

# SURGICAL MANAGEMENT OF ESTROGEN HAZARDS IN DOGS

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Estrogen keeps the world stable and beautiful. But one of its unwanted indirect influences is hydrophobia in human causing 30,000 human deaths per year in India (Nandi, 2008). So following the sermon of Grandfather Bhishma at the end of Kurukshetra battle that human is the great ABC (animal birth control) programme has started. Slogan of the movement is “each one stitch one” bitch.

## Rabies Control

### A) i) Sterilization in Male

**Surgical method** Castration or bilateral orchidectomy by open or closed method is well established and practised.

**Chemical method :** Bilateral intratesticular injection of calcium chloride solution (20% w/v) 1-2 ml as per the testicular size results induction of permanent (irreversible) chemosterilization in male dogs through germ cell apoptosis vis-à-vis necrosis alongwith concomitant production of reactive oxygen species (ROS) in testicular level as well as significant diminution in testosterone concentration without imposition of any general stress response, metabolic toxicity or any toxic and unwanted side effects (Jana et al 2002; 2004; Jana & Samanth, 2006; 2007). Degenerated germ cell and ledig cells are replaced by fibrous tissue and hyaline tissue.

**A) ii) Sterilization in female** Panhysterectomy site of incision is of surgeon's choice. But ventral midline or paramedian approaches are gravity dependent, injury prone, cause increased post-operative pain on sternal recumbency as evidenced by increased heart rate and respiratory rate ratio. Post-operatively mid line approaches cause acute or chronic incisional hernia, wound dehiscence, eventration and wound infection (Slatter, 2003). This is why “Grid incision” at right flank involving muscle splitting and having stronger suture-tissue interface is better. Right flank oblique incision is the best for easy access of both the ovaries and uterus upto the level of internal orifice of cervix. Removal of both the

ovaries is must. It has no estrogen withdrawal osteoporotic effect even after 8-11 years (Johnston et al, 2001; Ashoke Kumar et al, 2009).

## Diseases control

The pet dog was the only companion of Dharmaraj Yudhisthir on the way to Heaven at the end of Kurukshetra. Present day worth of dog is multifaceted. The estrogen related problems in canines faced in our daily practice can be surgically managed as described below.

### B) i) Pyometra –

The fluctuation of the level of estrogen and progesterone in estrous cycle and failure of conception followed by infection causes pyometra. It is urgent as that of appendicitis in human. Both are empyema. Cystic ovary, hormonal imbalance, cystic endometrial hyperplasia followed by accumulation of pus in uterus are rarely cured by medicines or the treatment is costly or usefulness of post-treatment uterus is controversial and the delay sometimes invites more problems like tumors. In a survey work among 130 Norwegian Canine practitioners 98% considered surgery as primary treatment in closed pyometra whereas 80% considered that with antibiotic, fluid, sometimes PGF<sub>2α</sub> and fluid alongwith methylergometrin in open pyometra (Anderson and Farstad, 2006). Among them 100% removed uterus and 98% removed ovaries.

In few instances as observed by the author even after removal of both the ovaries and uterus stump pyometra caused headache. Though the principle of treatment for stump pyometra is surgery, antibiotic with ecbolic, routine feeding of natural anti-estrogenic diet like table mushroom, soyabean cake and green tea augmented by intermittent administration of aromatase inhibitor (e.g. Tab Aromasin, Pfizer India Ltd). controlled the recurrence. Hence estrogen (E<sub>2</sub>→70-89 pg/ml) comes probably from

alternate source like adrenal gland, adipose tissue and other.

In closed pyometra, if prostaglandin fails, method used by Feldman and Nelson (1989) for inserting drains through cervix can be followed using A.I. Gun under C-arm fluoroscopic control. If drains are failed advanced cases after proper fluid therapy are operated at mid-ventral incision under light xylazine sedation and intravenous administration of diluted ketamine and calmpose.

#### **B) ii) Persistent estrous**

Symptom : Prolonged period of cornification of cells of vaginal wall, receptivity, tail flagging and vulvar swelling.

Diagnosis : Ovarian follicular cysts or tumors in USG

Treatment : Ovariohysterectomy (OHE)

#### **B) iii) Estrogen induced Tumours :**

- a) Mammary tumours
- b) Genital tract tumours

#### **a) Mammary Tumors**

Influence of estrogen and progesterone is well established for occurrence of mammary tumor in bitches. But ovariohysterectomy (OHE) during mastectomy at the age of 8-11 years can't control the recurrence of mammary tumors because of the presence of presensitized estrogen receptors (ER) which remain active from the secondary sources of estrogen after OHE. Risk of mammary tumors is 0.05% if OHE is done before first estrous cycle, that is 8% if OHE is done after first heat cycle and is 26% if OHE is done after second heat cycle. No protective benefit is available if it is done after 3<sup>rd</sup> heat cycle (Statter, 2003). It has been observed in our clinical practice also.

**Types of mammary masses (Benign)** 50% of total masses are benign e.g. fibroadenoma, mixed, adenoma, mesenchymal tumors, myoepithelioma and ductal papilloma.

**Malignant** Adenocarcinoma, ductal carcinoma, spindle cell carcinoma, Anaplastic carcinoma, squamous cell carcinoma, epithelial-carcinoma, mesenchymal-sarcoma, anaplastic carcinoma, squamous cell carcinoma, mucinous carcinoma, malignant myoepithelioma, carcinoma or

sarcoma in a mixed tumor, carcinosarcoma, extraskeletal osteosarcoma and osteochondrosarcoma. Histologically more than 5-6 pigmented granules in nucleus is indicative of cancer.

#### **Histological carcinoma**

- Grade 0 – Carcinoma in situ within the gland
- Grade 1 – Gland + Surrounding tissue
- Grade 2 – Gland + Surrounding tissue + Vascular + lymphatic Invasion
- Grade 3 – distant metastasis.

#### **Clinical staging**

Stage I – T<sub>1</sub>N<sub>0</sub>M<sub>0</sub>      T<sub>1</sub> = <3 cm dia

Stage II – T<sub>2</sub>N<sub>0</sub>M<sub>0</sub>      T<sub>2</sub> = 3-5cm dia

Where T = tumor size

Stage III – T<sub>3</sub>N<sub>0</sub>M<sub>0</sub>      T<sub>3</sub> = >5cm dia

N = Lymph node metastasis

Stage IV – T<sub>any</sub>N<sub>1</sub>M<sub>0</sub>

M = distant metastasis

Stage V – T<sub>any</sub>N<sub>any</sub>M<sub>1</sub>

**Prognosis** If estrogen or progesterone receptors are present, tumor is of better prognosis. About 50% of the cancers having those receptors others are not having. Receptor detection is costly affair.

**Treatment protocol will be** + OHE + Mastectomy + antiestrogenic diet and drugs like exemstene followed by chemotherapy with agents like doxorubicin/doxorubicin + cyclophosphamide/paclitaxel. Diet should be protein and fat rich and less carbohydrate diet is to be given. Tamoxifen works well in women but not in bitches. Tamoxifen use sometimes causes pyometra in bitches. It is used in dogs to treat prostate cancer.

#### **Removal of tumors**

- i) Lumpectomy tumor diameter <1 cm
- ii) Mastectomy tumor diameter >1cm
- iii) Regional mastectomy Cranial chain no.3 to 1
- iv) Radical mastectomy caudal chain no. 5 to 3

#### **b) Tumors of the genital tract**

Female genital tract tumors are ovarian tumors, oviductal tumors, uterine tumors, cervical tumors, and vaginal and vulval tumors. Histological classification after Kennedy *et al* (1998) are of several types e.g. granulosa cell

tumors, thecoma, interstitial cell tumor, Dysgerminoma, teratoma, embryonal carcinoma, papillary adenoma, cystadenoma, papillary adenocarcinoma, rete adenoma and haemangioma leiomyoma of ovary, tumor like lesions and cysts in and around ovary; adenoma, adenocarcinoma and lipoma of oviduct; adenoma, adenocarcinoma, fibroma, leiomyoma, leiomyosarcoma and several cysts of uterus; papilloma, urothelia carcinoma, malignant melanoma, leiomyoma, alveolar sarcoma, malignant lymphoma, haemangioma and CTVT of vagina and vulva including cysts of vulva.

Post-estrous uterine bleeding for a long period refractory to medicinal treatment is suspected for uterine tumour. Treatment is ovariohysterectomy. In most of the cases bilateral polycystic ovaries are found. Cervical tumor occurrences are less. Vaginal tumor cases are very frequent and approximately 3% of all canine tumors. The main etiology of these tumors are estrogen. From vaginal tumors also estrogen receptors (ER) have been detected. Simple surgical removal of vaginal tumors invites its recurrence until ovaries are removed. In bleeding benign growth of vulva and vagina of 8 bitches surgical growth removal alongwith OHE, resulted normal health and body weight gain without any recurrence upto one year after surgery as observed by the author. One case of alveolar sarcoma of vagina has been well

managed by OHE, antiestrogenic diet and aromatase inhibitor. Detection of Estrogen receptor (ER) and Progesterone receptors (PR) in genital tract tumors and mammary tumours will be helpful for treatment modalities in future.

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