

A KEEPER'S POINT OF VIEW OF DESLORELIN CONTRACEPTIVE USE WITH 0.2 SLOTH BEARS (*MELURSUS URSINUS*)

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According to the AZA Wildlife Contraception Center, Gonadotropin-Releasing Hormone Agonists (GnRH Agonists) such as deslorelin (Suprelorin®) implants are considered the safest reversible contraceptives for use in carnivores. Unfortunately, dosages and duration of efficacy are not well established for all species. Using this contraceptive method with two of our female sloth bears, we learned that side effects may vary greatly between individuals. Our 10 year old female, who has been on this implant for more than a year, has not exhibited any effects other than weight gain. Our 13 year old female, who was implanted for the first time, exhibited major mood swings along with sudden weight gain. It is unknown whether the side effects seen can be correlated with the implant, its dosage or may simply be the result of variation in individual response.

DESLORELIN IMPLANTS

The brand name Suprelorin® (deslorelin) implant, manufactured by Peptech Animal Health, Australia, is a GnRH Agonist (Gonadotropin-Releasing Hormone Agonist), which temporarily suppresses the reproductive endocrine system and prevents production of pituitary (FSH and LH) and gonadal hormones (estradiol and progesterone in females and testosterone in males). The effects, similar to those following an ovariectomy or castration, are reversed after the hormone content of the implant is depleted. Deslorelin initially stimulates the reproductive system, which can result in estrus and ovulation in females, followed by a down-regulation of the system. Species with induced ovulation (such as bears) may ovulate and become pseudo-pregnant when first treated. In some seasonal breeders, estrus and ovulation may be induced even during the non-breeding season. To suppress this initial stimulation, supplemental progestin treatment for 15 days (7 day prior to and 8 days after implantation) with Megestrol acetate is recommended. During the transition phase at the end of the period of contraception, estrous behavior or even copulation may occur. Side effects are similar to those associated with ovariectomy or castration, especially the potential for weight gain if diet is not controlled. (AZA Wildlife Contraception Center, <http://www.stlzoo.org/animals/scienceresearch/contraceptioncenter/>).

Suprelorin® comes in both 6 and 12-month formulations. Durations of efficacy should be considered minimums and dosage recommendations should only serve as guidelines as individuals may respond differently. Data from various species has shown that while individual responses may vary widely, they seem to be consistent for each individual. (AZA Wildlife Contraception Center, <http://www.stlzoo.org/animals/scienceresearch/contraceptioncenter/>).

SUBJECTS

Sloth bear: Hana

Date of birth: 12/19/94

Starting weight: 93kg (4/10/08)

Implant: 2 Suprelorin® 9.4mg implants (deslorelin; 12-month formulation)

Date of implant: 4/10/08

Supplemental contraception: 490mg Megestrol acetate oral suspension SID given 4/3/08-4/16/08

Reason for implant: To prevent estrous and possibility of reproduction with maturing 2.5yr old male cub

Sloth bear: Khali

Date of birth: 12/27/98

Starting weight: 97.1kg (11/4/06)

Implant: 2 Suprelorin® 9.4mg implants (deslorelin; 12-month formulation)

Date of implant: 5/3/07

Supplemental contraception: N/A; was previously implanted w/ an MGA implant which was removed 5/3/07 due to infection and replaced with deslorelin implant

Date of re-implant: 5/7/08

Reason for implant: To prevent estrous and reproduction with male companion

BEHAVIORAL CHANGES SEEN AFTER IMPLANTATION

HANA

- Major mood swings: would shift between being extremely irritable and aggressive, calm and lethargic, and flirty and solicitous.
 - Began fighting and exhibiting extreme aggression towards 2.5yr old cub to the point that they had to be separated in order to protect him from further injury. (This resulted in the cub being permanently separated before the normal weaning process was completed.)
 - Exhibiting aggression towards other bears (by digging at and slamming against their doors when passing by their enclosures as well as making threatening vocalizations).
- Less responsive to keepers: difficult to shift, train and interact with.
- Started pacing in yard and stalls.

KHALI

- No changes noticed.

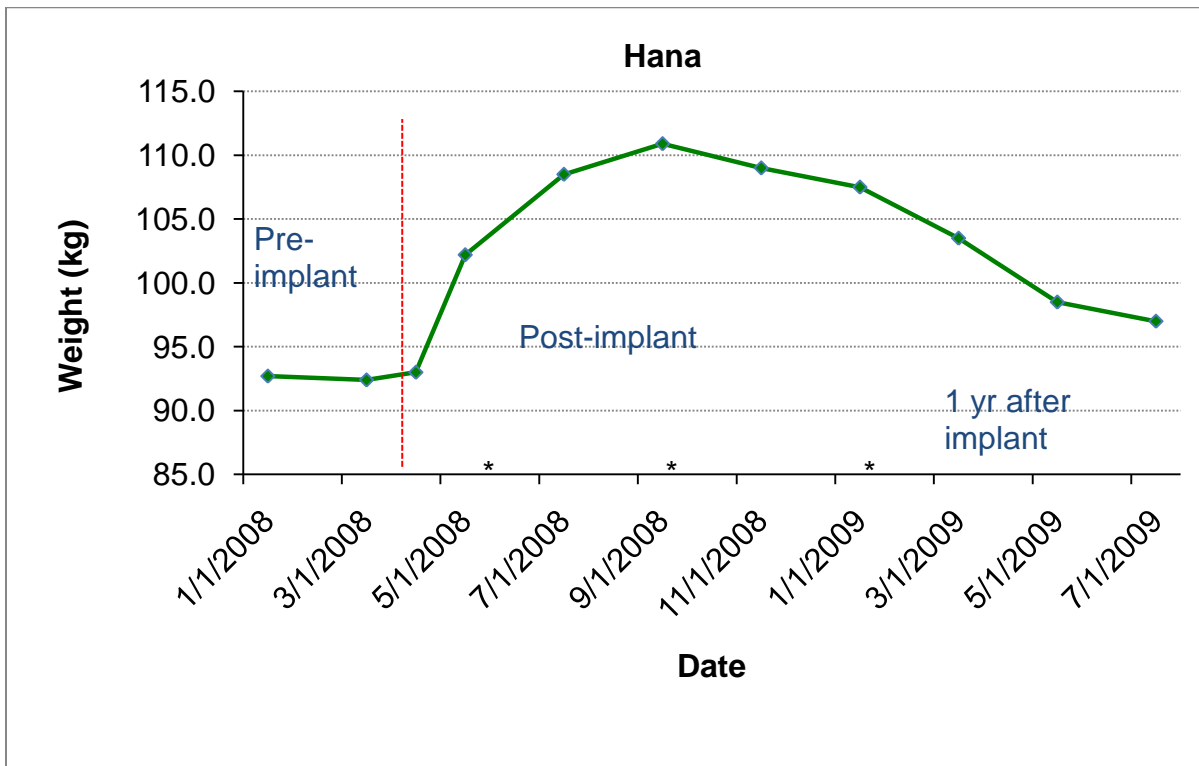
PHYSICAL CHANGES SEEN AFTER IMPLANTATION

HANA

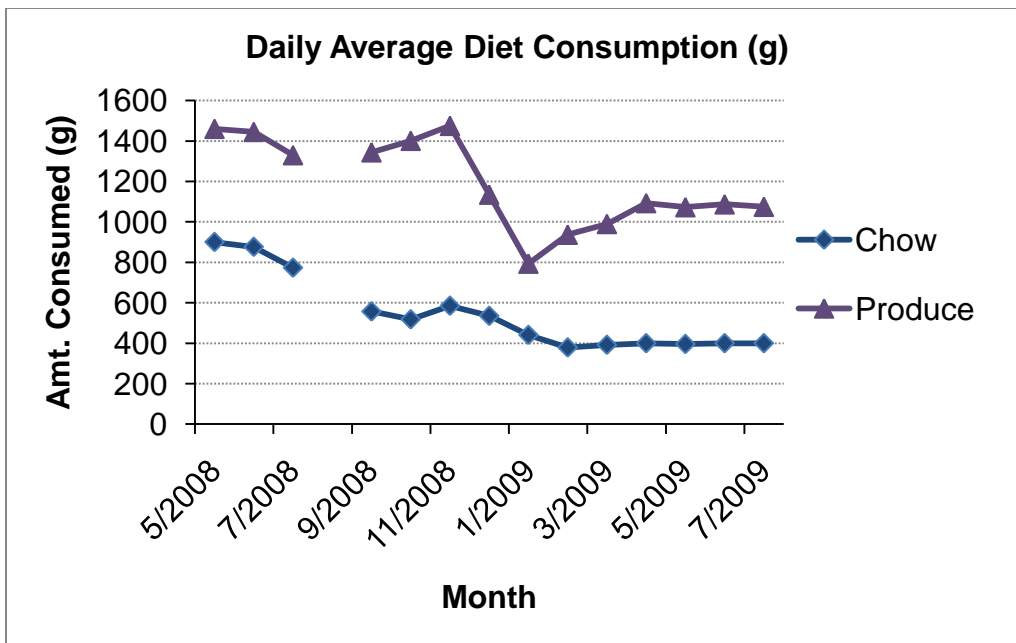
- Lethargy and a dazed state noted 4 days after implantation.
- Swollen mammary glands (mammary development) noted 5 - approximately 25 days after implantation.
- Increased appetite 7 days after implantation, followed by decreased appetite for at least 6 months after implantation.
- Pink genitalia noted 7 days after implantation.
- Generalized allergic-like reaction (lots of scratching) noted 6 – 9 days after implantation.
- Steady weight gain noted despite decreased food consumption and diet reductions.
- No evidence of estrus or ovulation following “reversal” of implant a year later.

KHALI

- Weight gain noted.



* = diet reductions



Hana's Original Diet

450g Mazuri omnivore chow

450g Hills adult dog food

450g grapes

800g orange

225g variable fruit (pear, apple, mango, cantaloupe, tomato, honeydew, beet)

*** Diet Changes** (post implant & no longer w/ cub)

6/08 – Hills adult dog food switched to Hills light dog food

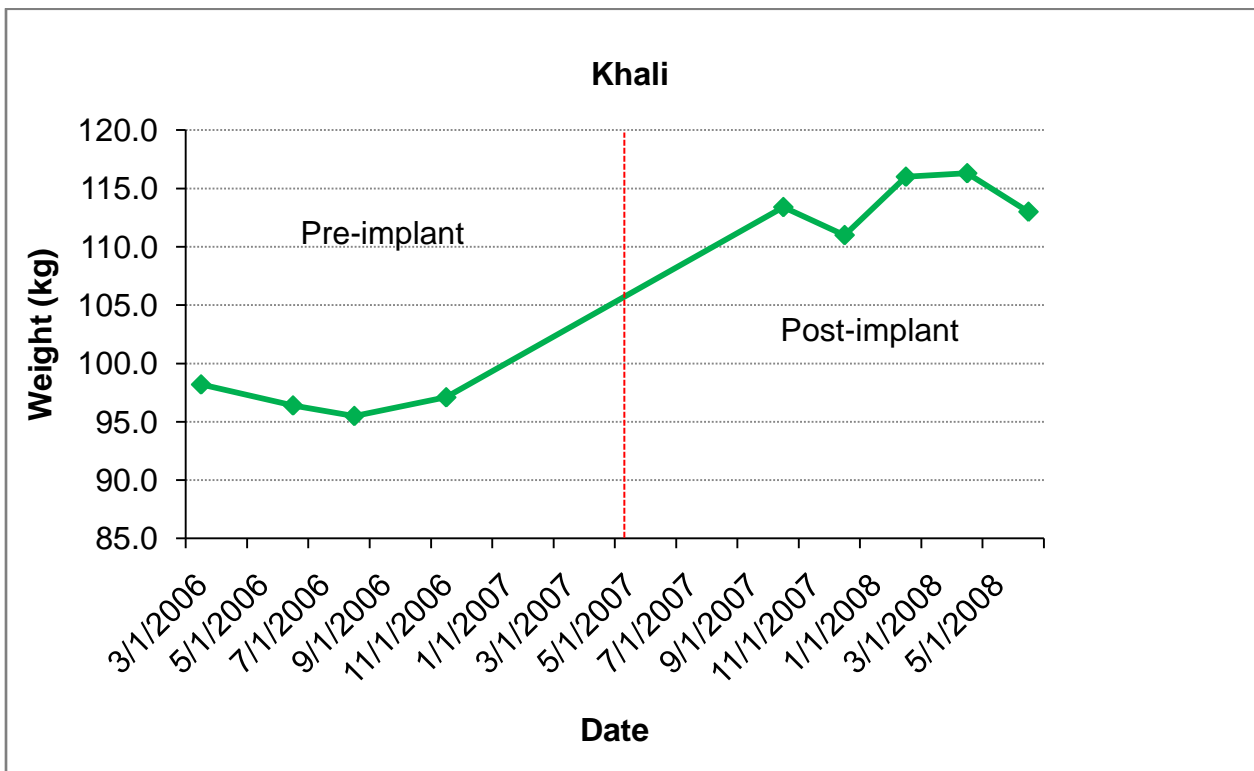
9/25/08 - reduced to 300g Mazuri omnivore chow & 300g Hills light dog food

1/24/09 - reduced to 200g Mazuri omnivore chow & 200g Hills light dog food; also reduced to 400g orange

Hana *Implanted 4/10/08

| Date | 1/17/08 | 3/6/08 | 4/10/08 | 5/30/08 | 7/17/08 | 9/11/08 | 11/13/08 | 1/23/09 | 3/26/09 | 5/28/09 | 7/23/09 |
|-------------|---------|--------|---------|---------|---------|---------|----------|---------|---------|---------|---------|
| Weight (kg) | 92.7 | 92.4 | 93.0 | 102.2 | 108.5 | 110.9 | 109.0 | 107.5 | 103.5 | 98.5 | 97.0 |
| Gain/Loss | | -0.3 | 0.6 | 9.2 | 6.3 | 2.4 | -1.9 | -1.5 | -4 | -5 | -1.5 |
| % Body Wt | | 0% | 1% | 10% | 6% | 2% | -2% | -1% | -4% | -5% | -2% |

*Switched to light canine chow 6/08; diet reduced 9/08 & 1/09



Khali's Diet 2/21/07 - Woodland Park Zoo (adjusted seasonally per consumption)

2.5lbs (1130g) Mazuri omnivore chow
 1 apple
 A few grapes
 4 variety items (1/2 banana, 1 cup blueberries, 2/3 cup grapes, 1 orange, 2/3 pear, 1/8 cup raisins, 1 boiled egg, 3/4 cup mealworms, 1/2 cup peanuts, 1.5T jelly, 1.25T honey)

*Do not have diet change or consumption data
 *Keeper notes indicate approx. 1/2 chow left uneaten most days from 5/07-10/07

Diet Change 12/27/07 - National Zoo

200g Hills light dog food
 600g Mazuri omnivore chow
 200g apple
 200g sweet potato
 200g romaine
 1 variable produce item (400g pear, grapes or banana; 800g orange, cantaloupe or honeydew; 1000g turnip)

Khali *Implanted 5/3/07

| Date | 3/11/06 | 6/2/06 | 8/10/06 | 11/4/06 | 10/23/07 | 12/17/07 | 2/14/2008 | 4/10/2008 | 6/6/2008 |
|--------------------|---------|--------|---------|---------|------------|----------|-----------|-----------|----------|
| Weight (kg) | 98.2 | 96.4 | 95.5 | 97.1 | 113.4 | 111.0 | 116.0 | 116.3 | 113.0 |
| Gain/Loss | | -1.8 | -0.9 | 1.6 | 16.3 | -2.4 | 5.0 | 0.3 | -3.3 |
| % Body Wt | | -2% | -1% | 2% | 17% | -2% | 5% | 0% | -3% |

*No weights were obtained between 11/4/06 & 10/23/07 due to exhibit move (WPZ)

*Transferred to National Zoo 11/27/07

Hana's Behavioral & Physical Changes Post Implantation

| Date | Behavioral Changes | Physical Symptoms | Comments |
|---------|--|---|---|
| 4/3/08 | | | Start Megestrol Acetate |
| 4/10/08 | | | Deslorelin implants given |
| 4/14/08 | difficult to shift – sat in chute and stared | lethargic; in a daze | |
| 4/16/08 | very cranky; fighting with cub (had to be separated due to continued aggression and injuries to cub) | swollen mammary gland; increased appetite; lots of scratching seen | Last dose of Megestrol Acetate |
| 4/17/08 | continued aggressive behavior towards cub despite physical separation (mesh door between them); not responsive to female keepers; very responsive to male curator; paying no attention to cub crying in adjacent stall | pink genitalia; mammary development; allergic-like reaction (lots of scratching seen all over body); little appetite AM | |
| 4/18/08 | paying no attention to cub in adjacent stall – spent most of day outside away from him; no aggression seen towards cub | lots of scratching seen | |
| 4/19/08 | exhibiting solicitous behavior (showing genital area); mouthing mammary glands | lots of scratching seen; mammary glands slightly less swollen | Start 3-day course of analgesic for mammary swelling and scratching |
| 4/20/08 | less responsive to keepers than usual; pacing; otherwise more calm & no aggression seen towards cub in adjacent stall | not much appetite | |
| 4/21/08 | very aggressive towards cub when reunited (separated again due to continued aggression and injuries to cub) | mammaries still swollen; decreased appetite | Last dose of analgesic |
| 4/24/08 | vocal threats towards cub in adjacent stall; heard vocalizing (whimpering?) softly while alone | | |
| 4/25/08 | aggressive towards cub in adjacent stall | | |
| 4/26/08 | not responsive to keepers PM, pacing a lot, seems out of sorts | decreased appetite; refusing honey | |
| 4/28/08 | reluctant to shift; distracted | refusing treats | |
| 4/30/08 | very aggressive towards cub in adjacent stall (visual access to cub taken away and 2 doors put between them from here on); pacing PM | | |
| 5/1/08 | pacing in rain | | |
| 5/2/08 | distracted and not responsive to keepers; not herself; aggressive towards other bears when shifting past their enclosures | not very interested in treats | |
| 5/9/08 | charging mesh, pacing and running around enclosure (reaction seemed to be correlated with seeing pregnant volunteer who she used to be fine with) | | |
| 5/10/08 | difficult to shift past enclosure with other bears | | |
| 5/11/08 | pacing | | |

| | | | |
|--------------------|--|---|---|
| 5/12/08 | acting more normally; responsive to keepers | mammaries back to normal | |
| 5/16/08 - 5/22/08 | difficult shifting; especially past other female bear's enclosure | | |
| 5/23/08 | adult male showing interest in her (did mesh door intros) – no interest from her towards male | | |
| 5/28/08 - 6/2/08 | aggressive towards adult male in adjacent enclosure (mesh door intros) | | |
| 6/14/08 - 9/30/08 | difficult shifting – not interested in food, enrichment, training or going outside; sleeping a lot | decreased appetite; leaving a lot of food; still gaining weight | (Behavior similar to when she “dens up” for the winter) 2 diet decreases between 6/08 & 9/08 |
| 8/3/08 - 8/25/08 | Still showing some aggression towards adult male during intros; sleeping a lot during intros | | Mesh door intros with adult male tried again; full contact intros also tried (unsuccessful) |
| 11/26/08- 12/13/08 | Starting to shift well; playing and acting silly; behaving more like herself | | |
| 12/27/08 | refusing to shift inside PM | | |
| 2/11/09 | sniffing where adult male had travelled in yard previously | | |
| 2/11/09 - 3/21/09 | adult male showing interest in her feces | | |
| 3/25/09 – 4/1/09 | interest shown towards adult male; adult male interested in her | | Mesh door intros tried again (successful) |
| 4/9/09 – 8/09 | playing with adult male; flirtatious behaviors seen (showing genital area; allowing sniffing/licking of genital area); no copulations seen | No evidence of estrus or ovulation | Successfully put with adult male Did not come into heat during breeding season |

CONCLUSIONS

We caution anyone interested in using deslorelin contraception with their bears to consider the possible side-effects and variation in individual response to this birth control method. We do not recommend using this contraception as a way to keep a female and her male cub together for a longer period of time without risk of the cub breeding with the female. Our attempt to do this using deslorelin resulted in an abrupt rejection and separation of the cub from the female.

Without investigating more cases of deslorelin use, we cannot say how common any of these side effects are, or even if the side effects exhibited by these two bears were definitely correlated with the deslorelin. It is possible that Hana was ready to separate from her 2.5 yr old cub and may have done so just as abruptly regardless of the implant. Khali's weight gain may have been correlated with her move to a smaller enclosure. Although we cannot say for sure, we suspect deslorelin was the major factor in the behavioral and physical changes we saw in these bears. The AZA Wildlife Contraception Center states that while individual responses may vary widely, they seem to be consistent for each individual. We have continued to implant Khali with deslorelin each year but will not use this method of contraception for Hana in the future.

Our final caution regarding the use of deslorelin contraception is that it is not immediately reversible. The contraception reverses when it wears off approximately a year later, but it cannot easily be removed once implanted without invasive exploratory surgery to locate the implants under the skin. Due to the extensive nature of this type of removal, we left Hana on the implant. More than a year after implantation, we still wait for Hana's estrous cycle to return to normal.

REFERENCES AND ACKNOWLEDGEMENTS

- AZA Wildlife Contraception Center, <http://www.stlzoo.org/animals/scienceresearch/contraceptioncenter/>
- Rana Bayrakci, Woodland Park Zoo, for providing information on Khali prior to her transfer to Smithsonian's National Zoological Park