3.16 PRIMATE REPRODUCTION and CONTRACEPTION

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Part 1. Primate reproductive physiology and tips on monitoring reproductive cycles

CHIMPANZEE REPRODUCTION

<table>
<thead>
<tr>
<th>Development</th>
<th>General</th>
<th>Wild</th>
<th>Captive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>Early oestrous swellings are usually small and irregular. Menarche (sign of first menstruation) occurs 1 –1.5 years after first swellings. Oestrous swellings do not reach maximum size until after menarche. Once swellings occur, they copulate frequently. May become pregnant for the first time from 4 months to 2 years after menarche.</td>
<td>First oestrous swelling 8.5 – 9.5 years. Menarche typically occurs at 11 years Pregnancy may occur from 11 years 4 months of age to 13 years.</td>
<td>First oestrous swellings 5.5 – 7.5 years. Menarche typically occurs 6.5 – 9.0 years. Pregnancy may occur from age 7 to 11.</td>
</tr>
<tr>
<td>Male</td>
<td>Mounting, thrusting and intromitting can occur as young as 2 years</td>
<td>Rapid testicular occurs growth between 9-10 years. Socially mature at 15 years</td>
<td>Rapid testicular occurs growth between 6-7 years. Adult weight and dentition occurs between 8 and 9 Need to be sociably capable of successful copulations which can occur between 11 and 12 years. Some aged 7-9 years have sired offspring</td>
</tr>
</tbody>
</table>

Oestrous Cycle
Duration usually last 34-37 days
Oestrous cycles continue through out life and have been observed in females of 45 years and older and females behaviour may change through out the cycle. Males increase time spent with a female when she is swollen. They are more likely to groom her and examine or manipulate her swelling. Copulation can occur at any stage in the oestrous cycle, including pregnancy and menstruation. Anovulatory swellings can occur during pregnancy. Copulation coincides with maximal swelling and peaks in the morning.
Cycle divided into 4 phases

<table>
<thead>
<tr>
<th>Phase</th>
<th>Duration</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-swelling phase</td>
<td>6-7 days</td>
<td>begins first day after the end of menstruation skin is quiescent</td>
</tr>
<tr>
<td>Swelling phase</td>
<td>17 –18 days</td>
<td>The perineum becomes increasingly swollen but may fluctuate during the day at maximal swelling (tumescence) it is free of wrinkles and shiny and last 6-7 days (out of the 17-18 days). Ovulation occurs on the last day of maximal swelling and can be predicted by labial occlusion of the medial surfaces of the labia minora pressing together so that the vagina appears as a slit.</td>
</tr>
<tr>
<td>Post-swelling phase</td>
<td>10 days</td>
<td>Swelling is rapidly lost over 4 days and then becomes quiescent</td>
</tr>
<tr>
<td>Menstruation phase</td>
<td>3 days</td>
<td>begins usually 6 – 12 days from the start of detumescence menstrual discharge duration and quantity can vary, sometimes it can be missed by observers.</td>
</tr>
</tbody>
</table>

Gestation

Gestation Period: 227 days ± 12 days = 32.5 weeks (31-34 weeks)

Signs of Pregnancy

- Initially signs maybe difficult to observe, because menstruation and oestrous swelling can continue for the first months of gestation. However, the swelling maybe smaller in size and less regular.
- Swellings can disappear by the end of the first trimester although in some females the swellings can continue throughout the gestation period.
- Morning sickness has been described (more common in primiparous females)
- Irregularity of appetite
- Mammary enlargement and self-manipulation and/or visual inspection of the nipples
- Distension of lower abdomen maybe noticed in the last few months.

Impending Parturition

Signs of Impending parturition

- Increased nipple manipulation
- Slight bulging of the perineal area
- Increase in frequency of urination and projectile like expulsion of the urine maybe seen several weeks before birth
- Females may taste urine and rub on nose one week before birth
- Some females become lethargic and lose appetite one week before birth
Within 24 hours, the rump may appear concave and vaginal dilation can be seen.

Parturition

Labour is usually 30 – 40 minutes but can be up to 8 hours

- Females become restless and take various postures
- Small amounts of blood and amniotic fluid are seen
- Other chimps inspect the genital area
- Straining may be observed
- The female will often hold, catch or pull the neonate and then retrieve and cleans it immediately
- Placenta is often delivered within minutes and the mother will break the cord. The placenta and fluids are often consumed by the mother.
- Some neonates have to be assisted because they cannot cling well and will often nurse irregularly in the first five days.
- Females with prior exposure to other infants are more likely to show good maternal behaviour.
- Other chimps particularly females show intense interest in the offspring and will often touch it. Some females will often take the youngster to care for it. This is normal but abduction can occur which is not acceptable by the mother.

Resumption of Oestrous Swellings

- No activity occurs due to the presence of lactation
- Usually 14 months to 4 years
- Several swellings may occur before fertilisation may occur.

Interbirth Interval

- Wild → Average is 5 years 8 months
- Captive → 2 years 10 months to 6 years 6 months have been recorded.
MANGABEY REPRODUCTION (courtesy of CERCOPAN)

Red Capped Mangabey Reproductive Data

Age at 1st Birth (months). Calculated from captive born individuals only as these are the only ones with accurate age. 
n=7. Mean: 47.4. Std Dev: 12.7

Birth interval (months) 

Average time to next birth after infant death (months) (n=6)

Measuring of Mangabey sexual swellings
Scale of 0-4
4 - Being the highest
0 - Not in season
2? - Means Onset of Swelling
2? - Dwindling or Reducing Swelling
? or ? - Can also be determined by Redness of swelling.

NB: Pale swelling may mean reducing of oestrus
Part 2. Primate Contraception

REASONS FOR CONTRACEPTION

- Space issues – good management
- Prevent hybridisation
- Temporary/ reversible while in captivity
- Do we know the relatedness of the individuals under our care? DNA Analysis can assist with this. If you don’t have access to this, contraception is recommended in the interim until relatedness can be ascertained.

CONTRACEPTION OPTIONS

- Surgery – permanent, dangerous under field conditions
  - Male (social issues)
    - Vasectomy (occasionally reversible)
    - Castration
  - Female (degree of surgical difficulty)
    - Ovariectomy
    - Ovariohysterectomy
    - Tubal Ligation
- Husbandry (abstinence)
  - Separating animals – eg. Bachelor groups
- Physical barriers - IUD’s
- Chemical

See below for the latest AZA and EAZA recommendations for non human primates.

IT IS RECOMMENDED THAT WHATEVER OPTION A SANCTUARY Chooses, THEY SHOULD FEED THEIR INFORMATION ON CONTRACEPTION TYPE/ SUCCESS ETC INTO THE INTERNATIONAL ANIMAL CONTRACEPTION DATABASE.

As at 2009, the European contact for this database is Dr. Sue Walker, based at Chester Zoo UK (s.walker@chesterzoo.org).

Chemical Contraception

1. Synthetic progestins

General Problems
- Blocking ovulation, causing thickening of cervical mucous, slowing ovum transport, and/or interfering with implantation or fertilisation
- May still get follicle growth and enough oestrogen production to cause oestrus behaviour
- Ovulation may also occur, even though no pregnancy
Reversibility
- Confirmation on documentation that ovulatory cycles have resumed
- CIRCULATING hormone will be gone within days
- Reproductive history, age, health, thin, fat, partner fertility

Contra Indications
- Don’t use implants in pregnant animals, due to possibility of prolonged gestation, stillbirth, abortion. However, there are numerous anecdotal reports where an implant has been inadvertently inserted early in an unknown pregnancy, with no apparent effect on the pregnancy, and offspring being born normally.
- Have been prescribed for lactating women – considered generally safe for nursing infants
- Not recommended in juveniles – lack of data
- Probably cause weight gain in all species

Implant - Implanon
This is an implant which is inserted subcutaneously whilst the animal is under general anaesthesia. It contains the active ingredient etonogestrel (68mg/ implant), and is effective for up to 3 years. It is a human product, and has been widely used in women in Europe and Australasia, however it is only recently gone on the market in the USA. Each implant costs ~€150. Anecdotally this implant has used successfully in chimpanzees, mandrills and gorillas (Various zoo reports, author personal experience).

Implant latency to effectiveness
- Individual variation
- Threshold levels of the hormone in the blood by 1-3 days post IM and within 1 week post SC insertion.
- As pre-ovulatory follicles are difficult to suppress, if cycle stage is not known, SEPARATE animal for 1 – 2 weeks (IM Vs SC)

The following material comes from the AZA Contraception Advisory Group

[http://www.stlzoo.org/animals/scienceresearch/contraceptioncenter/contraceptionrecommendatio/contraceptionmethods.htm](http://www.stlzoo.org/animals/scienceresearch/contraceptioncenter/contraceptionrecommendatio/contraceptionmethods.htm)  (Accessed 11th May 2009). Note that implanon (above) has only recently become available in the USA, but has been widely used in Australasia and Europe for over 10 years.

THE USE OF ANY CONTRACEPTIVE IN NON-DOMESTIC ANIMALS IS CONSIDERED EXPERIMENTAL
(M=MALE-DIRECTED, F=FEMALE-DIRECTED METHOD)

Implant - MGA (melengestrol acetate)
Manufacturer - ZooPharm division of Wildlife Pharmaceuticals, Colorado, USA.
Product Information - MGA implants are the most frequently used and consequently the contraceptive method for which we have the most information in the Wildlife
Contraception Center database. Melengestrol acetate is a synthetic progestin. MGA implants contain 20% melengestrol acetate by weight in a silastic matrix. **Because different species require different dosages, implants are not interchangeable. Please check with the WCC regarding implants that are not being utilized.** Although duration of MGA implant efficacy may vary by individual and species, the continued recommendation is to replace them at 2-year intervals.

**Storage** – Implants should be stored at refrigeration temperatures (4°C).

**Sterilization** – MGA implants should be inserted using sterile surgical technique. In addition, it is recommended that implants be gas-sterilized with ethylene oxide followed by de-gassing at room temperature for a minimum of 2 weeks prior to use. Because the implants are porous, they must be de-gassed longer than metal instruments. Inadequate de-gassing may result in residual gas that may evoke a tissue reaction. If ethylene oxide sterilization is not available, the implant may be rinsed with alcohol and dried with sterile gauze prior to placement. Sterilization with a cold-soak solution is not recommended, because the chemicals can be absorbed and/or MGA may be leached from the implant. Low temperature hydrogen peroxide gas sterilization (STERRAD) is replacing the more dangerous EtO process in most hospitals. (More information can be found at www.sterrad.com). Our lab test found no difference in MGA release rates after implant sterilization with the STERRAD system, but long-term efficacy of these implants has not yet been evaluated. Because heat may change the structure of the MGA, implants should not be autoclaved.

**Insertion** - Implants should be inserted between the scapulae intra-muscularly if possible, but, if subcutaneous placement is necessary, place implant in a “tunnel” created by blunt dissection of fascia away from the incision. Migration may be controlled by suturing the implant in place at the time of insertion. Implant loss can be reduced by properly sterilizing implants before insertion, using sterile insertion technique, and separating the animal from conspecifics during the period of healing. (NOTE: in some taxa such as the callitrichids and small prosimians, steel sutures have been successful in preventing over-grooming and implant removal by conspecifics, thereby avoiding the need to separate animals). **The implant’s presence and location should be confirmed whenever the animal is handled.**

**Monitoring implant placement** - Identification transponder microchips inserted in MGA implants can be used to confirm presence and location. Implants cannot be supplied with transponders already in place; however, chips can be inserted in implants that are longer than the chip. Using sterile procedure, puncture implant longitudinally with needle containing transponder chip (it comes sterile) and insert into implant as you would under the skin. Insert implant into animal using standard surgical technique as outlined above. Secondly, stainless steel suture or comparable material may be incorporated into the implant to make it visible on radiographs prior to sterilization.

**Implant disposal** – used implants received from ZooPharm or Ed Plotka should be disposed of in proper waste containers after use.

**Latency to effectiveness** - Although individuals vary, threshold levels of the hormone should be reached in the blood within 1 to 3 days following IM insertion and within 1 week after SQ insertion. However, pre-ovulatory follicles are difficult to suppress, so, if cycle stage is not known, extra time must be allowed. Therefore,
separation or alternative contraception should be used for at least 1 week (if IM) or 2 weeks (if SQ) following insertion.

**Estrous cycles during treatment** - MGA may effect contraception by blocking ovulation, causing thickening of cervical mucus, slowing ovum transport, and/or interfering with fertilization or implantation. However, follicle growth may continue and sometimes be accompanied by estrogen production sufficient to cause estrous behavior. Ovulation may occur even though pregnancy does not ensue. Higher progestin doses may be preferred, so that estrous behavior is prevented, but may not be effective in completely suppressing follicle growth and some estradiol production.

**Duration of efficacy and reversibility** - Implants are considered effective for at least 2 years and possibly much longer, depending on species and individual differences, but in some cases have been found to be effective for as much as 5 years when left in place. This means that **implants should be replaced every 2 years to insure contraception, but should be removed when pregnancy is desired.** For this reason too, old implants should be removed when a new one is placed to avoid administering a higher than intended dose. Once the implant is removed, the circulating MGA clears very rapidly, so that ovulation and conception may occur within days, although actual latency is usually longer and will depend on the individual.

**Use during pregnancy** - Synthetic progestins like MGA are not recommended in pregnant animals because of the possibility of prolonged gestation, stillbirth, abortion, etc. in some species, although the effect may depend on dose. Progestins in late pregnancy seem not to interfere with parturition in primates, but this may be a taxon-specific phenomenon.

**Use during lactation** - Progestins are sometimes prescribed for lactating women and are considered generally safe for nursing infants.

**Use in pre-pubertals or juveniles** – Future reproduction was not affected in calves of domestic cows on MGA-treated feed, but no studies of pre-pubertal treatment with MGA or other progestins have been conducted with other species, so possible long-term effects on fertility are not known.
Precautions – MGA can cause weight gain in all species. Possible deleterious effects on uterine and mammary tissues vary greatly by species; see cautions for each taxon. Consideration for seasonal breeders - Treatment should begin at least one month before the anticipated onset of the breeding season. However, in canids, treatment should begin more than two months before the time of anticipated estrus, because proestrus increases in estradiol can begin as much as two months before estrus, and it is known that this endogenous estradiol can exacerbate deleterious effects of progestins on the uterus and mammary glands. This synergy of estradiol and progestins may also occur in other carnivores, such as mustelids and ursids. Reporting Requirements - All institutions must submit a complete Contraception Center Survey to the AZA Wildlife Contraception Center. The product will no longer be sold to any institution that fails to submit the annual survey. Request for purchase – MGA implants may be purchased by prescription through ZooPharm. All prescriptions should be written using their protocol and MUST include an authorization number designated by the AZA Wildlife Contraception Center. MGA implants cost $30/gram (As of June 1st 2008) plus shipping and handling. To request authorization for ordering MGA implants, please complete the Implant Request Form and submit to: Sally Boutelle, Program Coordinator AZA Wildlife Contraception Center Saint Louis Zoo 1 Government Drive St. Louis, MO 63110 314-646-4595; fax: 314-646-5534 Contraception@stlzoo.org Injection - DEPO-PROVERA® (medroxyprogesterone acetate) Manufacturer – Pfizer Product information - With the second most numerous records in the Wildlife Contraception Center database, Depo-Provera® has been used most often in reproductively seasonal species (e.g., prosimians, bears, pinnipeds), species in which anesthesia for implant insertion is problematic (e.g., giraffes, hippos), and as an immediately available interim contraceptive (e.g., if an implant is found missing or has not been ordered). Medroxyprogesterone acetate is a synthetic derivative of progesterone administered as an acetate salt with anti-estrogenic activity. Dose - Dosage studies have not been conducted for most species. Recommended doses and injection intervals vary according to species and experience. Current reports have indicated that 2-5 mg/kg body weight every 2-3 months has been effective (the higher dose for smaller species and the lower dose for larger ones). However, New World monkeys require as much as 20mg/kg monthly. For especially large species for which body weights may not be available, such as hippos, see Taxon-Specific Recommendations. Latency to effectiveness - IM injection is roughly equivalent to implant insertion, i.e., separation or alternative contraception should be used, conservatively, for 2 weeks, but at least for 1 week. Estrous cycles during contraceptive treatment - Synthetic progestins may effect contraception by blocking ovulation, causing thickening of cervical mucus, slowing
ovum transport, and/or interfering with fertilization or implantation. However, follicle growth may continue and sometimes be accompanied by estrogen production sufficient to cause estrous behavior. Ovulation may occur even though pregnancy does not ensue. Higher progestin doses may be preferred, so that estrous behavior is prevented, but may not be effective in completely suppressing follicle growth and all estradiol production.

**Duration of efficacy and reversibility** - Duration of efficacy, and thus latency to conception following last injection, can be extremely variable and has been seen to vary from 4 weeks to 2 years in some individuals. In general, the recommended dose (2.5-5 mg/kg BW) is effective for at least 2 months in most species. Hippos and giraffe have been treated at lower doses and appear to need re-treatment every 6 weeks. New World primates require higher doses at more frequent intervals.

**Use during pregnancy** - Progestins are not recommended in pregnant animals because of the possibility of prolonged gestation, stillbirth, abortion, etc. in some species, although the effect may depend on dose. Progestins in late pregnancy seem not to interfere with parturition in primates, but this is a taxon-specific phenomenon. Because of the variability in duration of efficacy for Depo-Provera, special caution should be used when treating females that might be pregnant.

**Use during lactation** - Progestins are sometimes prescribed for lactating women and are considered generally safe for nursing infants.

**Use in pre-pubertals or juveniles** - Future reproduction was not affected in calves of domestic cows on MGA-treated feed, but no studies of pre-pubertal treatment with MGA or other progestins have been conducted with other species, so possible long-term effects on fertility are not known.

**Consideration for seasonal breeders** - Treatment should begin at least one month before the anticipated onset of the breeding season. This does not include however canids or other carnivores due to the potential for progestin side effects addressed in the corresponding taxonomic sections below.

**Precautions** - Progestins likely cause weight gain in all species. Possible deleterious effects on uterine and mammary tissues vary greatly by species; see cautions for each taxon. In the human literature, Depo-Provera® has been linked to mood changes. Because it binds readily to androgen receptors and is anti-estrogenic, females may experience male-like qualities (increased aggression, development of male secondary sex characteristics, etc.)

**Reporting requirements** - All institutions using Depo-Provera® are asked to submit a complete Contraception Center Survey to the AZA Wildlife Contraception Center. It is essential that accurate records of doses and intervals be maintained and results reported to the Wildlife Contraception Center Database to contribute to dosage development.

Please submit surveys to:
Sally Boutelle, Program Coordinator
AZA Wildlife Contraception Center
Saint Louis Zoo
1 Government Drive
St. Louis, MO 63110
314-646-4595; fax: 314-646-5534
Contraception@stlzoo.org
The Pill
- Various progestin plus estrogen analogues
- Follow human protocol – so must take each day
- Treatment can begin in any phase of the cycle, but may not be effective in the first month if treatments begins near the time of ovulation - Impractical in most situations

PROGESTIN-ONLY PILLS
- Ovrette® (norgestrel) pills – 0.075mg
- Jolivette® (norethindrone) pills – 0.35mg
- Micronor® (norethindrone) pills – 0.35mg
- Nora-Be® (norethindrone) pills – 0.35mg
- Nor-QD® (norethindrone) pills – 0.35mg
- CamilaTM (norethindrone) pills – 0.35mg
- ErrinTM (norethindrone) pills – 0.35mg

The limited data in the WCC database regarding the use of these orally active progestin-only contraceptives is primarily for great apes and a few Old World monkeys.

Manufacturer – See brand details and the list of manufacturers: BC Pills

Product information – A progestin-only oral contraceptive pill consists of synthetic progesterone, either norgestrel or norethindrone, without estrogen.

Latency to effectiveness - As with implants and injections, separation or alternative contraception should be used for 1-2 weeks after initiation of treatment.

Estrous cycles during contraceptive treatment - Synthetic progestins may effect contraception by blocking ovulation, causing thickening of cervical mucus, slowing ovum transport, and/or interfering with fertilization or implantation. However, follicle growth may continue and sometimes be accompanied by estradiol production sufficient to cause estrous behavior. Ovulation may occur even though pregnancy does not ensue. Higher progestin doses may be preferred, so that estrous behavior is prevented, but may not be effective in completely suppressing follicle growth and some estradiol production.

Duration of efficacy and reversibility - Duration of efficacy may not be much more than one day, so pills must be administered daily. Following cessation of treatment, rapid clearance can result in ovulation within a few days, but actual latency to conception will vary by individual.

Use during pregnancy - Progestins are not recommended in pregnant animals because of the possibility of prolonged gestation, stillbirth, abortion, etc. in some species, although the effect may depend on dose. Progestins in late pregnancy seem not to interfere with parturition in primates, but this is a taxon-specific phenomenon.

Use during lactation - Progestins are sometimes prescribed for lactating women and are considered generally safe for nursing infants.

Use in pre-pubertals or juveniles - Future reproduction was not affected in calves of domestic cows on MGA-treated feed (another synthetic progestin), but no studies of pre-pubertal treatment with MGA or other progestins have been conducted with other species, so possible long-term effects on fertility are not known.
**Consideration for seasonal breeders** - Treatment should begin at least one month before the anticipated onset of the breeding season.

**Precautions** – Progestins likely cause weight gain in all species. Possible deleterious effects on uterine and mammary tissues vary greatly by species; see cautions for each taxon.

**Reporting requirements** - All institutions using Progestin-only pills are asked to submit a complete Contraception Center Survey to the AZA Wildlife Contraception Center. It is essential that accurate records of doses and intervals be maintained and results reported to the Wildlife Contraception Center Database to contribute to dosage development.

Please submit surveys to:
Sally Boutelle, Program Coordinator
AZA Wildlife Contraception Center
Saint Louis Zoo
1 Government Drive
St. Louis, MO 63110
314-646-4595; fax: 314-646-5534
Contraception@stlzoo.org

2. **GnRH Implants**

**SUPRELORIN® (deslorelin) IMPLANTS**

**Manufacturer** – Peptech Animal Health, Australia

**Product information** – Suprelorin® (deslorelin), a GnRH agonist, effects contraception by temporarily suppressing the reproductive endocrine system and preventing production of pituitary (FSH and LH) and gonadal hormones (estradiol and progesterone in females and testosterone in males). The observed effects are similar to those following ovariecotomy or castration, but are reversed after the hormone content of the implant is depleted. As an agonist, deslorelin first stimulates the reproductive system, which can result in estrus and ovulation in females or temporary enhancement of testosterone and semen production in males. Then, down-regulation follows the initial period of stimulation. Although deslorelin can also be an effective contraceptive in males, we recommend its use primarily in females, since monitoring efficacy in females by suppression of estrous behavior or gonadal steroids in feces is more straightforward than ensuring continued absence of sperm in males, since most institutions cannot perform regular semen collections. It can, however, be used to ameliorate aggression in males but higher dosages are usually needed.

Deslorelin implants are available in two formulations: 4.7-mg for a minimum of 6-month, and 9.4-mg for a minimum of 12-month contraception. Deslorelin has been tested primarily in domestic dogs and cats, which makes it most suitable for carnivores, and it has successfully reduced aggression in male lion-tailed macaques. However, it appears not to be effective in male bovids or marsupials. It is currently in use in a number of species but the primary taxonomic group treated has been carnivores.

**Storage and Expiration** – Implants should be stored at refrigeration temperatures (4°C). Expiration date is stamped on individual implant packages. If implant expires
prior to placement, contact Sally Boutelle (contraception@stlzoo.org) for the actual longevity of the implant.

**Insertion** – The implant comes pre-loaded in an insertion device. The recommended site of implant placement is SQ between the shoulder blades. The area should be clipped and cleaned using standard surgical prep techniques. A fold of skin should be lifted and held between the thumb and fingers as the obturator (sent with the implant) is inserted. To prevent breakage of the implant during insertion, the barrel of the obturator should be slowly withdrawn as the implant is expelled. The implant should be held steady as the obturator is removed to insure release of the implant so that it remains in place under the skin.

**Latency to effectiveness** - Because the initial effect is to stimulate the reproductive system, it is important to either separate treated animals from opposite sex individuals during the period of enhanced fertility or use another form of contraception. Females treated with deslorelin should be considered fertile for 3 weeks following insertion. Males may remain fertile for 2 or more months, until residual sperm either degenerate or are passed (as following vasectomy). Lessening of aggression in some male primates treated with deslorelin or other GnRH agonists was not seen for 6-12 months, but the delay may have been due to an inadequate initial dose.

**Suppression of initial estrus/ovulation** – The estrus and ovulation that can occur within 2 weeks following implant insertion can be suppressed with supplemental progestin treatment for 15 days (7 days prior to and 8 days after implant insertion). Megestrol acetate tablets are the simplest form for short-term progestin administration, with the tablet offered as a treat to insure ingestion. Depo-Provera® should not be substituted for Megestrol acetate, because its initial high levels and sustained release can interfere with Suprelorin® efficacy. MGA implants can be left in place for 2-3 weeks following Suprelorin® implant insertion, but then should be removed to prevent interference with the down-regulation action. Leaving them in place longer may compromise Suprelorin® efficacy.

**Estrous cycles during contraceptive treatment** - Deslorelin first stimulates, then suppresses estrus in females. Species with induced ovulation (e.g., felids, some mustelids, bears) may ovulate and become pseudo-pregnant (also canids) when first treated. In males, initial stimulation may be accompanied by increased aggression or sexual interest. Estrous behavior or even copulation may occur during a transition phase near the end of the period of contraceptive efficacy.

**Duration of efficacy and reversibility** – A new 12-month formulation containing 9.4mg deslorelin should be effective for approximately twice as long as the smaller (4.7mg) implants that have been supplied in the past. However, the dose needed per-kg-body-weight with the new 9.4mg implants is about twice that of the existing 4.7mg implants. For animals effectively contracepted for 6 months with two 4.7mg implants, two 9.4mg implants will be necessary, but the period of efficacy will be double (12 months). For 6 months contraception, one 9.4mg implants will not substitute for two of the 4.7mg ones. These dose recommendations should only serve as general guidelines, because individual animals may respond differently. Stated durations of efficacy should be considered minimums. The smaller implants may actually be effective for more than 6 months, and the larger ones for more than 12 months, in some animals. Data from various species have shown, responses may
vary widely between individuals, but that the response from one individual tends to be consistent and if an individual reverses earlier than expected it will consistently do so. If it is not possible to wait for signs of reversal to determine duration of efficacy for the animal, then for continuous contraception the small implants should be replaced at 5- to 6-month intervals and larger ones at 11- to 12-month intervals.

Use during pregnancy - GnRH agonists should not be used during pregnancy, as they may cause abortion.

Use during lactation - No known contraindications once lactation has been development.

Use in pre-pubertals or juveniles - Because deslorelin suppresses gonadal steroids, its use may delay epiphyseal closure of the long bones, resulting in taller individuals, similar to the effects of pre-pubertal spaying and neutering in domestic dogs and cats. GnRH agonist use in prepubertal domestic cats was followed by reproductive cycles after treatment ceased. However, species differences may occur.

Consideration for seasonal breeders - In females, GnRH agonists can induce estrus and ovulation even during the non-breeding season in some taxa. In males, GnRH agonists can transiently stimulate testosterone production even during the non-breeding season. Treatment should begin more than two months prior to the anticipated breeding season to prevent initiation of spermatogenesis, because it appears that suppression of sperm production is more easily accomplished before it has commenced and time must be allowed for passage of residual sperm, as following vasectomy.

Precautions - In general, the effects on weight should be similar to those from ovarioectomy or castration. Preliminary data indicate that increased appetite will result in weight gain, especially in females, unless food is restricted. In males, muscle loss may result in overall weight loss if not replaced by fat. In sexually dimorphic species, males may become the size (weight) of females. Animals may lose secondary sex characteristics (e.g. lions may lose the mane while being treated with deslorelin).

Reporting requirements - All institutions using deslorelin must submit a complete Contraception Center Survey to the AZA Wildlife Contraception Center. The product will no longer be sold to any institution that fails to submit the annual survey.

Request for purchase - Deslorelin implants are available to AZA accredited institutions as part of a research trial coordinated by the AZA Wildlife Contraception Center as part of an agreement with Peptech Animal Health, Australia. This product is not commercially available in the United States at this time. For those institutions outside the U.S. interested in deslorelin, contact Peptech Animal Health directly for information at www.peptech.com. For AZA accredited institutions in the U.S. please submit the Deslorelin Agreement Form to:
Sally Boutelle, Program Coordinator
AZA Wildlife Contraception Center
Saint Louis Zoo
1 Government Drive
St. Louis, MO 63110
314-646-4595; fax: 314-646-5534
Contraception@stlzoo.org
REVERSIBLE VASECTOMY

This technique has been used successfully in thousands of lab rodents and humans (90% success rate in more than 4,000 cases: Silber & Grotjan 2004), but has only been attempted in a few exotic species, so should be considered experimental. Reversals have been accomplished in bush dogs (DeMatteo et al. 2006) and most recently in a Przewalski's Horse. Initial vasectomies have been performed in chimpanzees but reversals not yet attempted. Thus, the procedure should not be used in males likely to be recommended for subsequent breeding until more experience is gained with a broader range of species.

To increase the chance of successful reversal, it is important that an "open-ended" vasectomy be performed, leaving the distal (testicular) end open to permit leakage, which allows a pressure-relieving granuloma to form, minimizing vas or epididymal damage (Silber 1977a). The proximal (abdominal) end can be cauterized, providing an effective seal which prevents spontaneous recanalization (Silber 1976, 1977a,b).

Reversal surgery is possible subsequent to other vasectomy procedures but requires a very difficult anastomosis of the vas to the epididymis to reverse. The "open-ended" vasectomy permits reversal via the much simpler vasovasostomy (Silber 1977a, 1978, Silber et al. 1977).

Open-Ended Vasectomy Procedure - The typical midline incision used in neutering results in difficulty freeing the proximal end of the vas deferens during the subsequent reversal procedure. Rather, the vas should be isolated from the cord via a small incision in the upper scrotum or at the external inguinal ring. Because the thickness of the scrotal skin may preclude the scrotal approach used for humans, a 1- to 1.5-cm incision should be made over the external inguinal ring. The vas deferens should be kept moist by pulsatile irrigation with heparinized saline (2500U heparin/500 ml NaCl) to avoid post-operative scarring. After the vas deferens is transected, the abdominal (proximal) cut end should be cauterized by inserting a needle electrode about 1 cm internally. If only the mucosa is cauterized, leaving the muscle is unharmed, a very tight seal will form to achieve blockage. The distal end should be left open for leakage to release pressure.

Vasovasostomy - Dr. Sherman Silber, the physician who pioneered the technique, has offered his services to the zoo community to perform reversals. If there is sufficient interest among zoo veterinarians, we can organize training session in the technique. Otherwise, Dr. Silber should be contacted to perform the surgery. In general, the procedure entails making an incision over the upper scrotum and external ring similar to the original incision for the vasectomy, exposing the vas deferens longitudinally by blunt dissection, facilitated by placing a small Penrose drain underneath the vas. The distal and proximal ends of the vasa are held with vasovasostomy clamps and the scarred ends of both sides are resected. Translucent fluid is aspirated from the distal cut end with 22 g medicut and 1-cc syringe to check for the presence of sperm. Absence of sperm in the fluid may indicate an epididymal blockage which makes successful vasovasostomy unlikely. However, if the original vasectomy was open-ended, this complication is very unlikely. The vasovasostomy is performed using 9-0 nylon interrupted mucosal sutures and 8-0 nylon interrupted muscularis sutures.
Latency to Effectiveness - Latency to disappearance of sperm following vasectomy will depend on the species and individual, perhaps as long as 2 months, until residual sperm either degenerate or are passed.

Precautions - Vasectomy is not recommended for species with induced ovulation because mating will result in female pseudopregnancies with prolonged periods of progesterone elevation, which can cause pathology of uterine and mammary tissue. Endogenous progesterone and progestin contraceptives cause similar disease.

Contact for More Information - Dr. Sherman Silber (DrSherm@aol.com)

References:
IUD’s

- Intra Uterine Devices.
- Very cheap – 1000CFA each
- Some skill required to place
- Poor success rate in juveniles or individuals that haven’t given birth (nulliporous) – will fall out
- BUT – don’t alter social hierarchy or oestrus cycles
- Acts as a physical barrier

**IUD Placement 1**
Measure uterine depth

**IUD Placement 2**

Withdraw device into sleeve with string.
Set depth marker from previous uterine measurements

IUD Placement 3

Which contraception method to use?

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CHIMPANZEE AND GORILLA
Recommendations (Does not include Implanon, as American recommendations, however, the authors would put implanon as currently the most reliable chemical contraceptive for Apes.)

1. MGA implant (F)
2. Birth Control Pills (for females that reliably take medicated treats) (F)
3. Depo-Provera (F)
4. GnRH Agonists - Gonadotropin Releasing Hormone Agonists are considered the safest reversible contraceptives, but dosages and duration of efficacy are not well established for all species.
   - Suprelorin® (deslorelin) Implants (F or M)
   - Lupron® Depot Injection (F or M)

(a) Cautions
(1) Chimpanzee sexual swelling: available data show that females exhibit partial to normal swellings on birth-control pills, and partial to no swellings on MGA, with differences likely due to relative doses or pill regimen that includes a placebo week.
(2) Combination birth control pills are NOT recommended during the first year of lactation because the Estrogen can suppress milk production.

Research and Monitoring
   (1) Surveillance for deleterious effects Contact Dr Sue Walker s.walker@chesterzoo.org (Europe) or Sally Boutelle contraception@stlzoo.org (USA)

OLD WORLD MONKEYS
Recommendations
1. GnRH Agonists - Gonadotropin Releasing Hormone Agonists are considered the safest reversible contraceptives, but dosages and duration of efficacy are not well established for all species; males may require higher doses. Side effects are generally similar to those associated with gonadectomy, especially the potential for weight gain unless diet is controlled.
   - Suprelorin® (deslorelin) Implants (F or M)
   - Lupron® Depot Injection (F or M)
2. MGA implant (F)
3. Depo-Provera® injection (2.5-5 mg/kg body wt. at 45-90 day intervals throughout breeding season) (F).

Cautions
(1) No deleterious effects noted, although caution is suggested with progestin use

Research and Monitoring
(1) Chart sexual swelling in species for which it applies
   (b) Surveillance for deleterious effects - Contact Dr Sue Walker s.walker@chesterzoo.org (Europe) or Sally Boutelle contraception@stlzoo.org (USA)