Repeat breeding in domestic animals

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Repeat Breeders

Definition
A cow/buffalo that has normal estrus & estrous cycle yet fails to conceive after 3-4 or more inseminations

Repeat Breeders are defined as a heterogeneous group of sub-fertile cows with no anatomical abnormalities or infections, that exhibit a variety of reproductive disturbances in a consistent pattern over three or more heat cycles of normal duration (Perez Mana and Espana, 2007)
A manifestation by the animal due to multifactorial etiology

Global Problem

Modern day high producing Holstein cows due to intensive selection for high yields have reduced fertility (Dobson et al., 2007)

Incidence: 06 to 35%

2nd most common reproductive disorder

More common in cows vs buffaloes
ETIOLOGY  Fail. Fert & EED

Predisposing Factors
Nutrition  Negative energy balance
   High Protein changes uterine pH & decrease P4
   Micronutrients Ca, P, Mg, Cu, Zn, Vit A, E, Se

Endocrine dysfunction (suprabasal P4)
Infection/reproductive tract abnormality
Poor semen quality
Age
Genetic
Immunologic Antisperm antibody
Peri-Parturient disease
Stress  Heat most important
Repeat Breeding

**Male**
- AI
  - Poor semen quality
  - Cryo-preservation damages
  - Frozen sperm ½ life
  - Buffalo semen season
- Natural Service
  - Poor Nutrition
  - Over-Use

**Female**
- Nutritional Inadequacies
  - Lack of energy (NEBAL)
  - Excess of Protein
  - Deficiency of Minerals vitamins
    - Specially Vit A, C, E and Se, Ca and P
- Hormonal dysfunction
  - Ovarian cysts
  - Supra-basal Progesterone
  - Low LH
  - Low luteal progesterone
  - Aberrant estrus
- Reproductive tract abnormality
  - Ovaro-bursal adhesions
  - Kinked cervices tubal blockage
- Infections Endometritis
  - Bacteria, viruses, protozoa, fungi
- Genetic problems and Immuno-infertility
- Stress like heat, cold etc
- Environmental pollutants
- Metabolic disorders
- Peri-parturient disorders
- Housing

**Other factors**
Serives required per conception is the standard for assesment of the problem

- At conception rates of 70, 60, and 50 percent 2.7, 6.4 and 13.0% of healthy cows require 4 services to conceive.

- Low conception rates could be because of sub-optimal semen quality, faulty AI, poor hygiene and with poor CR the number of services required may further increase hence it remains difficult to define the repeat breeding problem for individual cows however, in herds----------------
Indices to assess the severity of herd problem of infertility

<table>
<thead>
<tr>
<th>Assessment Index</th>
<th>Normal</th>
<th>Slight problem</th>
<th>Moderate problem</th>
<th>Severe problem</th>
</tr>
</thead>
<tbody>
<tr>
<td>% pregnant to a given service</td>
<td>&gt;65.0–60.1</td>
<td>50.1–60.1</td>
<td>45.0–50.0</td>
<td>&lt;50.0</td>
</tr>
<tr>
<td>Services/ Conception of all served cows</td>
<td>&lt;1.54–1.66</td>
<td>1.99–1.66</td>
<td>2.2–2.0</td>
<td>&gt;2.2</td>
</tr>
<tr>
<td>Calving to service interval Days</td>
<td>&lt;60.0–65.0</td>
<td>70.0–65.1</td>
<td>85.0–70.1</td>
<td>&gt;85.0</td>
</tr>
<tr>
<td>Days Open (Calving to conception)</td>
<td>&lt;80.0–82.5</td>
<td>85.0–82.6</td>
<td>100.0–85.1</td>
<td>&gt;100.0</td>
</tr>
<tr>
<td>% submission of all calved cows</td>
<td>&gt;80.0–70.1</td>
<td>60.1–70.0</td>
<td>45.0–60.0</td>
<td>&lt;45.0</td>
</tr>
<tr>
<td>Non detected estrus</td>
<td>&gt;10.0–14.9</td>
<td>19.9–15.0</td>
<td>40.0–20.0</td>
<td>&gt;40.0</td>
</tr>
<tr>
<td>Heat detection rate</td>
<td>&gt;90.0–85.1</td>
<td>80.1–85.0</td>
<td>60.0–80.0</td>
<td>&lt;60.0</td>
</tr>
<tr>
<td>18-24 day return intervals</td>
<td>&gt;65.0–62.5</td>
<td>60.1–62.4</td>
<td>50.0–60.0</td>
<td>&lt;50.0</td>
</tr>
<tr>
<td>% needing 3 services</td>
<td>&lt;12.3–15.9</td>
<td>24.9–16.0</td>
<td>30.2–25.0</td>
<td>&gt;30.0</td>
</tr>
<tr>
<td>% needing 4 services</td>
<td>&lt;4.3–6.3</td>
<td>12.4–6.4</td>
<td>16.6–12.5</td>
<td>&gt;16.6</td>
</tr>
<tr>
<td>Culled as empty / year</td>
<td>&lt;5.0–7.1</td>
<td>10.1–7.2</td>
<td>13.0–10.0</td>
<td>&gt;13.0</td>
</tr>
</tbody>
</table>
Diagnostic Methods

- Record Analysis
- Visual
  - Proper estrus detection
  - Proper mating events
  - Colour, consistency of cervico-vaginal mucus

Vaginoscopic examination to exclude growths, adhesions

Uro-vagina uncommon can spoil semen
Recto-genital palpation

- Uterine tone at AI - subjective
- Follicle at AI
- Ovulation depression
- Early CL day 5 Sub-optimal
- Early Embryonic deaths Not possible to be detected as most deaths occur before day 20
Laboratory Tests

- Uterine pH
  - Normal pH 7.3
  - 6.9 and 8.0 suggest endometritis
- White side test to detect metritis
  - Cervical mucus + NaOH, Boil
  - Yellow colour indicates metritis
- Cervical mucus penetration assay
- Hemizona assay more to assess sperm function
- Metabolic profiles Glucose, Ca, P
- Karyotyping on lymphocytes
Other Tests

- Uterine biopsy and cytology

- PMNs > 18% suggest endometritis
In Vivo imaging techniques USG
Ultrasonography

- Luteal ovarian cyst
- Follicular ovarian cyst
- Uterine fluid accumulation
- Mucometra
Colour doppler  The frequency of a Doppler shift is typically between 100 Hz and 11 kHz, determines echogenecity and blood flow and hence can determine physiological status of follicles/ CL etc..

Power-mode image of vascularization (yellow-orange) of the corpus luteum of a cow

Schematic representation of a cow’s pelvic area
Magnetic Resonance Imaging

Magnetic resonance imaging is based upon relaxation of hydrogen protons in a large magnetic field after a radio-frequency pulse (RF) has deflected the proton spin transversely.

- Three dimensional images can predict ability of follicles to produce steroid and ovulate and hence can predict the exact physiology.
CT Scan (Computer assisted tomography)

- Uses X-Rays for diagnostic purposes

Only in the developmental stage in veterinary medicine
Hysteroscopy / Laparoscopy

- Evaluates morphology of live tissues
- Received little attention in bovine because of the cervix
- Flexible hysteroscopes more common
Hormone Assays

- RIA
- ELISA
- ECLIA

Immunosorbent assay

Progesterone assay

LH

Patency testing
Diagnosis of herd problem can be attempted but the diagnosis of cause of repeat breeding in an individual animal is extremely difficult.

**Therapy**

- Evaluate semen
- Evaluate for anatomic defects
- Evaluate for nutrition and management and advice appropriate measures of correction
- Evaluate reproductive hygiene and insemination procedures and adopt corrective measures
Herd

Correct deficiencies
Treat Bulls for minor problems
Change Bulls or evaluate semen
Vaccinate for infectious disease

Individual animal

Combating Uterine Infection
Monitoring for Ovulation/Cysts
Therapy of luteal insufficiency
Improving AI techniques
Improving management
Specific corrective measures

- Genital tract infection
  Intrauterine/parenteral antibiotics

Prostaglandins

Immunomodulators
  Oyster glycogen 500 mg in 50 mL PBS I/Ut.
  LPS 100 µg in 30 mL PBS I/Ut

Agents to alter Uterine environment
  Antioxidants: 4 mM Taurine + 50 mM fructose in PBS before AI
  Vitamin C Inj Ascovet 20 mL before AI
  Enzymes: Trypsin, Chymotrypsin, papain I/Ut.

Uterine motility stimulants
  Mifepristone, clitoral massage
Hormonal therapy

- Correction of Ovarian dysfunction
- Delayed ovulation
- hCG Injection Pubergen/Chorulon 1500-3000 IU at AI
- GnRH 100 Ug IM at AI
- PG at AI
- Antiprolactin Bromocryptine 10 mg orally 12 h before and at AI
- Dextrose 500mL IV at AI plus Bovine insulin 0.2 IU/Kg IV
- Clomiphene 300 mg orally
- Metformin 2000-4000 mg orally
Ovarian Cysts

Single IM injection of Progesterone
Vaginal progesterone implants
100 Ug GnRH
Ovsynch protocol
PG + GnRH (day 0) + PG (day 14)
Transvaginal US guided aspiration

Mucometra
Pott Iodide 10-15 gm daily with feed for 5-7 days
Ifer-H 2 mL SC
Luteal Insufficiency

- hCG injection at 4-5 days of AI
- Progesterone injection 500 mg at 5 days of AI
- Progesterone vaginal implants.
- Recombinant Bovine Somatotropin 500 mg SC at AI
- Antiestrogens Tamoxifen citrate ??
- GnRH at AI and at day 14-16
- Bovine insulin on day 8, 9 and 10 of estrus

Feeding of fish oil
Nutritional Management

- Management of dry cows important
- Advice not to feed more than 10% of rumen degradable proteins
- Dry cows should be fed low energy high fibre diet with more of chopped straw
- Feeding of anionic salts with Ca and P
- Injections of vitamin A, E and C important
Timing of AI/ Semen deposition

- Multiple AI in long estrus periods
- Training of AI Personnel
- Deep Intrauterine AI

Avoiding Periparturient disorders
- Metabolic diseases Ketosis/milk fever
- Parturient problems

Immuno-infertility
- More anecdotal
- Give vitamin C, E and dexamethosne
- Change the bull or semen
Other therapies  Acupuncture and Intraperitoneal AI or embryo transfer.

- Repeated inseminations
- Mineral vitamin supplements
- Cooling of heat stressed cows/ buffaloes
- Adequate hygiene at parturition & at AI
- Regular and frequent check of semen
- Addition of sperm motility enhancers when liquid semen is used eg. caffeine
- Prevention of natural mating with scrub bulls
Repeat breeder cow/buffalo → Exclude effects of season

Herd

Female

Investigate and advise

1. Nutrition (preparturient)
2. Collect samples for investigation of infectious disease
3. Reduce stress
4. Metabolic profiles

Male

AI

1. Evaluate semen and AI techniques

Natural mating

1. Infectious disease
   (i) Trichomonas
   (ii) Campylobacter
2. Semen evaluation
3. Age of bull

Individual

1. Investigate for abnormalities of genital organs like ovaro-bursal adhesions, cystic ovaries, tumours, stenosis, etc.
2. Investigate for subclinical endometritis. When no tests possible, treat on presumptions if there is a history of periparturient disease.
3. Monitor ovulations/oestrus cycle length
   (i) Provide ovulation induction treatments at AI
   (ii) Repeat AI/consider I/U AI
4. If animals do not settle, treat for luteal insufficiency.
5. Supplement with vitamins A, E and C and Ca, P and Se.
6. PSP dye test – if both fallopian tubes occluded. Exclude such animals.
7. Cytogenetic-karyotyping
Embryonic losses are reported to be 20%–30% in ewes, goats and sows

- The major reason for embryonic mortality is likely to be inadequate luteal function
- Consumption of toxic plants
- The injection of GnRH between days 10 and 13 after mating
- Progesterone FGA Day 4 after mating
Mare Embryonic Resorption

- Endometritis
- Alterations in progesterone levels, the uterine and oviductal environment, maternal age and postpartum breeding have all been implicated with causing EED, either directly or indirectly.
- Foal heat breedings
- Retarded development of the embryo
Progesterone supplementation is probably the most common method of treatment.

Administration of Regumate starting from Day 5 and continued till Day 120 and tapering thereafter.
Embryonic losses in camels

- Occurs between Day 20-90 of gestation
- Incidence 5-20%
- Diagnosis USG, plasma progesterone
- Day 15 and 35 important
Reasons of Embryonic losses in Dogs

Infectious Reasons

*Brucella canis*: The most important clinical signs are abortion in late pregnancy (after 45\textsuperscript{th} day) in bitches.

Although there are no clinical signs prior to abortion, a serosanguinous discharge may be observed for 1-6 weeks following abortion.

Recommended antibiotics for *B. canis* treatment are minocycline (25 mg/kg SID, 21 days) and ihydrostreptomycin (5mg/kg IM, 7 days) combined, tetracycline (30 mg/kg BID, 21 days) and streptomycin (20 mg/kg IM, 14 days) combined and per os enrofloxacin for 4 weeks.
• Fetal death, mummification, abortion, premature birth and stillbirth may occur if pregnant bitches are infected with canine herpes virus.

• **Neospora caninum:** *Neospora caninum* is a protozoan of which its final host is dog. *Neosporosis* causes early fetal death, mummification, fetal resorption and weak neonatals in pregnant bitches (6,8,11,12). However, it is not definite yet if *N. caninum* is the primary reason of natural aborts of bitches or not
• **Non-Infectious Reasons**

**Hypoluteodism:** Hypoluteodism is due to insufficiency of plasma progesterone concentration. The best option accepted in hypoluteodism treatment is daily administration of 0.1 mg/kg *Megestrol acetate* up to 62nd day of pregnancy.

• **Drugs:** Adverse effects of drugs in pregnant cause congenital malformation of embryo or fetus due to teratogenic effect or cause fetal resorption or abortion because of embryotoxic effects.
# Classification of drugs according to their safety during pregnancy

<table>
<thead>
<tr>
<th>Safe</th>
<th>Careful Operational Safety</th>
<th>Risky</th>
<th>Contraindicated</th>
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<tbody>
<tr>
<td>Amoxicillin</td>
<td>Antiemetics</td>
<td>Amikacin</td>
<td>Prednisolone</td>
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<tr>
<td>Ampicillin</td>
<td>Atropine</td>
<td>Amphotericin</td>
<td>Primidone</td>
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<tr>
<td>Antacids</td>
<td>Cimetidine</td>
<td>Aspirin</td>
<td>Propranolol</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>Diazepam</td>
<td>Amitraz</td>
<td>Salicylates</td>
</tr>
<tr>
<td>Clavulanic acid</td>
<td>Diphenhydramine</td>
<td>Betamethasone</td>
<td>Thiacetarsamide</td>
</tr>
<tr>
<td>Diethylcarbamazine</td>
<td>Dopamine</td>
<td>Captopril</td>
<td>Tobramycin</td>
</tr>
<tr>
<td>Digitalis</td>
<td>Furosemide</td>
<td>Chloramphenicol</td>
<td>Valproic acid</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Ketoconazole</td>
<td>Cortisone</td>
<td>Phenylbutazone</td>
</tr>
<tr>
<td>Fenbendazole</td>
<td>Metoclopramide</td>
<td>Dexamethasone</td>
<td>Phenytoin</td>
</tr>
<tr>
<td>Ivermectin</td>
<td>Ranitidine</td>
<td>Flumethasone</td>
<td></td>
</tr>
<tr>
<td>Lincomycin</td>
<td>Sulfasalazine</td>
<td>Flunixinmeglumine</td>
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<tr>
<td>Mebendazole</td>
<td>Sulfonamides</td>
<td>Gentamicin</td>
<td></td>
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<tr>
<td>Miconazole</td>
<td>Theophylline</td>
<td>Ibuprofen</td>
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<tr>
<td>Neomycin</td>
<td>Thyroxine</td>
<td>Indomethacin</td>
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<tr>
<td>Piperazine</td>
<td>Trimethoprim</td>
<td>Levamisole</td>
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<tr>
<td>Praziquantel</td>
<td>Metronidazole</td>
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<tr>
<td>Pyrantel</td>
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<tr>
<td>Sucralfate</td>
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The above lectures are also explained in video lectures at my YouTube Channel Govind Narayan Purohit

Kindly share the videos and subscribe to my channel if you like them

Thanks