1 Pharmacological agents acting upon the reproductive system

2

3 Gonadotrophins

- Stimulate reproductive activity in anoestrous animals
- Stimulate animals to breed during their non-breeding season
- Superovulation for embryo transfer
- For diagnostic use (e.g. in testing for rig horses)

4 GnRH and analogues

- Produce reflex secretion of LH
- Limited effect on FSH
- Causes luteinisation of a large follicle
- Causes ovulation of pre-ovulatory follicles
- May help recruit follicles in suboestrous animals

5 GnRH and analogues

- 1) In oestrus synchronisation programmes (ovsynch)
- 2) In superovulation programmes to tighten the time of ovulation
- 3) In the mid-luteal phase, to try to increase pregnancy rates
- 4) To stimulate oestrus in anoestrous animals (not very efficient!)

6 Gonadotrophins: LH

- LH is not available
- hCG is used in horses (and cows) to tighten timing of ovulation
- hCG is used for endocrine challenge tests
- hCG can be used to stimulate libido in low-libido males (better than testosterone)

7 Controlling the time of ovulation

8 hCG challenge test for rigs

9 Gonadotrophins: FSH

- FSH is available as recombinant or abattoir-derived material
- Used for superovulation
- Has a short T½ so has to be given often
- Is the only hormone that can be used to superovulate mares

10 Typical superovulation regimen for cattle

11 Gonadotrophins: eCG

- Equine Chorionic Gonadotrophin (also known as Pregnant Mares' Serum Gonadotrophin)
- Long T½ so can be given once
- But has variable LH activity, as well as its FSH activity
- … hence superovulation responses are unpredictable (so FSH is now more favoured)

12 Gonadotrophins: eCG

- Also used to stimulate ovulation rate in out-of-season breeding in sheep
- And to improve responses of anoestrous beef cattle to oestrus induction / synchronisation regimens
- In both, it is acting by 'boosting' endogenous gonadotrophin activity

13 Steroids: Oestrogens

- Affect uterine muscle and blood flow
- Stimulate uterine immunity
- Causes oestrous behaviour (after progesterone priming)
- Weakly luteolytic
- Affects follicular waves
- Promotes mammary development

14 Oestrogen:- uses in oestrus synchronisation programmes

- To regulate follicular waves, by causing regression of all large antral follicles and emergence of a new follicular wave
- To cause +ve feedback secretion of LH
- To augment oestrus behaviour

15 Oestrogen:- other uses

- To stimulate uterine immunity and responsiveness to oxytocin
-
- To treat misalliance in dogs, by altering tubal transport of gametes/zygote
-
- To cause oestrus behaviour, in (e.g.) ewes that are used in sheep AI centres

16 Oestrogen:- disadvantages of use

- Down regulates hypothalamus OE-Rs in postpartum period

- Long-term treatment results in masculinisation
- Treating bitches runs the risk of causing pyometra
- Behavioural oestrus DOES NOT mean that there is physiological oestrus

17 Progesterone and progestagens

- Progesterone can be given by injection or absorbed through the vaginal mucosa
- Progestagens can be absorbed orally (monogastric animals) or (some) through the vaginal mucosa
- Or can be given as s/c implants (e.g. in the ear)

18 Progesterone and progestagens

- Progesterone (injection, CIDR
- Altrenogest (Regumate; oral in sow and mare)
- Megestrol
- Proligesterone
- Hydroxyprogesterone
- Medroxyprogesterone
- Flugestone
- Norgestomet (ear implant in cow)

19 Effects of progestagens

- Cause -ve feedback on gonadotrophin secretion
- Stimulate (short term) synthesis and accumulate of gonadotrophins in the pituitary
- Eliminate oestrus behaviour in females
- Reduce aggressive/masculine behaviour in males

20 Uses of progestagens

- Main use is in oestrus synchronisation programmes or in the treatment of anoestrus
- Inducing out-of-season breeding in horses and sheep
- Regulation of the bitch's oestrous cycle
- Treatment of aggressive/wandering dogs
- Treatment of pseudopregnancy in dogs
- Augment pregnancy rate in cattle (mares)

21 Controlling oestrus with progesterone: principle

22 Intravaginal progesterone inserts
23 Inserting norgestomet implants
24 Early breeding in mares
25 Progesterone and oestrogen for treating bovine anoestrus
26 Progesterone and gonadotrophins for treating anoestrous beef cattle
27 Progesterone and gonadotrophins for inducing out-of-season breeding in sheep
28 Problems of progestagens
- Adversely affect uterine immunity, so there are potential contraindications in animals with uterine/vaginal infections
- Long-term progesterone treatment reduces conception rates
- Predisposes to pyometra in the bitch
- Long-term treatment results in increased appetite and fluid retention (esp. in the bitch)

29 Androgens
- Use for anabolic effect (anabolic steroids)
- Control of the oestrous cycle in the bitch (safer than progestagens?)
- SHOULD NOT be used to stimulate libido in low-libido males

30 Antiprogesterone
- Being developed as an abortifacient for the bitch (safer than misalliance injections)

31 Pseudopregnancy in the bitch
32 Prostaglandins
- PGF2α causes luteal regression
- and has a moderate ecbolic action
- PGE2 may have useful pharmacological actions within the reproductive tract

33 Prostaglandins
- Given by
- Intramuscular injection
- Injection under the mucosa of the vagina
- Intracervical pessary

34 Use of prostaglandins

- Oestrus synchronisation
- Induction of oestrus (e.g. in non-observed oestrus)
- Induction of oestrus in cows with uterine infection and a persistent corpus luteum
- Induction of parturition (full term) in cows
- Maybe use PGE to force cervical dilation (e.g. in sheep with 'ringwomb')

35 Manipulating oestrus by controlling the length of the luteal phase with PGF2α

36

37 Gonadotrophin and PGF2α to induce or synchronise oestrus (Ovsynch)

38 Progesterone, oestrogen and PGF2α to induce or synchronise oestrus (Genermate)

39 Drugs that act upon uterine muscle

- Oxytocin: contraction, also milk let-down
- Prostaglandin F2α: short-term ecbolic action
- Ergot alkaloids (ergotamine, ergotoxine)
- Clenbuterol (smooth muscle relaxant)
- Isoxpurine (smooth muscle relaxant)
- ["ecbolic" = making uterine muscle contract]

40 Control of expulsive forces in parturient cows