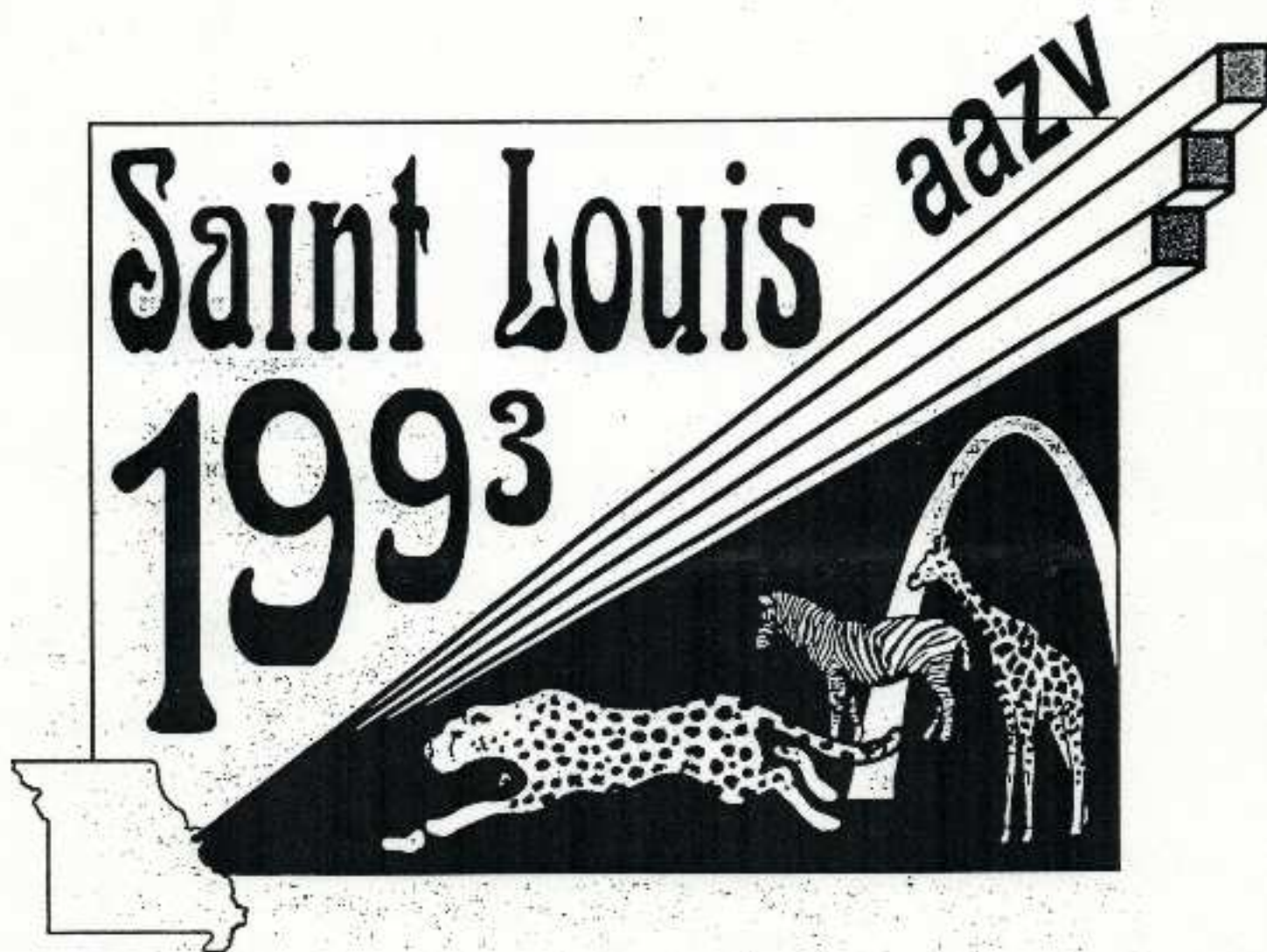


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## IMMUNOCONTRACEPTION IN ZOO ANIMALS: VACCINATING AGAINST PREGNANCY

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Three years of research with immunocontraception of captive female exotic species with a porcine zonae pellucidae (PZP) vaccine have been completed. As of June 1993, 17 zoos in 6 countries are participating in these studies. A total of 173 animals representing 35 different species have been immunized, including 24 species of ungulates, 8 carnivores and 3 species of bears (see below). As of June 1993 results are known for 11 of these species. Contraceptive efficacy ranged from a low of 77% for tur to a high of 100% for tahr, sika deer and Przewalski's horses. Based on the results of this research, as well as 6 years of PZP immunocontraceptive research with feral horses, 4 years with white-tailed deer and 15 years with nonhuman primates, the data indicate that (1) PZP immunocontraception is highly effective across a wide range of species, (2) there are differences in contraceptive effectiveness according to the type of adjuvant used, (3) no significant health problems result from PZP immunocontraception over 3 years in captive exotic species or in white-tailed deer or feral horses after 4 and 6 years respectively, (4) the vaccine is safe to give to pregnant animals, (5) the vaccine can be administered remotely, by dart, (6) a single annual booster inoculation is sufficient to extend contraception for a second year and (7) the contraceptive effect of PZP immunization is reversible after short-term use (up to 2-3 years).

Issues of concern include (1) the number of inoculations necessary for contraceptive antibody titers (2) the amount of PZP antigen necessary for contraception, (3) appropriate adjuvants, (4) the most effective delivery systems, (5) and long-term effects upon ovarian function, after 5-7 years of consecutive treatment, and research during the past year has focused on these potential problems. Species with well-defined seasonal breeding lasting 1-3 months can be treated successfully with a single inoculation and will produce contraceptive antibody titers for up to 200 days following administration. Species with longer breeding seasons can be treated with two inoculations given over 4-5 weeks. Preliminary evidence indicates that the "standard" dose of PZP antigen (65  $\mu$ g of antigen or about 5,000 zonae)



can be reduced to between 50%-90% and still generate contraceptive antibodies. From an economic viewpoint, this means that the cost of contraception can be reduced from the current \$25/dose to somewhere between \$2.50-\$12.50/dose.

The concern over adjuvants arose primarily because of the possibility that Freund's Complete Adjuvant (FCA), which has previously been shown to be highly effective in generating high antibody titers, may lead to tuberculosis-positive test reactions in animals thus treated. Also, a small percentage of these animals produced small abscesses. A recent study of alternative adjuvants indicates that Freund's Incomplete Adjuvant (FIA), Carbopol® (Goodrich Co., Cleveland, OH), FIA = Quil-A (Superfos Specialty Chemicals, Vedback, Denmark) and DEAE-dextran (Sigma Chemical Co., St. Louis, MO) all produce contraceptive antibody titers when used with PZP vaccine. Muramyl dipeptide, and Ribi Adjuvant System did not produce contraceptive antibody titers.

Remote delivery is possible, but not all delivery systems are adequate because of the high viscosity of the antigen/adjuvant emulsion. The system which has provided the best results thus far is the Pseudart® 1.0 cc barbless dart (Pseudart, Inc., Williamsport, PA) fired from a Pseudart capture rifle, blowpipe or CO<sub>2</sub>-powered pistol.

Long-term effects of the PZP vaccine upon ovarian function are not well understood and are the most important focus of the studies that are currently underway. While there is no evidence for debilitating side effects from PZP immunocontraception through 6 years of treatment, most available data indicate that developing ovarian follicles may also become the focus of action for anti-PZP antibodies, as well as ovulated ova, and that ovarian pools of oocytes may be depleted by prolonged use of the vaccine. Two species, rabbits and dogs, appear to have ovarian function disrupted even after short-term use; but there is no evidence of this in other species thus far. Reversibility of the contraceptive action of PZP after short-term use (1-2 years) has been documented in domestic mares. The majority of feral horses treated for 4 consecutive years demonstrated ovulatory cycles based on urinary estrone conjugates and behavior. At the Bronx Zoo a muntjac contracepted in 1991 produced a fawn in 1993, and at the Toronto Metropolitan Zoo, 3 of 6 tur contracepted in 1990 produced kids in 1993. At the Zoologischer Garten Koln, 3 banteng, which were contracepted in 1991 and which subsequently stopped demonstrating estrous cycles, were all cycling again in 1993. A protocol for the study of long-term effects of PZP contraception upon ovarian function and reproductive tract histopathology has now been developed and will be implemented in future studies. There can be no guarantee that unanticipated long-term effects will not appear, but annual updates of data will be provided to all participating zoos as this research progresses. We do not recommend that valuable animals in SSP breeding programs be treated with the PZP vaccine until the data base for long-term effects is broader.

Species treated as of June 1993 are given below. Those marked with asterisks have been treated successfully; for all others, data were not yet available at the time this abstract was prepared. These species included Przewalski's horse, \* banteng, \* sambar deer, \* axis deer, \* sika deer, \* muntjac deer, \* Himalayan tahr, \* North American wapiti, \* white-tailed deer, \* West Caucasian tur, \* African lion, tiger, black buck, Indian wolf, North American bison,

pygmy hippo, addax, ibex, onager, river hippo, impala, kudu, giraffe, waterbuck, fallow deer, aoudad, mouflon sheep, cougar, jaguar, bobcat, leopard, European brown bear, Kodiak bear, Asiatic black bear, Asian small-clawed otter. Contraception failed to be achieved in the river hippo but may have been the result of a lack of adjuvant or poor injection. Although contraceptive effectiveness has not yet been assessed, very high antibody titers have been achieved in the Indian wolf, African lion and tiger.