

6TH INTERNATIONAL SYMPOSIUM
on Non-Surgical Contraceptive
Methods of Pet Population Control

ACC & D

BOSTON | JULY 22-24, 2018

Reproductive Biology 101

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Repro 101

A brief introduction to cat and dog reproductive biology

G. Robert Weedon, DVM, MPH



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Repro 101

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Alliance for Contraception
in CATS & DOGS

Mission: Our mission is to advance non-surgical fertility control so as to effectively and humanely reduce the number of unwanted cats and dogs.

acc-d.org



imagine...

preventing unwanted litters without surgery

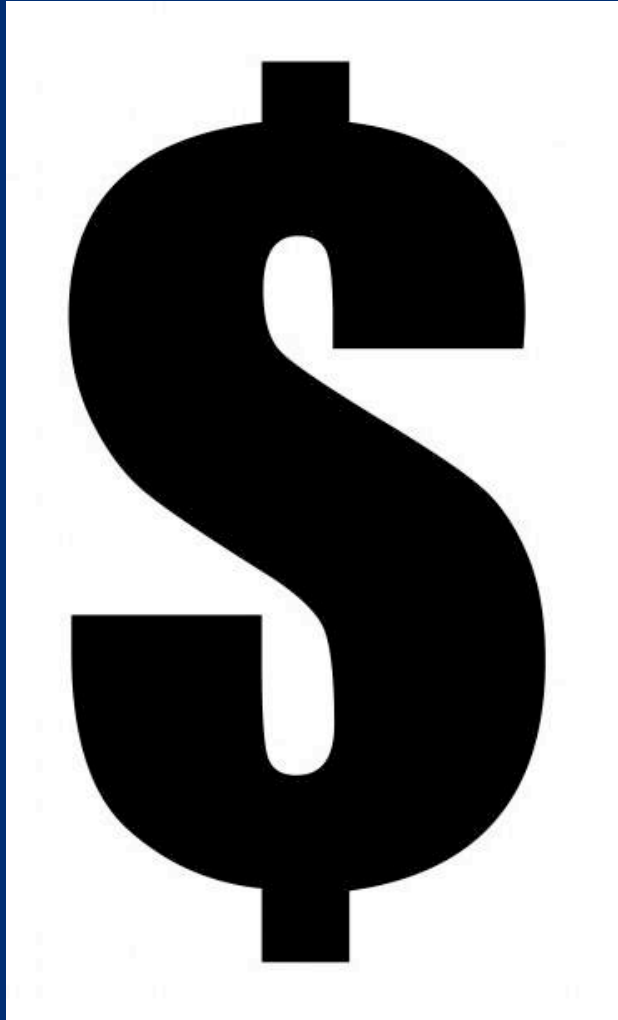
Overview of tonight's discussion:

- Canine Reproduction
 - Anatomy
 - Physiology
- Feline Reproduction
 - Anatomy
 - Physiology
- Control of Reproduction



Why nonsurgical sterilization instead of traditional spay/neuter?







What does the science tell us?



“In the absence of juvenile sterilization, 91% of adult intact females would need to be sterilized annually to halt population growth. In comparison, **with a 3-year nonsurgical contraception program, an annual contraception rate of 60% of female juvenile and adult intact cats would be required to halt population growth, assuming that treated cats were retrapped at the same rate after 3 years.**”

What does the science tell us?



“Within population type, a given implementation rate of the TR strategy results in the most rapid rate of population decline and (when populations are isolated) the highest probability of population elimination, followed in order of decreasing efficacy by equivalent rates of implementation of TNR and temporary contraception. Even low levels of demographic connectivity significantly reduce the effectiveness of any management intervention, and continued abandonment is similarly problematic.”

To save more lives.....



...we need more options.

A Cure for Euthanasia?

“A nonsurgical sterilant could reduce the global population of homeless dogs and cats, but there hasn’t been money to develop one—until now”



A Cure for Euthanasia?

A nonsurgical sterilant could reduce the global population of homeless dogs and cats, but there hasn't been money to develop one—until now

NINETY KILOMETERS SOUTHWEST OF Montgomery and a few decades shy of the modern world lies Oak Hill, Alabama, the smallest town in one of the poorest counties in the state. There are 22 homes, one gas station (which doubles as a general store), and a post office staffed by a single employee.

Oak Hill doesn't have much—but it does have cats. Cats that congregate in barns and under sheds. Kitchens here are long-waisted, treatments and vetting shops. Pregnant queens abandoned in the woods. Tooms are their main source for food.

There are no animal control services in Oak Hill, so the cats keep breeding. And dying. Cats roam down the state highway, beside about three or four, and those that do make it to overgrown fields, farmsteads and barns are euthanased within days.

A few fortunate felines find their way to the back porch of David Fuller, a retired electrician engineer who, as a contractor for NOAA, spent years ensuring that remote components destined for space survived their environment. These days, Fuller and his wife do the same for Oak Hill's cats. They trap the ones they can and try to find homes for them. They bottle-feed kittens whose

eyes have been closed shut by star. And they drive on long each week to the nearest Wal-Mart, where they load their pet bags (most with 4.5-lb bags of dry cat food).

Thirty-five feral cats and Fuller's property house, and he uses one of another 16 on his neighbor's farm in a nearby town. Despite Fuller's best intentions, however, he can't possibly keep up. He's running out of people to give the cats to, and the overflowing adoption will no longer take them. He's spayed and neutered a few, but he can't long-grafted the \$100 surgeries. And so the cats keep breeding.

The problem isn't confined to Oak Hill. It occurs everywhere throughout the United States and dogs but enough to put their numbers, and developing one with Congress find the people in— as China and India—date even worse. In the U.S., millions of dogs and cats are abandoned in US shelters each year, and many are shot and poisoned around the globe. “There's almost no hope of any kind of dent in the problem with just,” says Anne Briggs, the president of Portland, Oregon-based Alliance for Companion in Care and Dogs (ACCAD).

For the past decade, ACCAD and human organizations have pushed nonsurgical alternative to chemical spay/neuter drugs—something cheaper and it's such as a vaccine or a “booster,” Briggs says, would let us reach far more cats with the same money. Researchers have developed similar products for wildlife; they have trained cat-sufficiency or population control in companion animals. The funding and interest has a further progress.

That may be about to change thanks to a U.S. Institute named Cary Dickinson, has announced \$75 million



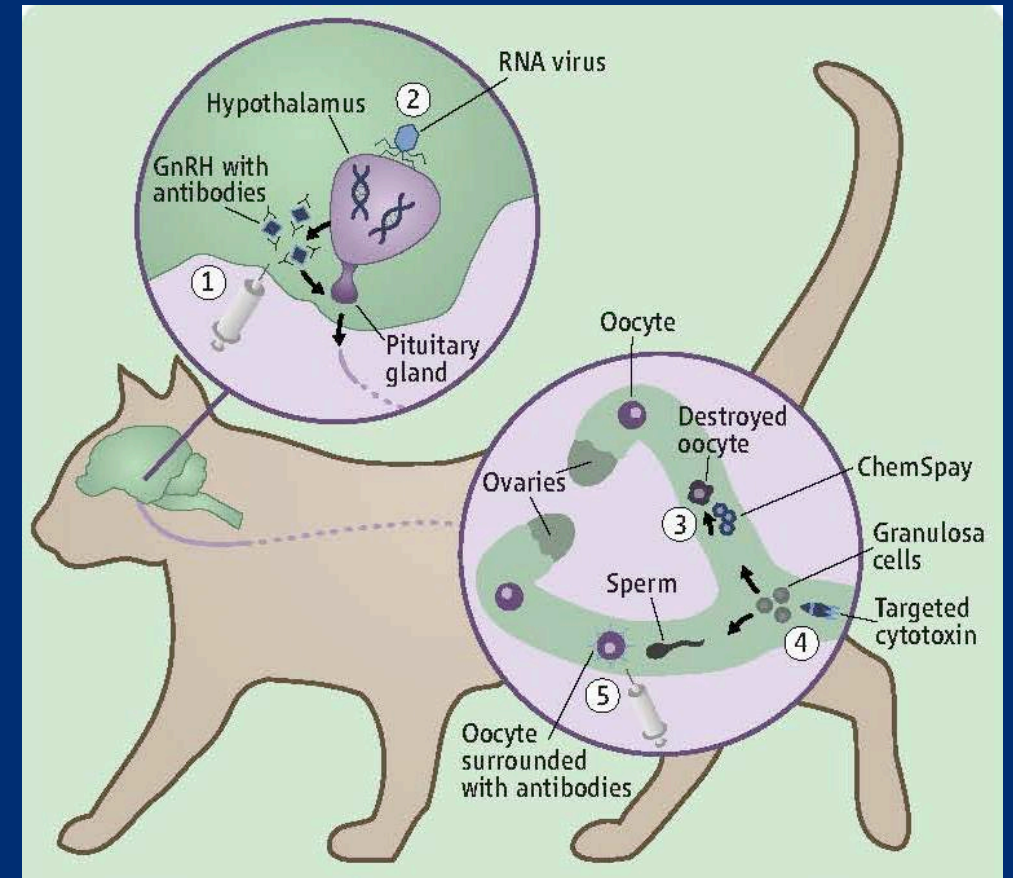
Vagabonds. About 22 million stray cats roam the streets of the United States.

1400 18 SEPTEMBER 2009 VOL. 322 SCIENCE www.sciencemag.org
Fuller/Dickinson

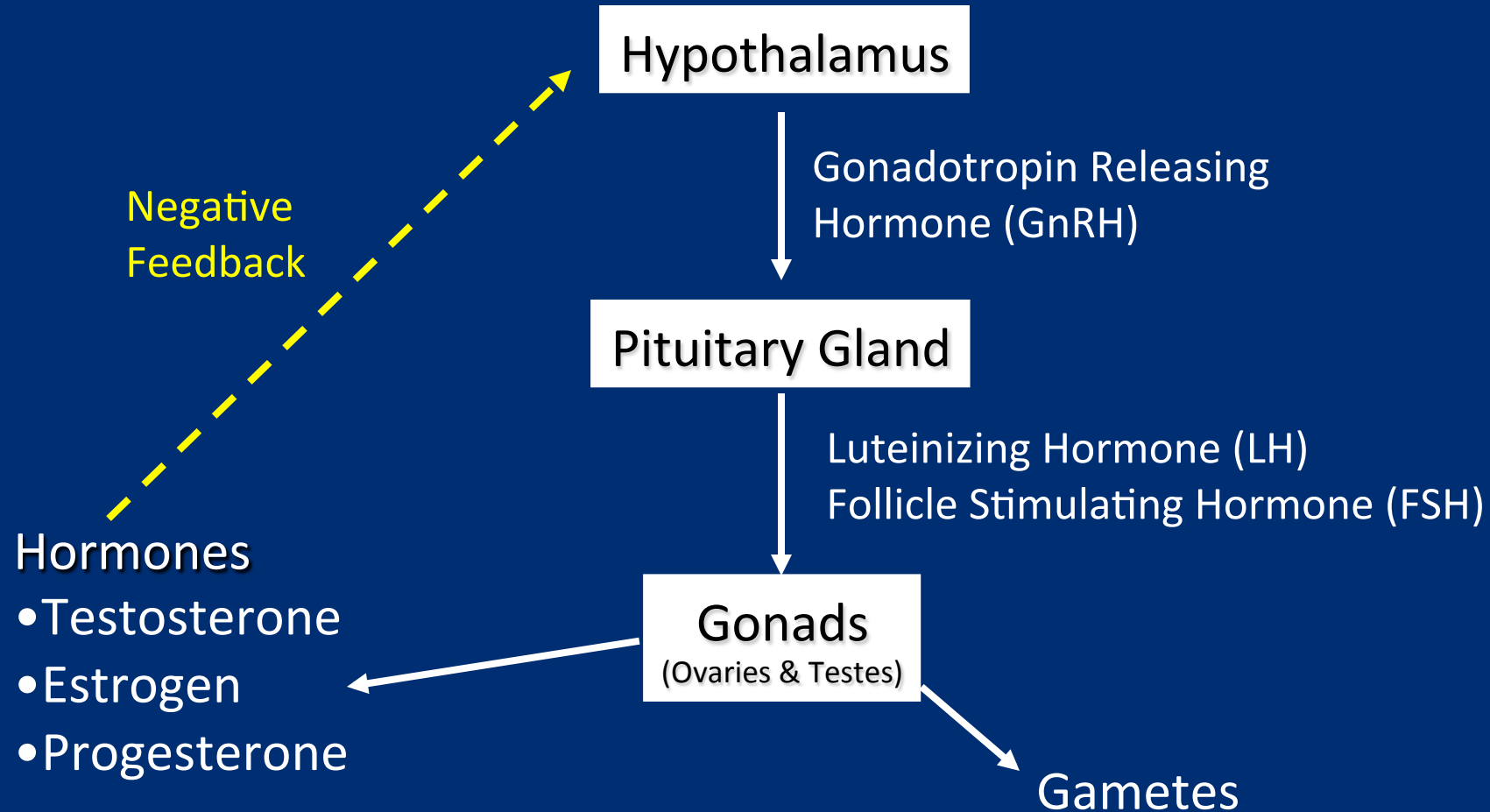
A Cure for Euthanasia?

Researchers are looking into a number of ways to permanently sterilize cats and dogs without surgery, including:

- (1) a vaccine that would block the release of sex hormones,
- (2) a virus that would genetically silence fertility pathways,
- (3) a chemical that would destroy eggs,
- (4) a targeted cytotoxin that would destroy cells necessary for the production of sperm and eggs, and
- (5) a vaccine that would block sperm from entering eggs.



Reproductive Physiology

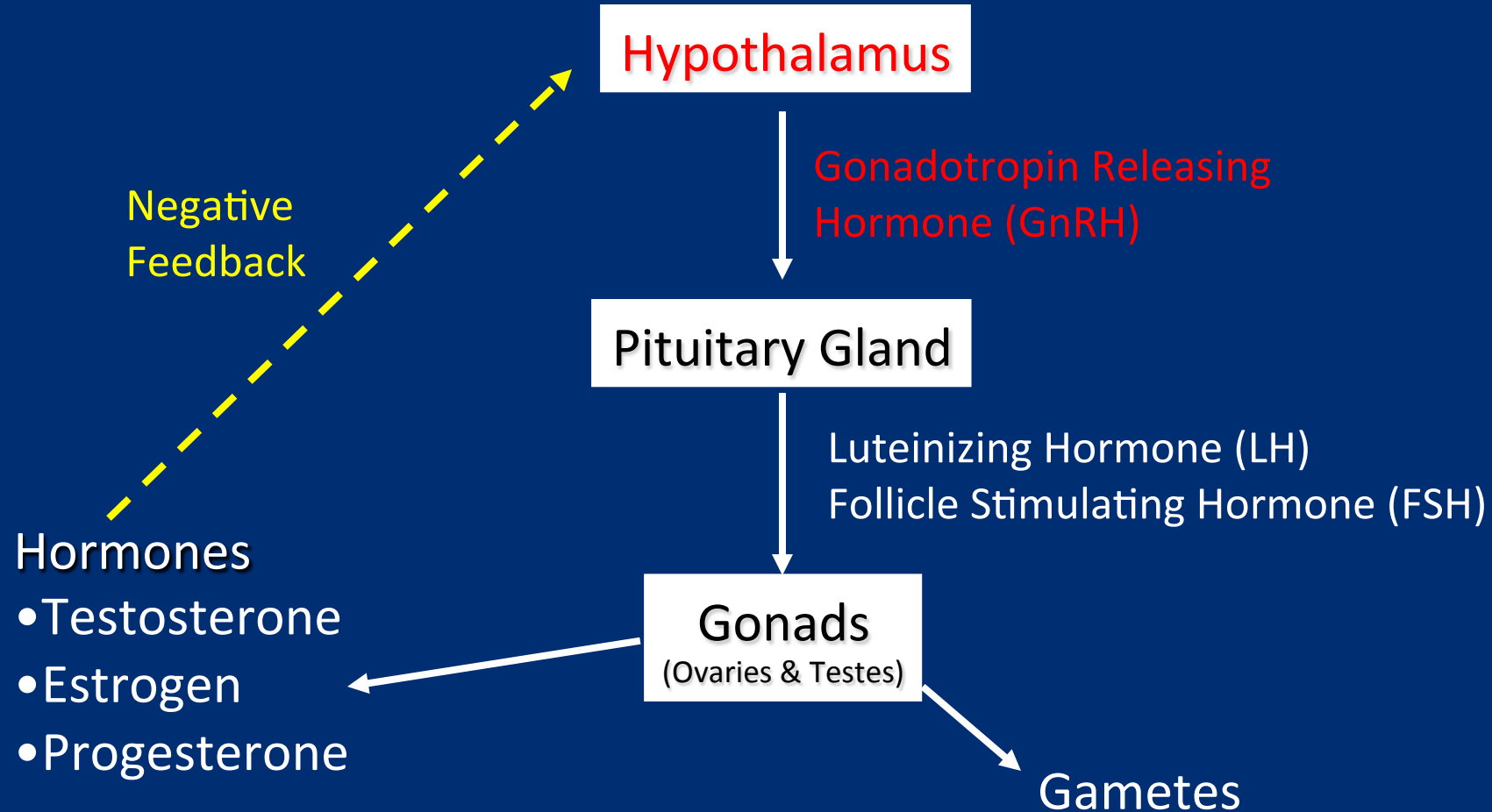


Reproductive Physiology

- Brain

- The major control center for reproduction is the brain, where specific neurons synthesize gonadotropin-releasing hormone (GnRH) under a number of influences, such as light levels, body condition, age, and the blood levels of various hormones.
- One of the most interesting things about brain secretion of GnRH is that it is secreted in pulses and not continuously. The pulses are important – if GnRH is not delivered in pulses, it does not have the normal effect on the reproductive system.
- Interfere with GnRH, and you interrupt all of reproduction in both males and females. In fact, not only is reproduction interrupted, but the species-specific reproductive behaviors are disrupted as well.

Reproductive Physiology

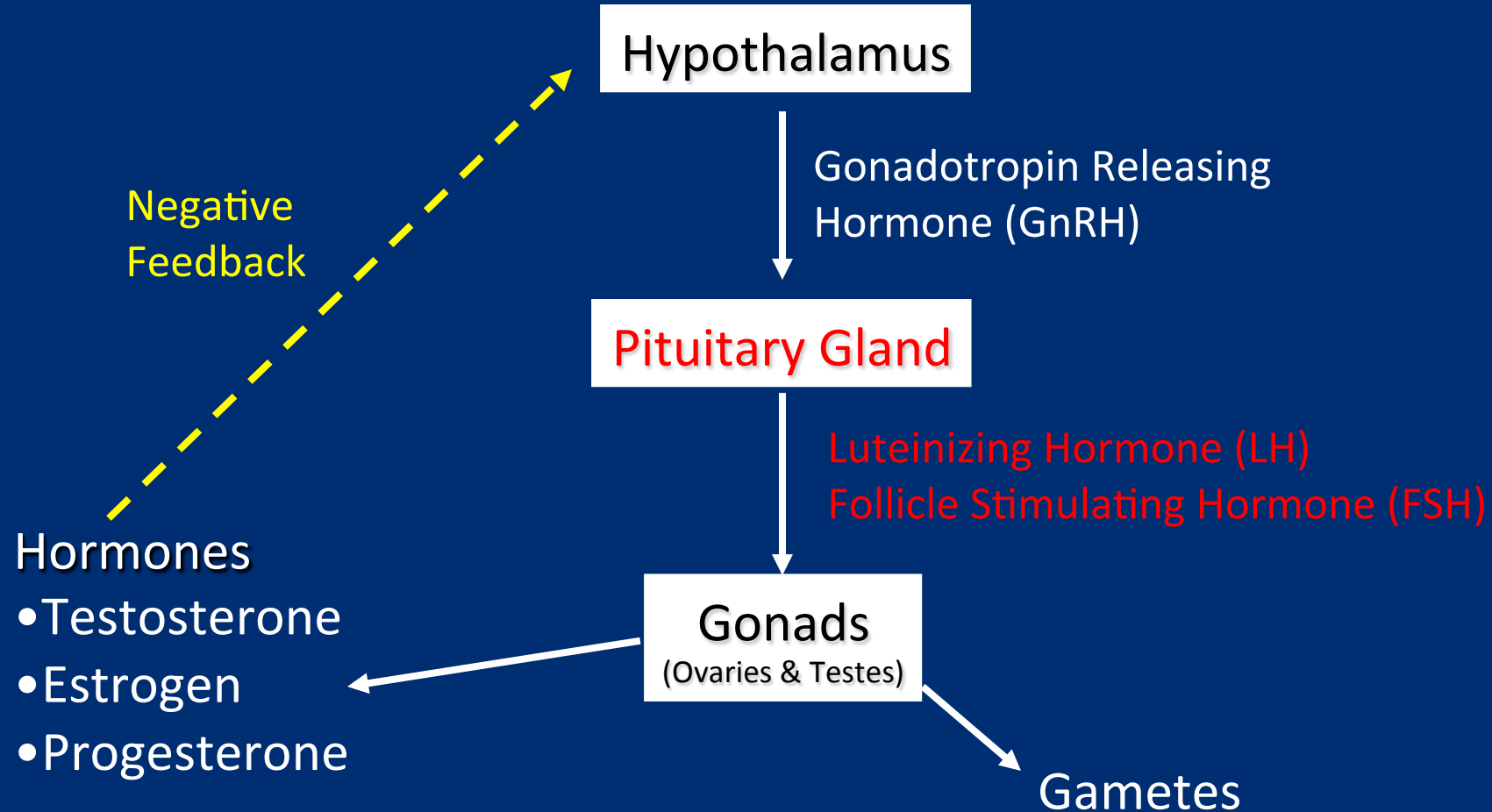


Reproductive Physiology

- **Pituitary**

- The pituitary gland has specific cells – the gonadotrophs – that have receptors for GnRH that bind to the peptide.
- Once the GnRH binds to its receptor on specific pituitary cells, it causes the release of two larger protein hormones called gonadotropins – luteinizing hormone (LH) and follicle-stimulating hormone (FSH) – which are secreted into the blood. As the brain gives off pulses of GnRH, these pulses reach the pituitary and cause the pituitary to give off pulses of LH and FSH.

Reproductive Physiology

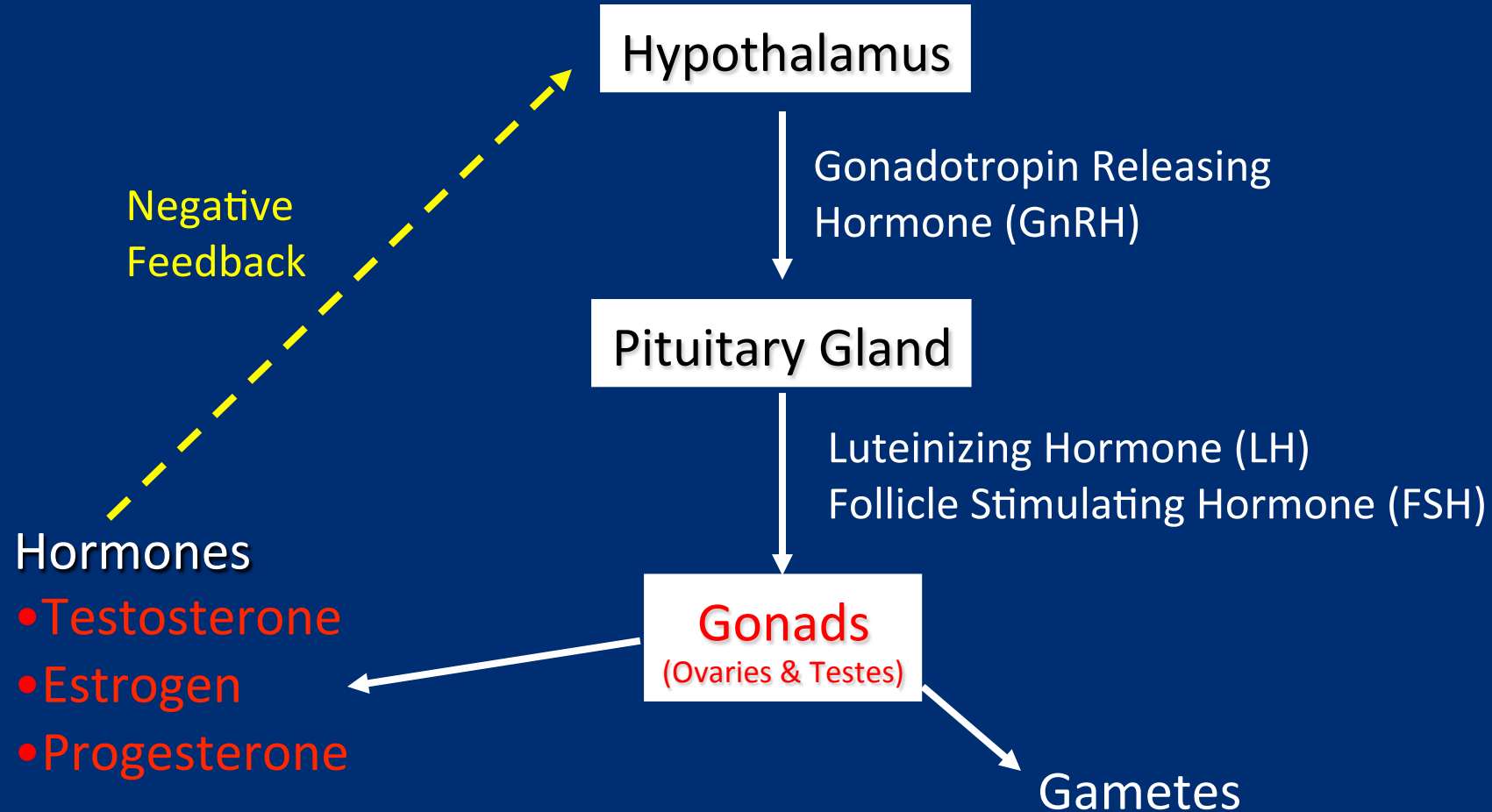


Reproductive Physiology

- Gonads (Ovaries and Testes)

- Once the pituitary secretes LH and FSH, they travel in the blood to the gonads – ovaries in females and testicles in males. These two hormones bind to receptors on the gonads. They coordinate the estrous cycle (heat) of the female and are important in the production of estrogen and progesterone. In the male, FSH and LH are important for sperm maturation and stimulation of the production of testosterone.
- When the steroid hormones (estrogen, progesterone and testosterone) are secreted from the female or male gonads, these hormones travel in the blood to the brain, where they turn off the secretion of GnRH. This is called **negative feedback**.

Reproductive Physiology



The Bitch

Puberty - 6 mo.

Monoestrus

- One estrus during breeding season

Estrous Cycle

- Proestrus
- Estrus **Heat**
- Metestrus or Diestrus
- Anestrus

Estrous Cycle (Non-Pregnant)

Proestrus (9 days)

- Vulva swollen
- Bloody discharge
- Attracted to male but does not mate

Estrus (9 days, ovulation day 2)

- Accepts male
- Straw-colored discharge

Metestrus or Diestrus (90 days)

- False pregnancy

Anestrus (5 months)

- Sexual inactivity

Estrous Cycle - Pregnant

Proestrus (9 days)

- Vulva swollen
- Bloody discharge
- Attracted to male but does not mate

Estrus (9 days, ovulation day 2)

- Accepts male
- Straw-colored discharge

Pregnant Metestrus/Diestrus (50 - 60 days)

- Pregnancy
- Parturition (63 days from ovulation)

Anestrus (5 months)

- Sexual inactivity

Canine Fertility

- The onset of the first estrous cycle (puberty) of an individual bitch is expected between 6 and 10 month of age but may not begin until she has reached 2 years of age. The interestrus interval is normally 4-13 month, with 7 month the average.
- The anestrus phase of the estrous cycle normally lasts 1-6 months. It is marked by ovarian inactivity, uterine involution, and endometrial repair. An anestrus bitch is not attractive nor receptive to male dogs.
- During proestrus, the bitch becomes attractive to male dogs but is still not receptive to breeding, although she may become more playful. A blood-tinged vulvar discharge of uterine origin is present, and the vulva is mildly enlarged. Estrogen rises from basal anestrus levels to peak levels in late proestrus, while progesterone remains at basal levels until rising at the LH surge. Proestrus lasts from 3 days to 3 weeks, with 9 days average.
- Estrus lasts 3 days to 3 weeks, with an average of 9 days.

Canine Fertility

- Estrogens

- Increased estrogen causes an increased turnover rate of vaginal epithelial cells, resulting in the progressive cornification seen on vaginal cytology.

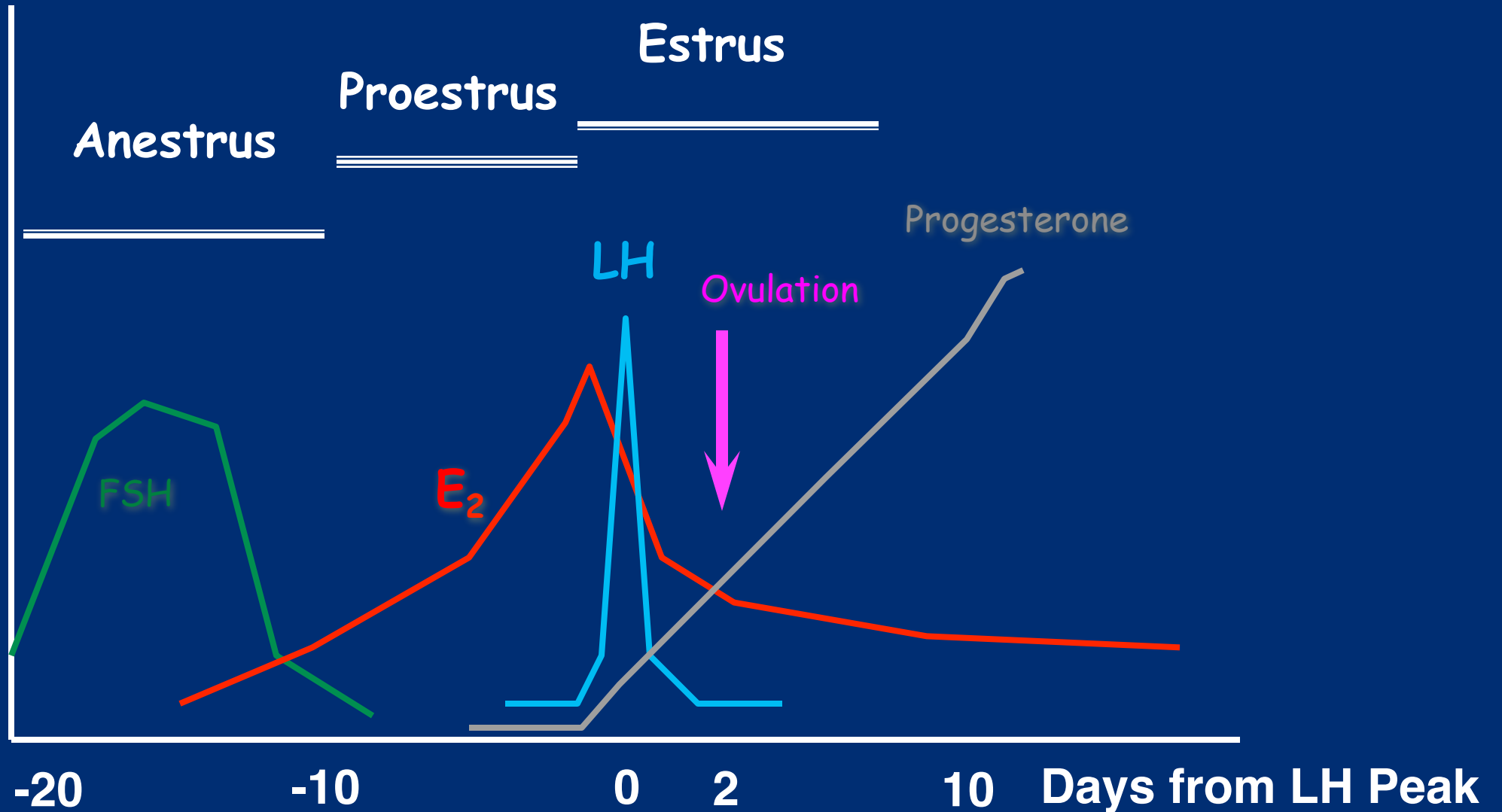
- Luteinizing Hormone

- At the end of the follicular phase of the estrous cycle, a marked increase in LH over usual baseline values develops over 24-48 hours, followed by a return to baseline values. This surge is thought to occur in response to the decline in estrogen levels and increase in progesterone levels. The LH surge triggers ovulation, making it the central endocrinologic event in the reproductive cycle of the bitch.

- Progesterone

- Progesterone levels begin to rise at approximately the time of the LH surge (prior to ovulation). Rising progesterone acts synergistically with declining estrogen to reduce edema of the vulva and vagina. During metestrus, plasma progesterone concentrations are high. They usually plateau at 10 to 30 days after ovulation. In non-pregnant bitches, the progesterone secretion declines slowly and reaches a basal level at about 75 days after the start of the luteal phase.

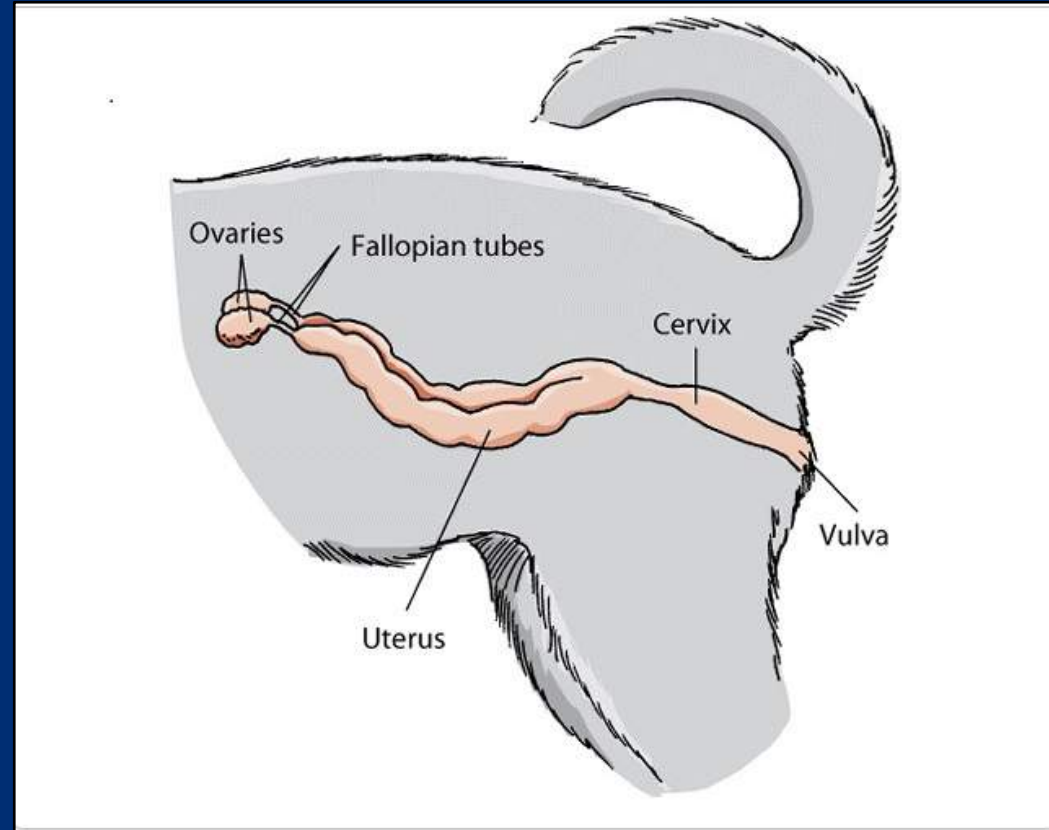
Hormonal Changes



Canine Female Reproductive Anatomy

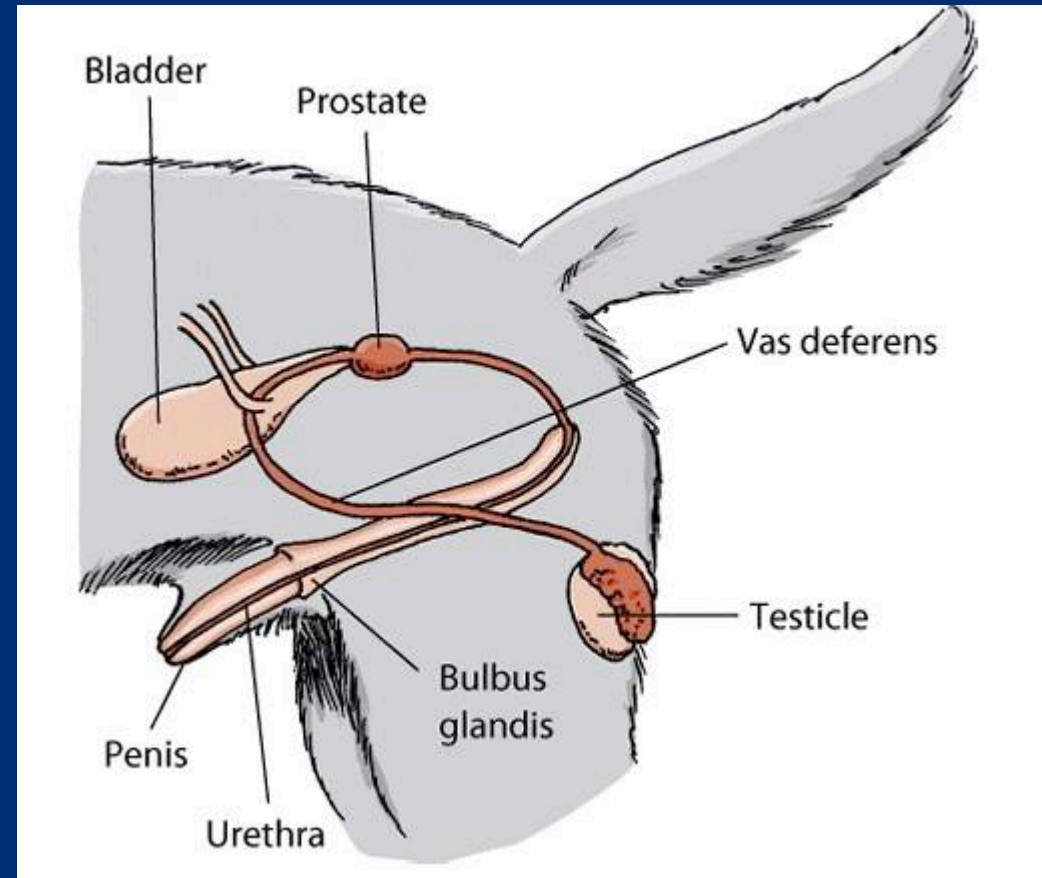
The female genital tract includes:

- vulva,
- vagina,
- cervix,
- uterus,
- oviducts, and
- ovaries.
- As well as the mammary glands found on the chest and abdomen.



Canine Male Reproductive Anatomy

In males, the genital tract provides a pathway for sperm cells and semen. The epididymis connects the testicle to the ductus deferens, which carries sperm to the urethra. Sperm mature and are stored in the epididymis. The accessory sex glands, such as the prostate, create the fluid portion of semen.



Feline Reproduction

Female-Queen

Male - Tom

Puberty

- 4 - 9 months

Estrous Cycle

- Seasonal
 - January to September
 - House cats may cycle year round

Estrous Cycle

Pro-estrus

- 1 - 2 days
- Attracted to males
- Rubs head and neck on objects
- Vocalization, posturing and rolling

Estrus

- Accepts male
- 4 - 6 days if male present, 10 days if no male
- Ovulation is induced by mating
- Affectionate to aggressive towards owners

Estrous Cycle

Proestrus if queen did not ovulate

- 8 - 10 days

Diestrus after ovulation

- pseudopregnancy - 40 days
- pregnancy - 60 days

Anestrus 3 - 4 months

Feline Fertility

- Female cats go through puberty, defined by onset of their first estrus, at an average age of 8-9 months, with a range from 4-18 months.
- Cats are seasonally polyestrous, cycling for an average of about 6 days every 2-3 weeks from January through mid-October.
- The seasonal anestrus from mid-October through December is defined by day length; cats maintained under artificial lights for 12 continuous hours daily will cycle year-round and may exhibit increased fertility.
- Cats are induced (reflex) ovulators. An external trigger, usually coitus, stimulates release of gonadotropin releasing hormone (GnRH) from the hypothalamus. This stimulates release of luteinizing hormone (LH) from the pituitary within 2-4 hours, which will then cause ovulation in 1-3 days.

Feline Fertility

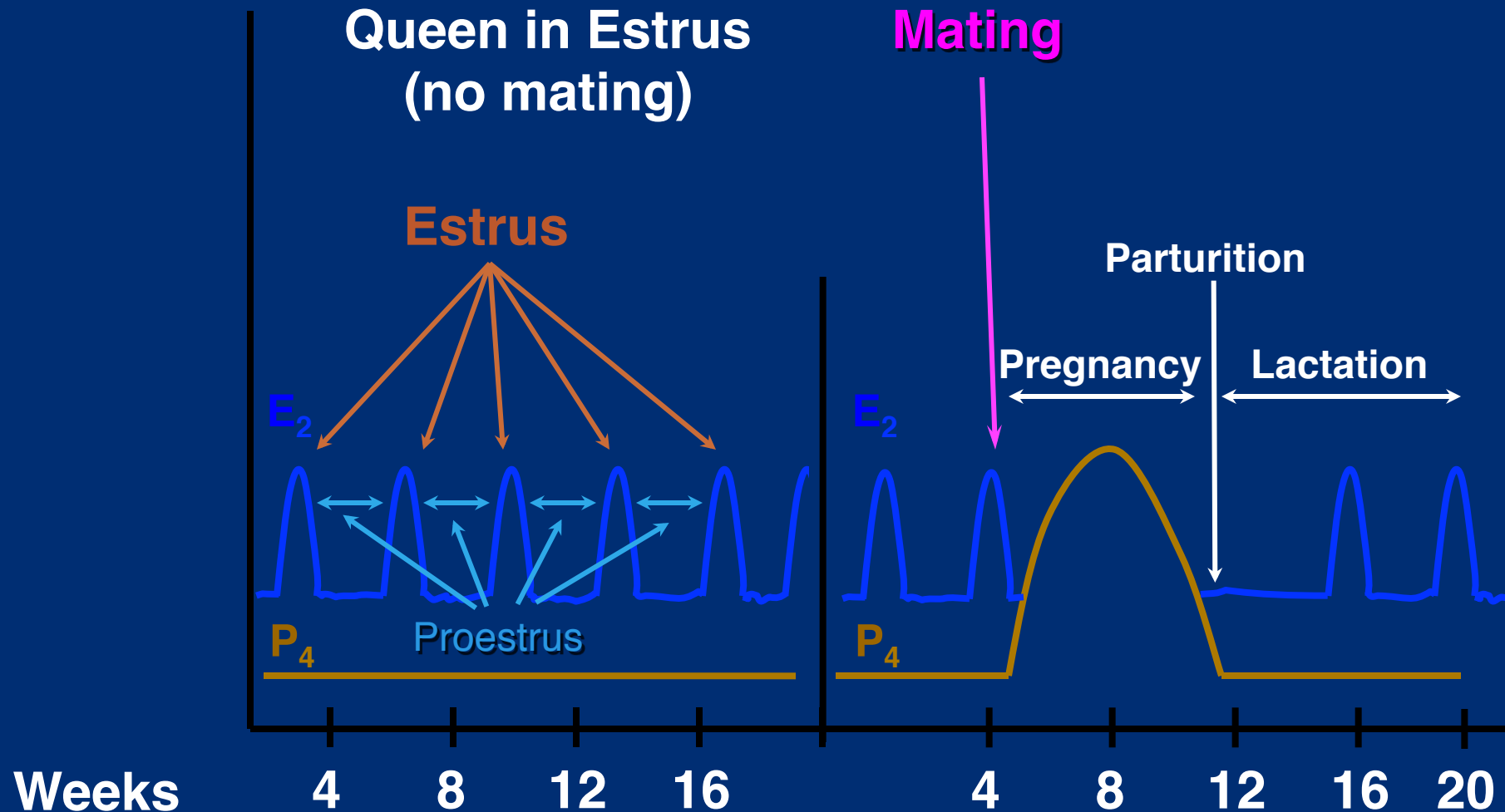
- Tom cats go through puberty, defined by first appearance of sperm in the ejaculate, at 8-12 months of age.
- The penis of male cats is encircled at the level of the corpus cavernosum glandis by 100-200 cornified papillae, commonly called penile spines. These are androgen-dependent; they appear at 6-7 months of age and disappear after castration.



Feline Fertility

- Historically, it was thought that the engorged penis of the tom and/or the penile spines stimulated the cervix of the queen to induce ovulation. Watson and Glover recently demonstrated that queens will not emit a characteristic coital vocalization when the cervix is probed, but will when the posterior vagina is stimulated. They also showed that the erect penis of the tom cat is too short and too large in diameter to reach the cervix of the queen, suggesting that stimulation of the posterior vagina is necessary for ovulation induction in this species.
- Mature tom cats are capable of mating repeatedly over a 4-5 day period without a decrease in sperm numbers.

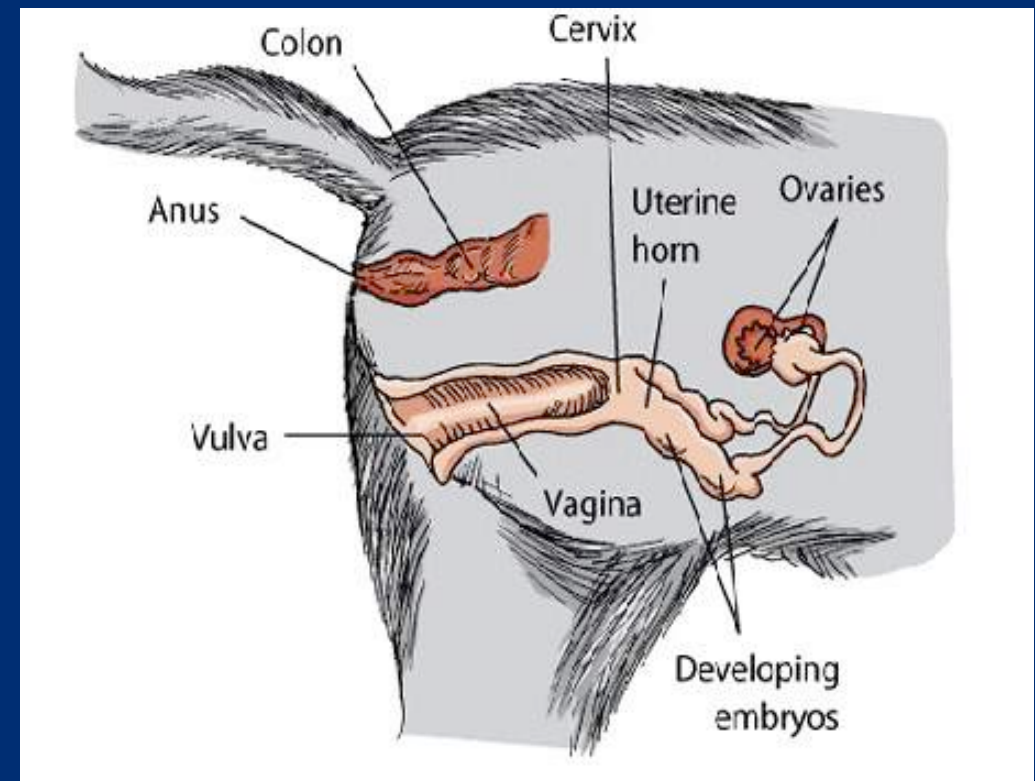
Hormonal Changes in the Queen



Feline Female Reproductive Anatomy

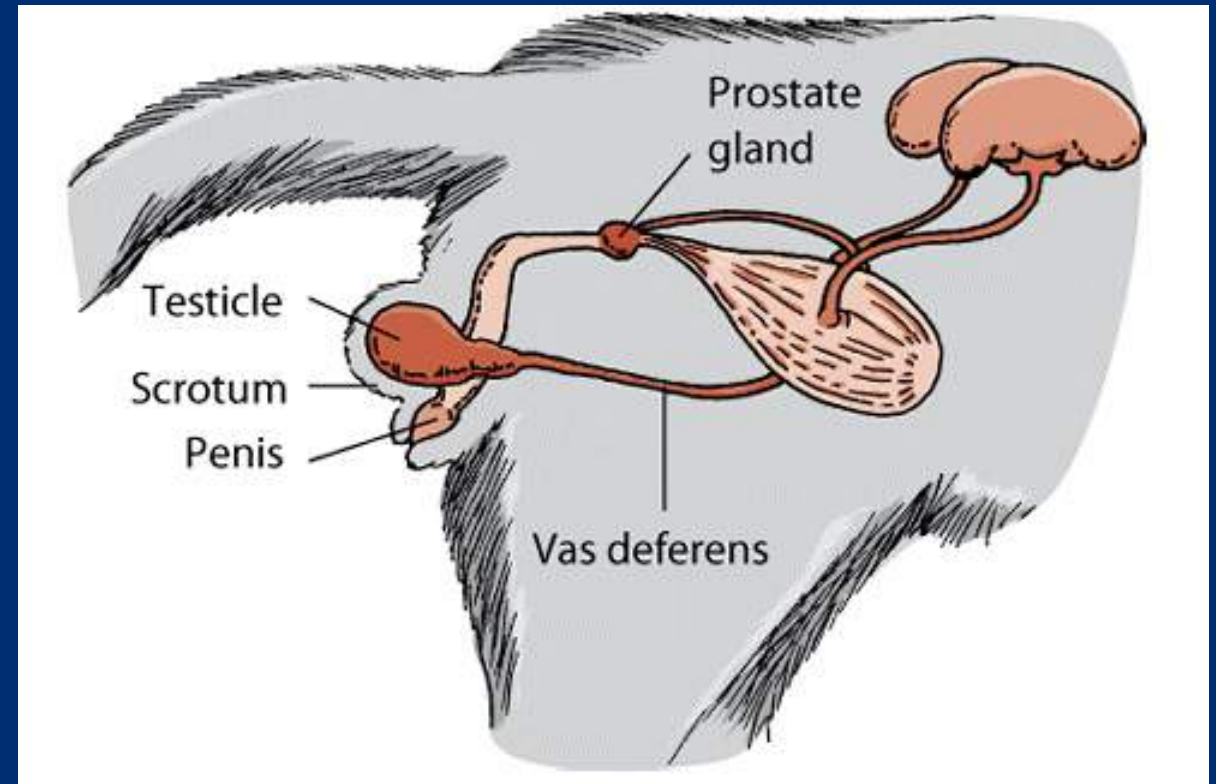
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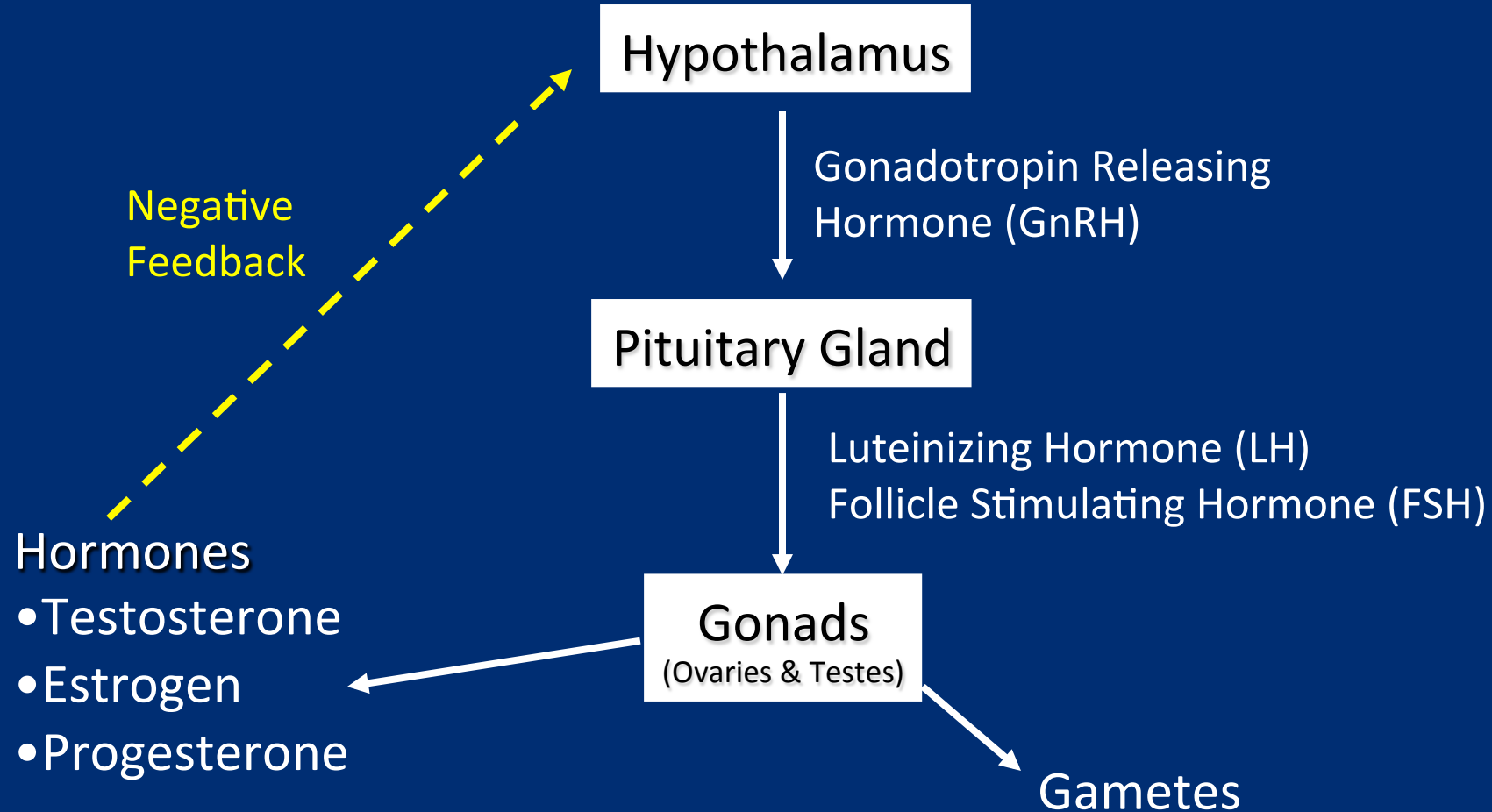


Feline Male Reproductive Anatomy

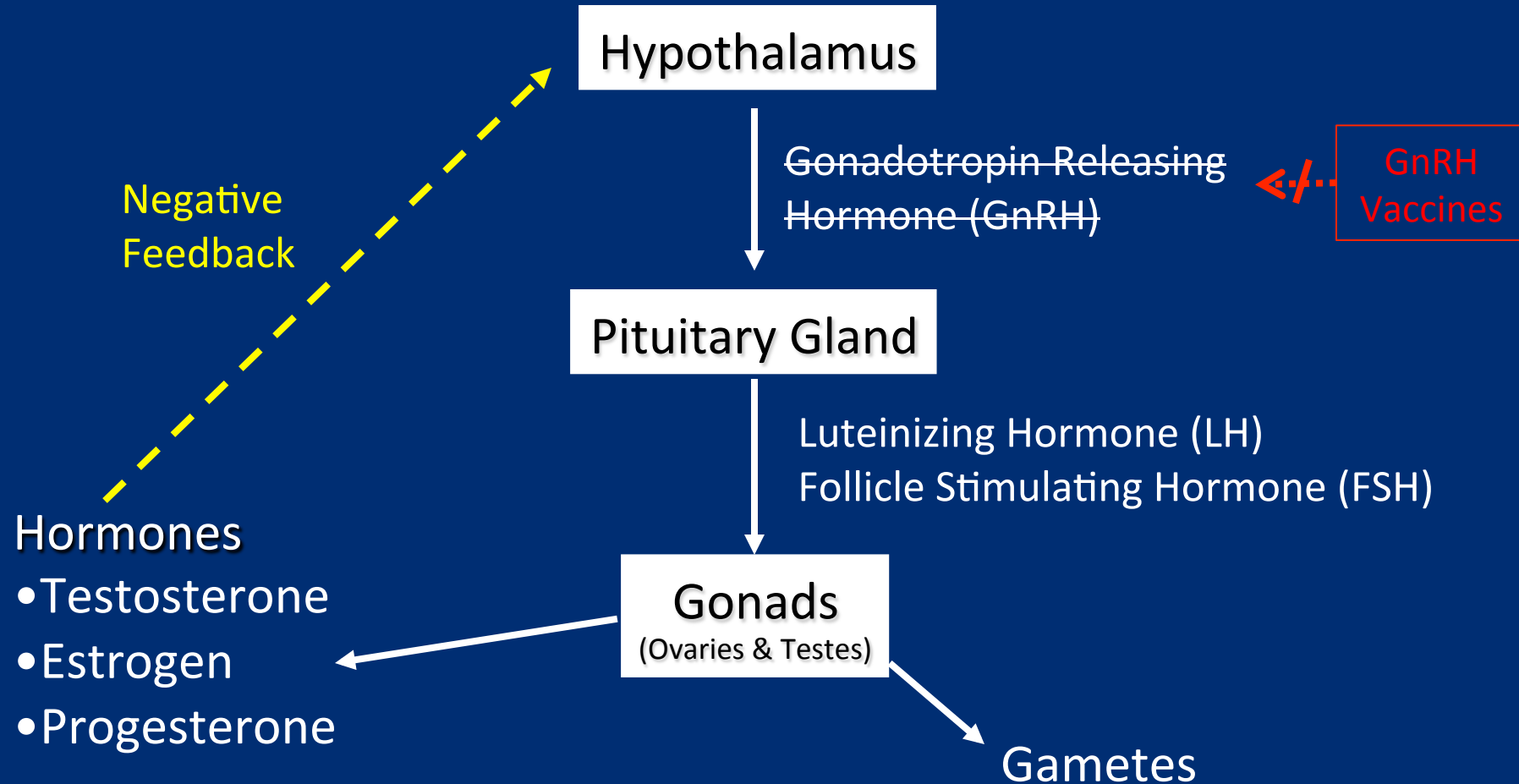
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Reproductive Control



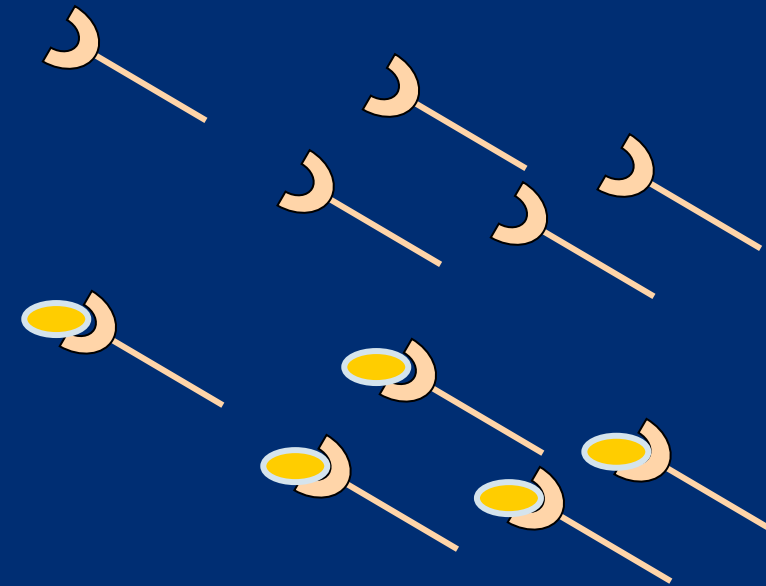
Reproductive Control



Slimmy receives a rabies vaccine.

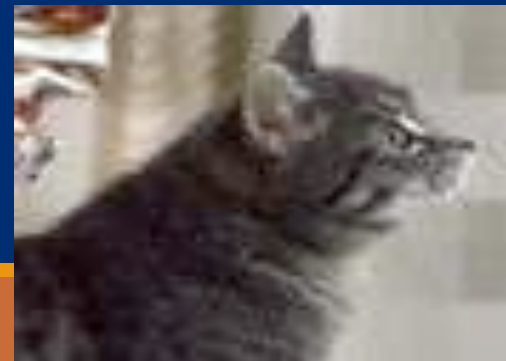


Her body makes antibodies against the virus.



If exposed to the virus, circulating antibodies bind it. The virus does not reach its receptor.

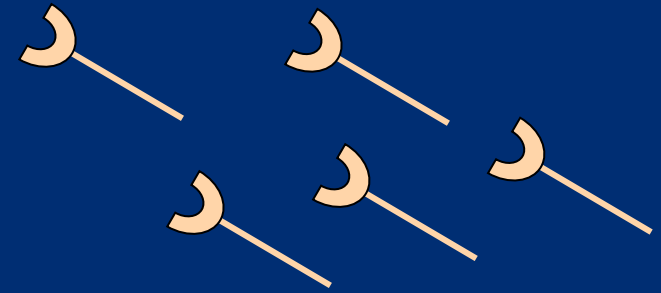
Slimmy does not contract clinical rabies.



Hey, thanks!

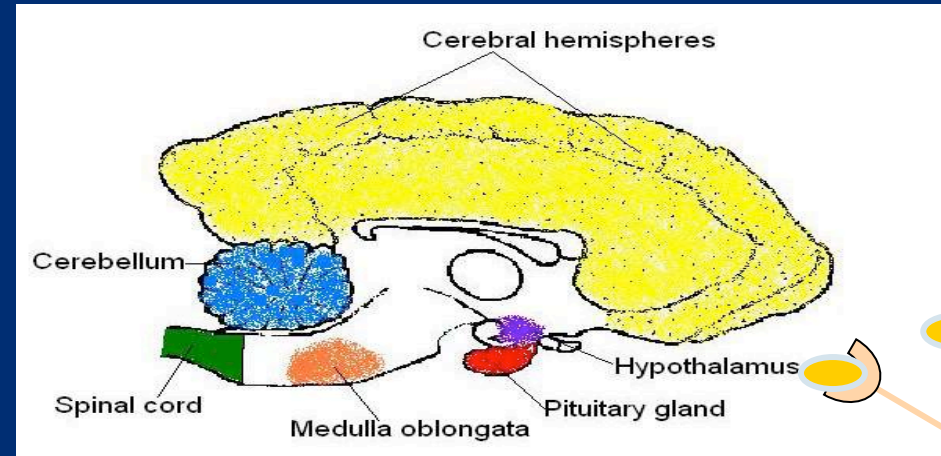
Slimmy receives a GnRH vaccine.

Her body makes antibodies against her own GnRH.



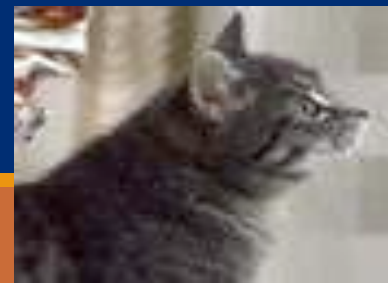
When her hypothalamus releases GnRH, antibodies bind it.

GnRH does not reach its receptors in the pituitary.



FSH and LH are not released.

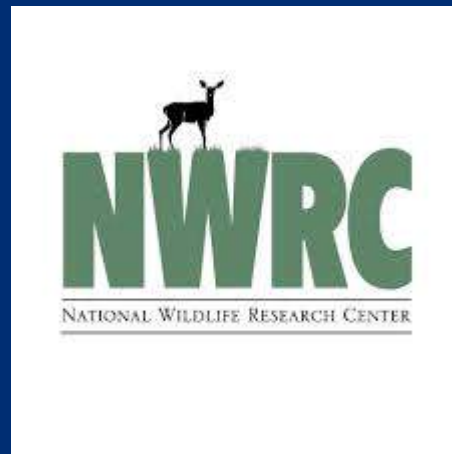
Slimmy is contracepted.



GonaCon

Overview:

- Developed by USDA-NWRC
- EPA registered for use in white-tailed deer (2009) and wild horses and burros (2013)
- Contraceptive effect in many other species



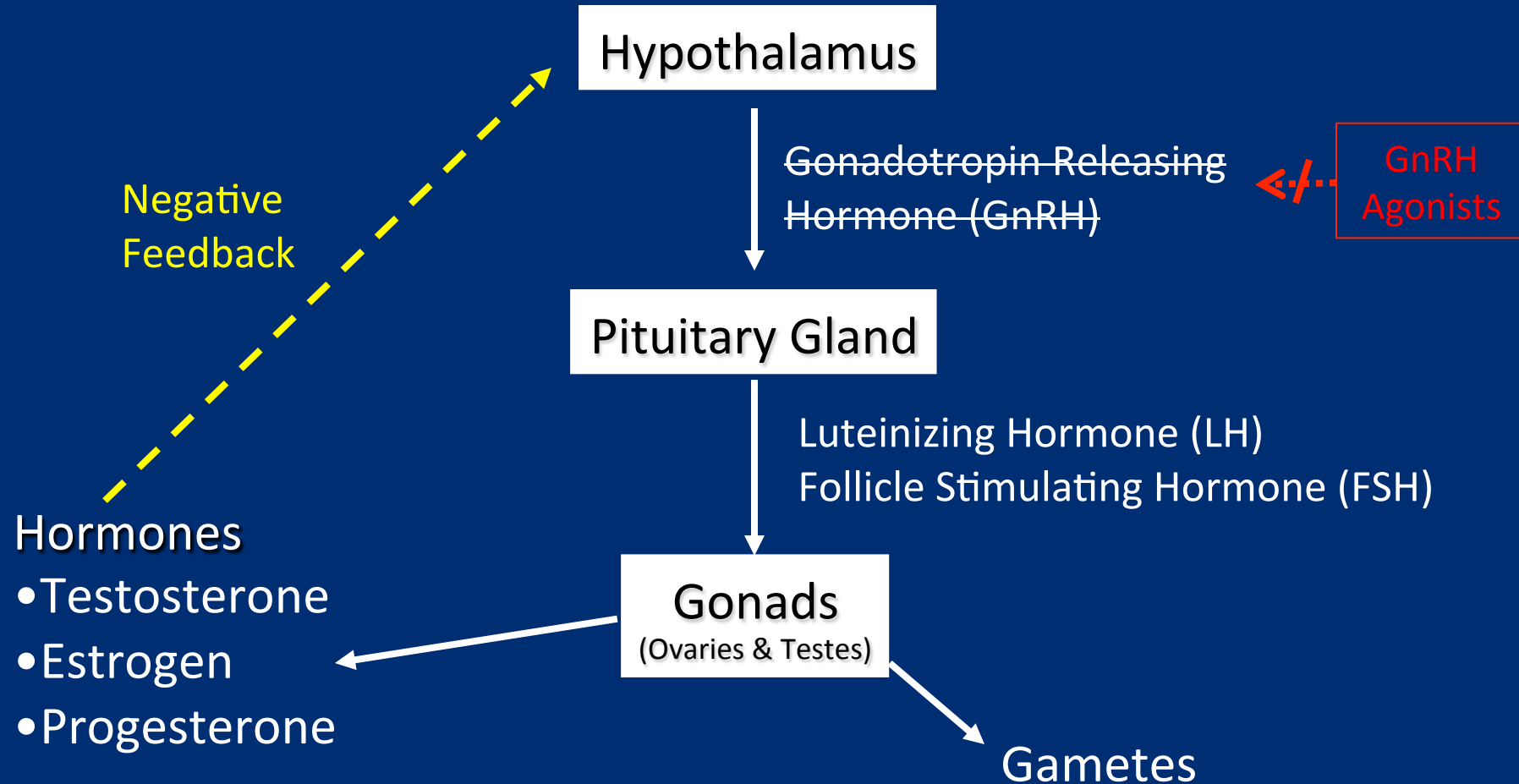
GonaCon

- Dr. Levy's studies demonstrated safety, efficacy & suppression of sexual behaviors in male & female laboratory cats.
- ACC&D's field trial in wild-bred cats did not show the same efficacy.



Photo: Julie Levy

Reproductive Control



Deslorelin / Suprelorin®

VIRBAC, formerly Peptech Animal Health

- GnRH agonist
- Delivered by implant
- Approved in Australia, New Zealand and EU for male dogs
- FDA-indexed product to treat adrenal tumors in ferrets
- Research also conducted with:
 - Female dogs
 - Male/female cats



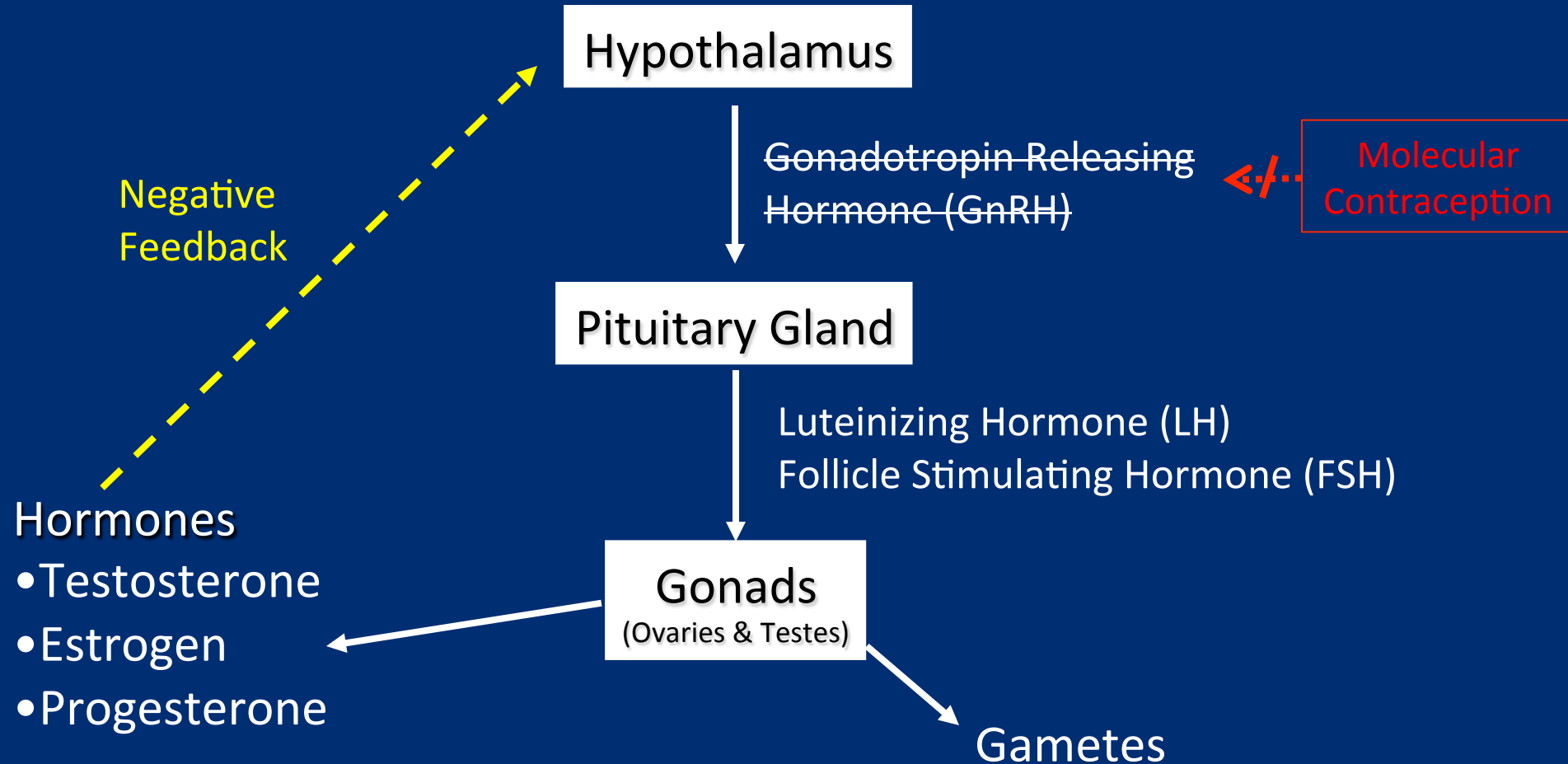
Dogs with No Names

Dr. Judith Samson-French
and her team implant
dogs on First Nations
Reserves with Suprelorin.

dogswithnonames.com





Reproductive Control

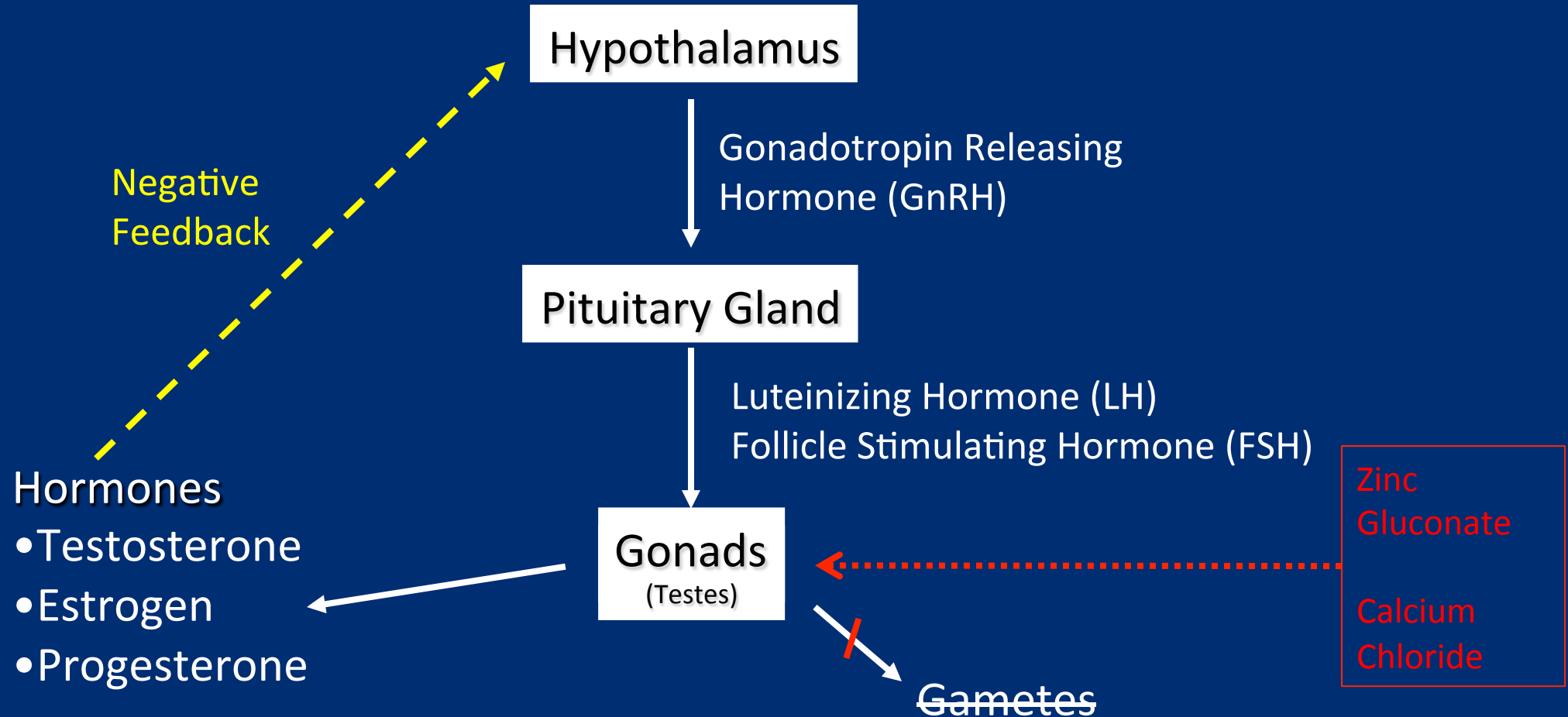


Chemical sterilization

The use of chemical compounds which destroy and/or render ineffective essential component(s) of the reproductive system

- Current approaches are for males
 - Zinc gluconate neutralized by arginine
 - 
 - Calcium chloride
 - 

Reproductive Control



New York Times

December 2, 2013

“New Strides in
Spaying and
Neutering”



Wall Street Journal

November 26, 2014

“Too Many Dogs: A Simple Solution”

Too Many Dogs: A Simple Solution for Sterilization - WSJ



ESSAY

Too Many Dogs: A Simple Solution

A cheap, quick, relatively painless procedure could make a big dent in overpopulation. What's stopping it?



A cheap, quick, relatively painless procedure could make a big dent in canine overpopulation. What's stopping it?

3 MONTHS FOR JUST \$1 ACT NOW

[http://online.wsj.com/articles/too-many-dogs-a-simple-solution-for-sterilization-1417187544\[1/29/2014 10:08:58\]](http://online.wsj.com/articles/too-many-dogs-a-simple-solution-for-sterilization-1417187544[1/29/2014 10:08:58])

Zinc Gluconate

Zinc gluconate used in a sterilization clinic in the Dominican Republic (2010)



Calcium Chloride

Calcium Chloride castration of male dogs.

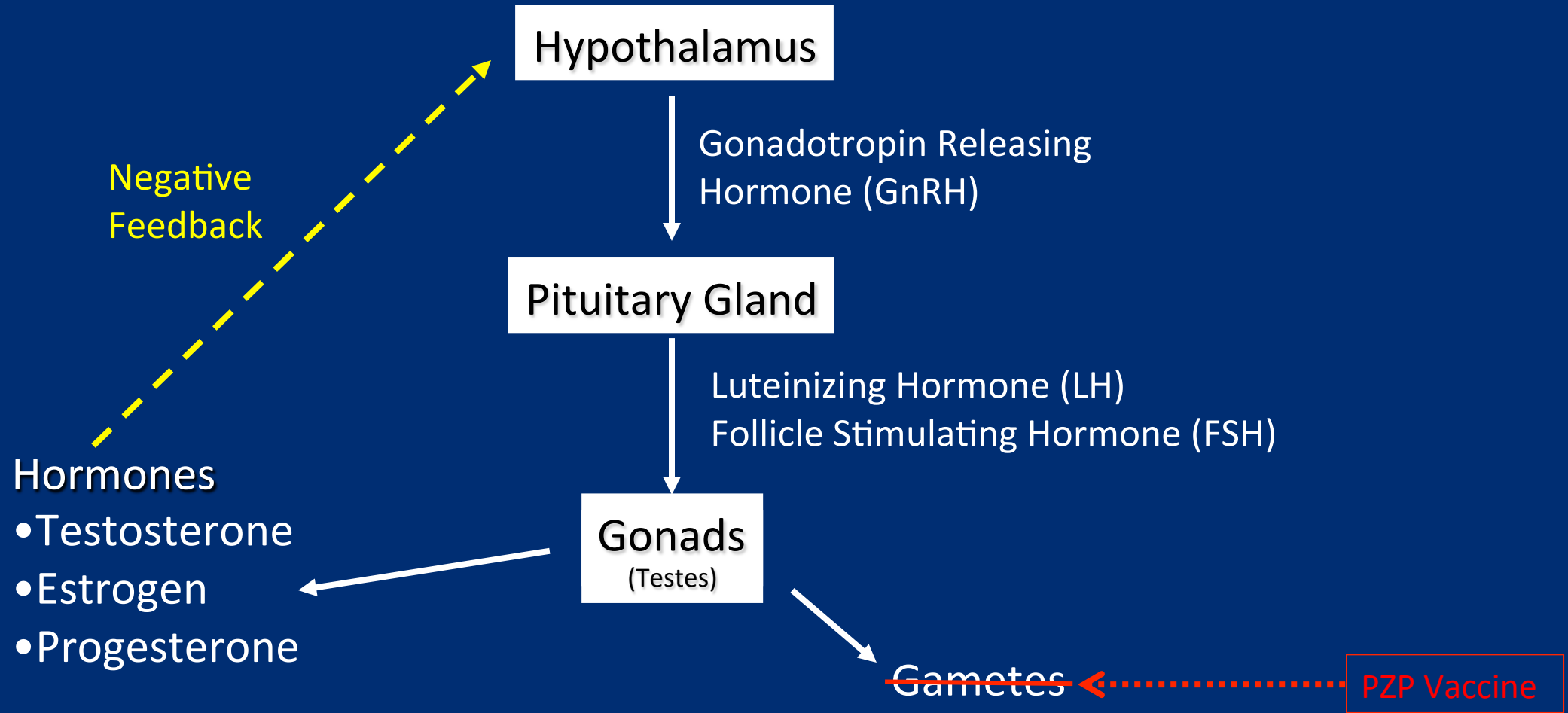


Calcium Chloride

ACC&D Position Statement on Calcium Chloride:

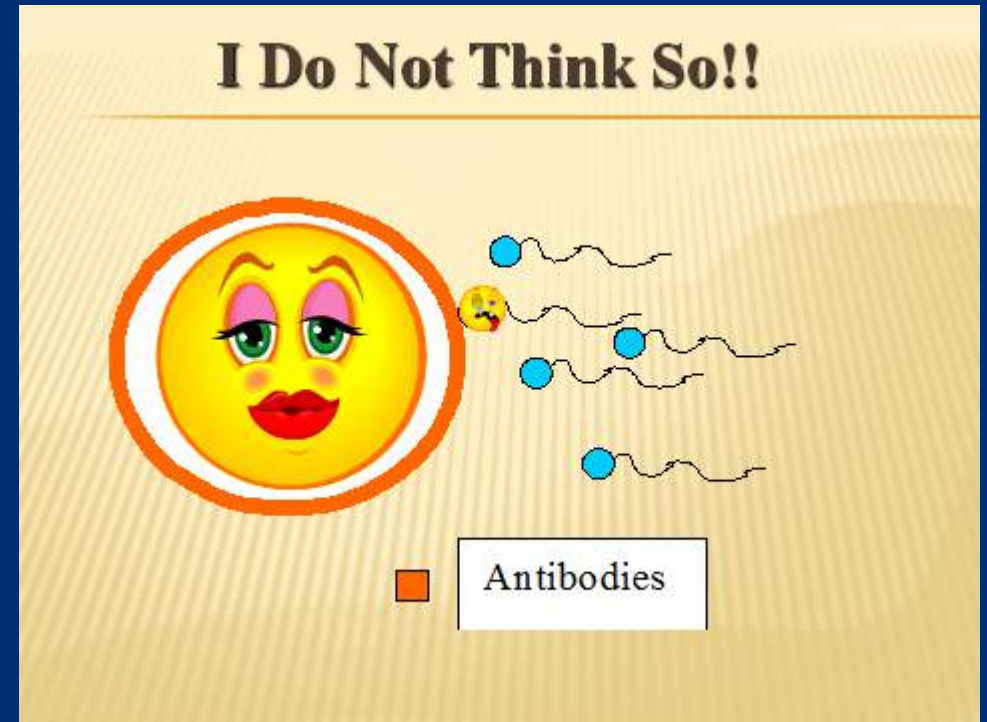
- To our knowledge, CaCl_2 has not been reviewed or approved by any regulatory agency for use as an animal sterilant.
- ACC&D believes that the current use of intratesticular CaCl_2 as a sterilant should be considered experimental.

Reproductive Control



Porcine Zona Pellucida (PZP) Vaccine

The anti-PZP antibodies interfere with fertilization by binding to the ZP glycoprotein receptors that surround the egg of the treated female animal, blocking the binding and subsequent penetration of sperm.



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*Thank you for attending this
primer on reproduction.*



Alliance for Contraception
in CATS & DOGS

acc-d.org



imagine...

preventing unwanted litters without surgery



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Questions?