SHORT COMMUNICATION

COMMENTS FROM THE AZA CONTRACEPTION ADVISORY GROUP ON EVALUATING THE SUITABILITY OF CONTRACEPTIVE METHODS IN GOLDEN-HEADED LION TAMARINS (*LEONTOPITHECUS CHRYSOMELAS*)

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Abstract *Animal Welfare 2002, 11*: 343-348

Reversible contraceptives, such as melengestrol acetate (MGA) implants, have become an invaluable tool that captive-animal managers use to maintain various species in social groupings while avoiding unwanted pregnancies. The American Zoo and Aquarium Contraception Advisory Group (AZA CAG) monitors the efficacy, reversibility, and safety of contraceptives used in captive exotic mammals worldwide. Because so few data exist on contraceptive efficacy and safety in exotic species, it is critical that evaluations reflect an understanding of the mechanism of action of the active ingredient as well as of the delivery system. The following discussion addresses the concerns of the CAG over the manner in which De Vleeschouwer et al (Animal Welfare 2000, 9: 251–271) analysed MGA implant reversibility data in golden-headed lion tamarins.

Keywords: *animal welfare, Callitrichidae, contraception, golden-headed lion tamarin, melengestrol acetate, reversibility*

Introduction

Reversible contraception has become an invaluable tool that captive-animal managers use to maintain various species in social groupings while avoiding unwanted pregnancies. A survey-based study by De Vleeschouwer *et al* (*Animal Welfare 2000, 9*: 251–271) evaluated one such contraceptive, the melengestrol acetate (MGA) implant, in golden-headed lion tamarins (GHLT) (*Leontopithecus chrysomelas*). The American Zoo and Aquarium Contraception Advisory Group (AZA CAG) monitors the use of this synthetic progestin, along with that of other contraceptives used in captive exotic mammals worldwide, via an annual survey. The objectives of the CAG include monitoring contraceptive efficacy, reversibility, and safety. The following discussion addresses the concerns of the CAG over the manner in which De Vleeschouwer *et al* (2000) analysed the MGA implant reversibility data in golden-headed lion tamarins.

Point 1

On p 254 of the paper by De Vleeschouwer *et al* (2000), the following assumption is made: "Longevity for MGA implants was assumed to be about two years." This assumption is central to the way the results of this study are interpreted. It is likely that this assumption originated from the CAG recommendations which suggest replacement of MGA implants every two years. This recommendation should not be interpreted to mean that implants are no longer effective after two years. The CAG has emphasised that the use of MGA implants in exotics is experimental, and has recommended that MGA implants be replaced after two years for four reasons: because experience has shown that these implants are effective for at least two years; because there is no assay to monitor MGA presence that has been validated for exotics; because scant research has been done to document resumption of ovarian cycling with an implant in place; and because determining efficacy duration for each species/dose by allowing implants to wear out results in unwanted births and surplus animals. Additionally, the fact that no two individuals are physiologically identical results in individual variation in the length of efficacy for a contraceptive. For these reasons, the CAG considers a contraceptive bout for an implant as ongoing until the implant is removed or determined to be lost (DeMatteo 1997).

That three female GHLT conceived with an MGA implant in place 25–29 months following insertion is important but inconclusive information on their duration of efficacy. These cases provide important baseline information that the CAG uses to determine for a particular species the minimum MGA dose and the implant configuration required in order for conception to be effectively ruled out for a two-year period. The fact that some females are capable of conceiving with a two-year old implant in place should not lead one to assume that all two-year implants are expired. Instead, it is the MGA dose, implant size, and physiology of the animal which determines duration of implant efficacy.

We suggest that it is inappropriate to include the 21 GHLT females with MGA implants still in place because no assays were performed to determine whether the females were or were not still reproductively suppressed by the two-year old implants. MGA implants may be effective for longer than two years, as was documented with female Hamadryas baboons (*Papio hamadryas*) at the Saint Louis Zoo. The sexual swellings of these two baboons were completely suppressed even though their MGA implants were 43 and 73 months old. However, within days of removing the implants, both females developed sexual swellings.

When the 21 implanted GHLT females are removed from the analysis, seven females remain. The data presented for these females are inadequate to evaluate reversibility for two primary reasons. First, there is no information regarding variables within the social group that could have an impact on the females' ability to conceive (ie presence of fertile males, dominance status, etc). Second, there is no information on the amount of time that elapsed following MGA implant removal and the determination that the contraceptive was irreversible. Such information is critical to understanding whether there is truly a problem with reversibility in GHLT following contraception with MGA.

Analysis of CAG survey data indicates that in at least two of the seven GHLT female subjects, only three or four months had elapsed before the MGA implants were deemed irreversible by De Vleeschouwer *et al* (2000). Specifically, in their annual CAG survey, the Antwerp Zoo reported that several GHLT had implants removed in May 1999 as part of a reversibility study. The current article under review received final acceptance in October

1999. This would allow only a very limited time for those females to reverse (ie to return to fertility) prior to the initial submission of the article.

Table 1 shows that the time taken to reverse in the related golden lion tamarin (*Leontopithecus rosalia*), for which more long-term data exist, varied from 1 to 26 months. Variation in time to reversal was also seen in other Callitrichidae (Table 1). Time to reversal varies for numerous reasons, including individual differences, female age, parity prior to contraception, mate access, female weight, and reproductive quality of her mate.

Point 2

The statement that this study demonstrates that "there is some evidence for a higher frequency of stillborn infants than before implantation" (p 259) is misleading. The authors clearly state later that "it is unclear whether the higher proportion of stillborn infants is really due to implantation, since the stillbirths did not always occur in the first litter after implantation" (p 259). In addition, although the authors discuss the effect of age on litter size, the effect of age on percentage of stillbirths is not discussed. A more appropriate analysis would include all available birth records (ie studbook data) and would not be limited to the pre- and post-contraceptive births of females implanted with MGA.

Point 3

The statement that this study demonstrates that "medical side-effects of MGA implants seem to be infrequent, but for some females uterine changes have been reported" (p 259) must be interpreted with caution. When pathologists find any abnormality on biopsy or necropsy, a great deal of care is taken in connecting a cause with an effect. This caution is a result of knowing that there are many environmental and genetic components that can potentially produce similar results. The CAG works closely with a veterinary reproductive pathologist to analyse data both from control animals without contraception and from animals treated with contraceptive. This comparison is critical in separating problems associated with contraception from those resulting from other factors.

Point 4

On p 261, the following information is incorrect: "The AZA CAG report mentions that eight out of 13 golden lion tamarins whose implants were removed did not resume reproduction." The report (DeMatteo 1997) actually states the opposite. That is, five out of 13 golden lion tamarins whose implants were removed did not resume reproduction, while eight did resume reproduction. In other words, 60% of the females that had had implants removed in order to allow reproduction had conceived at the time that DeMatteo (1997) was compiled.

Conclusion

The purpose of the above comments is to provide additional pertinent information accumulated through the AZA CAG's contraception database on related and other primate species that can be used to evaluate the conclusions drawn by De Vleeschouwer *et al* (2000). Because so few data exist on contraceptive efficacy and safety in exotic species, it is critical that evaluations reflect an understanding of the mechanism of action of the active ingredient as well as of the delivery system. And although it is impossible to control all the variables, it is necessary to account for these variables (ie animal age, reproductive history, weight, variable duration of implant efficacy, etc) in the interpretation. The universal aim of all

Table 1 **Summary of data contained in the AZA CAG Contraception Database for Callitrichidae females which had an MGA implant removed to allow reproduction.** Unk, unknown.

Species	Number of MGA implants removed for reproduction (total number inserted)	Female's age when implant removed for reproduction (years)	Parity	Duration implant removed for reproduction in place (months)	Successful reversal	Interval: implant removal to conception (months)	Interval from removal date to last report date or animal death (months)	Infant status	Comments
Callimico goeldii	6 (114)	4	No	19	Yes	10.75	---	Live	
		6.5	Yes	21.5	No	---	53	---	Unidentified mineral density/calcification in uterus or bladder noted two years earlier.
		5	Unk	27	No	---	5.5	---	Female died 5.5 months after implant removed.
		10	Yes	9	Yes	9.5	---	Abortion	03/12/99 Abortion. Based on vulva swelling (02/01/99) foetus age estimated as one month.
		7.5	No	9	No	---	12	---	Female died 12 months after implant removed.
		10	No	9.5	No	---	16	---	
Callithrix jacchus	13 (27)	5	Yes	19.5	No	---	3.5	---	Birth pending as of 02/98 but no follow-up provided.
		6	Yes	18	No	---	3.5	---	Birth pending as of 02/98 but no follow-up provided.
		6	Yes	19	No	---	3.5	---	Birth pending as of 02/98 but no follow-up provided.
		4	Yes	6.25	Yes	0.5	---	Live	
		6	Yes	19.5	No	---	3.5	---	Birth pending as of 02/98 but no follow-up provided.
		5	Yes	7	Yes	0.5	-	Live	
		5	Yes	6.75	Yes	0.5	-	Live	
		8	Yes	7	Yes	4.25	-	Live	
		8.5	Yes	19.5	No	---	3.5	---	Birth pending as of 02/98 but no follow-up provided.
		5.5	Yes	21.5	Yes	2	---	Stillbirth	C-section performed. Foetus was full term but a stillbirth.
		6	Yes	9	Yes	4	---	Live	
		5	Yes	9	Yes	1.25	---	Stillbirth	Delivered by C-section.
		4.5	Yes	5	No	---	15	---	
Leontopithecus chrysomela	8 (83)	8	Yes	26	Yes	3	---	Live	
		11	Yes	15.5	Yes	5.25	---	Stillbirth	Over the next 2.25 years, this female had three more births all of which were live.
		11	Yes	11.25	No	---	23	---	Female bred but failed to conceive prior to death two years after implant removed. Her mate did sire offspring with another female after her death.
		6	No	18	No	---	33.5	---	Female died three years after implant removed.
		8.5	Yes	22.5	No	---	2	---	Female part of contraception reversibility study.
		8	Yes	17.5	No	---	0.5	---	Pregnant at start of bout. Gave birth ten days after implant inserted.
		6	Yes	14.25	Yes	2.75	---	Unknown	Female part of contraception reversibility study.
		7.5	Yes	13.5	No	---	1.5	---	Female part of contraception reversibility study.
Leontopithecus rosalia	22 (275)	5.5	Yes	21.75	Yes	21.75	---	Live	
		10.5	Yes	18	Yes	9	---	Live	
		4.5	No	12.75	Yes	25.75	---	Live	
		3	No	21.25	Yes	2	---	Live	
		10.5	Yes	22.5	Yes	2	---	Live	
		7	Yes	19	Yes	2	---	Live	
		6	Yes	20.25	Yes	1	---	1 Live and 1 Stillbirth	

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Species	Number of MGA implants removed for reproduction (total number inserted)	Female's age when implant removed for reproduction (years)	Parity	Duration implant removed for reproduction in place (months)	Successful reversal	Interval: implant removal to conception (months)	Interval from removal date to last report date or animal death (months)	Infant status	Comments
		8.5	Yes	12.25	Yes	0.5	---	1 Live and 1 Stillbirth	
		6	No	37	No	---	7.5	---	Transferred 7.5 months after implant removed. Lost to follow-up.
		4	Yes	26.5	Yes	10	---	Unknown	Young found dead.
		10.5	Unk	13	No	---	63.5	---	Female died 5.25 years after implant removed.
		8	Yes	6.5	No	---	5	---	Female died five months after implant removed during transport.
		7	Yes	25	Yes	10.75	---	Live	
		5.5	Unk	9	No	---	80	---	02/04/00 Removed cystic right ovary.
		9	No	45.75	No	---	40	---	
		10.5	Unk	21.75	No	---	42	---	
		15.5	No	34.5	No	---	55.5	---	Reported that both this female and her mate are old.
		10	No	18	Yes	Unk	---	Abortion	Foetus of unknown of age but early gestation.
		16.5	No	18	No	---	9.5	---	Physical exam nine months after implant removed revealed that this female is no longer reproductive.
		6	Unk	10	Yes	12.25	---	Stillbirth	Note that this female was exposed to heavy smoke inhalation in first quarter of pregnancy.
		5	Unk	16.75	Yes	8	---	2 Live and 1 Stillbirth	
		9.5	Yes	5	Yes	0.5	---	2 Stillbirth	Another stillbirth one year and again 1.5 years later.
Saguinus imperator	1 (14)	9.5	Yes	19	Yes	0.25	---	Stillbirth	Reported that infant stillborn and possibly premature.
Saguinus oedipus	14 (273)	14	Yes	38.25	Yes	0.25	---	Live	
		11.5	Yes	33.25	Yes	0.75	---	Live	
		5	No	43.25	Yes	0.5	---	Live	
		4	No	32.75	Yes	11	---	Live	
		8.5	Yes	24.25	Yes	15.5	---	Live	
		8	Yes	19.25	No	---	26	---	
		6	No	16	Yes	0.5	---	Live	Another live birth 14 months later
		5	Yes	11.25	Yes	0.75	---	Live	
		6	Unk	26	No	---	5.5	---	
		7	No	24	Yes	0.5	---	Live	Another live birth 5.5 months later.
		5.5	Yes	Unk	Yes	0.5	---	Live	Insertion date not reported. Duration of implant possibly 24 months based on other available information.
		3	Unk	13	No	---	7	---	
		6	Yes	8.25	No	---	11	---	
		11	No	2	No	---	5	---	

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animal managers, veterinarians, and the CAG is to determine which contraceptives are safe and effective for each species.

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