Medical Management of Reproductive Disease in Psittacines

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The majority of avian species have reproductive organs on the left side, but rudimentary right-sided ovaries or oviducts may persist into adulthood.1 The ovary is located at the cranial aspect of the left kidney and is suspended by the mesovarium. The ovary is comprised of multiple yolk filled follicles, which resembles a bunch of grapes. The arterial blood supply is derived from the short cranial renal artery, which has multiple branches within the mass of follicles. The oviduct is located in the left dorsocaudal coelom and is suspended by the mesosalpinx. It is divided into five sections: the infundibulum, magnum, isthmus, shell gland (uterus), and vagina. The infundibulum “catches” the ovum, and this is the site of fertilization. The egg-white, albumen, is deposited in the longest section of the oviduct, the magnum. Shell formation occurs in the uterus, and the egg spends the majority of its time in this location.

The most important environmental factor to stimulate reproductive activity is photoperiod. Photoreceptors in the retina and pineal gland become sensitized which stimulates release of gonadotropin releasing hormone (GnRH) from the hypothalamus.3 Most species respond to increasing day length, and maximum stimulation occurs with 12–14 hours of light. Rainfall stimulates reproductive activity in certain species such as zebra finches and cockatiels. The presence of a mate, or perceived mate (mirror or human care-giver) is another powerful reproductive stimulus in many avian species. While birds with physical contact with a mate will have the most stimulation,4 auditory contact with a male conspecific has also been shown to induce cycling in females of certain species such as budgerigars and ring-necked doves. Nesting material and/or the presence of a nesting box has also been shown to stimulate egg-laying and plasma luteinizing hormone (LH) secretion in cockatiels and other cavity-nesting species.5,6

Chronic egg-laying is a common reproductive disease of pet psittacines, especially cockatiels and lovebirds. Egg-laying is extremely metabolically taxing on the avian body. The amount of calcium in a single chicken egg contains approximately 10% of the total body reserve of calcium, about a third of which is derived directly from medullary bone.7 If unresolved, chronic egg-laying can lead to hypocalcemia and subsequent dystocia. Affected birds are often not housed with a mate; therefore, it is imperative to address environmental stimuli (see above) in the treatment plan.

Numerous causes contribute to avian dystocia including malnutrition, chronic stress, hypocalcemia, obesity, salpingitis, and malformed eggs. Clinical signs include straining to pass droppings, blood in the droppings, wide-based stance, visible coelomic distension, dyspnea, and generalized weakness or lethargy. Lameness and pelvic limb paresis may also be seen secondary to compression of sciatic nerves by the egg. Metabolic disturbances, such as post-renal azotemia, may occur secondary to urinary and fecal outflow obstruction. The egg is often palpable in the coelom, but a single “bird-in-box” radiograph (which does not require restraint or anesthesia) can confirm the presence of a shelled egg.

Similar to other organs, the avian oviduct can be affected by inflammation, infection, and neoplasia. Oviductal impactions occur secondary to several of these disease processes and consist of a conglomeration of inspissated egg material, excess albumin, and mucin. In the author’s experience, this is a common occurrence in aged chickens. Ectopic ovulation can occur spontaneously, or as a result of a diseased oviduct. The ova may then be reabsorbed or can lead to coelomitis - either sterile or septic. Ovarian cysts, oophoritis, and ovarian neoplasia have all been reported in avian species. Domestic chickens are the only known non-human animal that spontaneously develops ovarian neoplasia. There is a high prevalence in this species, and the disease is age-related.8 Ovarian disease can also lead to coelomitis and coelomic effusion. Due to the compartmentalization of the avian peritoneal cavities, ovarian tumors are often confined to the intestinal and left dorsal hepatic cavities and egg-yolk peritonitis is often initially found in the intestinal peritoneal cavity.1

Medical management of the avian dystocia involves supportive care including heat support, fluid therapy, calcium supplementation (if indicated) and analgesics. Oxytocin is usually not efficacious in
birds as the avian equivalent, mesotocin, does not stimulate uterine contraction - arginine vasotocin (AVT) controls oviposition in avian species. The exact mechanism of AVT induced uterine contraction is unknown, but it likely stimulates local production of prostaglandins including E1.9 Commercially available prostaglandin E2 creams (Prepidil® Gel, dinoprostone cervical gel, Pharmacia & Upjohn Co, New York, NY) can also be utilized topically on the vent of an affected bird to help with egg expulsion. These medications are very expensive (thousands of dollars per tube), and have variable efficacy in the author’s experience.

If medical management fails, or if the bird is decompensating, ovocentesis is recommended. This involves aspiration of the egg contents with a large gauge (16 or 18 gauge) needle. General anesthesia is recommended to ensure the patient remains still for the procedure, and to help with relaxation of the vent and uterine musculature. Ideally, the egg would be manipulated such that the shell is visible through the cloaca with the assistance of a speculum. If this is not possible, percutaneous ovocentesis can be performed by aspirating the contents of the egg through the coelomic wall. The egg should collapse, and any visible egg-shell fragments can be removed. The remaining shell fragments should pass on their own within several days.4 If they do not, surgical removal is often indicated. Broad-spectrum antibiotics and analgesics should be prescribed following this procedure due the risk of salpingitis.

The hypothalamic-pituitary-gonadal axis controls avian reproduction, similar to most other vertebrates. The initiating factors in this hormonal cascade are gonadotropin-releasing hormones (GnRH). These peptide hormones are transported to the anterior pituitary gland, which in turn, stimulates the release of luteinizing hormone (LH). Most vertebrates, including birds, possess multiple forms of GnRH, which can be classified into three major forms - GnRH-I, GnRH-II, GnRH-III. Their ability to stimulate LH, and possibly FSH, release from the anterior pituitary is variable depending on species, sex, and reproductive status of the bird. In addition, multiple types of GnRH receptors have been identified, which are subdivided into mammalian and non-mammalian receptors.14 The incongruities between avian and mammalian GnRH peptides and their receptors may explain the reduced efficacy of synthetic GnRH-agonists including leuprolide acetate and deslorelin acetate in avian species.

Leuprolide acetate (Lupron®, TAP Pharmaceuticals Inc.) is a synthetic, GnRH agonist available as a depot formulation to provide long-term treatment for various reproductive diseases in humans including prostatic hyperplasia and precocious puberty.15 In avian species, it is used most commonly for treatment of excessive egg laying and to decrease undesired reproductive behavior. In addition, there are several published reports which describe its use for management of ovarian neoplasia in cockatiels along with periodic coelomocentesis.18,19

Although leuprolide acetate has been used extensively in many avian species, few controlled clinical trials exist which examine the efficacy of this drug. Leuprolide acetate was found to reversibly prevent egg laying in cockatiels after a single intramuscular injection. Specifically, the treated cockatiels had a 12–19 day delay in egg laying compared with a control group.20 A single injection of leuprolide acetate administered to nonbreeding adult Hispaniolan Amazon parrots (Amazona ventralis) at a dose of 800 μg/kg IM reduced plasma sex hormone levels for less than 21 days.21 In addition to unknown efficacy in most avian species, the published dose range is wide, from 100 to 1200 μg/kg IM.22 The recommended dose range and treatment interval for most psittacines is 400 to 1000 μg/kg IM every 2–3 weeks.23,24 This may not be financially feasible for all clients, as long-term treatment is usually required.

Deslorelin acetate (Suprelorin®F, Virbac, Fort Worth, TX) is another GnRH agonist that is formulated into a subcutaneous, controlled-release implant designed for use in dogs for reversible suppression of testosterone production, and thus contraception, for six to twelve months, depending on implant size. It is currently commercially available as a 4.7 mg or 9.4 mg implant, and is considerably less expensive than repeated treatments with leuprolide acetate. Recently, the 4.7 mg deslorelin implants have become available in the United States as an FDA Indexed Minor Use/Minor Species product under for management of adrenal cortical disease in domestic ferrets. The implants come from the manufacturer in a preloaded needle with a separate applicator syringe, similar to a microchip.

Similar to leuprolide acetate, deslorelin acetate is primarily utilized to decrease reproductive behaviors and egg laying in avian species. It has also been used successfully for long-term management of non-resectable ovarian neoplasia in cockatiels19,28 and Sertoli cell tumors in budgerigars29. In addition
to treatment of ovarian neoplasia, there is evidence that GnRH agonists, such as deslorelin acetate, have chemopreventative effects in domestic chickens against development of ovarian neoplasia. However, the only prospective controlled studies to date on deslorelin acetate in birds are in chickens, quail, and pigeons. Chickens treated with a 4.7 mg deslorelin acetate implant reduced egg production for a mean of 180 days whereas a 9.4 mg implant inhibited egg production for 319 days. In Japanese quail, a single 4.7 mg deslorelin acetate implant reversibly decreased egg production in 6 out 10 birds for 70 days. Plasma sex hormones, specifically 17β-estradiol and androstanediol, were significantly lower in the treatment than in the control group on day 29, but at no other time points. Pigeons implanted with a single 4.7 mg deslorelin implant had reduced egg production for 5–7 weeks and reduced serum LH concentrations for 84 days compared with control birds.

Endogenously, avian reproduction is controlled by the hypothalamo-pituitary-gonadal axis. However, there are numerous exogenous elements that have a considerable influence on reproduction such as photoperiod and presence of a true or perceived mate. As such, any treatment that affects only the endogenous reproductive hormone cascade, including GnRH agonists, will be rendered less effective if the environmental factors are not also addressed simultaneously. Therefore, GnRH agonist therapy should not be utilized as a sole therapy for reproductive disease in any avian species.

REFERENCES