Contraception in yellow-footed rock-wallabies (*Petrogale xanthopus*)

2.4.5. Contraception possibilities

The information below was collected by the EAZA Reproductive Management Group (RMG). For additional information, see the EAZA RMG website www.egzac.org or contact contraception@chesterzoo.org.

Males

Surgical

If permanent contraception is desired, a surgical procedure is the recommend option in male marsupials. This procedure involves permanent contraception by surgical gonadectomy (castration) or the surgical interruption of a segment of the vas deferens (vasectomy). Side effects of castration should be similar to those in domestic species i.e. weight gain and the loss of secondary sex characteristics, but this is data deficient. Vasectomy should not impact testosterone-mediated behaviours.

Chemical

Gonadotrophin Releasing Hormone (GnRH) vaccine: GnRH vaccines, such as Improvac (guideline below), cause the production of anti-GnRH antibodies by the immune system, neutralising endogenous GnRH activity. This results in a reduction of FSH and LH production by the anterior pituitary and, ultimately, in the inhibition of testosterone secretion from the testes and spermatogenesis.

- **GnRH Protein Conjugate (Improvac): Intramuscular injection formulation -** Two injections of 400µg are given 35 days apart and boosters are usually administered every 6 months, although duration can vary between individuals. Latency to effectiveness can be up to 6 weeks so separation of the sexes is recommended if possible. In seasonal breeders initial injections should be administered at least 6 weeks prior to the breeding season. Improvac is designed to be fully reversible; there are currently no reversals on the database however studies have shown reversibility in other species within a two year period. It must be taken in to consideration that younger individuals will take longer to reverse in comparison to older individuals. Permanent changes to the reproductive system resulting in infertility has been seen in other species, notably in elephants. The effects of Improvac have not been well researched in marsupials.

GnRH agonists such as Suprelorin implants or Lupron injections are not known to be effective in male marsupials.

Females

Surgical

If permanent contraception is desired, surgical removal of the ovaries (ovariectomy), removal of the ovaries and uterus (ovariohysterectomy), removal of the uterus (hysterectomy), or the clamping or blocking of the fallopian tubes (tubal ligation) are possible. Prior approval from the EEP coordinator

is required as the procedures are not reversible. Weight gain can be a common side effect of ovariectomy, and can be managed by reviewing diet and food presentation.

Chemical

Gonadotrophin Releasing Hormone (GnRH) vaccine: GnRH vaccines, such as Improvac (guideline below), cause the production of anti-GnRH antibodies by the immune system, neutralising endogenous GnRH activity. This results in a reduction of FSH and LH production by the anterior pituitary and, ultimately inhibition of ovarian follicular development.

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Gonadotrophin Releasing Hormone (GnRH) agonists: GnRH agonists, such as deslorelin (Suprelorin; guideline below) or leuprolide acetate (Lupron), reversibly suppress the reproductive endocrine system, preventing production of pituitary hormones (FSH and LH) and subsequently gonadal hormones (oestradiol and progesterone in females). The observed effects are similar to those following ovariectomy, but are generally reversible. GnRH agonists first stimulate the reproductive system, which can result in oestrus and ovulation in females soon after the implant is placed. The stimulatory phase can be prevented in females by treatment with a progestin or oral birth control pills for 2-3 weeks.

- **Deslorelin acetate (Suprelorin) subcutaneous implant:** 1 x 4.7mg implant is recommended for a **minimum** duration of 6 months and 1 x 9.4mg implant is recommended for a **minimum** of one year. Due to the initial stimulation of the reproductive system, sexes should be separated OR the first bout must also be supplemented with additional contraception e.g. oral megestrol acetate (2-5mg/kg body weight Ovarid/Megace) daily 7 days before and 7 days after placing the implant(s). Suprelorin is designed to be fully reversible. Treatment should start at least 1 month before the breeding season. In macropods deslorelin treatment might not inhibit the reactivation of a quiescent blastocyst and subsequent birth, but successfully inhibits follicular development and post-partum oestrus (in 4/5 animals[2]). We have 8 records of reversals in marsupials in our database. Four yellow-footed rock wallabies gave birth to live young 2-4 years after being implanted with 1x4.7mg implants, and four red kangaroos reversed between 2 months and 4 years after being implanted with 2x4.7mg implants. It is unknown whether implants were removed. In eastern grey kangaroos, 9.4mg implants have lasted for three consecutive breeding seasons in some individuals[1-3]. In order to increase the chances of a full reversal, place the implant subcutaneously in a place where is easy to locate to facilitate removal i.e. subcutaneously in locations with thinner skin such as the base of the ear, inner

thigh or arm, or umbilical region. Note that these implants are not designed for removal and disintegration may be the case which complicates locating and removing the implant over time. The most common side effect of Suprelorin is weight gain.

Progestin-based contraceptives: Progestin-based contraceptives function by interfering with fertilization by thickening cervical mucus, interrupting gamete transport, disrupting implantation, and inhibiting the LH surge necessary for ovulation (etonogestrel and levonorgestrel implants, medroxyprogesterone acetate injections).

- **Levonorgestrel implant (Norplant 2/Jadelle) Intramuscular or subcutaneous implant:** 1 rod of 75 mg should be sufficient for contraception in this species. Implants last 36 months in tammar wallabies[3] and anecdotal evidence suggests that implants last for 5-7 years in koalas. Treatment should start at least 1 month before the breeding season. In macropods progestogen treatment might not inhibit the reactivation of a quiescent blastocyst and subsequent birth, but successfully inhibits follicular development and post-partum oestrus thereafter[4]. Norplant 2/Jadelle is designed to be fully reversible and the implants have been shown to be reversible in tammar wallabies following removal.
- **Medroxyprogesterone acetate (Depo-Provera) Intra-muscular injection formulation:** The recommended dose is 5mg/kg body weight every 2-3 months respectively. Latency to effectiveness is approximately 1-3 days however it is recommended that sexes should be separated for one week or the first bout must be supplemented with additional contraception for 7 days. Treatment should start at least 1 month prior to the start of the breeding season. Depo-Provera is designed to be fully reversible and we have one reversal recorded in a red kangaroo in the database. The female conceived approximately 5 months after the estimated expiry date. As Depo-Provera is not an implant, you will need to wait until the product has cleared from the individuals' system before they can reverse. A side effect of Depo-Provera is that females may develop male secondary sex characteristics and there may also be an increase in aggression. There may also be a deleterious effect on the endometrium following prolonged use.
- **Etonogestrel (Nexplanon/Implanon): Subcutaneous implant –**The recommended dosage of Nexplanon/Implanon (etonogestrel 68 mg) for this species is ½ - 1 full implant. The implant is effective for approximately 2.5 – 3 years. If this is noticed and not desired, a higher dose is recommended. Nexplanon/Implanon is designed to be fully reversible, however we have no records of reversal in marsupials in the database. To increase the chances of a full reversal it is recommended that the implant is placed in such a way that facilitates removal (e.g. subcutaneously in the upper inner arm). A side effect of using Nexplanon/ Implanon is potential weight gain.
- **Megestrol acetate (Ovarid/Megace) Oral contraceptive:** 2-5mg/kg body weight is recommended for use 7 days before and 7 days after the placement of Suprelorin implants to suppress the stimulation phase. Treatment should begin in anoestrus.

Porcine Zona Pellucida vaccine: The PZP antibodies interfere with fertilisation by binding to the ZP glycoprotein receptors that surround the egg of the vaccinated female, blocking the binding and subsequent penetration of sperm.

- **PZP vaccine: Intramuscular injection formulation -** The first injection would consist of ~100ug of PZP protein. The recommended dose is 2 injections given typically 2+ weeks apart then a booster every 8 months for most species. For seasonal breeders, treatment should start 1-2 months before the breeding season. Latency to effectiveness is approximately 2-3 weeks after the final injection in year 1 therefore separation of the sexes from the initial injection until 2 weeks after the final injection is recommended. Reversibility differs between species; however the longer PZP is given the longer it takes for a female to come back to being fertile. It is therefore suggested that an individual is on PZP for no longer than 3 years if you want the female to breed. (Please visit WWW.SCCPZP.ORG for more information on the product and protocols). There are no contraindications for use during pregnancy and lactation. This product cannot be used in the UK.

References

1) Herbert et al. (2005). Long-term effects of deslorelin implants on reproduction in the female tammar wallaby (Macropus eugenii). Reproduction. 129(3):316-319. doi:10.1530/rep.1.00432.

2) Herbert et al. (2004). Effect of deslorelin implants on follicular development, parturition and post-partum oestrus in the tammar wallaby (Macropus eugenii). Reproduction. 127(2):256-273. doi:10.1530/rep.1.00094.

3) Wilson et al. (2013). Deslorelin implants in free-ranging female eastern grey kangaroos (Macropus giganteus): mechanism of action and contraceptive efficacy. Wildlife Research. 40(5):403-412. doi:10.1071/WR13050.

4) Nave et al. (2000). Contraceptive effects of levonorgestrel implants in a marsupial. Reproduction, Fertility and Development. 12(1-2):81-6.