BIOL30001 – Reproductive Physiology

Lecture 10.1: Manipulating Domestic Animal Reproduction I

- In an attempt to increase reproduction, or more importantly control it in terms of environmental manipulations and through diet and pharmacological interventions

Manipulating Reproduction

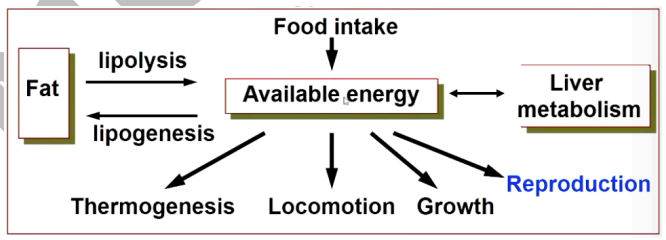
- Breeding at younger ages
- Advancing breeding season
- More frequent pregnancies
- Synchronisation of ovulation
- Induction of multiple ovulations
- Genetic improvement
- Artificial insemination
- Improved pregnancy rate
- Embryo transfer and associated techniques
- Pregnancy testing
- Control of birth timing

Increasing Fertility

- Many strategies that can be used – all about controlling reproduction
- Yellow = industry use
- Aim is to increase economy while decreasing labour

Nutrition, Energy and Reproduction

- Reproduction is definitely a luxury – a lot of things have to fall into place for it to successfully take place
- Animal must be in a state to be able to partition with extra nutrients
- Starvation
    - Anovulation
        - In a poor nutritional balance, it can lead to anovulation or sporadic ovulation
    - Inability to maintain pregnancy
        - Cannot invest enough nutrients – energetically costly for a mother
    - Inability to maintain lactation
        - Energy intensive for nutrient requirements
    - Suppressed sperm production
        - Can be hindered by low nutrition and stress
    - Altered behaviour
        - May not be able to attract partners as well



- Intense Exercise
    - Amenorrhea – often seen in gymnasts and athletes
- Obesity
    - Inhibition of ovulation
    - Inhibition of sperm production
        - due to accumulated adipose tissue surrounding the testes and therefore impaired thermoregulation
    - Behavioural modification
        - Lowered sex drive
    - Altered foetal nutrition
        - Incorrect partitioning of nutrients in the foetus
        - Obese women change the amounts of glucose sent to the foetus
        - Obese women tend to have quite small babies relative to their body size due to changed glucose diversion and partitioning
    - Parturition issues
        - Due to increased adipose tissue near the cervix

Nutrition

- Influence HPG axis acute and chronic effects – effects seen at the level of the brain
    - Patterns of LH secretion in a rhesus monkey on a normal day of feeding, during a day of fasting and during refeeding – the pulsatility is completely changed
- Nutrition and stress interaction
    - LH surges will be affected by increased cortisol levels
    - Ovulation number and egg quality – flush feeding
        - Farmers use this to their advantage; if they give more nutrients during a specific timeframe – there is potential for more offspring
        - Rather than overfeeding or underfeeding an animal – around conception (2-3 weeks before), the mothers are flush fed to increase the number of eggs that are ovulated – allows for twins or triplets

        - = less time + effort + more offspring
    - Sex ratio of offspring – in ruminants, can skew the sex
        - High energy diet = male offspring
        - High carbohydrate diet (+ negative energy balance) = female offspring
            - Farmers would want females in the offspring to allow for future breeding (milk)
            - Would want male offspring for the purposes of meat

Nutrition and Puberty

- Timing of breeding in sheep fed different diets to manipulate growth
    - In sheep the weight at which offspring go through puberty is ~35kg – however this does not occur if sheep are in the anestrus phase – don't go through puberty until they are 42kg when the breeding season starts
    - When it is breeding season, young will go through puberty at the right time
    - Group D is born right at the end of the breeding season and actually don't get a chance to go through puberty until the next breeding season – inefficient for the farmer (needs to feed and nurture for longer)
- Patterns of GnRH secretion in a rapidly growing and in a slowly growing lamb
    - In lambs that are rapidly growing, there are consistent GnRH pulses, however, in slowly growing lamb, GnRH pulsatility is uneven

Nutrition

- Resumption of cycles after calving and subsequent pregnancy rate
    - In cows, gestation is 9 months long – for a farmer to have an economic benefit, they would want their cows to have offspring once a year
    - This means, there isn't much gap between both pregnancies
    - This is dramatically affected by her body weight – 'body condition', which is a tactile measure of adipose across their body
    - Increase adipose deposition is actually better because she has extra reserves of energy to allow for another birth because leaner cows don't actually have a great capacity to carry offspring
    - Fatter cows generally have an increased ability to return to normal menstrual cycling again - needs several cycles before further conception
- Conception rate- bell-shaped distribution
    - If there is a low body condition score, she will have a decreased ability to conceive successfully – the same would occur if she had a very high body score.
    - The aim would be to achieve an optimal body condition score for greatest success
- Hormones related to this include: Leptin, Kisspeptin, Ghrelin and other hormones
    - Feedback onto the HPG axis and impact reproductive status
- Metabolic substrates
- Direct effect of nutrients

Nutrition: Micronutrients

- E.g. vitamin E and selenium
- Antioxidant – free radical scavenger
- Deficiency causes infertility in both males and females but by different mechanisms and effects vary between species
- In animals that have good nutrition, their conception rate is quite high compared to those with selenium deficiency – e.g. New Zealand cows
    - Reduced sperm motility and maturity
    - Rats: normal ovulation/mating but foetal loss after day 7
    - Cattle: silent heat, delayed conception, reduced fertilization, cystic ovaries, retained foetal membranes, metabolic disorders

Goats	Control	Selenium deficient
conception rate	93%	64%
infertile does	7.4%	36%
weaned kids/doe	0.89	0.36
milk fat (g/day)	41	36
milk protein (g/day)	32	28

Nutritional Factors

- Impact on females
    - Ovarian/oocyte
        - Energy (fat) content/ratio of the oocyte or zona pellucida – can be changed with fat
    - Uterine
        - pH environment may be impacted by tomatoes, capsicums (and other acidic foods)
            - Sperm swimming/signalling – viscosity
            - pH uterine inhospitable
            - proteins and secretions in uterus may also be affected by diet
        - Modulated lumen histotroph (nutrients – glucose, proteins)
    - Embryonic Loss
        - Glucose main substrate for embryo development – if there isn't enough nutrition, you impact the survival of the embryos
        - Modulated embryo – maternal communication (MRP): the larger the size of the embryo, the greater the amount of the interferon released – if you have a larger and faster growing embryo, you are more likely to get an embryo that will signal to the mother its presence (through the interferon) and therefore
        - Placentation failure – foetal reabsorption or abortion
- Impact on males
    - Testis development

        - Hormone regulation altered
        - Testicular mass and function
    - Sperm
        - Sperms themselves as composed of a number of fatty acids
        - Sperm tastes like your diet
        - Characteristics – low fatty acid diet = abnormal morphology

Manipulating Breeding Season

Why?

- Marketing – lambs
- Survival or young – don't want them born in peak Winter, would prefer birth in Spring
- Convenience – can synchronize feeding activities, can cross foster between young
- To fit artificial constraints e.g. horses – thoroughbred horses are all born on the same day – would want an individual born in the middle of the season

Methods

- Photoperiod
- Melatonin- can be added through very expensive implants
- Pheromones – can change the breeding season

Ram Effect

- Pheromones from ram induce increased LH pulsatility in ewes
    - Just before the breeding season, the farmer introduces a vasectomized ram that releases pheromones – this is enough to stimulate the start of that cycle in the females
    - Synchronization or ewes and lambing
    - Earlier breeding onset (seasonal) varies with bread
    - Allows maximization of use of valuable stud rams

Artificial Insemination

- First performed in 1800s in dogs
- Widespread commercial use began in 1950s when semen freezing and storing developed
- Facilitates genetics improvement of herds – easy way to access gene qualities from all around the world
- Global frozen genetics – avoids some quarantine restrictions for studs
- Insurance against death or injury
- Cost/benefit determines usage ($10-$100 straw)
- Heat detection – timing
    - E.g. cows are in heat for about 18 hours, the best fertilization rates occur insemination 12 hours after onset of heat
    - A female develops a lordosis when she is in heat – other females hump their female friends doggy style to signal to males they are ready to mate
    - KAMARs are little detection packs that release fluid when they have been humped on (visual cue)

Semen

- Collection
    - Artificial vagina – used in the dairy industry to collect semen
    - Bull ~12 billion (8mL) sperm per ejaculate
- Evaluation
    - Motility, morphology
- Dilution
    - Specialized media containing buffers and many cryoprotectants – mainly egg yolk, fructose (substrates for the sperm to survive)
        - Fructose for nutrients
        - Egg yolk for protection
    - Need 10-25 million sperm per straw – can be ready for use in 30 seconds
        - Pack in straws
        - Cool and freeze
        - Store it in liquid nitrogen – can be shipped all around the world
        - Thaw
        - Inseminate via cervix
        - Sexed semen – can actually get sex specific offspring from it – e.g. females = milk, males = mean

Improving Herd Genetics

- Desired improvements in productivity
    - Milk, meat, wool production
- Limited availability and high cost of top quality sires
    - E.g. top quality bull may be able to service 3-4 cows per day during breeding season – it can actually take six years to figure out if the bull is good or bad
- Proving bulls for AI at genetics Australia
- Large numbers → more accurate genetic diagnosis
- Faster time scale than with natural breeding

Pros and Cons of AI

Advantages	*Disadvantages*
• Increased production • Disease control • Sire availability (global) • Safety • Long term supply – upto 80 years	• Cost of semen • Technical skill to get sperm and inseminate as well • Can have lower success at conception • Potential for uterine injury or infection

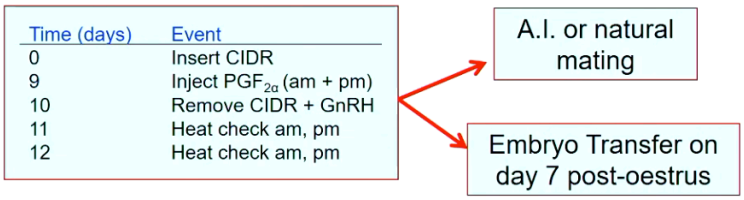
Synchronization of oestrus

Can be achieved through:

- Prostaglandin
  - Synthetic PGF2alpha– Cloprostenol administered to attempt to terminate the cycle and initiate oestrus
  - Induces luteolysis
    - As long as the animal is 11 days into the cycle, it causes the corpus luteum to regress and forces the follicle to grow very quickly and come out (speeds up ovulation)
    - The second injection will cause luteolysis and allows for tighter synchrony
  - One injection: oestrus 2-3-days after
    - CL only sensitive to PG after day 4 post-oestrus (or more)
  - Two injections 11(cow) or 9 (sheep) days apart – allows for increased synchrony – after first injections 80% might respond and the 20% may not. After second injection, most likely full synchrony will be achieved
  - Can be coupled with the use of a CIDR
  - Prostaglandins actually get removed from the body quite rapidly because they are very potent – removed by first pass by the lungs – therefore most effective to give PGs in the morning and evening
- Progestins
  - *e.g.* CIDR (controlled internal drug releasing device) – silastic implants put in the uterus, releases progesterone and
  - prolongs the cycle
  - Placed for 7-12 days then removed
    - physical removal of the CIDR will cause a drop in high levels of progesterone and mimic luteolysis
    - gets rid of any corpus luteum if it is still there – pulling out reduces the progesterone
    - CIDR + prostaglandin end the previous cycle and begin the next cycle (ovulation)
  - Check the animal for heat/ ovulation about 2 days after removal and then can add GnRH
- GnRH/hCG/eCG (PMSG)
  - Injection of GnRH as the CIDR is pulled out
  - Ovulation inducers
  - Ensure timing relative to AI, embryo recovery

Typical Oestrus Synchronization Program

- Many synchronization programs
  - Depends on species and country of use (legalization)
  - Depends on reason for synchronizing
- Different countries have different rules surrounding administration of specific agents e.g. CIDR in USA
- Lungs can take away/ get rid of 99% of PGs



Reasons for Synchronization – Most Economical Reasons

- Restart oestrous cycles after parturition – can be achieved by giving exogenous hormones
- Synchronized ovulations / inseminations for all cows at once
  - *e.g.* if sheep flock ovulated on one day then almost all births will occur over a one-week period
- Easier to schedule supplementary feeding – only need to feed extra during a specific period of time
- Reduces time needed monitoring oestrous events – can be condensed into a few days – using KMARS or tail-paints
- Cross-fostering much easier (lambs) if some were to die
- Treatments of young easier to manage together – more economical
  - castration
  - tail docking easier to do at optimum times
- Marketing of young coordinated

Ovulation and Parturition Induction

- Ovulation
  - Facilitate synchronization of oestrus
  - Multiple embryos for pregnancy recovery
  - Increase twinning/multiple offspring rate
  - Can be achieved by the following mechanisms
    - Stimulation- *e.g.* FSH, GnRH to promote follicle growth
    - Inhibition of dominant feedback mechanisms - Immunization with androstanedione-7-HSA (fecundin) against inhibin in order to allow more follicles to come through

- Parturition
    - Facilitate tighter calving/lambing interval
    - Dexamethasone – can be given to induce parturition and allow for entire herd to give birth around the same time (also more economical)
    - Increasing phased out- ethical implications
        - Because the farmer's objective is not necessarily the baby calf, but more the milk that the mother is producing following birth

Decreasing Fertility

- Why?
    - Suppression of behaviour (e.g. male aggression)
    - Management of cows and to stop in-breeding
    - Improved growth rates, taste (Boar-taint)
        - Increased production of androstenone and Skatole in fat (all the way from their testes into their meat and adipose tissue), results in bad taste; not desirable for consumers – important to try and stop this
        - Intact males (not castrated) grow better overall because testosterone has the added benefits of aiding muscle growth and bone growth but you would still want to remove behaviours that testosterone is responsible for
- Domestic, Companion and wild animals
    - Desexed e.g. castration (chemically or physically)
        - Vaccination- GnRH, GDF-9/ BMP-15 to stop the HPG axis
        - Small implant which sits under the skin – administers a chronically high dose of GnRH, closing down the system entirely (not pulsatile anymore, closes down the system) – good as it keeps animal intact, but closes down the reproductive system
        - Immunocastration
            - GnRH agonists (Deslorelin)