4- You are invited to assess the reproductive status of a recent parturient(300) dairy cows in a large dairy herd showing a copious muco-purulent discharge behind all cows, stacked on the inner sides of their tails and all cows exhibit a sever straining on rectal palpation. What is your diagnosis, suspected causes of such cases, your recommendation and interference? (10 Marks).

Good Luck

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1- Write briefly on the following and illustrate with examples whenever possible:

a- Estrous cycle in a cow (3 Marks).

- Estrus cycles are generally three weeks long, but normally can range from 17 to 25 days.
- Duration of the estrous cycle is often 1 to 2 days shorter in heifers than in cows.
- High seasonal temperatures do not seem to alter the length of the estrous cycle, but may reduce the duration of estrus, blood flow to the reproductive tract and concentration of various reproductive hormones.
- **According to the behavioral signs of estrus on the animal, estrus could be classified into four distinct phases as follows:**

  1- Proestrus (Day 19- Day 0): It is the period immediately preceding estrus. It begins when progesterone declines as a result of regression or luteolysis of the corpus luteum. Proestrus lasts from 2 to 5 days depending on the species.

  2- Estrus (Day 0): The period of estrus averages 12 - 18 hours under most conditions. Ovulation occurs approximately 24 to 30 hours after the onset of estrus. It is the most recognizable stage of the estrous cycle because it is characterized by visible behavioral signs including increased locomotion, phonation (Vocal expression), nervousness and attempts to mount other animals. At the end of this period, the female expresses her willingness to accept the male for mating. This willingness is referred to as standing estrus, and the characteristic mating posture is known as **lordosis** because of a characteristic arching of the back in preparation for mating. Lordosis is used as a diagnostic tool to identify the appropriate time to inseminate the female artificially or to expose her to the breeding male. Estradiol is the dominant hormone during this stage of the estrous cycle.

  3- Metestrus (Day 1-3): It is the period between ovulation and the formation of functional corpora lutea. Metestrus lasts two to five days which are usually required after ovulation before the newly formed corpora lutea produce significant quantity of progesterone.

  Diestrus (Day 4-18): It is the period of maximum luteal function. It is the longest stage of the estrous cycle and encompasses the period of time when the corpus luteum is fully functional and progesterone production is high. It ends when the corpus luteum is regressed (luteolysis). Diestrus usually lasts about 10 - 14 days, and is directly related to the length of time that the corpus luteum remains functional, i.e. produces progesterone.

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b- Methods of estrus synchronization in large ruminants (4 Marks).

1- **Progesterone based protocol:**
   a. Progesterone alone.
   b. Progesterone-prostaglandin combinations
   c. Progesterone - PMSG combination.

2- **Prostaglandin based protocol:**
   a. Prostaglandin alone.
   b. Prostaglandin-GnRH combinations
   c. Prostaglandin-Estradiol combinations.
3- **Other means of synchronization:**
   a. Physical disruption.
   b. Intrauterine infusions.
   c. Early 48 – hour weaning.
   d. Shang treatment

1- <u>Progesterone based protocol:</u>

Common progesterone products used for estrous synchronization:

- *Oral compounds*:
  - MAP :(6-methyl-17 acetoxy-progesterone)
  - MGA® (Melengestrol Acetate)
  - CAP: (6-chloro-Δ6-dehydro-17-cetoxyprogesterone)
  - DHPA (dihydroxyprogesterone acetophenide)
- *Intera-vaginal progesterone release device*
  - CIDR®: (Controlled-Internal-Drug-Release)
  - PRID:(Progesterone-Releasing-Intera-vaginal-Device)
- *Implant*:
  - Synchromate-B
  - Norgestomate.
- *Injection*: Progestin or progesterone.

Regimens of estrous synchronization with progesterone:

a. **<u>Progesterone alone</u>**

☐ The progestin is administered in feed or drinking water, as subcutaneous implants, by topical application, or as vaginal pessaries for a period exceeding the inherent lifespan of the corpus luteum (14 - 20 days) to prevent ovulation and estrus.

☐ The administered progestin does not affect the life-span of the CL which usually regresses 17 days after the previous estrus

☐ Example of some progesterone products used in feed and dose:
   MAP 180 mg/day.
   CAP 10mg/day.
   MGA 1mg/day.

1- Oral progesterone compounds:

- This system depends on treatment with MGA for 14 days or more (by feeding).
- All heifers will be in heat 2 to 6 days after the last day of MGA feeding and bulls can be turned in with heifers 17 days later.
- **Advantage**: Simple to implement, inexpensive, and heifers do not have to be handled
- **Disadvantage:** Not ideal for use with AI, but good strategy for use with natural service.

2- Intra-vaginal progesterone release device:

- CIDR® is a T-shaped devise; about 5 inches long; is inserted into the vagina of breeding females for 7 days.
- All heifers will be in heat 2 to 4 days after the last day of device removal.
- **Advantages:** Use of CIDR can induce puberty in some heifers
- **Disadvantages:** Relatively expensive protocol

3- Progesterone implant:

This system depends on an injection of 2ml of solution contain 5 mg estradiol valerate and 3 mg norgestomet at the timing of implant insert.

- *Synchromate B* is of polymeric implant which contains 6 mg of norgestomet.
- *Norgestomet implant* is an implant contains a synthetic progestin along with an estradiol valerate .
- The implant is removed 9 days later and most cycling heifers will return to estrus within 4 days. Females are bred 48-60 hrs later (av. 54 hrs).
- Producers who inseminate upon observation of estrus should do so during the second estrus following implant removal, when fertility is improved and some synchrony of cycle remains.
- **Advantage** - Simple to implement, inexpensive, and heifers do not have to be handled. Suitable for use in cycling heifers only.
- **Disadvantage** - Not ideal for use with AI, but good strategy for use with natural service. Not suitable in dairy cows. Presence of CL at time of use affect on the success and fertility after its withdrawal i.e. poor fertility if the implant is inserted into cows with without CL.

b. **Progesterone-prostaglandin combinations**

- If treatment with MGA is for 14 days or less, it must combine with a luteolytic agent ($PGF_{2\alpha}$) to successfully control time of estrus onset.
- 82% of treated animals will exhibit estrus within 17 hours (48 hours after $PGF_{2\alpha}$) and 100% within 32 hours (sooner than with PG treatment alone).
- Greater promise has been shown when PGF2α was given 16-18 days after the withdrawal of melengestrol acetate, thus avoiding the less fertile first estrus after progesterone removal.
- The combination treatment has some advantages:
  - It shortens the period of progestin treatment and thus possibly enhances the chances of conception.
  - It requires only one prostaglandin treatment.
  - It shortens the overall synchronization procedure.
  - It gives better synchronization.

1- MGA with Prostaglandins

System I:

This system depends on initial synchronization of females by feeding with MGA (0.5mg) for 14 days and $PGF_{2\alpha}$ is administered during the luteal phase of the subsequent cycle.

System II:

This system depends on feed MGA for 9 days (0.5mg/head/day) to prevent estrus in diestrus and proestrus animals then give $PGF_{2\alpha}$ on Day 8 to regress CL (s). Remove MGA on Day 9 (stop feeding) and cows will be in heat in 2-5 days.

2- CIDR® or PRID® plus $PGF_{2\alpha}$

- CIDR® or PRID® insert in the vagina keeps the serum levels of progesterone high enough to prevent ovulation and estrus for 7 days.
- $PGF_{2\alpha}$ is luteolytic when administered during diestrus, and should be given on day 6 (1 day before insert removal).

3- Norgestomet and $PGF_{2\alpha}$:

- During the 7- 9 days of implantation, norgestomet suppresses further ovulations, corpora hemorrhagicum become mature and susceptible to prostaglandin. Therefore, exogenous prostaglandin products administered near the time of norgestomet implant removal will allow synchrony of estrus and a high pregnancy rates.

c. **Progesterone plus PMSG combination:**

- This system depends on administration of progesterone (50mg) by injection for 14 days, PMSG (500IU) is administered on day 12and $PGF_{2\alpha}$ (cloprostenol; 500µg) is administered on day 15.
- This regimen synchronizes estrus in more than 72% of treated animals.

2- Prostaglandin based protocol:

- ***Principle of estrous synchronization with prostaglandin*:**
  - $PGF_{2\alpha}$ is an effective luteolytic agent during the mid luteal phase of the estrous cycle i.e. $PGF_{2\alpha}$ administered during days 5-17 of the estrous cycle will cause regression of the CL and subsequent return to estrus in 36 to 72 hours. Prior to day 5 the CL may not have sufficient receptor sites to respond to normal levels of $PGF_{2\alpha}$. After day 17 the CL usually is regressing.
  - $PGF_{2\alpha}$ administered between day 5 and 17 of the estrous cycle causes blood plasma progesterone levels to fall rapidly within 24 hours, followed by a rise in estrogen within 24 hours.
  - A pre-ovulatory peak of LH occurred on the average within 3 days and estrus occurred at about the time of the LH peak. Ovulation occurred about 24 hours after the onset of estrus.
- ***Reasons for wide variable response to synchronization of estrus regimens using $PGF_{2\alpha}$:***

  If $PGF_{2\alpha}$ given at any time of the cycle, only about 60 – 65% of the cows are expected to respond and this is due to:

  a) Absence of CL at time of $PGF_{2\alpha}$ administration i.e. anestrum.
  b) Age and reproductive status of animals:

- Heifers usually respond more quickly and more synchronously than cows; most heifers will begin standing to be mounted on the second day after treatment.
- Beef cows are slower to respond, most being in estrus on the third day after treatment.

c) Stage of corpora lutea development:
$PGF_{2\alpha}$ is effective only when administered to cycling cows between day 5 and day 17 of the cycle

d) Stage of the follicular wave:
Day 7 $PGF_{2\alpha}$ gets faster response due to ovulation of follicle from 1st follicular wave. Day 10 PGF has slower response due to ovulation of follicle from 2nd follicular wave.

- ***Most common $PGF_{2\alpha}$ products, commercial name and indications:***

Product	Active principle	Dose	Half-life	Indications
Lutalyse (5mg/ml)	Dinoprost (Natural compound)	25 mg	2 – 3 min.	beef cattle and dairy heifers
Estrumate (250ug/ml)	Cloprostenol sodium (Synthetic Analogue)	500 ug	3 - 4 hours	lactating or dry cows and heifers
Prosolvin (5mg/ml)	Fenprostalene (Synthetic Analogue)	15 mg	2 hours	beef cattle and non-lactating dairy heifers

- ***Requirements for high successful response to synchronization with $PGF_{2\alpha}$***

Response to $PGF_{2\alpha}$ products may be considered consistent if luteolysis or behavioral estrus occurs following treatment. In order to observe behavioral estrus as a result of $PGF_{2\alpha}$ treatment, several conditions must be realized as follows:

- Female must have CL susceptible to luteolysis.
- The endocrine mechanisms must function properly.
- The female must experience psychic estrus (not silent).
- Females has the opportunity to display estrous behavior (bull, teaser or other cows must be present).
- Good heat detection and recording.

- ***Regimens of estrous synchronization with prostaglandins:***

a. <u>Prostaglandin alone</u>

☐ **<u>Program I (blind system):</u>**
It is one of the basic prostaglandin synchronization schemes utilizes double $PGF_{2\alpha}$ injection, 11-12 days apart. Prostaglandin-treated cows can be inseminated once 80 hours (FTI) after treatment, or twice 72 and 96 hours after treatment. Alternatively, females can be bred by appointment 72 to 80 hours after the onset of estrus if observed on subsequent days.

☐ **<u>Program II:</u>**
Single $PGF_{2\alpha}$ injection with heat observation.

☐ **Program III:**
Observe animals for sings of heat for a period 5-6, and inject animals not detected in estrus on 5th day, then observe estrus and breed accordingly.

☐ **Program IV:**
On day 1; palpate all animals and inject those having CL. Observe estrus for 5 days. Inject the remaining animals on day 12 and breed accordingly.

b. Prostaglandin-GnRH combination:

- Procedure of the synchronized ovulation with $PGF_{2\alpha}$-GnRH combination starts with an injection of GnRH to stimulate ovulation and the start of a new follicular wave followed by $PGF_{2\alpha}$ 7 days later to induce regression of CL. A second injection of GnRH 36 – 48 hours after $PGF_{2\alpha}$ resulted in a synchronized ovulation 24-32 hrs later.
- A timed breeding 16-20 hrs after the second GnRH injection resulted in fertility similar to cows bred at normal estrus.
- The procedure has been very reliable to mature cows but less reliable in heifers, apparently because of differences in the follicular wave patterns of heifers.
- All protocols can be preceded by administration of two doses of $PGF_{2\alpha}$ 14 days apart (Pre-synch) and administration of the first GnRH 12–14 days later (Day 0).
- ***Ovsynch*** (GnRH- $PGF_{2\alpha}$ -GnRH): GnRH on Day 0, $PGF_{2\alpha}$ on Day 7, GnRH on Day 9, and timed AI (TAI) 16 h later.
- ***Co-synch***: as for Ovsynch but TAI occurs concurrently with GnRH on Day 9.
- ***Select-synch*** (GnRH- $PGF_{2\alpha}$): GnRH on Day 0, PGF on Day7 and AI on detection of estrus.
- ***Hybrid-synch***: GnRH – $PGF_{2\alpha}$-GnRH with heat detection until Hour 72, Timed AI at 72 Hours.

c. Prostaglandin-Estradiol combination:

☐ **Heatsynch (GnRH-$PGF_{2\alpha}$-Estradiol):**

➢ As for Ovsynch but second injection of GnRH is replaced by administration of estradiol on Day 8 and cows are inseminated on detection of estrus on Days 7–9 and time inseminated on Day 10 if not detected in estrus by that time.

➢ **Advantages:**

1- Uses the less-expensive hormone estrogen in place of the second GnRH injection of the Ovsynch protocol.
2- High percentage of cows that will show visual signs of estrus and improve breeding system of cows and consequently the conception rates.

➢ **Disadvantages:**

1- High percentage of false heat expression.
2- Lower percentage of ovulation (40%) as compared with the Ovsynch protocol (83%).

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c- Factors affecting age of puberty in a ewe.

1- Season of birth:

-Ewe lambs born early in the spring tend to reach puberty at younger age than those born later in the spring.
-The fall-born lambs begin cycles when they are 48-50 weeks of age;
-The spring-born lambs reach puberty at a much younger age and less synchronously.

2- Body weight:

- A minimum threshold body weight of lambs at puberty is necessary.

3- Nutrition:

- Lambs raised on a high plane of nutrition reach puberty earlier than those on a low plane.

4- Breed:

- Lambs of prolific breeds tend to reach puberty at a younger age.
- Puberty in ewe lambs does not occur at a fixed age, weight, or time of year.
- It appears to be due to a complex interaction of these factors with the season of birth.

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d- Positive signs of pregnancy in a cow (3 Marks).

a. Fetal membrane slip.
b. Presence of placentomes.
c. Palpation of fetus.
d. Pulsation or thrilling of the middle uterine artery.

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2- Mention the origin, functions, commercial preparations, Doses and practical uses of the following reproductive hormones in a cow: (10 marks)

a. Prostaglandin F2α (4 Marks). b- Gonadotrophic hormones (3 Marks).
c. Estrogen (3 Marks).

Hormone	Origin	Function	Commercial preparation	Dose	Practical uses
Prostaglandin F2α	**Endometrium**	CL lysis and increased myometrial activity.	Lutylase (Natural $PGF_{2\alpha}$) Estrumate (Synthetic $PGF_{2\alpha}$) estroPLAN (Synthetic $PGF_{2\alpha}$) ProstaMate(Synthetic $PGF_{2\alpha}$) Hemabate (Synthetic $PGF_{2\alpha}$) Juramate (Synthetic $PGF_{2\alpha}$) Sincrocio (Synthetic $PGF_{2\alpha}$) PRELOBAN(Synthetic $PGF_{2\alpha}$) Ciosin (Synthetic $PGF_{2\alpha}$) SincroProst (Synthetic $PGF_{2\alpha}$) Prostal (Synthetic $PGF_{2\alpha}$) Enzaprost (Synthetic	Natural $PGF_{2\alpha}$ (Lutylase®): 25-35 mg….5-7 ml Synthetic $PGF_{2\alpha}$ (Estrumate®): 500 µg….2 ml Synthetic $PGF_{2\alpha}$ (Prosolvin®): 15 mg…….2ml	• Synchronization of estrus in farm animals. • Treatment of persistent corpus luteum. • Evacuation of abnormal uterine contents • Preparation of donors and recipients in embryo transfer
Gonadotrophic hormones	**Pituitary gland**	**FSH** • Stimulate granulosa cells multiplication and development of LH receptors. • Facilitated the synthesis of estradiol through induction of aromatase E. activity. • Promotes follicular vascularity • It may be involved in formation of proteases which weaken the follicular wall prior to ovulation. • Adequate FSH-priming of the follicle is essential for the effects of LH, normal ovulation and C.L. development	**FSH** Folligone Fostim Anterion Prolan-A Gystyl	5000-10000 IU	**FSH** • Smooth inactive ovary • Super-ovulation for embryo transfer • Synchronization of estrous after sponge removal • Induction of estrous after farrowing • Induction of estrous during physiological anestrum
		LH: • Requires for the final stages of follicular	**LH:** Prolan	5000-10000 IU	**LH** • Delayed ovulation

		maturation and ovulation. • Stimulates granulosa cells to produce prostaglandins. • Stimulate cells in the ovarian to release histamine, • Plays an important role in formation and maintenance of the C.L.	Pregnyl Chorulon Premognyl Cystovet Profassi Novarel Humagon		• Anovulation • Cystic ovary (follicular cyst) • Prolonged estrus • Repeat breeder • Early embryonic death • In bull: improve the libido • Induce or hasten ovulation • Stimulate the onset of estrus after farrowing
Estrogen	**Ovarian follicle**	- Stimulate granulosa cells multiplication and development of LH receptors. - Facilitated the synthesis of estradiol through induction of aromatase enzyme activity. - Promotes follicular vascularity - It may be involved in formation of proteases which weaken the follicular wall prior to ovulation. - 5. Adequate FSH-priming of the follicle is essential for the effects of LH, normal ovulation and C.L. development	Estradiol benzoate Folon-5 Cyren-B Diethyl stilbesterol	5-20 mg	• Induction of abortion • In undesirable pregnancy, mummified fetus • Open cervix • In closed pyometra, retained placenta, mummified fetus • Weak and/or silent heat • Incomplete enucleation of CL • To antagonize P4 release • Priming of uterine contractility to action of oxytocin • Induction of lactation • E2 plus P4 • Initiation of estrous • Osteoporosis in aged females • Hormonal castration and fattening • Prostatic hyperplasia and urinary incontinence in dog

3- Compare clinically between the followings: (10 marks)

a- Cow in normal estrus and nymphomanic one (3 marks)

	normal estrus cow	**nymphomaniac cow**
Sterility hump	Absent	Present
Mucous	Thick stringy mucous	High amount, tenacious and opaque.
Animal behavior	Mounting and allow other animals to mount	Mounting and refuse other animals to mount.
Voice	No change	Change to masculine direction.
Pneumovagina	Not occur	May occur due to relaxation of ligaments
Homo-sexual behavior	absent	present

b- Graffian follicle and corpus luteum (3 marks)

	- Graffian follicle	corpus luteum
Texture	Fluctuated	Liver like
Presence of neck	Has no neck	Has a neck
Protrusion on the ovary	Non protruded	protruded
Secretory function	Secrete estrogen	Secrete progesterone
Association with stage of estrous cycle	Present during estrus	During diestrus
Size	1.5-2.0 cm in cow 4.5.-5.0 in mare	2.5-3.0 in cow 3-4 cm in mare
Response to pressure	Pit under pressure due to its fluid content	Not pit under pressure
Structure	Fluid containing cavity with thin outer wall	Solid mass of tissue, sometimes contain cavity
Shape	spherical	Cauliflower like
Surface	Smooth	rough

c- Different types of corpus luteum. (2 marks)

1. According to size and shape of CL alongside the change in the estrous cycle

Stage / Day	CL Changes, Description	Code
1 - 2	Ovulation depression& CH	OVD
2 - 3	Soft developing CL not exceed 1 cm in diameter.	CH1
3 - 5	Soft developing CL, 2 cm in diameter	CH2
5 - 7	Mature CL, more than 2 cm in diameter.	CH3
8 - 17	Fully mature CL, 2-3 cm in diameter	CL3

18 - 20	Firm, regressed CL, 1-2 cm in diameter.	CL2
0 - 1	Hard CL or C. albicans, less than 1 cm in diameter.	CL1

2. According to reproductive status of animal

Corpus luteum periodicum	Corpus luteum gravidities	Corpus luteum persistent
i.e. Cyclic CL	i.e. CL of pregnancy	i.e. CL persistent associated with uterine pathology
Persistent on the ovary during luteal phase that extend from Day 4 to day 18 after estrus.	Persist on the ovary during whole pregnancy in cow and associated with presence of fetus in the uterus to maintain pregnancy.	It persists on the ovary and be evident during repeat rectal examination for 21 days at 5-7 days intervals and associated with pathology of uterus e.g. pyometra due to disturbance of mechanism of luteolysis
Protruded on ovarian surface	Embedded in ovarian tissue	Embedded in ovarian tissue

d. True and false double cervix in a cow (**2 Marks**).

True double cervix	**False double cervix**
A band of tissue separate the two openings and extend to the caudal Os of cervix	A band of tissue present caudal to the Os of cervix.
The cervix actually divided into two longitudinal tubes	The cervix is devided externally into two openings, but the cervical canal is intact.
Fertility is reduced in case of AI	Fertility is little affected
During parturition may lead to dystochia	Lead the female to be repeat breeder

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4- You are invited to assess the reproductive status of a recent parturient (300) dairy cows in a large dairy herd showing a copious muco-purulent discharge behind all cows, stacked on the inner sides of their tails and all cows exhibit a sever straining on rectal palpation. What is your diagnosis, suspected causes of such cases, your recommendation and interference? (10 Marks).

- The case is: Chronic muco-purulent endometritis (E2):

- Signs and findings:

- The animal is repeat breeder.
- Copious milky or cloudy mucus with pus flakes.
- Rectally, the uterus is slightly enlarged, flabby and thickened. And the cervix is felt slightly lager and flabby.
- Vaginally, the cervix is congested and enlarged.

- Suspected causes:

- Abnormal parturition; abortion dystocia, fetotomy and retention of placenta.
- Delayed uterine involution.

- Peneumovagina or wind sucking,
- Unhygienic births help.
- Unhygienic instruments used for treatment or insemination.

- Advice to reduce the incidence of this pathological condition:

1- Hygienic births help.
2- The use of hygienic instruments and insemination technique.
3- The use of artificial insemination instead of natural breeding to reduce the transmission of pyogenic bacteria.
4- Prophylactic antibiotic after birth.

- Interference of this case can be done through:

a. Diagnosis:

-- History of repeat breeding,
-- Rectal examination,
-- Vaginal examination.
-- Bacteriological examination from collected mucus.
-- Sensitivity test for suitable antibiotics.

- Treatment:

- Evacuation of the uterine contents: by massaging of the uterus through rectum.
- Induction of estrous to dilate the cervix by using PGF2α e.g. cloprostenol acetate 25-35 mg i.m.
- Treatment of the causative organism by systemic administration of antibiotics
- Local antiseptic and/or antibiotic application e.g. Lugol iodine 1% or oxtetracycline.
- The animal never be mated or inseminated on the first two or three heats after recovery

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