

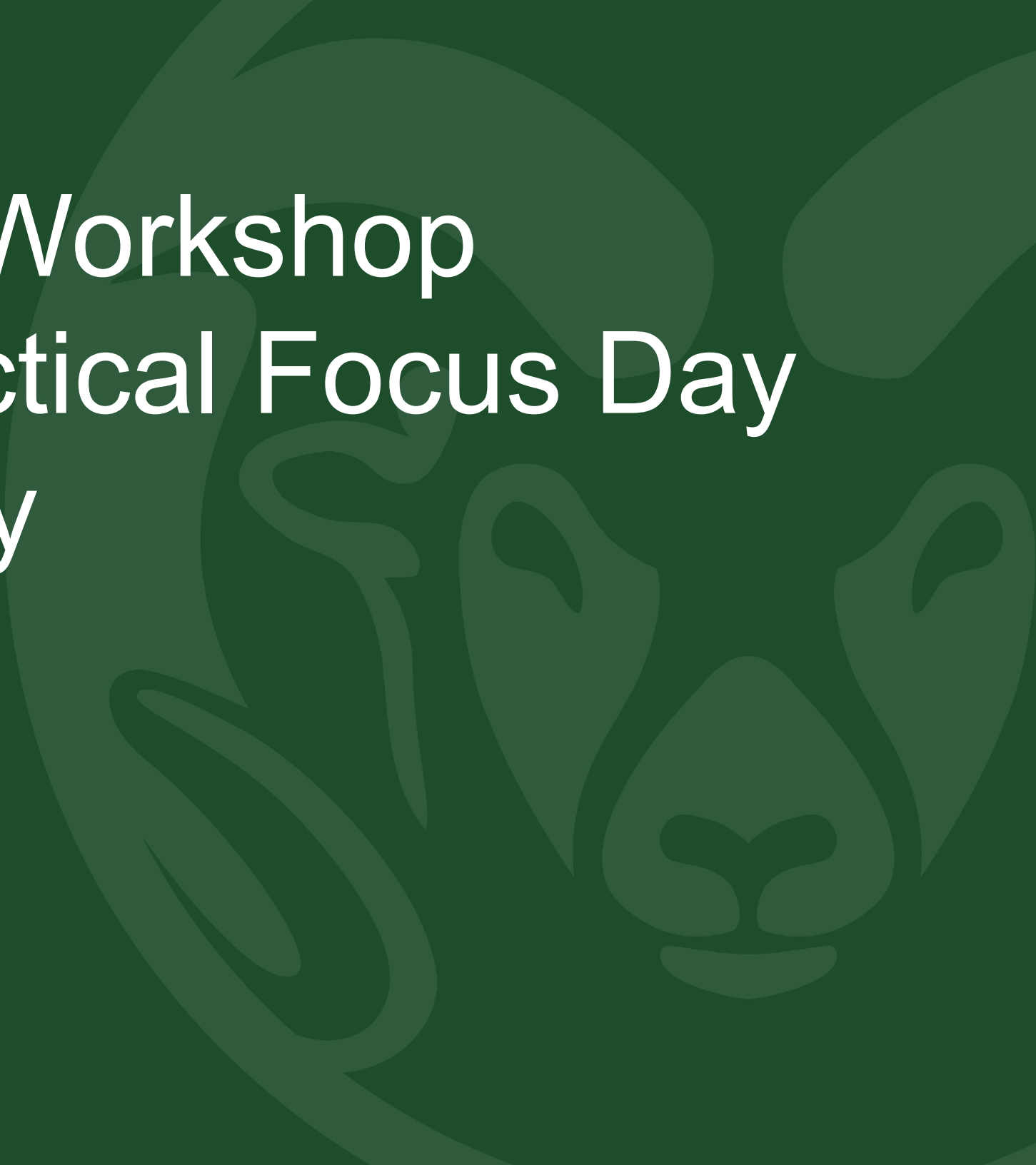
# IWBDA Breeders Workshop

## Reproduction Practical Focus Day

### Wednesday, 3 May

### 2023

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# The Breeding Female

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## Small Animal Reproduction

Greg Burns DVM

Diplomate, American College of Theriogenologists



VETERINARY HEALTH SYSTEM  
COLORADO STATE UNIVERSITY

# OVERVIEW

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- **Estrous Cycle Review**
- **Ovulation Timing**
- **OVT Abnormalities**
- **Normal Vaginal Flora**
- **Cystic Endometrial Hyperplasia CEH**
  - Pyometra
  - Mucometra
  - Endometritis



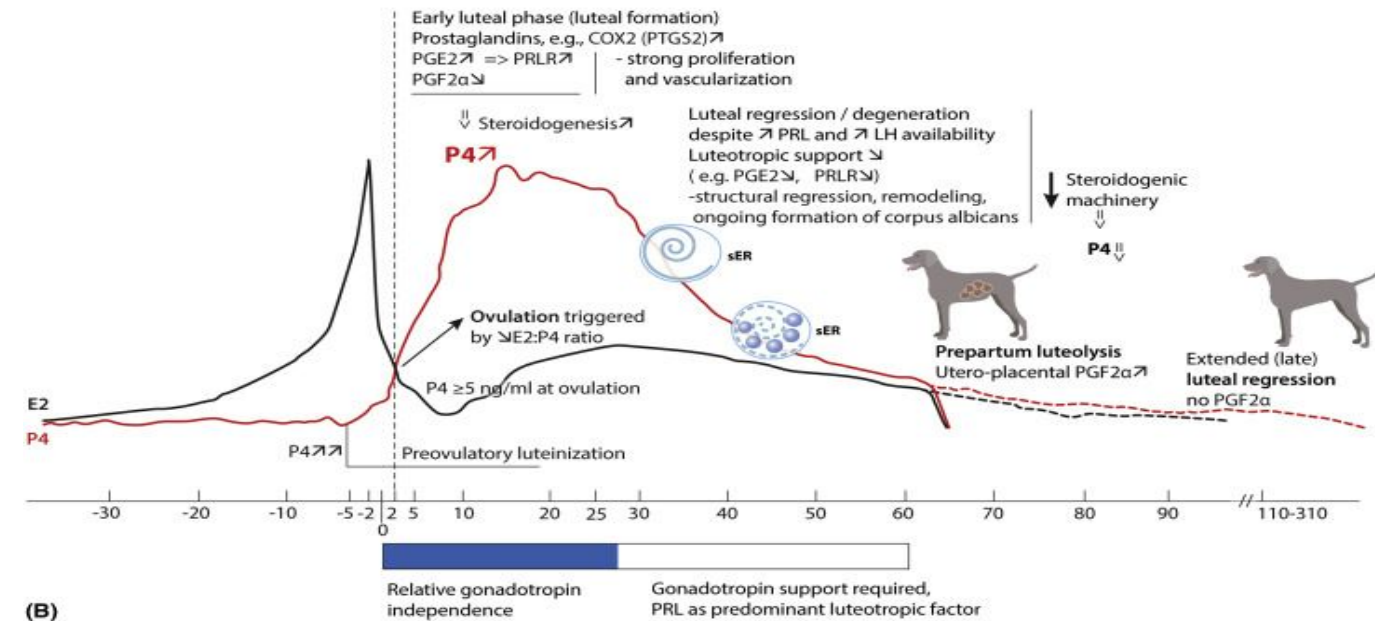
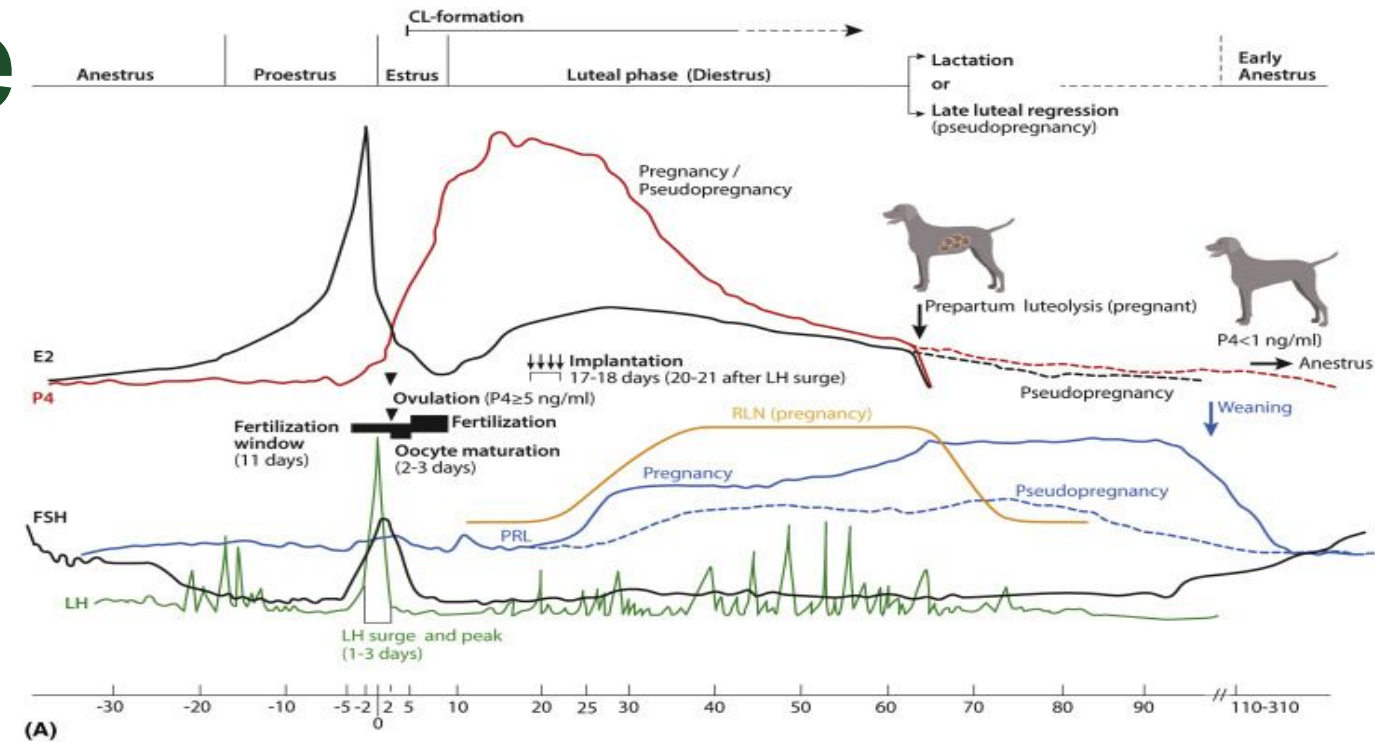
# Canine Estrous Cycle

Proestrus

Estrus

Diestrus

Anestrus



- Mariusz P. Kowalewski, in [Encyclopedia of Reproduction \(Second Edition\)](#), 2018



# Canine Estrous Cycle

True four stage cycle – Proestrus, Estrus, Diestrus, Anestrus

## Proestrus

- Reproductive tract getting ready for possibility of breeding/pregnancy
- Length – 1 day to 17 days (average of 9 days)
- Physical Changes
  - Vulva enlarges and becomes firm
  - Discharge – serous to serosanguinous
  - Attract male dogs but do not allow breeding
- Hormonal Changes
  - Estrogen rising and peaks
  - LH and Progesterone are low



# Canine Estrous Cycle

## Estrus

- Period of receptivity when ovulation occurs
- Begins first day female will accept male to be bred and ends first day she will no longer accept male
- Length – 3 to 21 days (averages 9 days)
- Physical Changes
  - Vulva somewhat less firm
  - Discharge – straw colored to serosanguinous
  - Stands to be bred and “flags” – moves tail dorsolaterally
- Hormonal Changes
  - Estrogen declining
  - Progesterone begins to rise (pre-ovulatory)
  - LH surge (narrow peak, 12-24h)



# Canine Estrous Cycle

## Diestrus

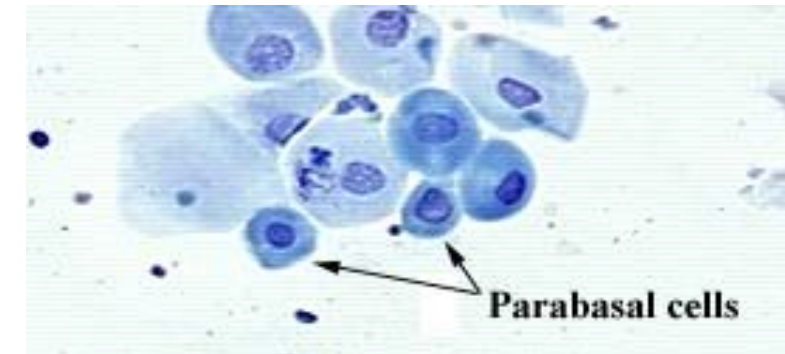
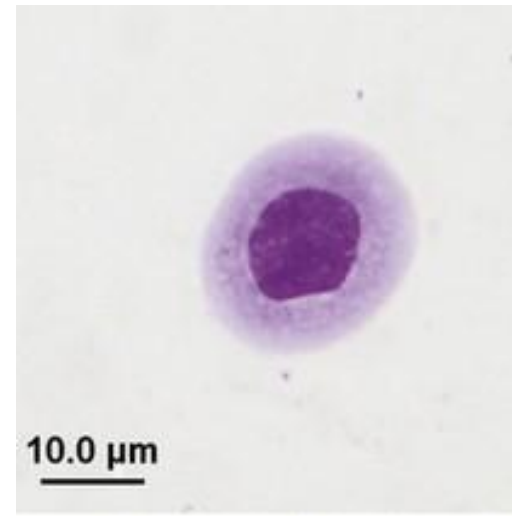
- Period following estrus when receptivity ends
- Two outcomes for dogs
  - 1) Successful breeding and subsequent fertilization of oocytes – pregnancy (gestation)
  - 2) No or unsuccessful breeding – pseudopregnancy
  - Both outcomes result in the same hormonal state, under the control of progesterone, solely from the corpora lutea (ovaries), for same period of time
  - The corpora lutea will continue to secrete progesterone **during pregnancy or non-pregnancy** (dogs do not experience maternal recognition of pregnancy to end diestrus) – **this is unique to the canine**



# Canine Estrous Cycle

## Anestrus

- “Quiet” reproductive period following diestrus
- Length – 4.5 – 5 months (average interestrus interval ~7 months, which includes ~2.5 months of other stages of cycle)
- Physical Changes
  - Typically, no physical changes
- Hormonal Changes
  - No significant hormonal changes during this period
- Vaginal Cytology
  - Predominate cell type is Parabasal





# Why is timing important?

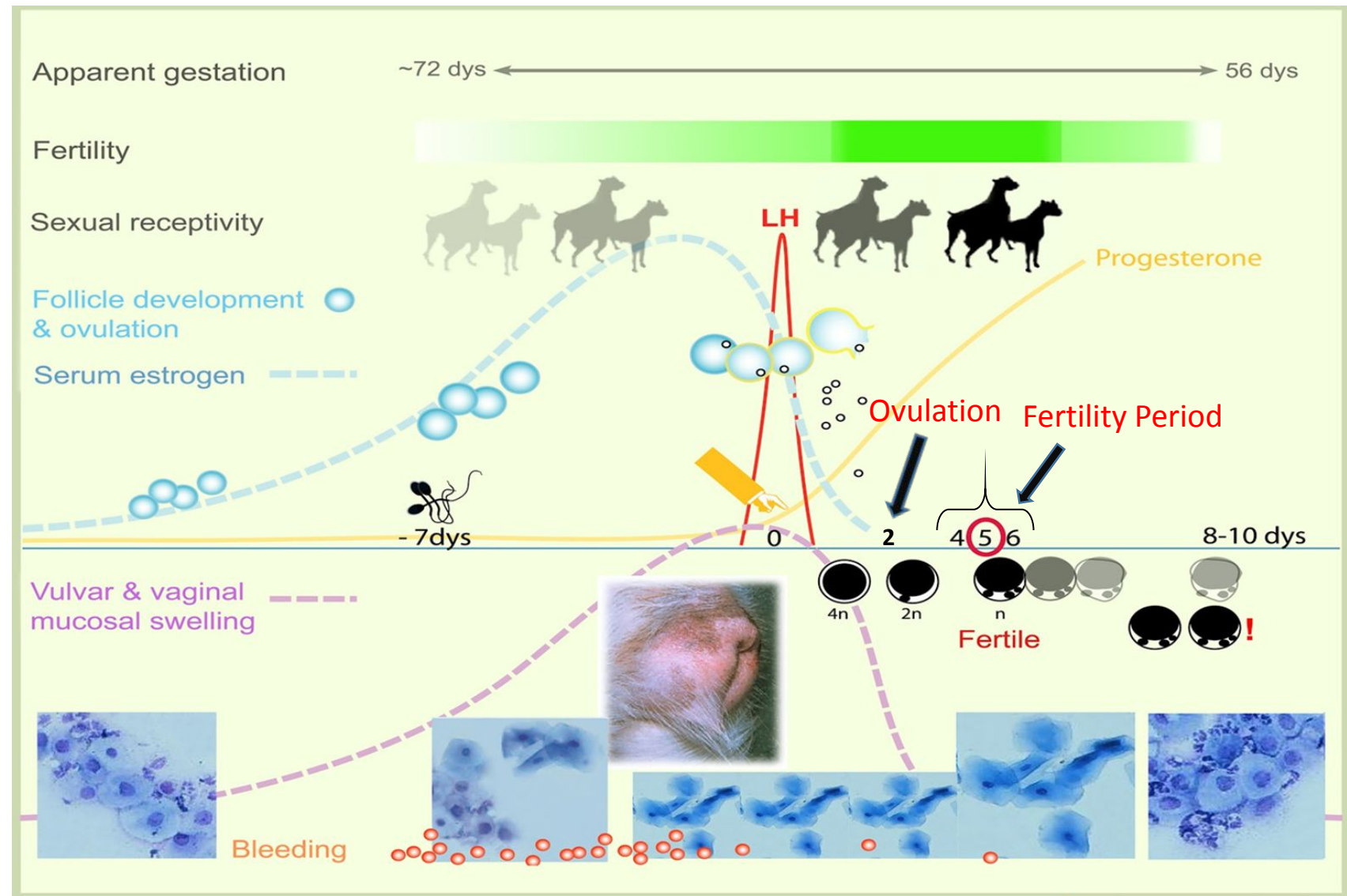
- ❑ Improper timing (poor breeding management) is the most common causes of infertility in the bitch
- ❑ Artificial insemination methods most often use attenuated semen samples
  - ❑ Fresh Semen is thought to last up to 9 (5-7) days in the female reproductive tract
  - ❑ Fresh-Chilled Semen is thought to last about 3-4 days
  - ❑ Frozen Semen is thought to last 12-24 hours





The bitch is in “heat” for approximately 3 weeks BUT there are only 3 days when oocytes capable of fertilization are present in the oviduct.

**So...how do we determine when this 3 day fertile period is occurring?**



# Ovulation Timing

BIOLOGY OF REPRODUCTION 17, 604–613 (1977)

## Changes in LH, Progesterone and Sexual Behavior Associated with Preovulatory Luteinization in the Bitch

PATRICK CONCANNON<sup>1</sup>, WILLIAM HANSEL and KENNETH MCENTEE

*Department of Animal Science,  
New York State College of Agriculture and Life Sciences, and  
Section of Theriogenology,  
New York State Veterinary College,  
Cornell University,  
Ithaca, New York 14853*

### ABSTRACT

LH and progesterone were assayed in plasma collected at 0800, 1600 and 2400 h daily from each of 6 Beagles during proestrus and estrus. The bitches' sexual behavior in response to males was assessed daily. Preovulatory LH surges lasting 24–40 h peaked ( $4.4\text{--}11.1$  ng/ml) at 2400 or 0800 h between three days before and one day after the onset of estrus. Estrous behavior in each bitch was observed only after an increase in progesterone. The initial increase in progesterone occurred either just prior to, or concomitant with, the initiation of the LH surge. Mean ( $\pm$  SEM) progesterone at  $-56$ ,  $-40$ ,  $-24$ ,  $-16$ ,  $-8$ ,  $0$ ,  $24$  and  $48$  h from the LH peak was  $0.7 \pm 0.1$ ,  $0.9 \pm 0.1$ ,  $1.2 \pm 0.1$ ,  $1.4 \pm 0.2$ ,  $1.5 \pm 0.2$ ,  $2.6 \pm 0.3$ ,  $3.2 \pm 0.4$  and  $5.4 \pm 0.6$  ng/ml. LH at the same times was  $1.7 \pm 0.3$ ,  $1.1 \pm 0.2$ ,  $1.5 \pm 0.3$ ,  $1.8 \pm 0.3$ ,  $4.9 \pm 1.0$ ,  $7.3 \pm 1.0$ ,  $2.0 \pm 0.3$  and  $1.4 \pm 0.4$  ng/ml. Ovulation time in the bitch was estimated by correlating results of gross and histological examination of ovaries removed from each of 10 Beagles during proestrus or estrus with LH and progesterone measured in plasma collected two to three times a day prior to obtaining the ovaries. Ovaries were removed from 6 of these bitches at approximately 4, 8, 20, 38, 44 and 50 h after the LH peak, when plasma progesterone was 1.3, 2.8, 4.2, 3.3, 4.4 and 6.9 ng/ml, respectively. The respective ovulated:nonovulated mature follicle ratios were 0:10, 0:6, 0:7, 0:8, 4:3 and 11:0. The sexual behavior of 6 ovariectomized bitches was observed daily for 5 weeks during which 16 days of estrogen treatment was initiated either 8 days before or 8 days after initiation of a 16 day progesterone treatment. Initial progesterone ( $4.8 \pm 0.4$  ng/ml plasma) had no effect. Induction of full sexual receptivity occurred 8 days after superimposing estrogen ( $65 \pm 5$  pg/ml plasma) on progesterone. Initial estrogen caused bitches to be attractive to males but failed to induce any acceptance of the males. Full sexual receptivity was induced within 18 h of superimposing progesterone on estrogen, was not affected by removal of estrogen 8 days later but was lost entirely within 18 h of progesterone removal after another 8 days.

The results suggest that, in the bitch: 1) ovulation occurs between 1 day before and 5 days after the onset of estrus and approximately 38–44 h following the LH peak; 2) follicle luteinization and increased progesterone secretion begins just prior to or concomitant with initiation of the LH surge some 60–70 h prior to ovulation and 3) the initial preovulatory rise in progesterone is synergistic with the preceding late-proestrous estrogen peak in eliciting estrous behavior.

“The early preovulatory increases in progesterone continuous with those observed after the time of ovulation and the dramatic preovulatory changes in follicle histology (Fig. 5-10) leave little doubt that in the bitch luteinization of follicles begins prior to ovulation. “



# Ovulation Timing

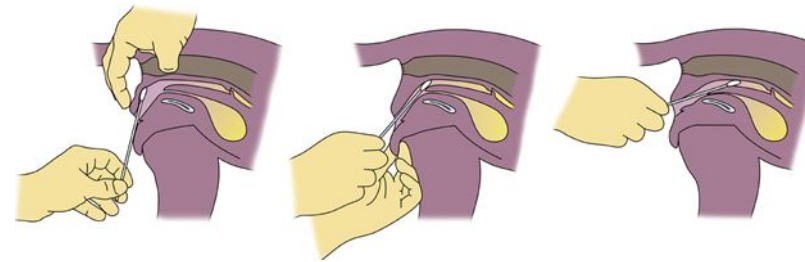
## □ Key Aspects of Ovulation Timing

- Timing of Insemination
- Site of semen deposition
- Number of effective sperm inseminated





# Ovulation Timing



Using Fertile-Focus

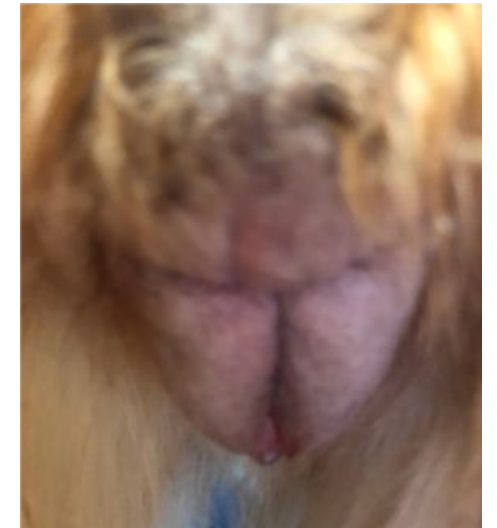


Not Fertile—Transitional—Fertile!



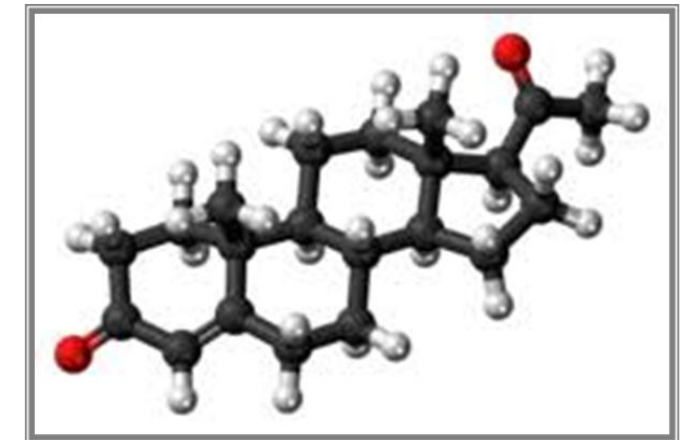
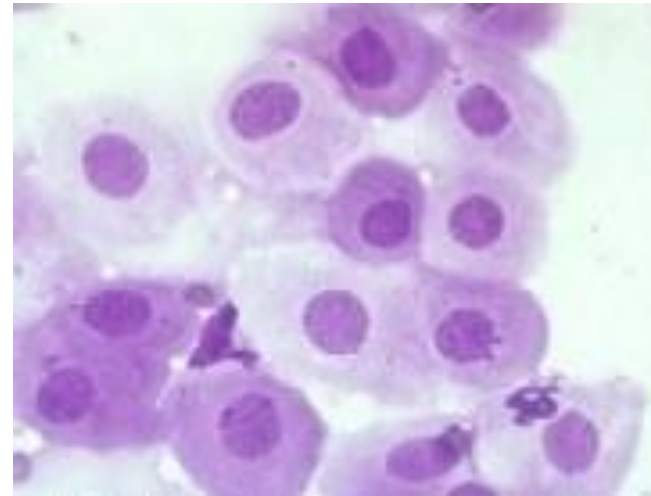
# Methods of Ovulation Timing

- Reproductive Behavior (estrus detection)
- Reproductive Anatomical Changes (estrus detection)
- Vaginal Cytology
- Vaginoscopy
- Endocrinology
  - Luteinizing Hormone (LH)
  - Progesterone Hormone (P4)



# Methods of Ovulation Timing

- Vaginal Cytology
- Vaginoscopy
- Endocrinology
  - Luteinizing Hormone (LH)
  - Progesterone Hormone (P4)

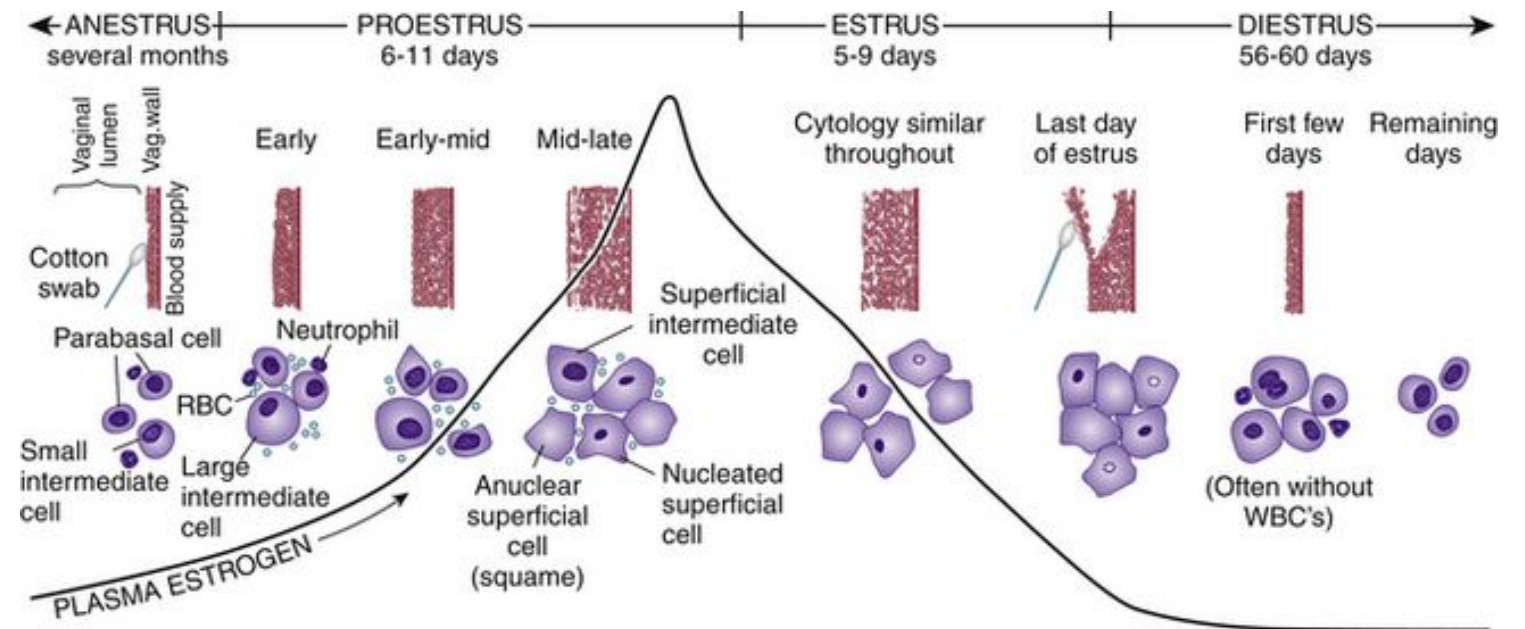
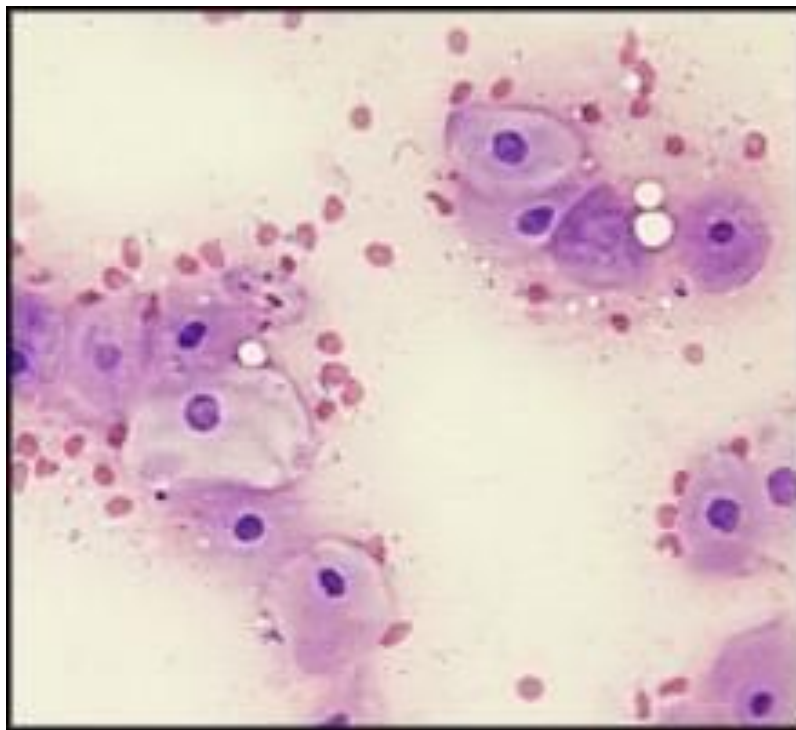




# Canine Estrous Cycle

## Proestrus

- Vaginal Cytology – “endocrine bioassay”
  - RBC’s present, WBC’s mostly absent
  - Predominant cell type is intermediate and moving to superficial epithelial



(From Feldman EC, Nelson RW: Ovarian Cycle and Vaginal Cytology. In: Feldman EC, Nelson RW, editors: Canine and feline endocrinology and reproduction, ed 3, Philadelphia, PA, 2004, Saunders, p. 755.

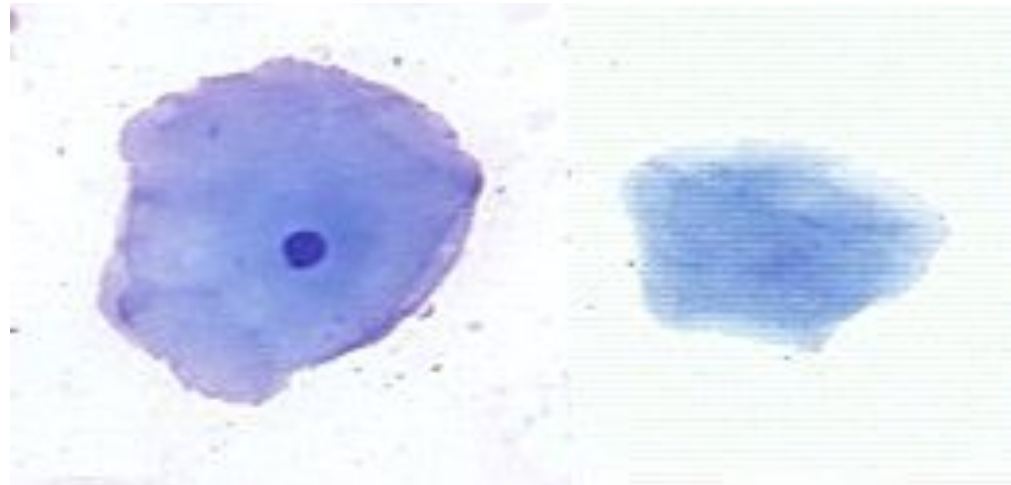




# Canine Estrous Cycle

## Estrus

- Vaginal Cytology
  - RBC's declining and sometimes absent, WBC's absent
  - Predominant cell type is cornified epithelial cell (>50% anuclear)

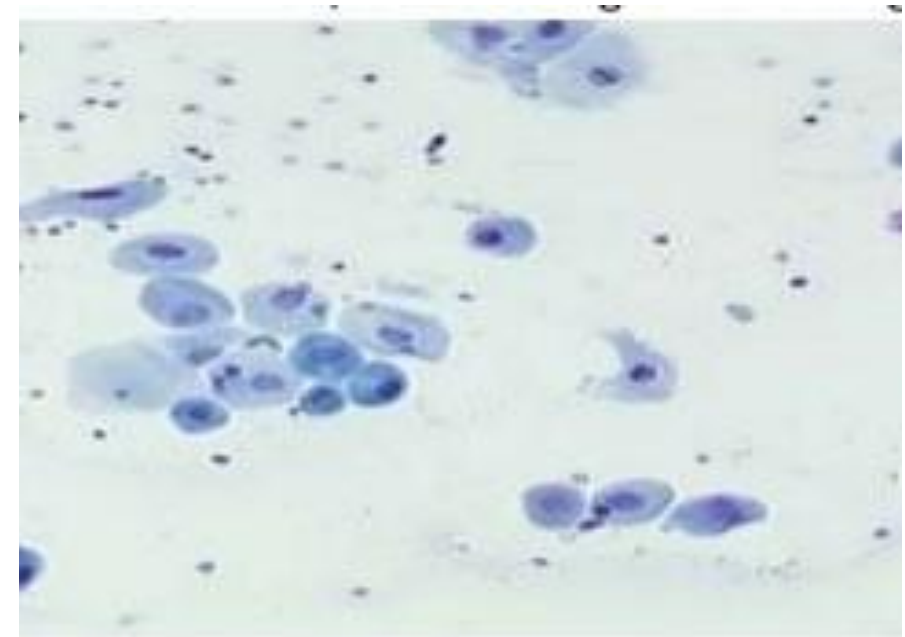
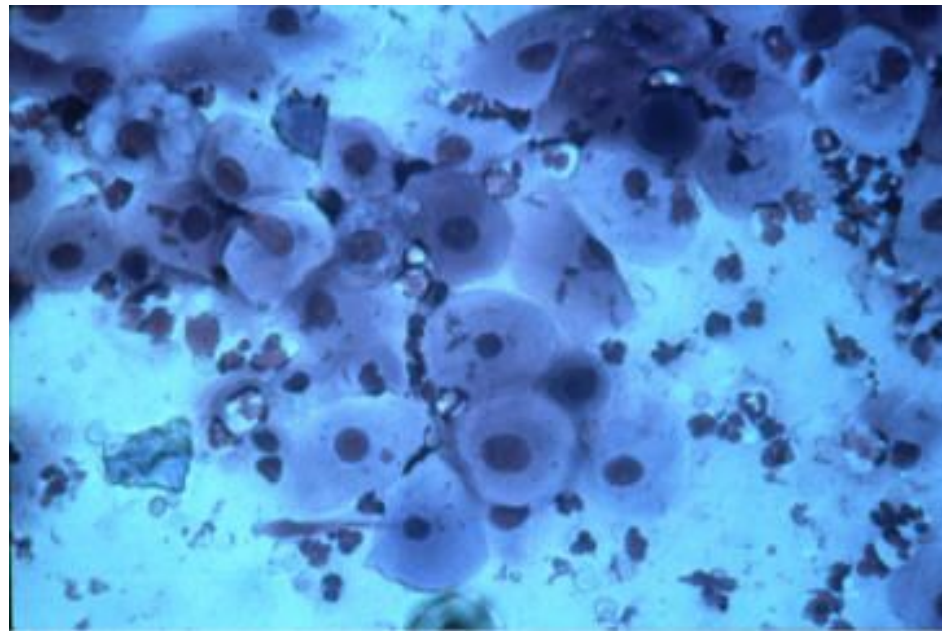


# Canine Estrous Cycle

## Diestrus

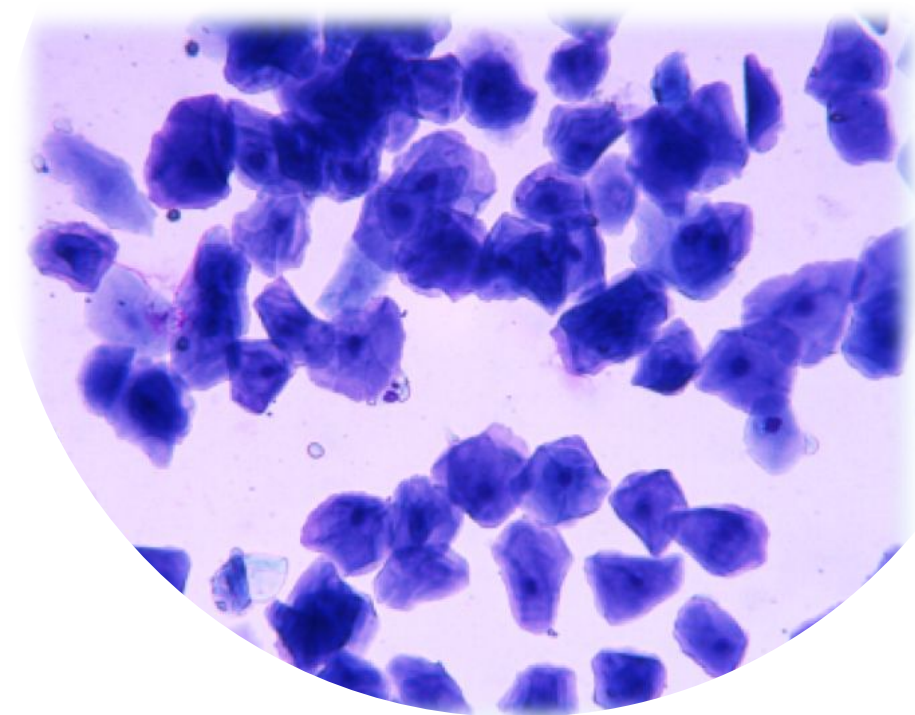
- Vaginal Cytology

- Predominant cell types are intermediate and parabasal (abrupt shift from cornified cells in 24-48h)
- WBC's present (sometimes abrupt “influx” of WBC's)



## Vaginal Cytology

- Vaginal cytology is an indirect measurement of ESTROGEN – “Endocrine Bioassay”
- Reflected by the % of superficial keratinized (cornflake) vaginal epithelial cells
- **Predictive value:** It will not tell you when ovulation has occurred BUT will identify the “fertilization period”



# Equipment: Basic Requirements for Vaginoscopy



Speculum and light source



- Rigid endoscope (minimum working length 29cm)
- Air insufflation- rectal insufflation bulb +/- shunt system
- Cold light source: xenon or LED
- Camera
- Cable
- Monitor







## Vaginoscopy

**Proestrus:** pink, moist, large edematous folds, little or no vaginal lumen

**Estrus:** becomes paler, drier and edema recedes – progresses through shrinking rounded to shrunken angular phase, large vaginal lumen

**Late estrus:** most fertile period! Dry, pale, shrunken angular, crenulated mucosa, large luminal space

**D1:** Loss of  $E_2$ : **SCI falls by > 20%**

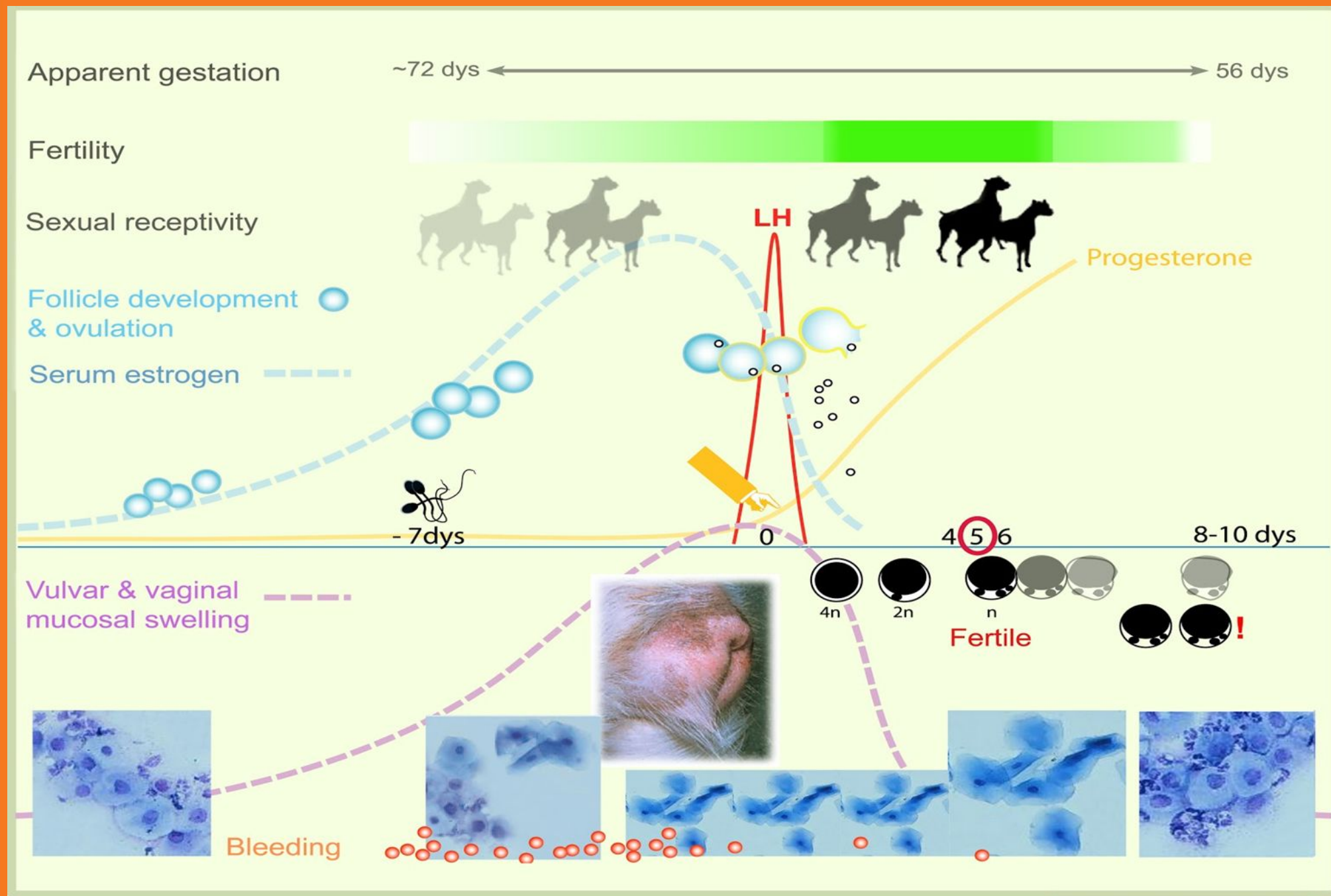
**Diestrus:** pink, flat moist folds often with brown mucky material

**KEY:** Assess level of crenulation, lumen size and mucosa color

**BREED NOW!**



# HORMONE ASSESSMENT



# Endocrinology

## Luteinizing Hormone (LH)

- Hormone produced by pituitary gland and peaks to cause ovulation
- Challenges for OVT
  - Very narrow peak in the canine. Usually peaks and returns to baseline within 24 hours
  - This makes daily testing necessary to obtain a true peak
  - Fertilization period is thought to begin 96 hours after LH peak



# Ovulation Timing - Canine

## Luteinizing Hormone (LH)



**1** Apply 3 drops of serum into well "1" using the provided pipette.



**2**



**3 Interpret Results**

*Negative: Test Line "2" is not evident or lighter than Control Line "3"*



*Positive: Test Line "2" is darker than or similar to Control Line "3"*

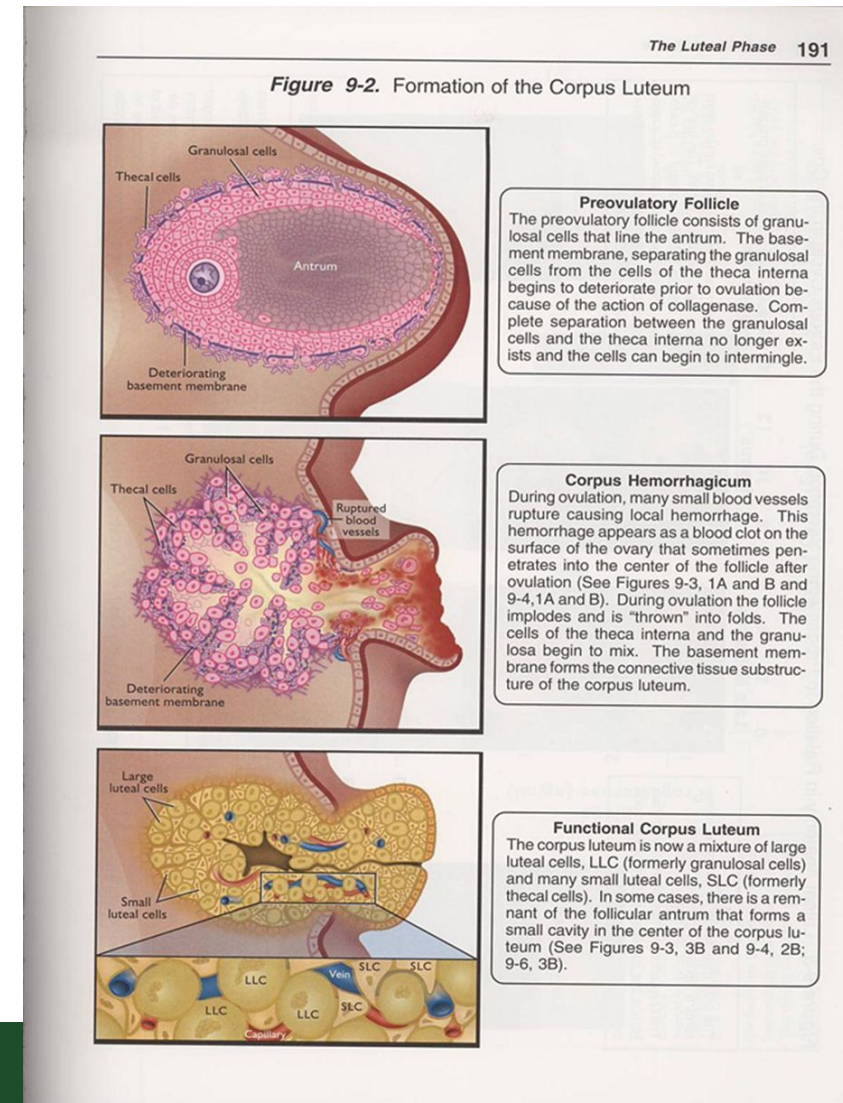
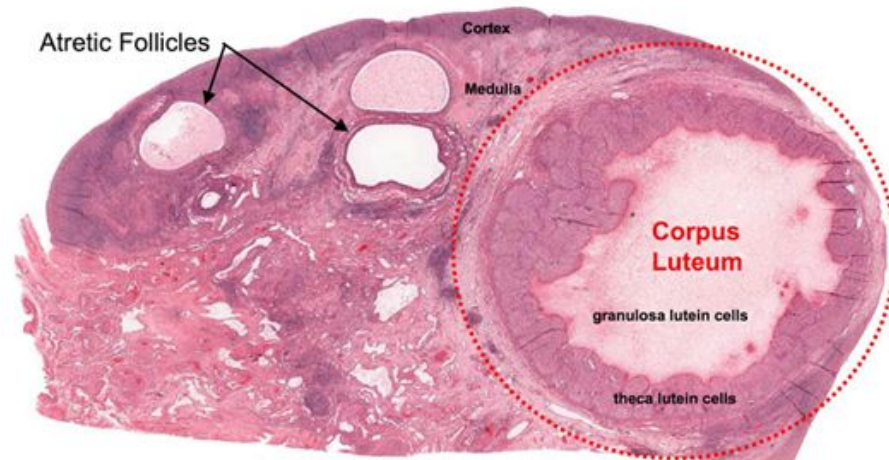




# Endocrinology

## Progesterone (P4)

- Steroid hormone produced by the corpus luteum (CL) for pregnancy maintenance in the canine
- Pre-ovulatory rise can be used for ovulation timing



Source: Senger, E., Pathways to Pregnancy and Parturition, Revised 2<sup>nd</sup> edition. Current Concepts Inc. Pullman, WA, 2003



## Progesterone

- **Qualitative Testing** – Testing that approximates or characterizes but **does not** measure the attributes, characteristics, properties, or **abundance** of a substance in a sample.
- **Quantitative Testing** – Testing that **measures absolute** or relative abundance (expressed as concentration) of a substance in a sample.

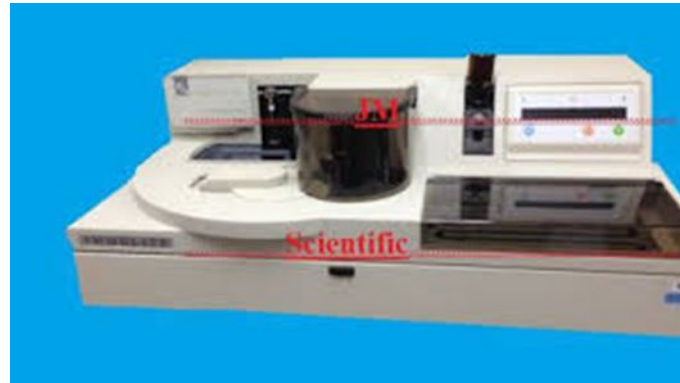
**We are interested in quantitative progesterone testing for accurate ovulation timing in the canine.**





# Qualitative Testing



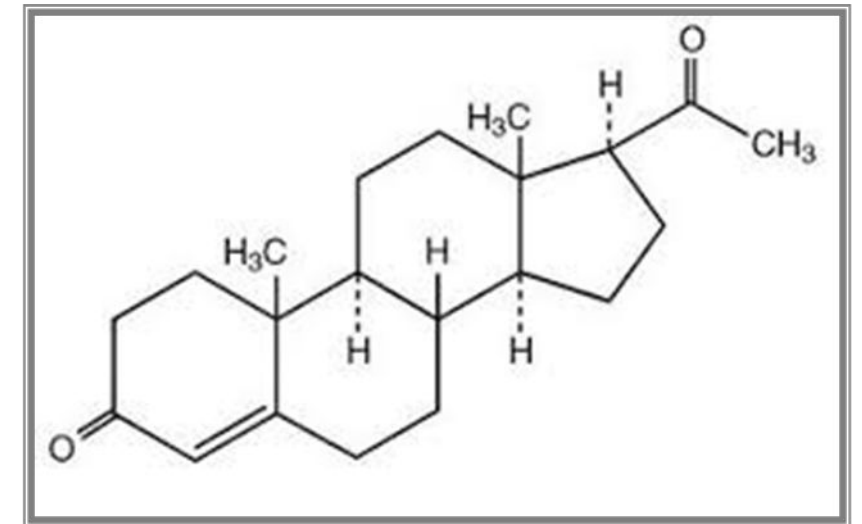
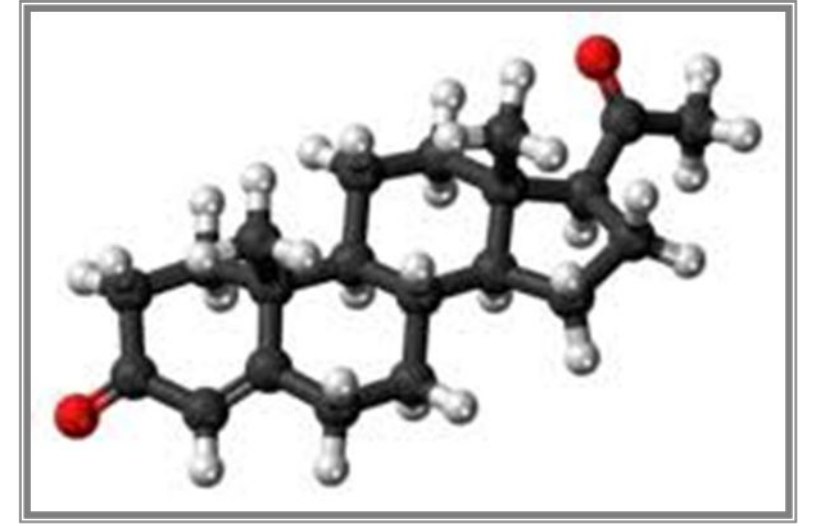


## Quantitative Testing



## Progesterone Testing

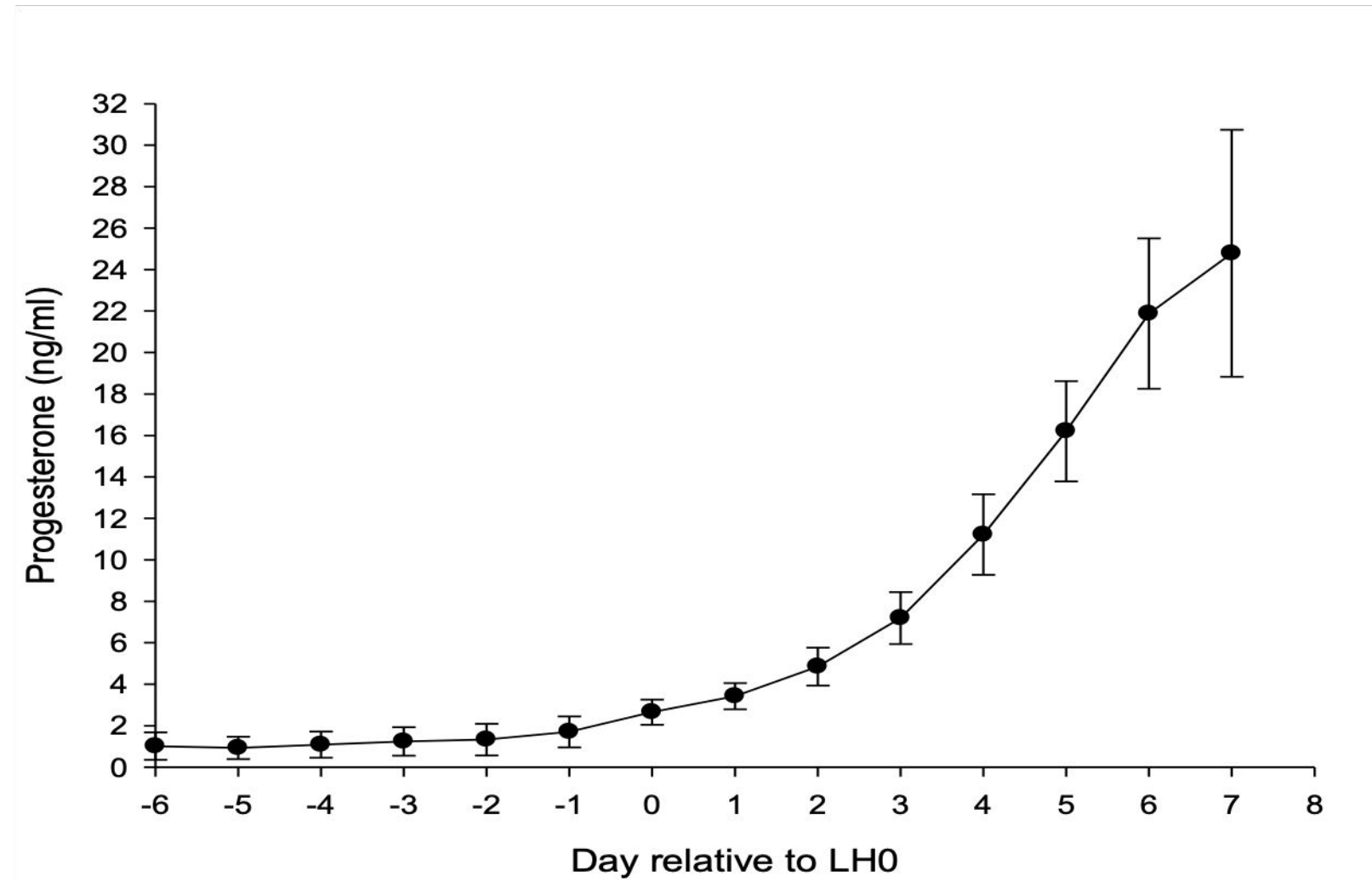
- Progesterone structure is the same for all species
- However, the same quantitative result is not always obtained from machine to machine or between species
  - Hormone folding
  - Protein binding
  - Cross reacting molecules
- Assay interference – lipid molecules
- Use a machine that is validated for the canine





# Progesterone Curve: Profile

Profile of mean ( $\pm$  SD) serum progesterone concentrations (4213) during estrus from 1300 individual bitches monitored for 1420 artificial inseminations. The progesterone profile was normalized to LH 0.

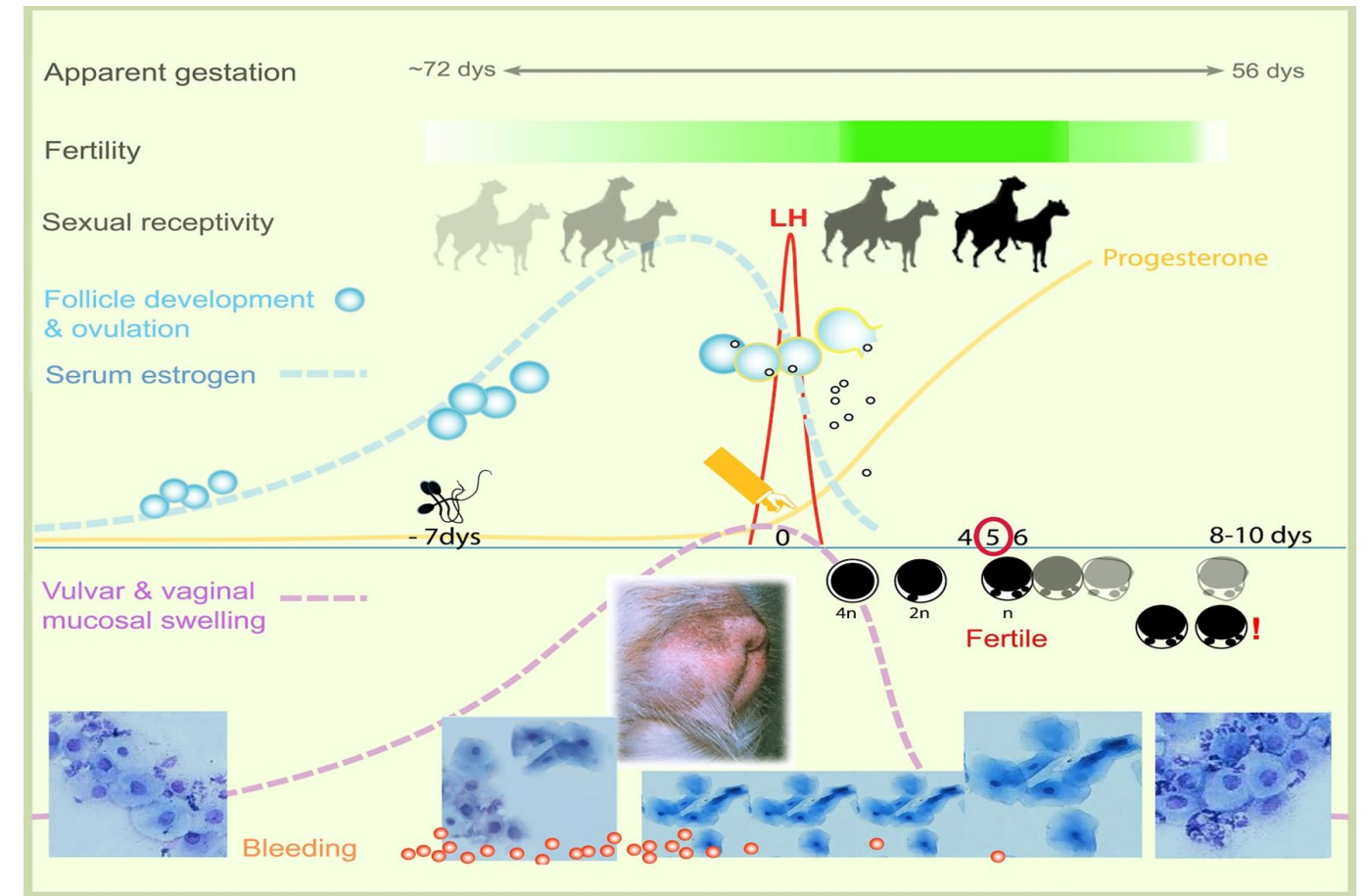


Hollinshead F.K. and Hanlon D.W. (2018) Normal progesterone profiles during estrus in the bitch: A prospective analysis of 1420 estrous cycles. *Theriogenology* 125, 37-42

# Progesterone Testing

- Fertility Period

- Begins 96 hours after the LH peak
- Begins 48 hours after ovulation
- Fertility period lasts 72-96 hours



# SUMMARY

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## PROGESTERONE MONITORING

□ Due to the predictability of the normal progesterone curve in the bitch serial progesterone measurements to confirm when LH0 is estimated to occur coupled with confirmation of a continual rise in progesterone concentrations until the day of AI will facilitate greater reproductive performance especially when using frozen semen



- Start testing at day 5-7 of proestrus and then every 2-4 days depending on progression, cytology and vaginoscopy findings
- Continuing monitoring every 2 d after determination of LH0 and ovulation until day of AI





# SUMMARY

## PROGESTERONE MONITORING

- Estimation of both LH0 and ovulation by detection of a rise in progesterone **>2 ng/ml and >5 ng/ml** respectively
- Confirmation of the fertile period by a continual rise in progesterone concentration **>10-20 ng/ml** within 4-6 d after the estimated LH0 or 2-4 d after when ovulation is estimated to occur
- Often the determination of when the LH0 and ovulation was estimated to occur is done retrospectively
- 'Slow' progesterone rises can be associated with smaller LS: clinically important when genetically valuable frozen semen is to be used



## Ovulation Timing - Conclusion

The intensity of estrus monitoring will depend on the type of semen planned  
for AI or mating

Natural mating/ fresh ejaculated semen:

Viable up to 7 days after NM/AI

Fresh chilled (shipped 24 h) semen:

Viable from 2-5 days after AI

**Frozen-thawed semen**

**Lifespan 6- 24 (48) hours after thawing and AI**



*Lifespan of all types of semen is variable depending on the dog's age, semen quality, fertility, extenders, handling , processing and storage conditions*



# When things don't seem quite right....

- Persistent estrus
- “Slow rise”
- Ovulation failure



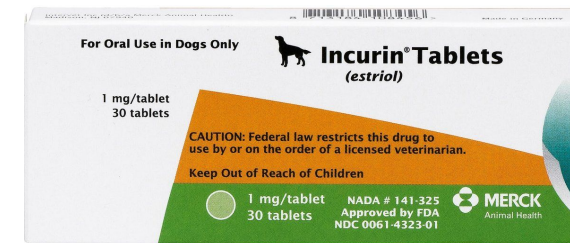
# Persistent Estrus (Prolonged Estrus)

- Defined as estrus that persists more than 21 days (does not include Proestrus)
- Clinical Signs
  - Consistent with **Estrogen** stimulation (“Heat”)
    - Vulvar swelling/serosanguinous discharge
    - Vaginal epithelial cornification
    - Behavioral estrus – standing to be bred, flagging
- Progesterone Level
  - Typically remains  $\leq 2\text{ng/ml}$  (dependent on cause)



# Persistent Estrus (Prolonged Estrus)

- Causes
  - Exogenous estrogen exposure – HRT creams/ointments, oral estrogen for urinary incontinence (Incurin®)
  - Endogenous estrogen production
    - Ovarian abnormalities
      - Follicular cysts
      - Granulosa cell tumors
    - Hypophysis or hypothalamus tumor



# Persistent Estrus (Prolonged Estrus)

- Advanced Diagnostic Testing
  - Ultrasound
    - Assess endometrium
    - Generally accepted that a “cyst” is  $\geq 8\text{mm}$
    - GCT
    - Sometimes normal
    - Inhibin level?
  - Surgery – Open or Laparoscopic
- Treatment
  - OE (Ovariectomy) or OHE (Spay)
  - Induce diestrus (or anestrus) using GnRH or hCG – results in luteinization, not ovulation (don't breed)
- Potential Risks (prolonged estrogen exposure)
  - Increased risk of pyometra
  - Bone marrow suppression



# “Slow Rise”

- Those that rise to 2.0ng/ml – 4.0ng/ml for more than 3 days followed by rapid (ovulatory) rise
- Possible causes
  - Delayed ovarian response to LH surge?
  - Inappropriate ovarian estrogen surge to cause ovulation?
  - Inappropriate pituitary delivery of LH?
  - Inappropriate receptor response to LH?
- Result is smaller litter sizes



# “Slow Rise”

- Type 1 example:
  - 1/1 – 1.5ng/ml
  - 1/2 – 2.2ng/ml
  - 1/4 – 2.4ng/ml ← LH Peak
  - 1/5 – 3.5ng/ml
  - 1/6 – 5.3ng/ml ← Ovulation
  - 1/7 – 10.8ng/ml
  - 1/8 – Fertility period begins this day

| Rate of P4 change | Semen type        |             |                   |                        |
|-------------------|-------------------|-------------|-------------------|------------------------|
|                   | Fresh             |             | Frozen            |                        |
|                   | Whelping rate (%) | Litter size | Whelping rate (%) | Litter size            |
| Slow              | 80                | 6.0 ± 3.1   | 71                | 3.9 ± 1.8 <sup>a</sup> |
| Normal            | 84                | 5.4 ± 2.7   | 70                | 5.4 ± 2.9              |
| Fast              | 80                | 6.0 ± 3.3   | 71                | 5.6 ± 3.1 <sup>b</sup> |

<sup>ab</sup> (within column) The litter sizes of bitches inseminated with frozen semen with slow progesterone curves were significantly smaller compared to bitches with fast progesterone curves (3.9 ± 1.8 vs 5.6 ± 3.1 pups per litter respectively; P<0.001) n=1420 oestrous cycles

Hollinshead F.K. and Hanlon D.W. (2018) Normal progesterone profiles during estrus in the bitch: A prospective analysis of 1420 estrous cycles. *Theriogenology* 125, 37-42





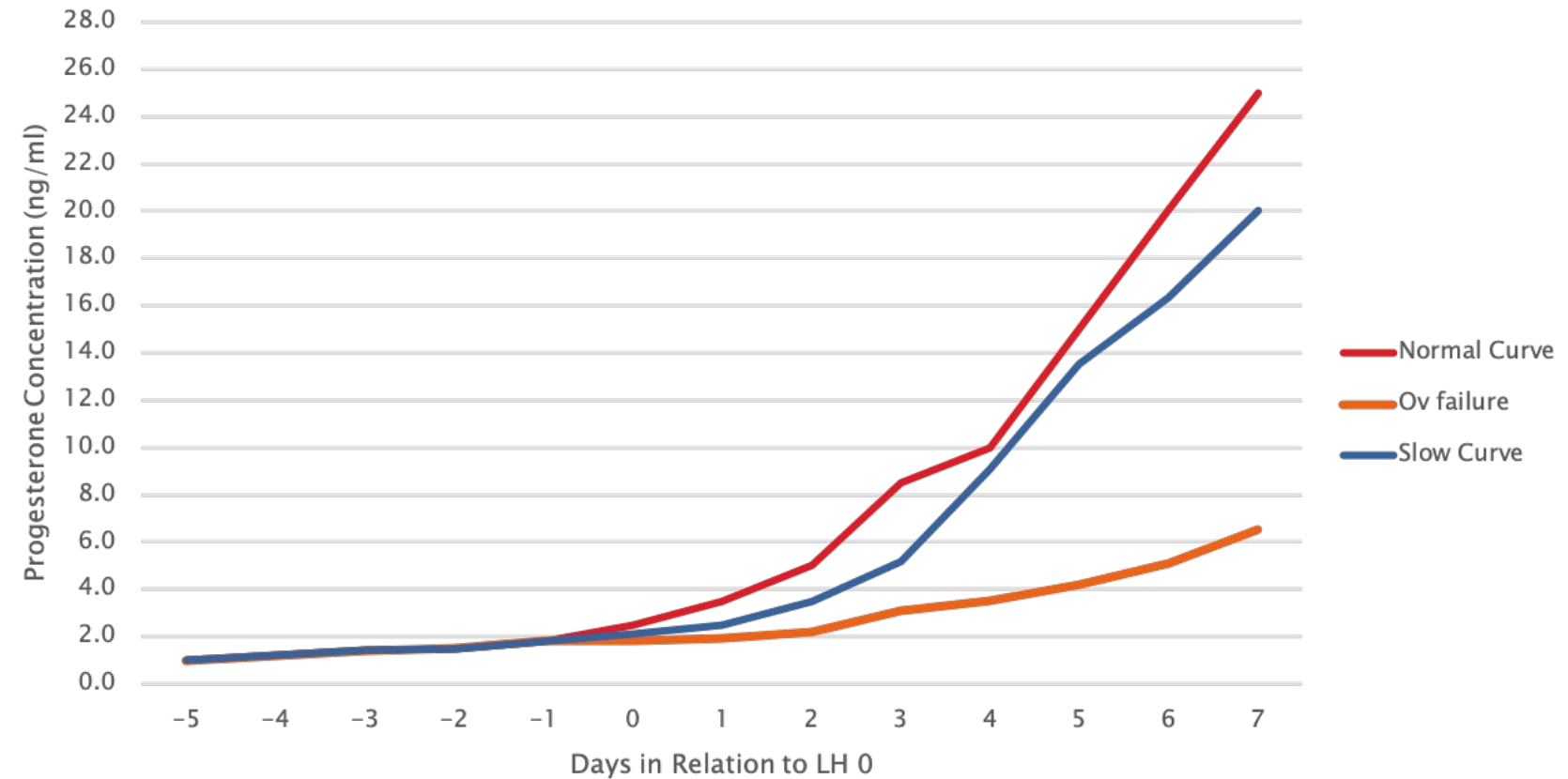


# PROGESTERONE PROFILES: SPEED

Abnormal progesterone curves: slow and ovulation failure

The litter sizes of bitches inseminated with frozen semen with slow progesterone curves were significantly smaller compared to bitches with fast progesterone curves ( $3.9 \pm 1.8$  vs  $5.6 \pm 3.1$  pups per litter respectively;  $P < 0.001$ ).

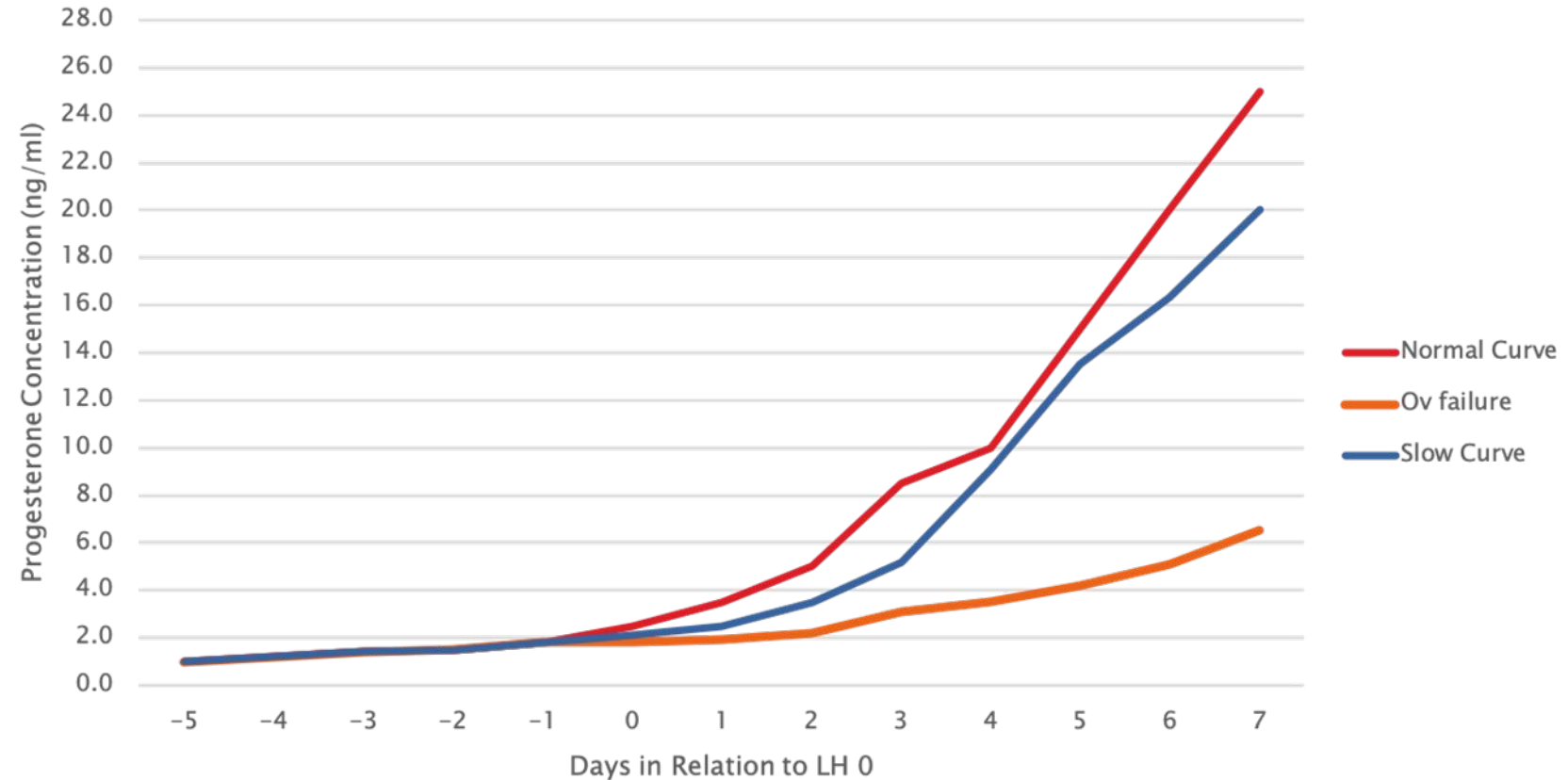
Care: in using a single and absolute P4 concentration of 15ng/ml to time AI



*Schematic graph illustrating different progesterone curves*

# Ovulation Failure (Luteinization)

- Progesterone level
  - 1/1 – 1.5ng/ml
  - 1/2 – 2.2ng/ml
  - 1/4 – 3.0ng/ml
  - 1/5 – 3.5ng/ml
  - 1/6 – 3.9ng/ml
  - 1/7 – 5.1ng/ml
  - 1/8 – 5.9ng/ml
  - 1/10 – 6.7ng/ml
  - 1/12 – 7.1ng/ml
  - 1/14 – 7.2ng/ml
  - 1/16 – 8.7ng/ml



Hollinshead F.K. and Hanlon D.W. (2018) Normal progesterone profiles during estrus in the bitch: A prospective analysis of 1420 estrous cycles. *Theriogenology* 125, 37-42

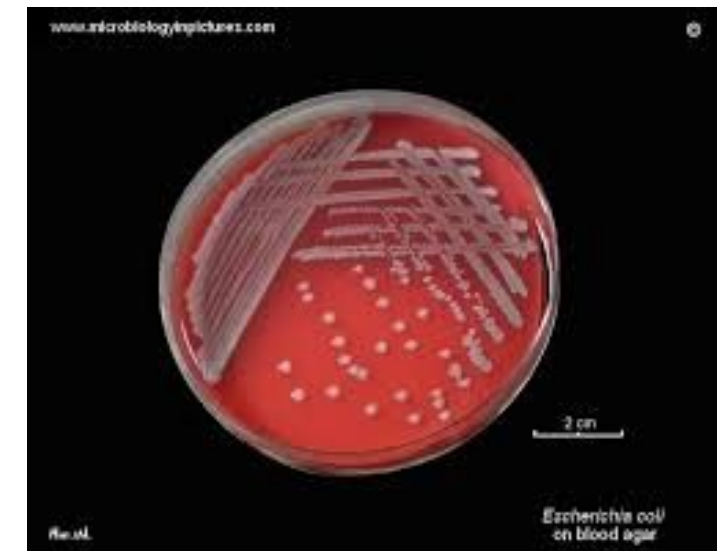


# Normal vaginal flora

- A mixed population of commensal bacteria is normally present within the vagina and plays an important role in homeostasis
- We typically do not culture normal bitches as part of a prebreeding work up (Infertility? Subfertility? Vulvar discharge?)
- Culture of a swab from this region is significant if there is a pure, heavy growth of a single bacteria, together with appropriate history and clinical signs (vulvar discharge, excessive neutrophils)

## Most common bacteria found in vaginal vault of healthy bitches

- *E. coli*
- *Streptococcus spp.*
- *Staphylococcus spp.*
- *Pasteurella spp.*



# Vaginal Cultures

“Because reproductive tract infection is caused by overgrowth of normal flora, the laboratory performing the culture always should be asked to provide a quantitative result, with culture of any single organism with moderate to heavy growth, or 3+ to 4+ growth on a four-point scale, considered relevant.

“Mycoplasma and ureaplasma organisms are part of the normal flora of the canine genitourinary tract.”

## Collection of tissue and culture samples from the canine reproductive tract

Margaret V Root Kustritz <sup>1</sup>

Affiliations + expand

PMID: 16750845 DOI: [10.1016/j.theriogenology.2006.05.003](https://doi.org/10.1016/j.theriogenology.2006.05.003)

### Abstract

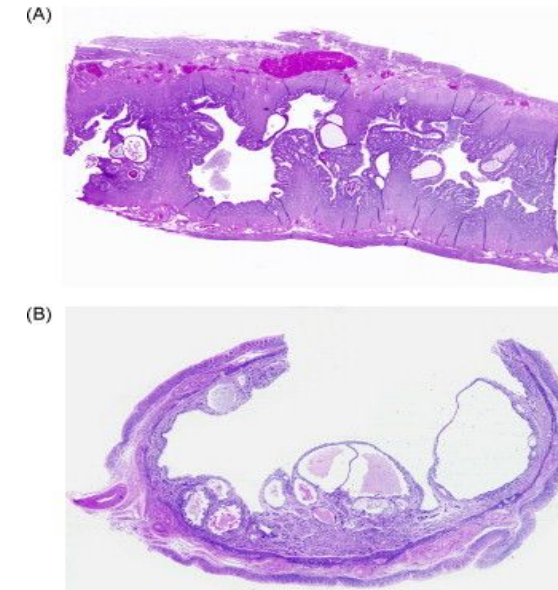
Definitive diagnosis of reproductive tract infection or other disease often requires sampling of tissue, either for culture or histopathology. Indications, sample collection technique, possible side-effects and interpretation of results are reviewed. Pertinent facts include: (1) collection of uterine biopsy specimens via laparotomy was associated with higher yield of diagnostic samples and fewer side-effects than other less invasive techniques; (2) vaginal culture samples should be collected from the anterior vagina to minimize number of contaminants in the sample; (3) collection of culture samples from the anterior vagina during proestrus or estrus, in the presence of discharge originating in the uterus, was a non-invasive technique for assessment for uterine infection; (4) samples for bacterial culture from mucosal surfaces, including the vagina and penis, must be quantitated to allow interpretation, with moderate to heavy growth of any single aerobic bacterial organism relevant; (5) mycoplasma and ureaplasma are part of the normal flora of the genitourinary tract in dogs and bitches and, because most laboratories cannot give reliable quantitative results, interpretation of positive results often is difficult; (6) collection of prostatic tissue samples for cytology or culture was more likely to yield a correct diagnosis than submission of ejaculated prostatic fluid.

# Cystic Endometrial Hyperplasia (CEH)

**Etiopathogenesis** - not completely understood

**Cystic Endometrial Hyperplasia (CEH )** - Hormone driven process from repeated exposure

- Estrogen influence
  - Promotes growth, vascularity of endometrium
  - Opens/dilates cervix
  - Increases number of progesterone receptors on endometrium
- Progesterone influence
  - Promotes secretion and proliferation of endometrial glands
  - Decreases local immunity
  - Closes cervix
  - “Quiets” endometrium – decreases contractibility



Cystic endometrial hyperplasia, pseudo-placental endometrial hyperplasia, and other cystic conditions of the canine and feline uterus  
[D.H.Schlafer](#)[A.T.Gifford](#)





# CEH in the Canine

## Etiopathogenesis – not completely understood

- CEH develops because of an abnormal uterine response to ovarian hormones (estrogen and progesterone)
  - Fluid (sterile) accumulates in endometrial glands and uterine lumen as an exaggerated response during the luteal phase (repeated, chronic influence of progesterone)
  - CEH mucometra/hydrometra is not always associated with inflammation and not typically a clinical disease (other than infertility)
  - Many patients with CEH are not symptomatic
- Current evidence suggests that Cystic Endometrial Hyperplasia (CEH) and Pyometra are separate entities
- CEH can also be induced (triggered) by trauma (biopsy), suture, irritants (cryoprotectants), etc.
- If bacteria are the trigger, **Pyometra is the result**

➤ *Theriogenology*. 2001 Apr 15;55(7):1509-19. doi: 10.1016/s0093-691x(01)00498-8.

### Cystic endometrial hyperplasia-pyometra complex in the bitch: should the two entities be disconnected?

H De Bosschere <sup>1</sup>, R Ducatelle, H Vermeirsch, W Van Den Broeck, M Coryn

Affiliations + expand

PMID: 11354710 DOI: 10.1016/s0093-691x(01)00498-8

#### Abstract

The uteri of 26 clinically healthy bitches and 42 bitches with a clinical suspicion of pyometra were examined histologically using a computerized image analysis system. Histologic lesions were characterised mainly by thickening or atrophy of the endometrium and by varying degrees of cystic changes of the glands. These lesions were observed in most of the clinically healthy bitches as well as in all of the clinically ill animals. In most of the ill bitches a variable degree of inflammation also was found. Some bitches with clinical signs indicative for pyometra had no inflammatory reaction in the uterus. These bitches were misdiagnosed as suffering from pyometra, confirming the difficulty of diagnosing pyometra by simple clinical examination. Determination of sex hormone serum levels revealed that all dogs in both groups were either in metestrus or in anestrus. Based on the results of this study the cystic endometrial hyperplasia-pyometra complex can be divided in two entities: a cystic endometrial hyperplasia-mucometra complex and an endometritis-pyometra complex. Both entities bear many similarities with each other, except for the inflammatory reaction in the endometritis-pyometra complex. It is concluded from this study that the latter complex probably does not necessarily follow the former, but that both can arise de novo.



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*Theriogenology* 70 (2008) 364–374

*Theriogenology*

[www.theriojournal.com](http://www.theriojournal.com)

### Mucometra, cystic endometrial hyperplasia, and pyometra in the bitch: Advances in treatment and assessment of future reproductive success

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#### Abstract

Pyometra is a common reproductive disorder which affects nearly one fourth of all female dogs before they reach 10 y of age. An association between pyometra and the most common uterine disease of the bitch, cystic endometrial hyperplasia, has been established, as the latter allows commensal bacteria originating from the vagina to proliferate in the uterus at the end of estrus. The progressive degenerative process in the development of cystic endometrial hyperplasia is usually proposed as the initiating lesion for pyometra in bitches; this is mediated by progesterone and potentially aggravated by estrogens. However, a separate process caused by local uterine irritation to trophoblastic reaction and bacterial proliferation has been recently proposed as an alternate mechanism leading to the development of pyometra. Pyometra is clinically distinct in pathogenesis, signs, treatment and prognosis from postpartum metritis or mucometra. Treatment of pyometra has historically involved ovariohysterectomy, however, during the last 10 y, numerous effective treatments have been proposed to treat both open and closed cervix pyometra with good success and future fertility. Among the treatments available, the use of repeated low doses of prostaglandins alone or in association with either dopamine agonists or progesterone-receptor antagonists has been demonstrated to be a viable alternative for valuable breeding dogs. © 2008 Elsevier Inc. All rights reserved.

**Keywords:** Mucometra; Cystic endometrial hyperplasia; Pyometra; Treatment; Dog

➤ *J Small Anim Pract*. 1975 Apr;16(4):249-57. doi: 10.1111/j.1748-5827.1975.tb05741.x.

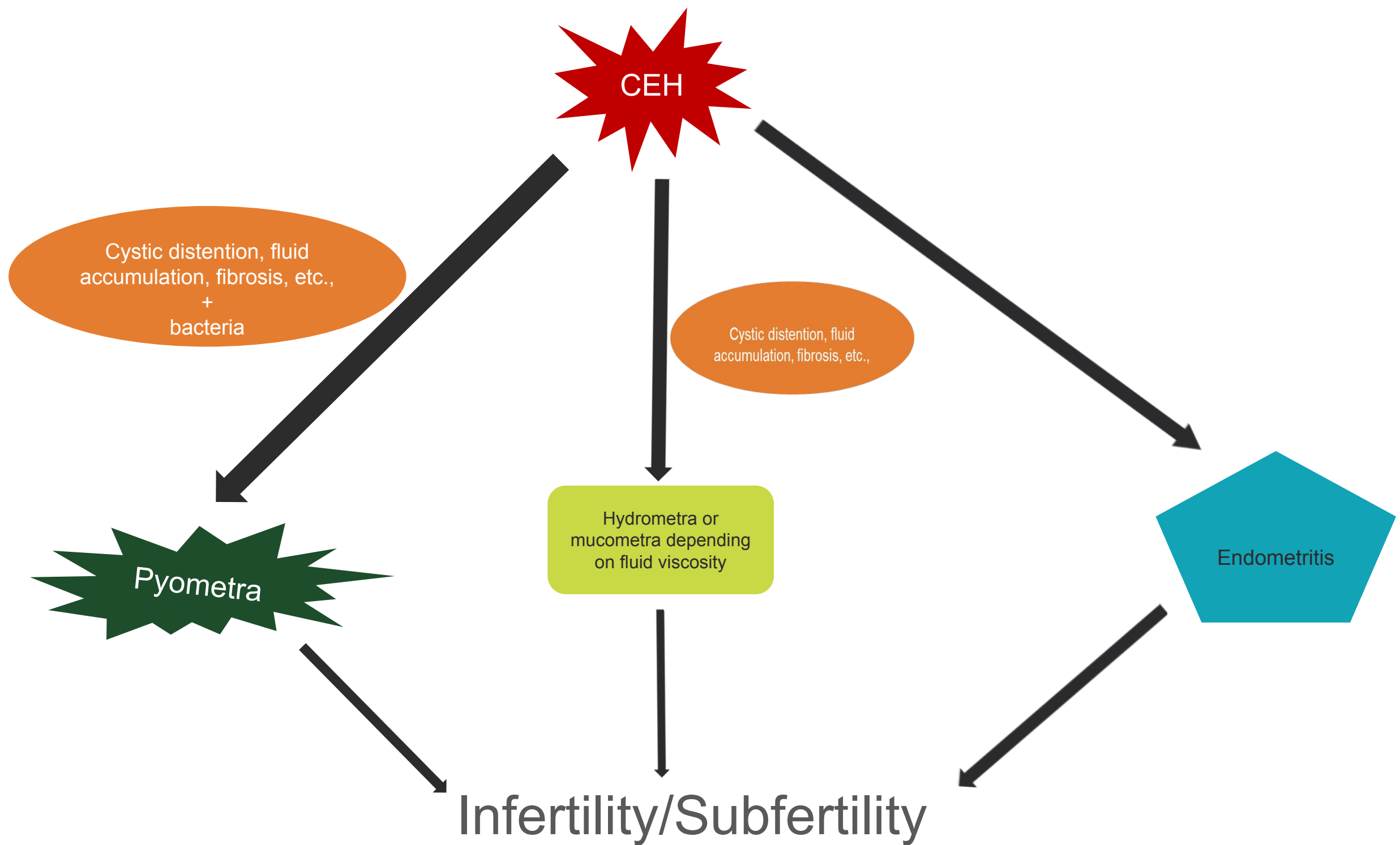
### The development of systic endometrial hyperplasia in the bitch following serial uterine biopsies

J C Hadley

PMID: 1170464 DOI: 10.1111/j.1748-5827.1975.tb05741.x





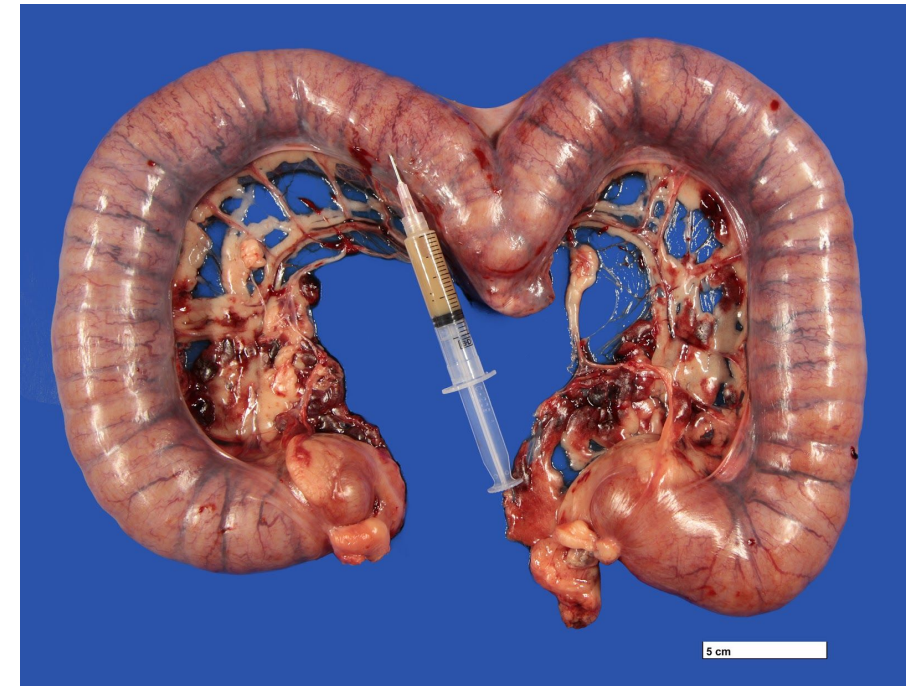


# Pyometra in the Canine

**Etiopathogenesis** - not completely understood

## **Pyometra – Endometritis**

- Pyometra can occur in the absence of CEH reinforcing the evidence that CEH and pyometra are separate entities
- Complex etiology
  - Bacteria
  - Immune dysfunction
  - Hormone
- Inflammation of endometrium always present
- These patients are clinically ill
- Bacteria include:
  - E. coli
  - Strep, Staph, Klebsiella, Proteus, Pasteurella



# Pyometra in the Canine

## Signalment

- 75% are nulliparous
- Mean age is 6 years

## Clinical Presentation – can vary greatly with patency of cervix – “open” v. “closed”

- Most commonly present 5 weeks post estrus
- Fever, lethargy, anorexia
- Vulvar discharge – mucopurulent – associated with cervical patency - “open”
- PU/PD, GI – vomiting/diarrhea
- Abdominal distention – typically associated with closed cervix
- Dehydration, hypothermia, sepsis – associated with severe cases

These patients usually (almost always) present in diestrus (luteal phase).



# Pyometra in the Canine

## Diagnosis

- History and Clinical Signs
  - Diestrus – signs of heat within the last 5 weeks
- Mucopurulent vulvar discharge (if cervix open)
- Blood Profile Changes
  - Marked leukocytosis with left shift (often >30,000)
  - Serum progesterone is typically >2ng/ml
  - Pre-renal azotemia
  - ALP, ALT increase (response to toxemia, diminished hepatic circulation?)
- Uterine Enlargement
  - Palpation
  - Radiography
  - Ultrasound



# Pyometra in the Canine

## Treatment

- **Ovariohysterectomy (OHE) – curative and preventative**
  - Stabilize first with IV fluid therapy, antibiotic therapy
- **Medical Therapy – no approved medication in the U.S. for this use**
  - Only if:
    - Significant contribution to genetic pool
    - 4y or less
    - Patent cervix
    - No or minimal biochemical changes (normal BUN, Cr, ALP, ALT)
  - **Prostaglandin – PGF<sub>2α</sub>**
    - 10-20ug/kg TID SQ
    - Can have significant side effects
      - Vomiting, Diarrhea, Hypersalivation, Abdominal Cramping
    - Requires several days (5-7 or so) of therapy and should be done in hospital
    - 73%-93% effective for complete resolution, 75%-87% fertility following therapy





# Pyometra in the Canine

## Treatment

- **Medical Therapy** – continued
  - **Dopamine Agonist** (prolactin inhibitor)
    - Will cause decrease on Prolactin (luteotrophic hormone)
    - **Cabergoline** (Dostinex)
      - Minimal side effects
      - Given once daily
      - 5ug/kg PO SID
  - **Progesterone Receptor Antagonist**
    - Remove progesterone block to open cervix and allow uterus to evacuate (contractions?)
      - Eventual luteolysis
    - **Aglepristone (antiprogestin) – RU<sub>534</sub>** – Not available/approved for us in the U.S. (special permit)
      - Minimal side effects
      - Two injections, given 24 hours apart
      - 10mg/kg SQ
      - 84%-93% for complete resolution, ~75% fertility following therapy (probably higher)





# Pyometra in the Canine

## Treatment

- **Medical Therapy** – continued
  - **Antimicrobial Therapy**
    - Start with broad spectrum and base on culture
    - Treat for 10-14 days post resolution of pyometra
  - **Prevention**
    - Not routine and controversial
    - Estrus suppression (2-3 months) to allow additional time for endometrial regeneration
    - Only drug approved for this use is a progestin – not appropriate in this situation
    - Mibolerone – androgen – not approved for this use in U.S, or in “breeding dogs”
      - Has been shown to be effective



# Mucometra in the Canine

## Clinical Signs

- Often no clinical signs – other than infertility
- May see mucous vulvar discharge when cervix is open

## Diagnosis

- Usually, no clinical signs but fluid in uterus – NOT lethargic, no fever, normal attitude/appetite
- Normal CBC, Chemistry profile
- If vulvar discharge – mucous and not purulent

## Treatment

- None/Monitor?
- Hasten evacuation of uterus
  - Prostaglandin –  $\text{PGF}_{2\alpha}$
  - Dopamine Agonist – cabergoline
  - Progesterone Receptor Antagonist - aglepristone



# Endometritis in the Canine

Etiopathogenesis - Unclear

## Clinical Signs

- Often no clinical signs – other than infertility

## Diagnosis

- Usually NOT lethargic, no fever, normal attitude/appetite
- Normal CBC, Chemistry profile
- Definitive diagnosis via transcervical catheterization by vaginal endoscopy – cytology, culture (most are bacterial)

## Treatment

- Choose a different breeding bitch (especially if not young and highly valuable)
- Anti-inflammatory therapy (NSAIDS)? Antibiotic therapy?



# Thank you

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