Contraception in bonobos (*Pan paniscus*)

2.4.5. Contraception possibilities

It should be noted that contraception is currently not recommended for bonobos. The information below was collected by the Bonobo SSP, AZA RMC and EGZAC. For additional information, see the EAZA Group on Animal Contraception (EGZAC) website http://www.egzac.org/ or contact contraception@chesterzoo.org.

Males

Vasectomy by surgical removal of a segment of the vas deferens is a practical and effective method of male contraception. However, the success of vasectomy, associated with difficulty of reversal, has made it less than ideal for male bonobo contraception.

Vas ligation using a metal clip for vas occlusion without severing the vas deferens has been performed in 5 bonobos in the SSP population as a possibly reversible technique. No reversals have been attempted in any of these animals. With vas ligation (as with all vasectomy techniques), there is a risk of spontaneous reversal as a result of recanalization of the vas. One such reversal was observed in a bonobo within a year after vas ligation. The reversal was detected due to the return of an opaque appearance to the ejaculate, which turns translucent after successful vasectomy. The spontaneous reversal necessitated the application of a second set of metal clips to the vas deferens of the affected animal. Monitoring semen quality from contracepted males over time is necessary to detect spontaneous reversal, which is identified by the presence of sperm in the semen. This follow-up analysis should be done at frequent intervals to guard against failure. Risks associated with the vas ligation procedure must be predetermined, and the possibility of infection must be evaluated. An institution should endeavour to enlist the assistance of human medical specialists before undertaking this procedure.

Females

It should be emphasized that contraception for bonobo females is appropriate only as a last resort, in a case when relocation for suitable breeding is not possible, and when relocation to a reproductively appropriate situation (e.g., with aged, non-cycling female; or to an all-male group) is not practical. Special consideration must be taken with potential social implications of preventing oestrus swellings.

Oral birth control pills (various brands): Use of birth control pills in apes is compromised by the difficulty in ensuring an animal's complete compliance with accepting and retaining the proper dose. Human birth control pills are available in different formulations of combined synthetic oestrogen and progestin. The human regimen for most formulations is 21 days of hormone treatment and 7 days of placebo, which results in withdrawal bleeding similar to menstruation. The majority of

apes contracepted with oral birth control pills have followed the same regimen. However, many bonobos have a longer cycle than 28 days, and some bonobos have received hormone for 28 or 35 successive days rather than 21, to more closely match their normal cycle. If oestrus behaviour is not desired, the placebo can be skipped for up to 12-16 weeks. If you start oral birth control pills, remember that it can take 2-4 weeks before the animal is actually contracepted, so you still have to separate the female from the males, if breeding is not allowed. Keller et al. (2010) noted breakthrough bleeding while on lower oestrogen dose oral birth control pills.Please see Agnew *et al*. (2016) for a review of oral birth control pill use in the bonobo SSP.

Etonogestrel (Implanon/Nexplanon) Intramuscular or subcutaneous implant: 1 rod is recommended, depending on the weight of the individual. Nexplanon in primates usually lasts between 2-3 years however this varies from individual to individual. There may be a low level of follicle production whilst on Nexplanon which can stimulate sexual behaviour or signs of oestrus such as skin swelling. Nexplanon will also thicken cervical mucus so even if ovulation does occur, sperm is inhibited. The first problem is knowing if the female has a sufficient dose of progestin to keep her effectively contracepted. There have been cases in various species where females showed oestrus, and may have even copulated but didn't conceive. If the implant is not in place or if the implant has been in for a minimum of two years then replace it with a new one.

Medroxyprogesterone acetate (DepoProvera) Intra-muscular injection formulation: Administration of this synthetic progestin is by injection, which may involve the use of darts to administer the drug or an anaesthetic event. The recommended dose is 2.5-5mg/kg body weight every 2-3 months respectively. Care must be taken to ensure administration of the full dose (Perkins 1995). 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. Depo-Provera is designed to be fully reversible and time to reversal varies greatly among females and can be as long as 2 years. As Depo-Provera is not an implant you will have to wait for the drug to clear from the individuals system and this length of time can vary between individuals is unpredictable in some cases. The effects of long-term administration of DepoProvera are not completely known. It may be best used as an interim contraceptive method. As recommended by the AZA Orangutan SSP, DepoProvera is best considered if females are at risk of becoming pregnant if there are delays in obtaining or administering another contraceptive method (Perkins 1995). 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.

Levonorgestrel implant (Norplant 2/Jadelle) Intramuscular or subcutaneous implant: 2 rods are recommended for this species. In primates, Norplant 2 usually lasts for 2-3 years however this can vary on an individual basis. There may be a low level of follicle production whilst on Norplant which can stimulate sexual behaviour or signs of oestrus such as skin swelling. Norplant however will also thicken cervical mucus so even if ovulation does occur, sperm is inhibited. The first problem is knowing if the female has a sufficient dose of progestin to keep her effectively contracepted. There have been cases in various species where females showed oestrus, and may have even copulated but didn't produce young. If the implant is not in place or if the implant has been in for a minimum of two

years then replace it with a new one. Complete healing should be achieved before reintroduction of the animal to others who may groom the implantation site and potentially induce loss of the implant. Norplant is designed to be full reversible however, the potential long-term side effects which could result in impaired fertility are not known. While a hypothetical loss of 10% fertility in human females is acceptable, it may not be so in the bonobo.

Intrauterine device (IUD): Physical considerations suggest the use of an IUD recommended for use in the human nulliparous female (i.e., the smallest size). Use of an IUD is complicated by the potential for removal of the device by the animal, a possibility countered by shortening of the removal strand. This, in turn, makes removal of the device when desired more difficult. Further, there is potential for complications should pregnancy be initiated in the presence of the device. Limited experience suggests a failure rate of approximately 5% (not dissimilar to the rate for human females) (Nadler et al. 1994; Porteous et al. 1994).

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 gonadal hormones (estradiol and progesterone in females, testosterone in males). The observed effects are similar to those following either ovariectomy in females or castration in males, but are reversible. GnRH agonists first stimulate the reproductive system, which can result in oestrus and ovulation in females or temporary enhancement of testosterone and semen production in males. The stimulatory phase can be prevented in females by treatment with a progestin or oral birth control pills for 2-3 weeks. This method has not been used to date in bonobos and only limited experience with this method is available in nonhuman primates.

Deslorelin acetate (Suprelorin) Subcutaneous implant: 1x 4.7mg is recommended for a **minimum** duration of 6 months and 1x 9.4mg is recommended for a **minimum** of one year. Up to three implants have been used in some cases if sexual behaviour or characteristics are not fully suppressed. Due to the initial stimulation of the reproductive system, the first bout must also be supplemented with additional contraception e.g. oral megestrol acetate (Ovarid/Megace) daily 7 days before and 8 days after placing the implants, or by continuing to administer birth control pills after implant placement. Suprelorin is designed to be fully reversible. In order to increase the chances of a full reversal, place the implant in such a way that facilitates removal. The most common side effect of Suprelorin is weight gain.

Weight gain is a common side effect associated with synthetic progestins and GnRH agonists, but less so with combination oral birth control pills. Because obesity can have serious health consequences, weight should be carefully monitored and diet managed as necessary.

Extensive data from humans and limited data from the AZA Wildlife Contraceptive Centre database indicate that oral birth control pills and the synthetic progestin products should be reversible in apes.