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FORMULARY AND PROTOCOLS IN EQUINE REPRODUCTION

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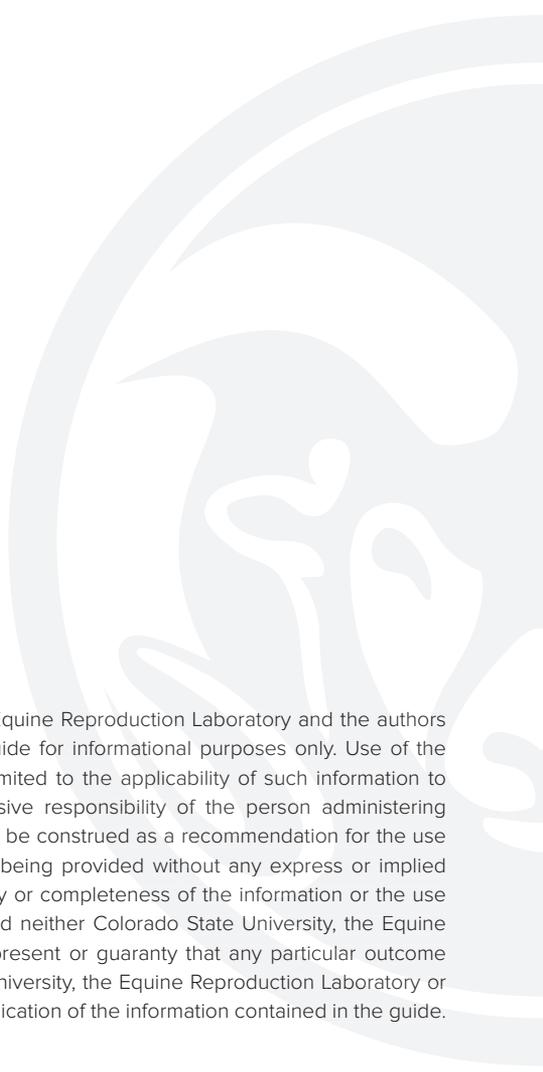
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PREFACE

The goal of this Formulary and Protocols guide is to provide veterinarians and veterinary students with medication dosages and therapeutic protocols used at the Equine Reproduction Laboratory, Colorado State University.

THIS GUIDE IS ORGANIZED INTO TWO SECTIONS:

1. FORMULARY

- Hormones
 - Intrauterine therapy
 - Uterine lavage
 - Miscellaneous medications
 - Systemic antibiotics
-

2. CLINICAL PROTOCOLS

The formulary contains up-to-date dosages and clinical indications for a wide variety of medications. The clinical protocols section contains descriptions of common reproductive treatment protocols.

ABBREVIATIONS

q 6 hr – every 6 hours

q 12 hr – every 12 hours

q 24 hr – every 24 hours

PO – oral route of administration

IV – intravenous route of administration

IM – intramuscular route of administration

qs – abbreviation for quantum sufficit,
a Latin phrase meaning “quantity required”

MEDICATION	DOSAGE, ROUTE, FREQUENCY	INDICATIONS
Altrenogest (Regu-Mate®) (2.2 mg/ml)	0.044 mg/kg, orally, q 24h	Suppression of behavioral estrus, synchronization of estrus, maintenance of pregnancy
Altrenogest (Regu-Mate®) (2.2 mg/ml)	0.088 mg/kg, orally, q 24h or 0.044 mg/kg, orally, q 12h (double dose)	Maintenance of pregnancy in high-risk mares
Buserelin*	10 to 50 µg, IM, q 6h to 12h	GnRH agonist; stimulation of follicular development in anestrous, transitional or acyclic mares
Cloprostenol (Estrumate®) (250 µg/ml)	250 µg, IM, once 50 µg, IM, q 24h for 2-3 days*	Termination of luteal activity, synchronization of estrus, termination of pregnancy, stimulation of uterine contractions (evacuation of uterine fluid); should not be administered in the early post-ovulation period due to adverse effects on development of the corpus luteum
Deslorelin acetate (SucroMate™)	1.8 mg, IM, once	Induction of ovulation

* medication reported to be used at other facilities; not in use at CSU

HORMONES

MEDICATION	DOSAGE, ROUTE, FREQUENCY	INDICATIONS
Deslorelin acetate (low dose)	50 to 100 µg, IM, q 12h	GnRH agonist; stimulation of follicular development in anestrous, transitional or acyclic mares
Dinoprost tromethamine (Lutalyse®) (5 mg/ml)	5 to 10 mg, IM, once	Termination of luteal activity; synchronization of estrus, termination of pregnancy, stimulation of uterine contractions (evacuation of uterine fluid); should not be administered in the early post-ovulation period due to adverse effects on development of the corpus luteum
Domperidone (Equidone® Gel) (110 mg/ml)	1.1 mg/kg, PO, q 12 to 24h	Dopamine antagonist; stimulation of lactation (agalactia) in postpartum mares, induction of lactation in nonpregnant mares, treatment of fescue toxicity

MEDICATION	DOSAGE, ROUTE, FREQUENCY	INDICATIONS
Estradiol (E₂)	5 to 10 mg, IM, q 24h	Stimulation of behavioral estrus in non-cycling or ovariectomized mares; used in conjunction with progesterone for estrus synchronization
Estradiol cypionate (ECP)	10 mg, IM, as needed	Stimulation of behavioral estrus in ovariectomized mares (long acting)
Human Chorionic Gonadotropin (Chorulon®) (hCG) (10,000 IU/vial)	2,500 IU, IV or IM once (dose range 1,500 to 3,000 IU)	Induction of ovulation
Human Chorionic Gonadotropin (Chorulon®) (hCG) (10,000 IU/vial)	10,000 IU, IV or IM, once	hCG stimulation test to evaluate horse for presence of testicular tissue (testosterone response test)

* medication reported to be used at other facilities; not in use at CSU

HORMONES

MEDICATION	DOSAGE, ROUTE, FREQUENCY	INDICATIONS
Gonadotropin releasing hormone (GnRH) - native	500 µg, IV or IM, once, 1 to 2 hours prior to breeding or collection	Increase libido in stallions with low libido
Oxytocin (20 units/ml)	20 units, IV or IM, q 6h to q 24h or as needed	Stimulation of uterine contractions (evacuation of uterine fluid), treatment of retained placenta, milk let-down
Oxytocin (low dose) (20 units/ml)	5 to 10 units, IV or IM, as needed	Induction of labor; administer 5 units followed by 10 units 15 minutes later; a majority of full term mares will rupture their chorioallantoic membrane within 5 to 15 minutes after the second dose of oxytocin
Oxytocin (20 units/ml)	60 units, q 24h, IM days 7 to 12 post ovulation	Suppression of estrus; induce formation of persistent CL
Progesterone -in-oil (P₄) (50 mg/ml)	150 mg, IM, q 24h	Suppression of behavioral estrus; synchronization of estrus and ovulation
Progesterone -in-oil (P₄) (50 mg/ml)	200 mg, IM, q 24h	Maintenance of pregnancy

MEDICATION	DOSAGE, ROUTE, FREQUENCY	INDICATIONS
Progesterone (long acting) (300 mg/ml)	1,500 mg, IM, q 7 days	Suppression of behavioral estrus, synchronization of estrus, maintenance of pregnancy
Progesterone /Estradiol P&E (50 mg P₄ plus 3.3 mg E₂/ml)	150 mg P ₄ /10 mg E ₂ , IM, q 24h	Synchronization of estrus, 'programming' time of ovulation in transitional mares, suppression of estrus
Prostaglandin E₁ (Misoprostol; Cytotec®) (100 µg/tablet)	1,000 to 2,000 µg, topically onto cervix, and within cervical lumen as needed	Cervical relaxation; tablets are crushed and added to DMSO gel or sterile obstetrical gel and applied to the surface and within the lumen of the cervix
Prostaglandin E₂ (dinoprostone cervical gel; Prepidil Gel®) (0.2 mg/ml)	1.0 ml gel applied to surface of each oviduct	Applied to surface of oviducts via laparoscope to 'unblock' oviducts suspected of luminal blockage with gelatinous masses that contain fibroblast cells
Sulpiride 5%* suspension (50 mg/ml)	0.5 to 1.0 mg/kg, IM, q 12h to q 24h	Dopamine antagonist; stimulation of lactation in postpartum mares; induction of lactation in nonpregnant mares; stimulation of follicular development in transitional mares

* medication reported to be used at other facilities; not in use at CSU

INTRAUTERINE THERAPY

INTRAUTERINE THERAPY

MEDICATION	DOSAGE, ROUTE, FREQUENCY	INDICATIONS
Acetylcysteine solution (20%) (200 mg/ml)	30 mls (6 grams) diluted into 150 mls sterile saline infused into uterus	Mucolytic; management of chronic uterine inflammation
Amikacin sulfate (250 mg/ml)	1 to 2 grams; buffer with 10 mls sodium bicarbonate (8.4 %) then qs to 50 mls with sterile saline	Antibiotic (Gram negative spectrum)
Amphotericin B (50 mg/vial)	100 to 200 mg reconstituted in 50 mls sterile saline	Antifungal agent
Ampicillin (1 gm vial)	1 to 2 grams, reconstitute in 50 mls sterile saline	Antibiotic (Gram positive spectrum primarily)
Ceftiofur (Naxcel®) (1 gm vial)	1 gram, reconstitute with 20 mls sterile water	Antibiotic (broad spectrum)
Ciprofloxacin (10 mg/ml)	500 mg; qs to 50 mls with sterile saline	Antibiotic (primarily Gram negative spectrum); should reserve for use against organisms resistant to other antibiotics

INTRAUTERINE THERAPY

MEDICATION	DOSAGE, ROUTE, FREQUENCY	INDICATIONS
Clotrimazole* (100 mg/ tablet)	500 to 700 mg in 50 mls sterile saline	Anti-fungal agent
Fluconazole* (200 mg/ tablet)	100 to 250 mg in 50 mls sterile water; to reconstitute, add 5 mls DMSO to 1 gram (5 tablets) of fluconazole to dissolve; divide into 4 aliquots of 250 mg each; qs to 50 mls with sterile water	Antifungal agent
Gentamicin (100 mg/ml)	1 to 2 grams; buffer with 10 mls of 8.4 % sodium bicarbonate; qs to 50 mls sterile saline	Antibiotic (Gram negative spectrum)
Kerosene (K-1)	250 to 500 mls	Chemical curettage of the uterus; used in mares with chronic mucus production; infuse into uterus with disposable tubing; lavage uterus the next day and daily for 1 to 3 days thereafter as needed

* medication reported to be used at other facilities; not in use at CSU

INTRAUTERINE THERAPY

INTRAUTERINE THERAPY

MEDICATION	DOSAGE, ROUTE, FREQUENCY	INDICATIONS
Lufenuron* (Program®) (270 mg/ packet)	540 mg in uterus suspended in 50 mls sterile saline, 270 mg applied to vaginal vault and clitoral area	Treatment of fungal endometritis (specifically for yeast organisms with chitin in cell wall)
Miconazole (1,200 mg insert)	1,200 mg insert deposited into uterus	Antifungal agent
Nystatin (100,000 USP units/gram; 30 gram vial)	5 grams suspended in 50 mls sterile water; or 0.5 million units	Antifungal agent
Penicillin (Potassium) (5 million units/vial)	5 million units; reconstitute in 50 mls sterile saline	Antibiotic (Gram positive spectrum)
Penicillin (Procaine) (300,000 units per ml)	15 mls; dilute to 50 mls in sterile saline	Antibiotic (Gram positive spectrum)
Ticarcillin/ Clavulanic acid (Timentin®) (3.1 gm per vial)	3.1 grams; reconstitute to 50 mls with sterile saline	Antibiotic combination; clavulanate blocks penicillinase; used for Gram positive organisms and <i>Pseudomonas aeruginosa</i>

UTERINE LAVAGE AND INFUSIONS

MEDICATION	DOSAGE, ROUTE, FREQUENCY	INDICATIONS
Ceragyn™	60 ml; uterine infusion	Anti-microbial peptide mimic; treatment of infectious endometritis; reduction of biofilm
Dimethyl sulfoxide (DMSO) (99%)	50 to 200 ml DMSO per liter saline; may repeat as needed; follow with lavage with 1 liter saline or LRS	Anti-inflammatory; uterine lavage to decrease mucus production; also effective in reducing biofilm
Hydrogen Peroxide (3%)	60 to 120 mls infused into uterus; follow the next day with lavage using sterile saline or lactated Ringer's solution (LRS)	Treatment of fungal endometritis
Lactated Ringer's Solution (LRS) or Normosol-R	1 to 4+ liters; repeat lavage until effluent fluid is clear	Uterine lavage (Note: neutral pH)
Povidone-iodine (Betadine® Solution) (1%)	10 to 15 mls added to 1 liter sterile saline	Treatment of bacterial or fungal endometritis; may also add povidone-iodine to tap water for uterine lavage of postpartum mare, mare with retained placenta, or mare with a pyometra

* medication reported to be used at other facilities; not in use at CSU

UTERINE LAVAGE AND INFUSIONS

MEDICATION	DOSAGE, ROUTE, FREQUENCY	INDICATIONS
<p>Saline (0.9%)</p>	<p>1 to 4+ liters; repeat lavage until effluent fluid is clear</p>	<p>Uterine lavage (Note: acidic pH)</p>
<p>Tris-EDTA and Tricide®</p>	<p>250 to 500 mls infused into uterus; then lavage uterus with lactated Ringer's solution (LRS)</p>	<p>Chelator of heavy metals; used as uterine infusion prior to antimicrobial therapy to reduce chelation and subsequent inactivation of antimicrobial agents; reduction of biofilm</p>
<p>Vinegar (Distilled White) (2%)</p>	<p>20 to 100 mls added to 1 liter sterile saline</p>	<p>Treatment of fungal endometritis</p>

UTERINE LAVAGE AND INFUSIONS

MISCELLANEOUS MEDICATIONS

MEDICATION	DOSAGE, ROUTE, FREQUENCY	INDICATIONS
Acepromazine (10 mg/ml)	10 to 20 mg, IV, once	Sedation; relaxation of cervix prior to embryo transfer
Aminocaproic acid (Amicar®) (250 mg/ml)	Loading dose: 40 mg/kg Maintenance dose: 10 to 20 mg/kg, q 6h	Blocks plasminogen; anti-fibrinolytic (management of ruptured uterine artery)
Benzotropine (Cogentin®) (1 mg/ml)	8 mg, IV, once	Priapism in stallions or geldings (administer early in course of disease)
Cabergoline*	2 to 3 mg, PO, q 12h - q 24h for 500 kg mare	Suppression of lactation
Calcium gluconate (23% Solution)	Add 100 to 150 mls to 1 liter of LRS; administer intravenously over 45 to 60 minutes	Adjunct treatment for retained placenta in hypocalcemic mares
Cerumene™* Squalane (25% Solution)	Topical application	Cerumenolytic agent; used to clean out clitoral sinuses if bacterial or fungal organisms are present and a potential nidus for subsequent reinfection
Clenbuterol* (Ventipulmin®) (72.5 µg/ml)	2.0 µg/kg, PO, q 12h	Tocolytic agent (blocks uterine contractions)

* medication reported to be used at other facilities; not in use at CSU

MISCELLANEOUS MEDICATIONS

MISCELLANEOUS MEDICATIONS

MEDICATION	DOSAGE, ROUTE, FREQUENCY	INDICATIONS
<p>Dexamethasone (2 mg/ml)</p>	<p>30 to 50 mg, IV or IM, once at time of mating or insemination</p>	<p>Anti-inflammatory; management of persistent mating induced endometritis</p>
<p>Diazepam (Valium®) (5 mg/ml)</p>	<p>0.05 mg/kg, 5 to 7 minutes before breeding or collection</p>	<p>Reduce anxiety in stallions with ejaculation problems</p>
<p>Firocoxib (Equioxx®) (20 mg/ml; injectable) (paste formulation in calibrated oral syringe also available)</p>	<p>0.1 mg/kg, q 24 hrs (injectable)</p> <p>Loading dose: 0.3 mg/kg, PO, once</p> <p>Daily dose: 0.1 mg/kg, PO q 24 hrs (oral paste)</p>	<p>NSAID; selective COX-2 inhibitor; may be used in treatment of placentitis to reduce inflammation</p>
<p>Fluconazole (200 mg/tablet)</p>	<p>14 mg/kg, PO, loading dose, followed by 5 mg/kg q 24h</p>	<p>Antifungal agent</p>
<p>Flunixin meglumine (Banamine®) (50 mg/ml) (paste formulation in calibrated oral syringe also available)</p>	<p>1.1 mg/kg, IV, once or PO (paste formulation)</p>	<p>NSAID; anti-inflammatory, anti-prostaglandin; analgesic; administered prior to transfer of an embryo; treatment of placentitis</p>

MISCELLANEOUS MEDICATIONS

MEDICATION	DOSAGE, ROUTE, FREQUENCY	INDICATIONS
Imipramine (50 mg/tablet)	1.76 to 2.2 mg/kg, PO, administered 1 to 2 hrs prior to xylazine	Chemical ejaculation of stallions; lowers the ejaculation threshold
Itraconazole*	3 to 5 mg/kg, PO, q 24h for 2 to 3 weeks or longer	Antifungal agent
Meclofenamic Acid (Arquel®)*	2.2 mg/kg, PO, q 12h	Prostaglandin inhibitor potentially used as adjunct therapy in embryo transfer
Mycobacterium cell wall fraction immunostimulant* (Settle™) (1.5 ml vial)	1.5 mls via intrauterine infusion or intravenous injection during early estrus (repeat as needed)	Immunostimulant; administered to mares with endometritis caused by <i>Streptococcus equi</i> subsp. <i>zooepidemicus</i> ; therapeutic goal is to enhance the innate humoral immune response in affected mares
N-Butylscopolammonium Bromide (Buscopan®) (20 mg/ml)	0.08 to 0.12 mg/kg, IV (40 to 60 mg) administered 5 to 10 minutes prior to transrectal palpation	Relaxation of rectal musculature (decrease rectal pressure)

* medication reported to be used at other facilities; not in use at CSU

MISCELLANEOUS MEDICATIONS

MEDICATION	DOSAGE, ROUTE, FREQUENCY	INDICATIONS
N-Butylscolopammonium bromide cream or gel (Buscopan®)	Topical cream or gel	Cervical relaxation; gel can be made by combining 5 mls of Buscopan® and 15 mls of sterile obstetrical lubricant or DMSO gel; applied to outside of cervix and within cervical lumen
Naloxone* (Narcan®)	20 to 40 mg, IV (shock dose: 0.03 mg/kg, IV)	Postpartum hemorrhage
Pentoxifylline 400 mg/tablet	8.4 mg/kg, PO, q 6h to q 8h	Management of placentitis
Pergolide mesylate Prascend® (1 mg/tablet)	0.002 to 0.004 mg/kg (1 to 2 mg total dose), PO, q 24h for 500 kg mare	Treatment of Equine Cushing's Disease; suppression of lactation
Perphenazine* (Trifafon®)	0.3 to 0.5 mg/kg, PO, q 8h	Fescue toxicosis

MISCELLANEOUS MEDICATIONS

MEDICATION	DOSAGE, ROUTE, FREQUENCY	INDICATIONS
Phenylephrine HCL (0.25 %) (Preparation H®)	Topical, as needed	Vasoconstrictive agent; topical treatment for bleeding vaginal vericose veins
Propanetheline bromide	30 mg, IV, once	Rectal relaxation; wait 5 to 10 minutes after administration prior to palpation
Reserpine* (Serpasil®)	2.5 mg, PO, q 24h for 7 to 10 days	Management of agalactia, behavioral modification
Sodium Bicarbonate (8.4 %)	10 to 20 mls added to aminoglycoside antibiotic prior to intrauterine infusion	Used to balance pH of aminoglycoside antibiotics (i.e. gentamicin)
Xylazine (100 mg/ml)	0.44 to 0.66 mg/kg, IV, 1 to 2 hours after imipramine	Chemical ejaculation of stallions; sedation

* medication reported to be used at other facilities; not in use at CSU

SYSTEMIC ANTIBIOTICS

SYSTEMIC ANTIBIOTICS

MEDICATION	DOSAGE, ROUTE, FREQUENCY	INDICATIONS
Ceftiofur sodium (Naxcel®) (50 mg/ml)	2.2 to 4.4 mg/kg, IV or IM, q 24h	Antibiotic (broad spectrum); used in equine reproduction for treatment of bacterial endometritis
Ceftiofur crystalline free acid (Excede®) (200 mg/ml)	6.6 mgCE/kg, IM; 2 doses 4 days apart	Antibiotic (broad spectrum); used in equine reproduction for systemic treatment of bacterial endometritis
Enrofloxacin (Baytril®) (100 mg/ml)	5 mg/kg, IV, q 24h	Antibiotic (broad spectrum); used in equine reproduction for treatment of bacterial endometritis, specifically for resistant <i>Pseudomonas</i> sp.; Note: intra-uterine therapy is associated with severe necrosis and is not recommended

SYSTEMIC ANTIBIOTICS

MEDICATION	DOSAGE, ROUTE, FREQUENCY	INDICATIONS
Gentamicin (100 mg/ml)	6.6 mg/kg, IV, q 24h	Antibiotic (Gram negative spectrum); used in equine reproduction for treatment of bacterial endometritis, chronic administration or administration to a dehydrated horse may result in acute renal failure
Penicillin (Procaine) (300,000 units per ml)	22,000 IU/kg, IM, q 12h	Antibiotic (Gram positive spectrum); used in equine reproduction for treatment of bacterial endometritis; severe procaine reactions may be observed after administration to susceptible horses
Trimethoprim-Sulfamethoxazole (960 mg tablets)	30 mg/kg, PO, q 12h	Antibiotic (broad spectrum); used in equine reproduction for treatment of mares with chronic endometritis or pregnant mares with bacterial placentitis

* medication reported to be used at other facilities; not in use at CSU

CLINICAL PROTOCOLS IN EQUINE REPRODUCTION

1. Artificial photoperiod to advance the breeding season
2. Stimulation of follicular development in transitional mares
3. Induction of a timed ovulation
4. Management of persistent mating-induced endometritis
5. Diagnosis and treatment of bacterial endometritis
6. Diagnosis and treatment of fungal endometritis
7. Progesterone supplementation in pregnant mares
8. Induction of lactation in a nurse mare
9. Diagnosis and treatment of placentitis
10. Prediction of foaling
11. Induction of labor
12. Treatment of retained placenta
13. hCG response test for detection of cryptorchid testes
14. Chemical ejaculation of a stallion

ARTIFICIAL PHOTOPERIOD

- The average date of the first ovulation of the year in mares maintained under ambient light conditions is **MID-APRIL TO EARLY MAY** in North America
- Provision of a stimulatory artificial photoperiod is used to advance the date of the **FIRST OVULATION OF THE YEAR**
- The artificial photoperiod should begin on or about **DECEMBER 1**
- Approximately **60 TO 70 DAYS** of an artificial photoperiod is necessary to stimulate ovulation; if the artificial photoperiod is applied appropriately, mares should ovulate by early to mid-February
- A minimum of **10 FOOT-CANDLES OF LIGHT** are recommended; this may be achieved by use of a 100 or 200 watt light bulb in a 12 x 12 foot box stall
- **INCANDESCENT OR FLUORESCENT LIGHTS** are both effective
- Automatic timers may be used to turn the lights **ON AT DUSK AND OFF AT 11:00 PM**
- Mares should be allowed an **8 HOUR PERIOD OF DARKNESS**; providing 24 hours of light is less effective
- Maintain the artificial photoperiod until at least **APRIL 1** or mares may revert back into anestrus
- Late-term pregnant mares due to foal in January, February or March may be housed '**UNDER LIGHTS**' to help ensure that they cycle after foaling and not experience post-partum anestrus

STIMULATION OF FOLLICULAR DEVELOPMENT IN TRANSITIONAL MARES

- Mares in **DEEP SEASONAL ANESTRUS** have ovarian follicles less than 20 mm in diameter
- **TRANSITIONAL MARES** have one or more ovarian follicles greater than 20 mm in diameter
- Mares may remain in transition for **SEVERAL WEEKS**
- Administration of **LOW-DOSE DESLORELIN** can stimulate follicular development in transitional mares
 - A dose of **50 µg of deslorelin** is administered intramuscularly twice daily
 - Treatment is discontinued when one or more follicles is at least **35 mm** in diameter
 - The follicle is allowed to mature without any hormone therapy for 24 hours (a **'coast'** period)
 - The mare is subsequently administered **hCG** to induce ovulation; note that administration of a 'high-dose' of deslorelin (i.e. 1.8 mg) is less effective at inducing ovulation in low-dose deslorelin treated mares
- Low-dose deslorelin therapy is **MORE EFFECTIVE IN TRANSITIONAL MARES** than mares in deep anestrus
- The **AVERAGE DURATION OF LOW-DOSE DESLORELIN THERAPY** is 5 days; treatment should be discontinued if no significant follicular development is evident after 10 days

INDUCTION OF A TIMED OVULATION

- It is common practice to administer either **HCG** (Chorulon®) or **DESLORELIN**
- Hormone therapy is generally effective if the mare is in behavioral **ESTRUS** and/or has endometrial **EDEMA** visible on ultrasonography and has a dominant follicle at least **35 MM** in diameter (i.e. in Quarter Horse, Arabian and Thoroughbred mares)
- Administration of **HCG** (2,500 IU, IV) will usually induce ovulation in approximately **36 HOURS**, whereas **DESLORELIN** (1.8 mg, IM) treatment typically induces ovulation in approximately **40 HOURS**
- Mares to be bred with frozen semen may be administered hCG or deslorelin to induce a **TIMED OVULATION** and make breeding management more efficient
 - *If **two (2) doses** of frozen semen are available, one can administer **deslorelin at 8:00 am** or administer **hCG at 12:00 pm (noon)** and anticipate ovulation at **12:00 am (midnight)**, in 40 or 36 hours, respectively. The mare is inseminated the evening before the anticipated ovulation and the morning after ovulation is confirmed*
 - *If **one (1) dose** of frozen semen is available, one can administer **deslorelin at 8:00 pm** and anticipate ovulation at **12:00 pm (noon)** 40 hours later and inseminate post-ovulation*
 - *In both scenarios, **ultrasound examinations** are performed at specified time intervals after hormone therapy in case of an early ovulation*

MANAGEMENT OF PERSISTENT MATING-INDUCED ENDOMETRITIS

- All mares experience **UTERINE INFLAMMATION** after either live cover or artificial insemination
- Inflammation **PEAKS AT 8 TO 12 HOURS** and is usually resolved by 24 hours in normal mares
- Endometritis may **PERSIST** for more than 24 hours in some mares
- **THERAPY** for persistent mating-induced endometritis (PMIE) includes:
 - **Uterine lavage** *to remove excessive fluid, inflammatory cells, dead sperm and debris:*
 - ◆ *The uterus is lavaged with sequential one-liter volumes of either sterile saline or lactated Ringer's solution until the effluent fluid is clear*
 - *Administration of* **oxytocin** *or* **prostaglandins**
 - ◆ **Oxytocin** *will stimulate uterine contractions for* **30 to 45 minutes**
 - ◆ **Cloprostenol** (*Estrumate*®) *will stimulate uterine contractions for* **2 to 4 hours**
- **PREVENTIVE MANAGEMENT** procedures on each subsequent cycle may include:
 - *Administration of* **dexamethasone** *(30 to 50 mg, IV) once at the time of breeding*
 - *Only breeding the mare* **one time** *to limit re-inflammation*
 - *Performing a* **uterine lavage** *4 to 6 hours after breeding*
 - *Prophylactic administration of* **ecbolic agents** *beginning 4 to 6 hours after breeding*

DIAGNOSIS AND TREATMENT OF BACTERIAL ENDOMETRITIS

- **DIAGNOSIS** of bacterial endometritis is based on:
 - **Culture** of a pathogenic organism from a uterine swab or low-volume lavage:
 - ◆ *The most common bacterial organisms are Streptococcus equi subsp. zooepidemicus, Escherichia coli, Pseudomonas aeruginosa and Klebsiella pneumoniae*
 - Presence of inflammatory cells (neutrophils) and possibly bacteria on uterine **cytology**
 - Detection of bacterial DNA using **PCR** analysis
- **TREATMENT** includes:
 - **Uterine lavage** to remove bacterial organisms and inflammatory debris
 - Infusion of an **antimicrobial agent** into the uterus for 3 to 5 consecutive days in estrus
 - ◆ *Selection should be based on results of antimicrobial susceptibility testing*
 - Empirical choice may include:
 - ◆ *Naxcel® or Timentin® as the only agent*
 - ◆ *A combination of a beta-lactam antibiotic (i.e. penicillin) plus an aminoglycoside*
 - **Systemic antibiotics** may also be considered; common options include:
 - ◆ *Ceftiofur crystalline free acid (Excede®); enrofloxacin (Baytril®); trimethoprim-sulfamethoxazole*

DIAGNOSIS AND TREATMENT OF FUNGAL ENDOMETRITIS

- Diagnosis of fungal endometritis is based on:
 - **Culture** of a pathogenic organism from a uterine swab or low-volume lavage
 - ◆ The most common fungal organisms are the yeast *Candida albicans*, and hyphate fungal organisms *Aspergillus fumigatus* and *Mucor* sp.
 - Presence of inflammatory cells (neutrophils) and possibly fungal organisms on **cytology**
 - Detection of fungal DNA using **PCR** analysis

- Treatment includes:
 - **Uterine lavage** to remove fungal organisms and inflammatory debris
 - **Infusion of an antifungal agent** into the uterus for 3 to 5 consecutive days in estrus
 - ◆ Our current choice for intrauterine infusion is nystatin
 - **Systemic administration of an antifungal agent** for 2 to 3 weeks
 - ◆ Fluconazole

- A **COMBINATION** of a systemic antifungal agent and an intrauterine antifungal agent may be more effective than either treatment alone in challenging cases

- It is common to subsequently culture the bacterium ***S. equi* subsp. *zoepidemicus*** after successful elimination of the fungal infection

PROGESTERONE SUPPLEMENTATION FOR PREGNANT MARES

- Progesterone is a steroid hormone required for **MAINTENANCE OF PREGNANCY**
- The vast majority of pregnant mares do not need progesterone supplementation
- In some clinical cases, progesterone supplementation should be considered in a pregnant mare:
 - **Small corpus luteum** *and/or evidence of uterine edema on ultrasound*
 - *Progesterone level less than 4.0 ng/ml*
 - *History of repeated pregnancy loss*
- Treatment protocols include:
 - *Administration of altrenogest (0.044 mg/kg, PO, q 24 hr)*
 - *Administration of long-acting progesterone once per week*
- Options for discontinuing supplementation include:
 - *Endogenous progesterone greater than 4.0 ng/ml in a mare treated with altrenogest*
 - *Ultrasound evidence of secondary corpora lutea formation (by approximately day 50 to 60)*
 - *Treatment until at least 90 to 120 days, at which time the placenta is producing sufficient progestagens to maintain pregnancy*
- **NOTE:** altrenogest is not detected in most traditional progesterone assays

INDUCTION OF LACTATION IN A NURSE MARE

- In the event that a young foal is orphaned by the unexpected death of its dam, **LACTATION CAN BE INDUCED** in another mare that may serve as a nurse mare
- The potential nurse mare must have **GIVEN BIRTH AND LACTATED PREVIOUSLY**, have good maternal instincts and have a gentle disposition
- Lactation can be stimulated by a combination of **ESTRADIOL-17 β** and a **DOPAMINE ANTAGONIST** such as domperidone or sulpiride; lactation can also be stimulated by administration of a dopamine antagonist alone
- Therapy for induction of lactation:
 - *Pre-treatment with **estradiol-17 β** (3 to 5 mg) for 2 to 3 days*
 - ♦ *The goal is to enhance the prolactin response to domperidone therapy*
 - *Administration of **domperidone** (Equidone®); 1.1 mg/kg (approximately 5 mls of Equidone® gel) once daily for 5 to 10 days*
 - *Begin hand-milking once lactation begins*
 - *Carefully introduce the foal to the nurse mare*
- **NOTE:** mares induced to lactate **do not produce colostrum**; an orphaned neonatal foal will need to be provided with an alternative supply of colostrum, a colostrum substitute or hyperimmune plasma

DIAGNOSIS AND TREATMENT OF PLACENTITIS

- Ascending bacterial **PLACENTITIS** is one of the most common infectious causes of abortion
- External **CLINICAL SIGNS** may include premature lactation, vaginal discharge or abortion
- Diagnostic techniques include:
 - *Ultrasonographic evaluation of the placenta per rectum to evaluate **placental thickness** (i.e. combined thickness of the uterus and placenta, CTUP)*
 - *Detection of placental separation from the uterus*
- Therapy for placentitis includes:
 - **Systemic antibiotics**
 - ◆ *Trimethoprim-sulfamethoxazole, twice daily for the duration of pregnancy (30 mg/kg, PO, q 12h)*
 - **Progestin supplementation**
 - ◆ *Altrenogest (i.e. Regu-Mate®), 0.088 mg/kg (double-dose), for the duration of pregnancy*
 - **Non-steroidal anti-inflammatory medications (options):**
 - ◆ *Pentoxifylline (8.4 mg/kg, PO, q 6h to q 8h), for the duration of pregnancy*
 - ◆ *Flunixin meglumine (1.0 mg/kg, IV) - as needed*
 - ◆ *Firocoxib (Equioxx® Paste); loading dose: 0.3 mg/kg; daily dose: 0.1 mg/kg, PO, q 24 hrs, for the duration of pregnancy*

PREDICTION OF FOALING

- The gestation length of mares is approximately 340 days in duration

- **CLINICAL SIGNS OF IMPENDING FOALING** include:
 - Mammary gland development
 - ◆ *Begins about 7 to 14 days prior to foaling*

 - **Waxing** of teat ends
 - ◆ *Approximately 70 % of mares 'wax-up'; mares that wax usually foal in 24 to 72 hrs*

 - **Increase in calcium** levels in mammary secretions
 - ◆ *A majority of mares have milk calcium levels greater than 200 ppm prior to foaling*
 - However, not all mares will reach 200 ppm; some mares will foal with a milk calcium level less than 100 ppm
 - ◆ *Most mares will foal within 24 to 48 hours after milk calcium reaches 200 ppm*

 - **Decrease in pH** in mammary secretions
 - ◆ *Mammary secretion pH is 7.0 to 7.4 in the days prior to foaling*
 - ◆ *pH of equine mammary fluid decreases to approximately 6.4 within 12 to 24 hrs prior to foaling*

- **NOTE:** changes in mammary pH may be less diagnostic than changes in milk calcium

INDUCTION OF LABOR

- **INDUCTION OF LABOR** may be indicated in a late-term pregnant mare for medical or management reasons
- Situations may include a previous history of giving birth to a stillborn foal, dystocia or injury during foaling, potential for neonatal isoerythrolysis or diagnosis of a potentially life-threatening condition such as placental hydrops.
- Ideally, **QUALIFICATIONS FOR INDUCTION OF LABOR** should include:
 - *Gestation length of at least 330 days*
 - *Mammary gland development*
 - *Waxing of the teat ends*
 - *Milk calcium levels of at least 200 ppm*
 - *Some clinicians also include relaxation of the cervix as a qualification for induction*
- The **TECHNIQUE** used at CSU for induction of labor is:
 - *Administration of 5 units (0.25 mls) of oxytocin intravenously*
 - *A second dose of oxytocin (10 units) is administered 15 minutes later*
 - *Most mares 'break their water' 8 to 10 minutes after the second dose of oxytocin*
- Mares induced to foal have a higher incidence of **RETAINED PLACENTA** than mares with a spontaneous delivery

TREATMENT OF RETAINED PLACENTA

- **RETAINED PLACENTA** is common after dystocia, obstetrical intervention, induction of labor and abortion
- Mares that experience one retained placenta are likely to retain their placenta in **SUBSEQUENT** births
- A placenta is considered to be retained in the mare after **3 HOURS**; considered a medical emergency
- **TREATMENT** for retained placenta may include some or all of the following, depending on clinical circumstances, duration placenta has been retained, medical condition of the mare, etc.:
 - *Administration of oxytocin (10 to 20 units, IV or IM)*
 - *Infusion of ~ 3 gallons warm water containing povidone-iodine into the allantoic cavity ("Burns Technique"); fluid is held within the allantoic cavity for 3 to 5 minutes before being evacuated*
 - *Uterine lavage (i.e. fluid is infused outside of the retained membranes)*
 - *Careful manual manipulation to disconnect retained chorioallantoic membrane from endometrium*
 - *Systemic antibiotics*
 - *Local infusion of antibiotics into the uterine lumen*
 - *Administration of a non-steroidal anti-inflammatory drug (i.e. flunixin meglumine)*
 - *Tetanus toxoid*
 - *Frog support pads or deep bedding*
 - *Administration of 100 to 150 mLs of 23% calcium gluconate added to 1 liter of Lactated Ringer's solution*
- **NOTE:** Cannulation of placental blood vessels followed by infusion of water may also be effective in resolution of a retained placenta

HCG RESPONSE TEST FOR DETECTION OF CRYPTORCHID TESTES

- Aggressive or stallion-like behavior in a gelding may indicate the presence of **CRYPTORCHID TESTES**
- Endocrine options for detection of the presence of cryptorchid testes include:

MEASUREMENT OF TESTOSTERONE IN A SINGLE BLOOD SAMPLE

CATEGORY	TESTOSTERONE LEVEL (PG/ML)
Gelding	< 100 pg/ml
Cryptorchid	200 to 1,000 pg/ml
Intact Stallion	> 1,000 pg/ml

HCG RESPONSE TEST

- *Initial blood sample is collected*
- **HCG** is administered (10,000 international units, IV)
- *Second blood sample is collected 1 to 2 hours later*
- *Both samples are analyzed for **TESTOSTERONE** concentration and levels compared*
- *An increase in testosterone level in the second sample suggests the presence of testicular tissue*

CATEGORY	TESTOSTERONE LEVEL (PG/ML)
Gelding	No change
Cryptorchid	Increased
Intact Stallion	Increased

CHEMICAL EJACULATION OF A STALLION

- Pharmacologically induced ex copula ejaculation, or chemical ejaculation, may be used to **COLLECT SEMEN** from stallions with physical disabilities, penile abnormalities, behavioral issues or ejaculatory dysfunction
- Semen collected by chemical ejaculation is typically **LOW IN VOLUME** and **HIGH IN SPERM CONCENTRATION**
- The procedure should be performed in a quiet place with minimal distractions (i.e. the stallion's regular stall)
- Clinical procedure:
 - Administration of **IMIPRAMINE HYDROCHLORIDE** (2.2 mg/kg, PO)
 - Administration of **XYLAZINE HYDROCHLORIDE** 0.3 to 0.4 mg/kg intravenously one to two hours later
- Passive emission of semen usually occurs within **3 TO 5 MINUTES** after administration of xylazine as the horse is becoming sedated
- Ejaculation may also occur **10 TO 15 MINUTES** after administration as the sedation is wearing off
- Semen can be collected using a hand-held cup attached to a long pole or into a collection device placed over the prepuce and tied over the back of the horse
- Chemical ejaculation is effective in **30 TO 75%** of horses treated

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