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The baboon (*Papio sp.*) as a model for female reproduction studies

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Abstract

Due to their size and anatomical similarity to humans, baboons make an excellent model for reproductive studies. Baboons have a simple short cervix, muscular uterus, ovaries just lateral to the uterus, and similar vasculature to that of humans. Because of the size of the animals, instruments designed for use in women can be readily used on baboons. Noninvasive determination of phase of estrous cycle is readily made by observation of changes in perineal sexual skin turgor and color. Some advantages of use of baboons compared to other nonhuman primates is that they are non-seasonal breeders, allowing for studies to be conducted year-round, have minimal infectious disease risks to humans as they do not carry Herpes B, and have a social structure allowing for easy group formation. Baboons serve as good models for many conditions in humans and should be considered for studies investigating reproductive issues.

Keywords

baboon; nonhuman primate; gynecology; contraception; research; model; reproduction

1. Introduction

Baboons (*Papio sp.*) are relatively large nonhuman primates that serve as good models for reproductive studies, as their reproductive tracts are similar to that of humans [1, 2, 3, 4.] Sexually mature female baboons typically range in weight from 14 – 18 kg, but can approach 30kg if obese [5.] Baboons have a relatively long life span and sexual maturity occurs at age 4–6 [6, 7, 8.] Females naturally experience an interbirth interval of approximately one to three years [6, 9,] which allows for multiple birthing event studies to be conducted in a reasonable timeline in this closely related species.

A significant positive consideration for the use of the baboon is the safety to personnel. All macaques are considered potential carriers of Macacacine (Cercopithecine) herpesvirus 1

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(Herpes B) which has a high rate of fatality when contracted by humans [10, 11, 12.] Since baboons are unable to carry this virus, handling and collection of blood and other body fluid samples involves lower risk than with macaques. Although large, baboons are relatively docile, and they can easily be trained to permit injections and observations without the need to handle the animals [8, 13.]

2. Reproductive cycles and pregnancy

Female baboons display large perineal sexual skin swelling, which predictably changes throughout the estrous cycle and pregnancy, making determination of phase of cycle easy to distinguish visually by a trained observer. Swelling occurs in response to estrogen and is maximal at the time of ovulation, resolving in the luteal phase [6, 8, 14, 15, 16, 17] (Figure 1.) Since these changes are predictable, careful monitoring can eliminate the need for invasive procedures, such as blood collection, to determine menstrual cycle stage. However, the engorged sex skin can also make visualization of the straight cervical canal difficult due to elongation of the vaginal vault. Therefore, transcervical procedures are optimally timed during the early follicular or late luteal phase when swelling is minimal [18.] Alternatively, hormonal contraceptive agents such as medroxyprogesterone acetate or combined oral contraceptives can be used to manipulate the cycle [15, 18.] Females typically become sexually mature between 4 and 6 years of age [19, 20.] In a closed colony at the Southwest National Primate Research Center (San Antonio, TX), females are maintained in breeding groups from approximately 6 years until 16 to 18 years of age. Aged baboons can experience menopause similar to humans, making reproductive problems more difficult to diagnose after this age [8, 21, 22.] Pregnancy can be diagnosed accurately by trained personnel observing changes in perineal sexual skin, bimanual palpation, and/or the use of ultrasound [8.] Gestation length is approximately 163–185 days [6, 8, 9, 19, 23, 24, 25.] Standard biometric ultrasound measurements are available to determine gestational age and growth profiles of fetuses [26, 27, 28, 29.] Infants are born more developed than humans, but depend on their dams for care and nutrition up to and beyond weaning. Typically, the infants are carried by the dams until approximately 5 to 6 months of age when the dam will wean the infant off the breast [6, 19, 30.] The infant will still cling to the dam (even if pregnant again), or other adults after weaning, learning the normal foraging and other behaviors of the adults [7.]

When pregnant, baboons have a single discoid hemochorial villous placenta [8, 31,] similar to humans. In comparison, macaques have a bi-discoid placenta and a slightly shorter gestation (168 days [6, 8, 32, 33.]) As with humans, some baboons will immediately return to cycling after delivery, and are therefore able to conceive rapidly [9.] Others do not resume cycling until the infant is weaned at 5 to 6 months [6.] Single births are typical, and twins rare but possible [6, 8, 34.] Unlike macaques which tend to be seasonal breeders, baboons are monthly ovulators with no breeding season [6, 8, 35.]

3. Social Biology

Social housing of baboons is readily achievable because they have a meld mold society which typically allows new members to join with minimal fighting and disruption to social

hierarchy. This is in contrast to macaques which are highly territorial and introduction of new individuals to the group may result in violent attacks. At SNPRC, a single fertile male baboon can cover a group of 15 or more females with a high pregnancy success rate [6, 8, 13.] Many males will accept unrelated offspring in the group, but care should be exercised, as some males will commit infanticide. Baboons have a mild temperament, and they can be readily trained to run through chute systems, making movement, observation, and treatment of animals relatively simple to accomplish [8.]

4. Gynecologic procedures

Because of their relatively large size, instruments such as vaginal speculums and dilators that are used in small women can be utilized effectively with no modifications in baboons. The cervix is easily visualized and relatively short and straight, making dilation simple and rapid [3, 7, 36.] In comparison, macaques have a relatively long tortuous cervix which can make dilation and catheterization difficult and prolonged [36, 37.] Like women, baboons possess paired ovaries lateral to the uterus and a midline simplex muscular uterus which is easily identified on transabdominal ultrasound [31.] The baboon has also proven to be a useful model for embryonic stem cells and artificial reproductive technologies (ART) due to its size, temperament, and similarity to humans [13.] The angle and orientation of the uterus is slightly different in primates as compared to humans due to adaptations allowing for different modes of locomotion [31.]

The vasculature supplying the pelvic organs in the baboon (*Papio sp.*) and human (*Homo sapiens*) are similar, with two branches coming from the internal iliac [39] and several anastomoses between uterine and ovarian arteries [31.] This is an important similarity, as transabdominal ultrasound can be used to monitor the infusion of agents into the uterus and potential uptake into the vasculature through the uterine or ovarian arteries. If visualization of the ovaries is required for reproductive studies, human vaginal probes can also be used because of the large size of the animal.

5. Conclusions

Baboons have already been used on a wide variety of reproductive studies, including pregnancy [40, 41, 42, 43,] fetal development [44, 45,] pharmacokinetics of compounds in pregnancy [46, 47,] abortifacient drugs [48,] nutrient restriction and the maternal/fetal relationship [49,] genetics [50,] endometriosis [51, 52,] hormonal [14, 16, 21, 53, 54, 55, 56,] temporary contraception [57, 58,] embryonic stem cells and ART [13,] pathology [59, 60,] and permanent contraception [18.] Their temperament and similarities to human anatomy warrant their continued use for reproductive studies. Significant advantages to the use of baboons in reproductive studies include their size, anatomy and physiology, the short straight cervix that can be easily cannulated, and increased personnel safety. Studies that require uterine sampling or administration of agents can typically be conducted in a less invasive manner (transcervically rather than laparoscopically) and with a shorter procedure time than those conducted in macaques. The use of baboons has already allowed for significant contributions to the advancement of knowledge and techniques associated with various reproductive studies, and will continue to play an important role in future studies.

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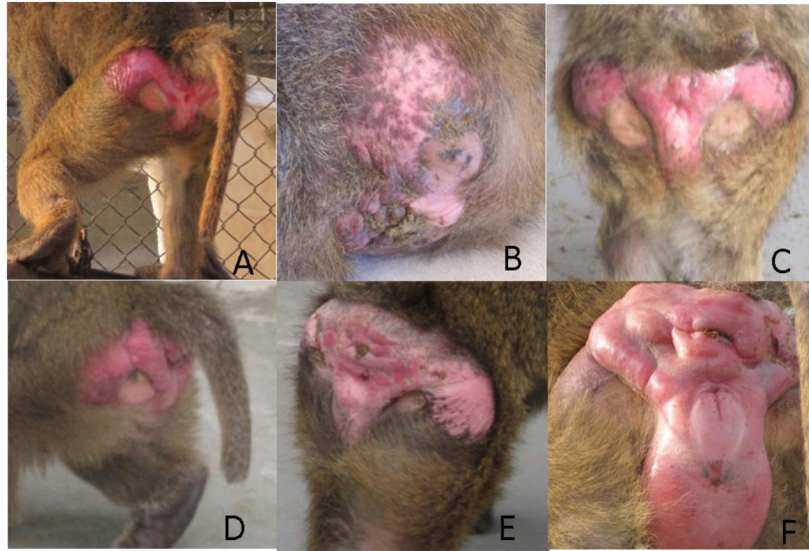


Figure 1. Perineal sexual skin swelling indicating phase of menstrual cycle. A. Score 0 and pregnant (bright pink/purple color). B. Score 0 not pregnant. C. Score 1 slight amount of swelling. D. Score 2 moderate amount of swelling. E. Score 3 significant amount of swelling. F. Score 4 fully swollen and ready to ovulate.