

Addressing challenges in developing and implementing successful in vitro fertilization in endangered species: an opportunity for humanity to “give back”



Thousands of wild animal species on our planet are threatened by extinction. This is due to a variety of factors primarily caused by humans, including loss of habitat, pollution, and over-exploitation (hunting to extinction). The primary goal of animal conservation is the maintenance of biodiversity, since the loss of any one species can disrupt the functioning of an entire ecosystem. Broad knowledge and understanding of reproductive physiology can help overcome fertility issues in these species. For example, we may be able to enhance natural mating in the wild, or in conservation centers. However, mating in captivity is not successful in many species or is impossible because the best genetic matching pairs are not in the same location. It is here that in vitro fertilization may be able to circumvent these mating difficulties and help maintain genetic diversity, especially in small, endangered animal populations (1).

Whereas most human medical treatments rely on preliminary animal experimentation and modeling, the notable exception to this rule is the practice of IVF. Since the birth of Louise Brown, virtually all clinical advances in IVF have been tested directly in humans. It is clear that the clinical experience in the human model is far greater than that in other species. Since we now find ourselves in a situation where other species might benefit from this experience, this gives humanity an opportunity to “give back” to the animal kingdom the benefit of the knowledge that we have acquired over the past 40 years in the treatment of human infertility.

Most wildlife infertility syndromes still have to be deciphered and valuable lessons can be learned from human reproductive medicine. In fact, reproduction has been adequately described in only about 250 species, with most of this knowledge concentrated in mammals and birds. For example, molecular causes of reproductive aging are largely unknown and likely diverse among species. Since reproductive aging is observed in captive wild species as well as humans, studies to prolong the reproductive life span in humans can likely also benefit wildlife (1).

Applying assisted reproduction to support the conservation of rare and endangered species was originally explored in the 1980s based on successes of these techniques in livestock species and humans (1). More than 35 years later, healthy offspring have been produced by artificial insemination or embryo transfer in no more than 50 wild species. It has often been difficult to progress from first births to repeated successes (2, 3). Except for a handful of mammalian species, primarily the giant

panda and the black-footed ferret, assisted reproductive technologies have not been broadly implemented and integrated into the management of rare and endangered populations. In addition, resources allocated to basic reproductive biology remain scarce (4) and too few investigators and specialized spaces are available for this research.

Knowledge and experience with human laboratory techniques are also highly relevant in the conservation of wild animal species. In particular, fertility preservation techniques, including cryopreservation of oocytes, sperm, and embryos may be directly applied to wild species facing extinction. However, significant differences exist in the reproductive physiology between species. For example, cell survival following cryopreservation techniques relies, to a great extent, on cell permeability to cryoprotectants and the water content of cells. Since these can be quite different among various species, cryopreservation techniques may have to be modified in order to apply them to wildlife. For example, oocyte diameter in the mouse is approximately 70 μm , whereas it is approximately 120 μm in the human. The human is therefore arguably a better model for oocyte cryopreservation in the cheetah, whose oocyte diameter measures about 110 μm . Thus, strategies for fertility preservation in humans, including the field of oncofertility, have significant secondary advantages for conserving biodiversity (5).

Systematic gathering and cryostorage of biomaterials from diverse wild species have been ongoing for over 25 years. These are aimed at maintenance of gene diversity and improvement of both captive (ex situ) and wild (in situ) animal management. There are commonalities between human and wildlife biobanking programs, including similar needs to coordinate sample and data collection. Other common goals include management of samples and financial sustainability. Thus, there is a need to build bridges between these two repository worlds, sharing what we do, addressing the substantial remaining challenges, and considering the advantages of a bigger, more integrated field of global biobanking science to benefit humans and diverse species.

In spite of preservation efforts, many populations of rare and endangered species are not sustainable and will go extinct in the next 50 years. Assisted reproduction has the potential to stem this tide by enhancing genetic diversity among existing species, strengthening those species that are fading away and preserving the future fertility, through cryopreservation, of those species that are on the brink of extinction. The value of assisted reproductive technology and cryobanking in animal conservation is undeniable but there is an urgent need for more options and faster progress. Human IVF clinicians and laboratories can support the ongoing efforts of established biodiversity preservation programs. Understanding the similarities and differences in reproductive physiology in human and wild animal models can enhance knowledge in both areas. Utilization of this knowledge and experience can give humanity an opportunity to “give back” to the animal kingdom an increased

chance for survival, as animal models have given to humans for the many years in the past.

Richard J. Paulson, M.D., M.S.^a

Pierre Comizzoli, D.V.M., Ph.D.^b

^a Department of Obstetrics and Gynecology, Keck School of Medicine, University of Southern California, Los Angeles, California; and ^b Smithsonian Conservation Biology Institute, National Zoological Park, Washington, D.C.

<https://doi.org/10.1016/j.fertnstert.2018.01.031>

You can discuss this article with its authors and other readers at

<https://www.fertstertdialog.com/users/16110-fertility-and-sterility/posts/29497-25640>

REFERENCES

1. Comizzoli P. Biotechnologies for wildlife fertility preservation. *Anim Front* 2015;5:73–8.
2. Thongphakdee A, Berg DK, Tharasanit T, Thongtip N, Tipkantha W, Punkong C, et al. The impact of ovarian stimulation protocol on oocyte quality, subsequent in vitro embryo development, and pregnancy after transfer to recipients in Eld's deer (*Rucervus eldii thamin*). *Theriogenology* 2017;91:134–44.
3. Tipkantha W, Thuwanut P, Maikew U, Thongphakdee A, Yapila S, Kamolnorranath S, et al. Successful laparoscopic oviductal artificial insemination in the clouded leopard (*noefelis nebulosa*) in Thailand. *J Zoo Wildl Med* 2017;48:804–12.
4. Wildt DE, Comizzoli P, Pukazhenthil B, Songsasen N. Lessons from biodiversity—the value of nontraditional species to advance reproductive science, conservation, and human health. *Mol Reprod Dev* 2010;77:397–409.
5. Comizzoli P, Songsasen N, Wildt DE. Protecting and extending fertility for females of wild and endangered mammals. *Cancer Treat Res* 2010;156:87–100.