Canine pregnancy

when something goes wrong

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When something goes wrong

- Failure to conceive
- Early embryonic death / abortion
- Abnormal pregnancy
- Health of the pregnant bitch
- Dystochia / C-secton
- Medication in pregnancy
Early pregnancy failure

- Mating is successful – no pregnancy

- Failure to concieve
  - anovulatory cycles
  - failure in fertilization

- Conception but pregnancy failure
  - early embryonic death
  - abortion
Anovulatory cycle

- Imbalance in hypothalamus-pituitary-ovary axis

- Clinically:
  - Heat often matures to standing heat
  - Progesterone rises to 10-15 nmol/l
  - Short interestrus interval
  - Split heat
Anovulatory cycle

• Diagnosis
  – flushing oviducts

• Treatment:
  Split heat – no treatment
  Suppression of the next heat with deslorelin implant or progestagens in order to get into balance with ovaries, pituitary and hypothalamus
Fertilization
Failure in fertilization

- Failure in transport of gametes in the genital track
  - Infection in the genital trace may disturb the transport of the gametes
- Old / defected gametes
  - Timing of mating
Failure in fertilization

• Diagnosis
  – flushing the oviduct / uterine horn after mating

• Undirect method
  – change the partner
When something goes wrong

- Failure to concieve
- Embryonic death / abortion
- Abnormal pregnancy
- Health of the pregnant bitch
- Dystochia / C-secton
- Medication in pregnancy
Early embryonic death

- Embryo = < 30 D fetus
- Dead embryo is absorbed – no vaginal discharge or other clinical symptoms
- Causes equal to abortion
<table>
<thead>
<tr>
<th>Day Range</th>
<th>Event Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>D0</td>
<td>LH max</td>
</tr>
<tr>
<td>D2</td>
<td>Ovulation</td>
</tr>
<tr>
<td>D4-5</td>
<td>Oocyte maturation</td>
</tr>
<tr>
<td>D5-7</td>
<td>Fertilization in the oviduct</td>
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<tr>
<td>D9-10</td>
<td>Embryos enter uterine horn</td>
</tr>
<tr>
<td>D12-17</td>
<td>Migration</td>
</tr>
<tr>
<td></td>
<td>◦ Ipsilateral horn 3 days</td>
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<td></td>
<td>◦ Contralateral horn 3 days</td>
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<tr>
<td>D17-18</td>
<td>Attachment to the uterine wall</td>
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<tr>
<td>D18-20</td>
<td>Implantation</td>
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</tbody>
</table>
Embryo development

• D21
  • Neural tube closure

• D30
  • Organogenesis completed
  • Fetal sac diameter 3 cm

• D40
  • eyelids, nails, furcoat, marks

• D42-45
  • bone calcification

• D46...
  • Tissue maturation, fetal growth
Relaxin - Questions!

- Can we use relaxin to indicate embryonic/fetal death, for how long?
- Does decrease in relaxin predict abortion?
Pregnancy detection

• Clinical signs
  – No specific signs, individually yes

• Palpation
  – 3-4 wk

• Ultrasound
  – Embryo sac 17 D from ovul.
  – Fetal heart beat 25 D from ovul.

• X-ray
  – After 45 D

• Relaksiini
  – After 25 D
Clinical signs

– Vulvar swelling lasts after heat

– Nipple enlargement from 3. wk on ..

– Inappetite 3-5. wks

– Mammary inlargement 5 wks ..

- Clear vulvar discharge 5. wk..

- Abdominal distension 5. wk..

- Fetal movement 7. wk..

- Males are interested
Palpation of pregnancy

– 3 wk
   Embryos about
   1.5 cm, round, elastic

– 4 wk
   About 2 cm, oval, elastic

– 5 wk
   Elasticity disappears,
   difficult to diagnose

– (7-)8 wk
   Fetuses are palpable
Embryo resorption / abortion

D degenerative (mucometra, hydrometra..)

A anomalies (hereditary, nutritional deficiencies...)

M metabolic (diabetes, hypothyroidism, adrenal diseases, hypoluteoidism)

N nutrition (undernourished)

I infection (brucella, E.coli, Str, Staph, Parvovirus, Toxoplasmosis..)

T tumors, toxins
Anomalías

- Most severe cases - no fertilization
- Severe cases – early embryonic death
- “milder” cases – full term puppies with various defects
Anasarca
Be careful!

Ultrasonographical finding of **transient** embryo malformation

- Transit fetal hydronephrosis
- Spontaneous resolution of anasarca

Anomalies

• Diagnosis:
  – During parturition / C-section
  – Ultrasonography in late pregnancy

• Treatment:
  – If the defect can be fixed
    – operation of the puppy
  – Mostly euthanasia
  – Hereditary aspect!!!
Metabolic

- Canine pregnancy is dependant on ovarian progesterone production
Hormones in gestation

- Luteotrophic
  - LH - pituitary
  - Prolactin - pituitary
  - Relaxin - placenta

- Luteolytic
  - PGF2α - placenta
  - Oxytocin - pituitary
Hypoluteoidism

- Progesterone < 15 nmol/l 4-5. week
- Not properly confirmed in dog
- Hereditary luteal dysfunction - In breeding bitches may be important to check for breeding soundness evaluation
Hypoluteoidism

• Diagnosis:
  – weekly progesterone testing necessary

Treatment (confirming diagnosis)
supplementation with
medroxyprogesteroneacetate 0.1 mg/kg SID
or
alternogest 0.08 mg/kg SID

- blood progesterone testing possible
- progestagens may cause masculinization of female fetuses and prevent lactation
Nutrition / Body condition

- Underweight
  - Low leptin and estrogen levels – disturbances in estrus cycle
  - Pregnancy toxemia

- Overweight
  - Problems in parturition

- Nutrition
  - Folic acid
    - Deficiency causes cleft palate
    - Develops within 30 days of pregnancy

  - Diet may influence epigenetic marks and modify gene expression in early pregnancy (Sinclair et al. 2007)
  - Dietary hyperthyroidism induced anestrus (Sontas et al. 2013)
Nutrition in pregnancy

• + 10% energy / week from D 40 until parturition

• Folic acid 5 mg PO starting before heat, continue until second half of pregnancy
Infections

- **Virus**
  - Herpes canis
  - Distemper
  - Parvo?

- **Bacteria**
  - Brucella canis
  - Other
    - Nonspecific (E.coli, Streptococcus sp, Staphylococcus sp, ...)
    - Specific (Salmonella, Listeria,..)
Infection

• Brucella canis

Brucellosis is an important zoonotic disease causing major economical losses in kennels
Brucella canis

Common

- Asia (Japan, China ..)
- Africa (South Africa, Nigeria, Tunis..)
- America, Canada

Sporadically in Europe

- Germany
- Czech
- Spain
- Hungary
- Austria
- Sweden
- Finland

Estimated seroprevalence 6-8 %

Free (2012)

Australia
New Zealand
Brucella canis

Transmission

- genital organs in coitus
- contaminated environment:
  (oral, nasal, vaginal discharge,
   traumatisized skin,
   conjunctiva, semen, urine)
Brucella canis

• Macrophages transfer bacteria into lymph nodes, spleen and genital organs
• In acute infection lymph nodes swell
• Bacteremia develops within 1-4 weeks and persists up to 6 months (~5.5 years)
• Incubation time
  2 weeks - 6 months
Brucella canis

• Clinical
  – abortions after 40 days pregnancy

• Subclinical
  – infertility
  – normal litters may be born
Brucella canis

• Both sexes may present
  – Lethargy
  – Weight loss
  – Lymph node enlargement
  – Discuspondylitis
  – Panophtalmia
Brucella canis

• Diagnosis
  – Serological
  – Blood culture
  – Tissue culture
  – Histopath.

• Treatment
  – No treatment is totally successful
  – Spaying / castration
  – Eradication of positive dogs in kennel
  – Euthanasia
Brucella canis

• Breeding dogs must be seronegative

• Eradication:
  – All seropositive animals
    • euthanasia
    • Spaying / castration + transferred from the kennel
  – Serological test from all dogs in kennel every 3 months until all samples are negative
  – Desinfection of the environment
Brucella canis
Finland

• 2008
  – Mixed breed bitch from abroad with diskuspondylits and eye symptoms – spayed, treated, recovered

• 2013
  – Pregnant bitch from abroad, whelped in Finland 10 puppies
    • Dam, 5 puppies and the male brucella positive
    • Bitch was euthanized

• 1960 brucellosis last time in Finland (bovine)

• 2009
  – 388 clinically healthy dogs examined serologically in 94 kennels
  – No antibodies was detected
Brucella canis
Sweden

• 2011
  • American staffordshireterrier
  • first case in Sweden
  • Serbian dog mated a bitch from Poland
  • abortion
  • euthanized
  • source of infection not identified

• 2013
  • Miniature schnauzer
  • abortion
  • euthanized
Other infections

• Opportunist bacteria
  – E.coli, Proteus, Streptococcus, Staphylococcus ...

• Special pathogens
  – Salmonella
  – Listeria
  – ...

May or may not give signs

*fluid in the uterus
*vaginal discharge
*infertility
*acute infection
Other infections

• Culture!
  – Vaginal discharge
  – Fetal fluids
  – Foetuses

If infection is suspected from previous pregnancy
  – sample from deep vagina before mating

• Antibiotics
  - short (10 days)
  - starting before mating–to term

Avoid unnecessary treatment – multiresistant strains of common bacteria!
Antibiotic treatment of healthy bitches with CEH

- Degenerative changes in endometrium
  - Decrease myometrial contractions after mating
  - Uterine fluid clears slower after mating
  - RI is higher – lower uterine perfusion

- Mating induced endometritis
  - Antibiotic treatment increased pregnancy rate

(England et al. 2012, Perturbed sperm-epithelial interaction in bitches with mating induced endometritis)
Infection

• Herpes canis
  – Primarily neonatal deaths
  – Early embryonic deaths? / abortions
Herpes canis

• Respiratory disease
  – Transmission through oronasal fluids
  – Mild disease, often unnoticed

• Vesicles in genitals (preputium, penis, vagina) may be a source of infection for the partner and the puppies born.
Herpes canis

- Latent carriers!

- Diagnosis
  - Serology
    - High for about 2 months after infection
    - Paired serum test 4 wk interval
  - Virus isolation /PCR
    - Swabs from fresh lesions
  - Autopsy of the puppies
Herpes canis - prevention

Isolation
  pregnant bitch
  3wk prep to 3 wk pp

Avoid stress

Desinfection

Vaccination

AI is recommended

• Vaccination:
  – Eurican herpes (Merial)
    • 1st 7-10 d after mating
    • 2nd 7-10 before parturition

If all dogs in the kennel are seropositive:
  no vaccination needed

If all seronegative:
  vaccinate and isolate
Herpes canis

• Bitch with herpes-litter, can be used normally for further breeding

• Not all reproductive problems are herpes!!!
Tumors / toxins

• Rare but possible
When something goes wrong

- Failure to conceive
- Embryonic death / abortion
- Abnormal pregnancy
- Health of the pregnant bitch
- Dystochia / C-secton
- Medication in pregnancy
Abnormal pregnancy outcome

Special cases

- Vaginal discharge
  - Most common sign in problems of pregnancy
- Torsio uteri
- Inguinal hernia
- Uterine wall rupture
Vaginal discharge

- **Clear mucus**
  - Common in 3-5 wk pregnancy, normal
  - Mucometra

- **Bloody discharge**
  - Placental detachment
  - Infection
  - Tumors
  - May be harmless if only few drops in early pregnancy

- **Pus**
  - Infection in uterus, vagina, bladder
  - Tumors in vagina, uterus

- **Green discharge**
  - Uteroverdin – always placental origin
  - Emergency case
Vaginal discharge – how to proceed

• Is there an infection?
  – Check the discharge
    • US
      – Liquid in the uterine lumen
    • Cytology
    • Culture

• How are the puppies?
  – US:
    • Heart beats
    • Circulation of placenta
    • Age of pregnancy
    • Feetal fluids

• How is the bitch?
  • Fever
  • Pain
  • General condition
  • Progesterone and relaxin assays
Torsio uteri

- Late pregnancy
- Large litter
- Large breed
- Acute abdominal pain
- Vomiting
- Vaginal discharge

- Treatment of shock
- After stabilization of the condition
  - Surgical correction
  - C-section / OHE
Inguinal hernia

• Usually symptomless
• Swelling of inguinal reagon, not painful, uni/bilateral
• Diagnosis – embryo/fetus detection with US

• If early preganancy – surgical correction

• In late preganancy and acute cases – C-section / OHE
Uterine wall rupture

- Case:
  - Whelped 4 days ago normally
  - Now contractions, pushing hard
  - C-section: abdominal anasarca puppy
  - Spayed – bitch survived
When something goes wrong

- Failure to conceive
- Embryonic death / abortion
- Abnormal pregnancy
- Health of the pregnant bitch
- Dystochia / C-secton
- Medication in pregnancy
Health status of the pregnant bitch

- Eclampsia
- Diabetes
- Pregnancy toxemia
- Odema
- Body condition - nutrients
Physiology of pregnant bitch

**Leukocytosis**
- *blood 25,000*
- *leucocytes in vaginal cytology!*

**Insulin resistance**
- direct or indirect influence of high progesterone on mammary GH secretion

**Increase in weight**
- *20-55%*
- *absolute additional need for proteins and energy*

**Feeding pregnant bitch**
- +150% energy of maintenance feeding during last 3 wk
- +200-300% during lactation
Physiology on pregnant bitch

Anemia
* 7-9 wk
* back to normal in 8-10 vko pp
* increase in plasma volume

progressive
normocromatic
normocytic

• PCV
  pregnant -30%
  pseudopregnant -20%

• Hemoglobin
  pregnant -30%
  pseudopregnant -20%
Eclampsia

Ca need increases towards the end of gestation

Milk secretion
Myometrial contractions

- Occasionally prepartum
- Usually during lactation (within 4 weeks pp)
- Small bitches with large litter
- Excess Ca in food during pregnancy
Eclampsia

Diagnosis:

- Lab: Ionized Ca in serum
- Panting
- Salivation
- Facial pruritus
- Stiffness, ataxia
- Restless
- Aggressive
- Hyperthermia
- Heart frequency high
- Convulsions

Treatment

- *10% calcium gluconate slow iv injection (1-20ml)
- *in uncontrolled seizures: diazepam 1-5 mg iv or barbiturates
- *hypoglycemia corrected if present
- *hyperthermia should be controlled
Gestational diabetes

insulin resistance

PU/PD
Polyphagia with weight loss
Pregnancy acromegalia
Macrosomia (oversized fetuses) – risk for dystochia
Gestational diabetes

Diagnosis

high blood sugar

Treatment

*insulin may be needed
decrease the dose
gradually towards parturition
*termination of pregnancy when the condition is severe
*oversized fetuses – c-section

70% of cases resolve after parturition
Pregnancy toxaemia

uncommon in dogs

small bitches with large litters and poor nutrition and/or anorexia
Pregnancy toxaemia

**Diagnosis:**
- ketonuria without glucosuria or hyperglycaemia
- hepatic function may be affected

**Treatment:**
- improve nutrition
- termination of pregnancy
Odema

Large breeds
Venous thrombosis should be ruled out with US

Treatment:
gentle exercise
diuretics with caution!
When something goes wrong

- Failure to conceive
- Embryonic death / abortion
- Abnormal pregnancy
- Health of the pregnant bitch

- Dystochia / C-section
- Medication in pregnancy
Parturition

Decline in progesterone
  - Clinically seen as body temperature drop
  - $< 5 \text{ nmol/l}$ – parturition starts within (12)-24 h

Change in temperature correlates with the size of the bitch
  - large $37^\circ\text{C}$
  - middle $36^\circ\text{C}$
  - small $35^\circ\text{C}$
• Full term pregnancy

  – 65 ± 1 D from LH max
  – 63 ± 1 D from ovulation
  – 57 D from cytological diestrus
  – 57-70 D from mating
Ultrasonographical examination of pregnancy

- Harmless
- Live fetuses
- Number of fetuses
- Duration of pregnancy / size of fetuses
- Malformations / Abnormal fluid accumulation
- Blood velocity / RI index may predict abortion
Timing of pregnancy  (D = LH max)

- 17-23 D
  small vesicle, no embryo
- 23-27 D
  small embryo attached to the uterine wall
25-35 D
  bipolar embryo attached in tubular yolk sac, skull ventricles
  heart beat from D 27..
- 35-37 D
  Most of the structures detectable
  Foetal diameter < uterine horn diameter
- 38-42 D
  Length of foetus = length of placenta
  > 48 D
  gall bladder, large pulmonal veins
- > 57 D
  peristalsis
- < 4 D before parturition teeth
X-ray / pregnancy

- Radiation!
- Bone calcification!
  - too early X-ray – false negative diagnosis
- Number of fetuses
- Dystocchia
Parturition

- Normal litter is born in approx. 8 hours (6-12h)
- > 24 hours, involvement is needed
Idiopathic preterm labor

- No infection, metabolic, congenital, traumatic, toxic cause identified
- Myometrial contractions

- Hypoluteoidism – cause or consequence
  - Does hypoluteoidism cause myometrial contractions or contractions cause luteolysis?
tocodynamometry
Idiopathic preterm labor

• Diagnos:
  – Based on history
  – Regular measurements of contractions ap

• Treatment:
  – Terbutaline 0.03-0.04mg/kg PO 8-12h
  – Early use(<40D) in bitches with history of PTL prevents myometrial contractions
  – Bitches studied carried to term without supplementation of progesterone
Cesarean section
Dystochia / C-section

• Indications for surgery
  • Full/overtime, no signs of parturition
  • Stage 2. (contractions) does not start – inertia uteri
  • Secondary inertia
  • Fetal fluids expelled, no puppy born within 2-3 hours – check!
  • Heavy contractions >30 min, no puppy
  • Health status of the bitch
C-section – anesthesia requirements

- Safe
  - for the bitch
  - and the puppies

- The bitch should quickly recover from anesthesia to be able to nurse the puppies

- Anesthetics cross placenta easily – depress breathing of puppies

- Newborn liver is not able to metabolize anesthetics
C-section - anesthesia

• All sedatives, pain killers and anesthetics penetrate placenta

• Quick removal of foetuses is essential for pup survival
  – First puppy should be born within 15 min from start of anesthesia

• Stabilize the bitch
  – Iv fluids
  – Check glucose and Ca – correct if needed

Dorsal recumbency may disturb circulation in vena cava leading to lower cardiac stroke volume and blood pressure
C-section - anesthesia

• Premedication (not recommended)
  – Morfin 0.3 mg/kg im or
  – Metadon 0.25 mg/kg iv or
  – Alpha-2-agonists (cardiovascular stress)
    Agonists available!

• Local anesthetic/epidural
  – Lidocain 2%
  – Good, bitch may move!

• Induction
  – Extra oxygen!
  – Propofol 6-8 mg/kg
    • Quickly metabolized by puppy liver
    Alfaxolone (neurosteroidal anesthetic)
    Ketamine may dause marked depression!

• Maintenance
  – Isofluran, sevofluran
C-section - anesthesia

• Pain control

• NSAIDs
  – May lead to kidney failure in puppies
  – A single dose perioperatively

• Opioids
  – Perioperatively
  – Pp if needed
Take home message
(Haga, 2014, EVSSAR Wroclav)

• Preoperative stabilisation
• Maintain blood pressure
• Preoxygenation
• Rapid airway control
• Several options for anaesthesia/analgesia are available
• Alpha-2-agonists, thiopental and ketamine less optional for neonates
Prognosis in C-section

- **Good**, both for the bitch and the puppies done within 12 h after beginning of 2\(^{nd}\) stage of labour
- **Fair** for the bitch, questionable for the puppies 12-24 h
- **Bad**, >24h whole litter is usually dead
- When the litter is dead, life of the bitch is quickly threatened
- **Be sure not to do elective c-section too early**
When something goes wrong

- Failure to concieve
- Embryonic death / abortion
- Abnormal pregnancy
- Health of the pregnant bitch
- Dystochia / C-secton
- Medication in pregnancy
Medication of the pregnant bitch

• Avoid any medication!

• Evaluate pros and cons

• Time of administration versus fetal development
Antibiotics

**May cause problems:**
- Chloramphenicol (bone marrow)
- Metronidazole (teratogenic)

**Do not use:**
- Fluoroquinolones (cartilage defects)
- Doxycycline, tetracycline (bone and teeth, toxic to mother)

**Safe:**
- Ampicillin
- Amoxicillin + clav.ac.
- Cephalosporins
- Clindamycin

**Use with caution:**
- Sulfadimethoxine
- Sulfonamides
- Trimetoprim
- Tylosin
Other drugs

- **Antifungals**
  - Ketoconazole
    - Teratogenic in rats
  - Miconazole
    - Safe topically

- **Anthelminths – safe:**
  - Fenbandazole
  - Ivermectin, selamectin
  - Praziquantel
  - Pyrantel

- **Pain killers**
  - NSAIDs
    - nephrotoxic
  - Opioids
    - Respiratory depression
      (nalozone antidote)

- **Anesthetics**
  - Ketamine (depression)
  - Isoflurane, sevoflurane
    (depression)
  - Propophol (depression)
Other drugs

• Corticosteroids
  – (cleft palate, other malformations, premature labour)

• Anticonvulsants
  – Diazepam
    (Congenital defect in rats)
  – Phenobarbital
    (rare congenital defects, bleeding tendency)
Thank you!