

## May Deslorelinacetate be used safely in bitches for contraception? A retrospective clinical study

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Section of small animal reproduction

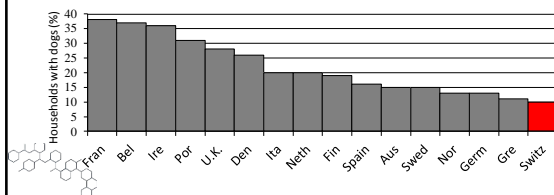


### Material and methods

- Background
- Aims
- Material and methods
- Results
- Conclusion

### Dog population in Switzerland

- Privately owned dogs: 0.5 millions (1 dog/16 habitants)
- Females: 62% spayed, males 35% neutered
  - No dog over-population
    - No stray dogs
    - Dog population in shelters constant
  - Strict laws (obedience training, microchip, registration)



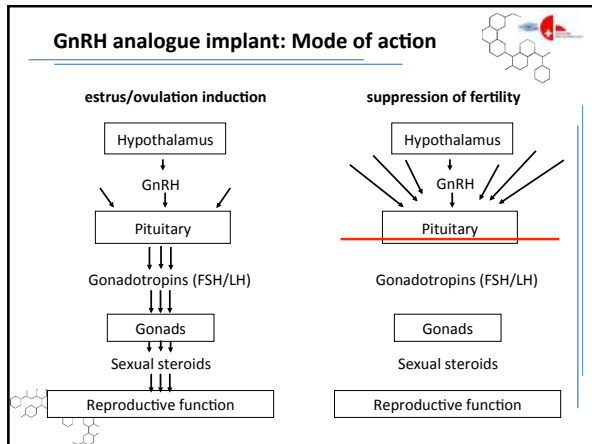
### Need for

Alternative to spaying (in dogs with a high risk for side effects of spaying)



Fully reversible contraceptive for future breeding bitches

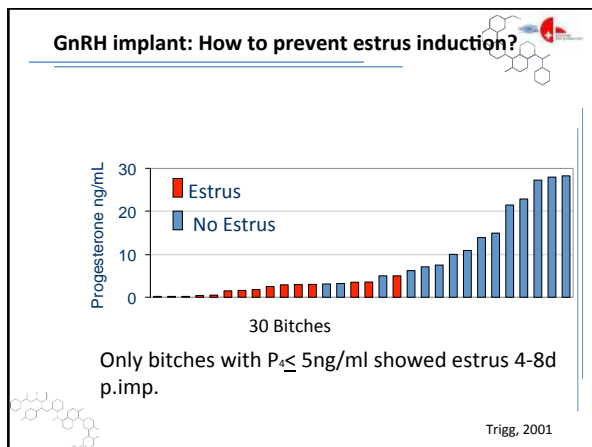




### GnRH analogue implant

Trigg et al., 2001: Use of a GnRH analogue implant to produce reversible long-term suppression of reproductive function in male and female domestic dogs

- Deslorelin at all doses increased duration of the mean interestrus interval and suppressed estrus for periods of up to 27 months
- 6/9 bitches became pregnant in first heat after recovery
  - 4 gave birth to healthy litters
  - 2 were necropsied close to parturition
    - treatment-induced effect on fertility is reversible
- No inflammation at site of implantation



### Off label use in bitches

In 2009 release of Suprelorin® (Deslorelinacetate)

- Temporary suppression of fertility in male dogs
- Off-label use in bitches:
  - To prevent induction of estrus, first application during diestrus (progesterone influence)

Effectiveness of Deslorelin Acetate for the Suppression of Heat in the Bitch ?

## Material and methods

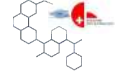


### Retrospective study

- Inclusion criteria:
  - Intact bitch
  - At least one Suprelorin® implant to suppress estrus
- Telephone interview with the owner (questionnaire)
- Interview with the veterinarian of the patient
- History of the dog
  - Time of first implantation
    - Stage of estrus cycle, weight of the dog
  - Implant size and number of retreatments
- Success of treatment
  - Side effects
  - Failure of estrus suppression



## Bitches

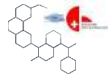


n=102

- Patients from our clinic (n=31)
  - Patients from 20 other veterinary clinics/practices (n=71)
  - 47 different pure breeds and 7 mongrels: Eurasier, Boxer, Cocker Spaniel....
  - Median weight 26 kg
- Implantation
- Time of first implantation: median age 21 months
  - P4 in 54 bitches (values above 5 ng/ml)
  - Dosage/dog: 4.7 mg, 2 x 4.7 mg, 9.4 mg
  - Frequency of implantation: 1 to 5 times
- Median observation period of 316 d



## Material and methods

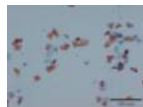


### Def: Failure of estrus suppression

#### Estrus signs

#### A: Major criteria

- Mating observed
- Acceptance for mating
- Estrogen level increased
- Superficial cells in vaginal smear



#### B: Minor criteria

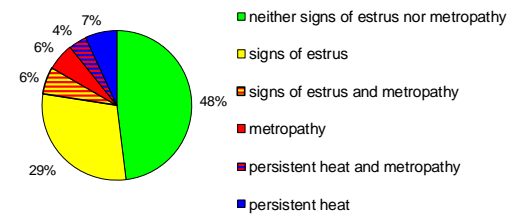
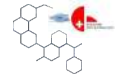
- Attractiveness to males
- Enlarged vulva
- Bloody vaginal discharge
- Bilateral alopecia



One major criteria, two minor criteria



## Results




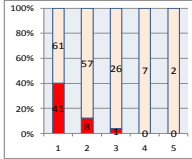
### Results: Failure of estrus suppression

47 bitches out of 102 (46.1%)

- 26 with a confirmed P4 > 5ng/ml

Risk factors?

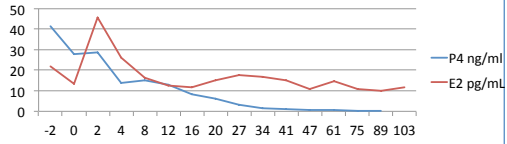
- Age: Bitches were older (31 months) than unaffected ones (19 months), P=0.003
- Frequency of implantation: 0.0026
- (Body weight: P=0.9)
- (Dosage / kg: P=0.167)
- (Progesterone >5ng/ mL: P=0.9)

### Failure of estrus suppression

Application of implant during diestrus does not prevent E2 increase: prospective study (Körber et al. 2013)

- 18 bitches implanted with 4.7mg Suprelorin
- 3 groups (diestrus, anestrus, estrus)
- In diestrus (n=8): increase of estradiol-17-β

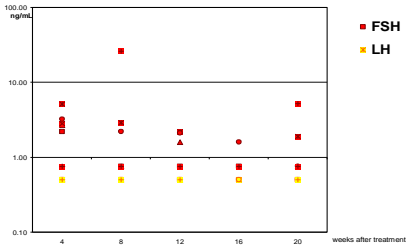


- Application in anestrus: induced heat
- Application in estrus: prolonged heat

### Failure of estrus suppression

Dogs with estrous signs

- FSH 0.4 – 12.5 ng/mL
- LH 0.6 – 3.0 ng/mL

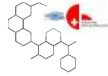


### Are there possibilities to avoid induced estrus?

- Pretreatment with Osaterone acetate 0.5mg/kg for 2 days prevented estrus signs and ovulation in 68,7% of the bitches
- Pretreatment with progestins: No consistent data
- GnRH-Antagonists only delay, but do not prevent the initial flare-up effect of GnRH-Agonists
- No effect with
  - Aromatase inhibitor anastrozole 0.1mg/kg
  - Anti-estrogen clomiphene acetate

Wright 2001  
Corrada 2006  
Sung 2006  
Hermo 2006  
Valiente 2009  
Fontaine 2011  
Anjofras 2011

### Prepubertal bitches

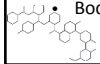


Trigg 2006:

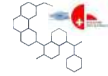
- 9.4mg deslorelin at 4 mo of age (n=6)
  - 9.4mg deslorelin at 7 mo of age (n=6)
  - Placebo at 4 mo of age (n=6)
- All bitches implanted at 7 mo of age showed estrus signs - 1-2 wk p.imp.
- No bitch implanted at 4 mo showed estrus signs during observation period (36 wk)
- Control group: 5 showed first estrus 12-28 wk p.imp.

Schäfer-Somi 2012

- 10 bitches (mean age 4 months) 4.7mg deslorelin
- No signs of estrus but increase in superficial cell index
- Body development unaffected



### Six prepubertal bitches in our study



Effectiveness

5 dogs (6-8 months) showed for 1-21 days signs of heat (2-13d after GnRH-treatment)

1 bitch (5.5 months) no signs of heat

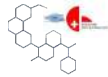
Retreatments

- Once n=2,
- Twice n=3
- Three times n=1

All owners are satisfied (n=1) or very satisfied (n=5)



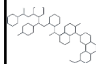
### Results: Persistent estrus



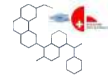
Persistent estrus: estrus signs lasted at least 7 d longer than in the regular cycle of the bitch (before implantation)

n=11

- Treatment required n=7
- OHE n=5, implant removal n=2



### Results: Persistent estrus





Persistent estrus: Noblesse, Borzoi, female, 7 years old



**Results: Uterine disease**


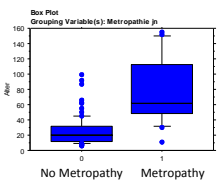
16 out of 102

Reduced general condition: n=6  
 Treatment : OHE (n=14)  
 Implant removal and conservative treatment (n=2)

**Results: Uterine disease**

16 out of 102, risk factor age!

Affected bitches are older (62 months) than unaffected ones (21 months), ( $P < 0.0001$ )

**Other side effects**

Urinary incontinence: n=4  
 Body weight changes  
 - Weight gain: n=28  
 - Weight loss: n=2  
 Pseudopregnancy: n=32 (+15)  
 Coat changes: n=29

Similar side effects are described in other studies

- Induced lactation
- Persistent estrus
- Ovarian cysts, depression and cystitis
- Behavioural changes
- Cystitis, Vomiting, allergic reaction

Fontaine 2011  
 Anjolras 2011  
 Arit 2012  
 Göricke-Pesch 2013

**Owners**

satisfied n=57  
 unsatisfied n=37  
 no comment n= 8


Retreatment:

- yes n=53
- no n=46
- not decided n=3

**Conclusion**

Deslorelin is an alternative to spaying

- in young bitches
- in bitches with high risk of side effects due to spaying



"Sheila"  
female Boxer, born May 07

**Conclusion**


Deslorelin is an alternative to spaying

- in young bitches
- in bitches with high risk of side effects due to spaying

Owner should be advised about

- possibility of failure of estrus suppression despite application during diestrus
- possible necessity of implant removal or spaying

Application at the umbilical region



Further studies are needed!

Thank you for your attention!



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