A Line of Dwarf Mice
Feline Reproductive Problems

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which prevent a cat from reproducing. Cats with a male appearance can be born with a uterus, and cats which outwardly appear to be female can have testes. There can also be physical defects of the external genital organs which prevent reproduction of the animal.

In addition to these defects, the sperm may be defective such as having coiled tails; being incompletely formed, or being immobile. Such conditions are often not diagnosed until the cat has failed to impregnate a queen. Then a semen analysis is done. This is not easy in cats that are not trained to accept semen collecting during sexual mating. Most animals need to be anesthetized and then electroejaculated to obtain sperm for examination. For this reason it is advisable to use the male first with a proven female, if that male is not successful then these tests are the next step. Because of the difficulty of routinely obtaining sperm from male cats, artificial insemination is rarely used.

Female cats are highly seasonal in their breeding cycle. They need 12 to 14 hours of light a day to cycle. If an animal is kept indoors in a darkened room, it will not cycle. When a female cat (queen) is in season behavioral changes occur. These are the only indication that the animal is ready to breed.

Cats are induced ovulators, unlike dogs which ovulate spontaneously during their heat cycle. The stimulation of the breeding process causes the brain to release luteinizing hormone, a substance which causes the follicles to release the ovum. Thus for ovulation to occur, the stimulation of mating is necessary. In some animals the stimulation to induce ovulation needs only to be slight. The process of taking a vaginal smear may induce ovulation in some queens.

Such smears can be of some assistance, but they may not provide an accurate picture of the stage of the queen's cycle. A more accurate method is monitoring the level of estradiol in the bloodstream. The level of this hormone is high during estrus (heat). This method is currently expensive and not practiced for most queens since the bloodtest has to be run every day.

It is best to breed a queen repeatedly to induce ovulation. Studies have found that the luteinizing hormone peaks within 90 minutes of repeated breedings. It is recommended to leave the queen and the male together for some time so they can breed more than once.

Once the queen has ovulated, progesterone levels in the blood rise. If the animal is pregnant, the level stays high for the first half of the pregnancy and then gradually declines by the time of birth (64 days). If the cat ovulates but does not become pregnant, the progesterone level will drop earlier (45 days) and the queen will come into season again. A cat can also have a false pregnancy.

The gestation period is about 64 days. In a difficult to breed queen, it is important to determine whether the animal ovulated and whether it is pregnant. Pregnancy can be detected as early as 20 days after ovulation through ultrasonography, but is generally performed at 21 to 28 days. Palpation can also detect embryos between 21 to 28 days of gestation.

A number of things can interfere with a successful gestation. The animal can have an undetected uterine infection or embryos may die due to chromosomal defects. It is possible for a queen to lose a litter later in pregnancy (abortion). This can be due to viral disease, such as a herpes infection, or to hormonal disorders. Thus early pregnancy detection is important as it helps the veterinarian with a diagnosis. Failure to carry full term presents a different medical problem from failure to conceive. Giving birth is easy for most queens, but there can be complications such as uterine inertia or malpresentation of a kitten. Veterinary help is indicated in each of these conditions. Dr. Meyers-Wallen said that a predisposition to uterine inertia could possibly be an inherited problem, and she advised studying the bloodline if such a problem occurs. She also said that Caesarean sections can be performed in cats, and that queen and kittens usually do fine.

She did stress that in most instances it is important to have kittens nurse as soon as possible. They receive the colostrum (protective antibodies) from the dam, and nursing stimulates the production of prolactin, a hormone necessary for milk production. Pyometra, uterine infection, can go undetected in cats and can be a cause of infertility. Pyometra can occur both in very young and in middle aged cats. Vaginal discharge may be undetected and other symptoms may be absent. Owners have to be very observant to detect this condition early. If it is not treated quickly and allowed to become chronic, kidney diseases can develop.

Pyometra can be treated with prostaglandin, a potent drug which causes the uterus to contract and expel the pus. The drug has some transient side effects such as panting, salivation, vomiting and restlessness. The level of white cells in the blood should be carefully monitored before and after treatment. The white cell count should go down within normal range after treatment. If the cell count goes down but then becomes elevated again, further treatment is generally indicated. Once treatment is completed, the queen should be bred on her next heat. Unfortunatly pyometra can recur, thus prostaglandin treatment is only recommended for breeding queens. The recommendation for pet cats with this condition is ovariohysterectomy (spay).

Cats should not be bred until they are mature and have reached their adult size and weight. Dr. Meyers-Wallen explained that very young queens generally are not good mothers. Cats can be bred twice a year if they are in prime health. She said that, although cats usually do not cycle while nursing, it is possible for this to occur.

She emphasized that good records are a great help to the veterinarian should problems arise. She also stated that vaccinations during pregnancy are not recommended, and that it is best to have the cat vaccinated and wormed prior to breeding.

Dr. Meyers-Wallen is associate professor of reproduction at the School. She is in the section of medical genetics and deals with genetic, pediatric, and reproductive problems of cats and dogs.

A Line of Dwarf Mice

Researchers at the Laboratory of Reproductive Physiology at the School have developed a line of dwarf mice produced by genetic ablation of growth hormone expressing cells. For the last two years, Dr. Ralph L. Brinster and Dr. Richard R. Behringer here at Penn, and Dr. Lawrence S. Mathews and Dr. Richard D. Palmer of the University of Washington, have been developing a method for selective ablation of specific cell lines in transgenic mice. Genetic ablation is a technique which utilizes genetic engineering to delete specific cells.

In multicellular organisms the diverse cell lineages which develop into organs, bone, tissues, etc. are generated from a hierarchy of stem cells. By using ablation techniques to delete specific cells, the relationships between stem cells and cell lineages can be studied. Such a system would be very valuable in studying the origin of distinct populations of cells which form tissues or organs in the body.

In these experiments, the switching region of the growth hormone gene was fused to part of the diphtheria toxin gene, and the hybrid gene was introduced into the animal's chromosomes by microinjecting the gene into the egg from which the animal developed. When the cells that make growth hormone began to differentiate in that animal and to make growth hormone, they also made the toxin. This killed any cell that made growth hormone but no other body cell. Thus the growth hormone cells never developed, and no cell that might arise from a growth hormone cell could be formed. A dwarf mouse developed. This demonstrated the utility of the method and established a model for dwarfism.

The dwarf mice are about one-third to one-half the size of normal mice. Growth hormone could not be detected in these animals and insulin-like growth factor 1, the blood level of which is stimulated by growth hormone, was reduced eight-fold in comparison to normal animals. The researchers found that the dwarf mice cease growth at approximately six weeks of age, maintaining a weight of 10 to 15 grams.

The research demonstrated that the genetic ablation of specific cell types in transgenic mice can be a useful method for understanding cell lineage relationships and the role of particular cell types in morphogenesis. It was also demonstrated that cell type produces a hormone, one can generate a hormone deficient animal model. The technique should be valuable in generating unique models of human and animal disease.