

DIETHYLSTILBESTROL AND IT'S THERAPEUTIC VALUE IN VETERINARY PRACTICE

By

Ratana Oonyawongse

Diethylstilbestrol is a synthetic substance of relatively simple structure, not containing the phenanthrine ring (1), produces reactions similar to those from estrone (2) The Council on Pharmacy (3) and Chemistry has adopted the name stilbestrol for the mother substance 4, 4'-dihydroxy stilbene, reserving the designation diethylstilbestrol for its more potent derivative 4, 4' dihydroxy-a:B diethyl stilbene. This substance was introduced by Dodds and his associates in 1937. (4) This substance is now included among new and non official remedies and has been judged by the Council to be a reliable therapeutic agent for those conditions recognized by it as suitable for estrogen thereapy.

THERAPEUTIC VALUE AND POTENCY AND TOXICITY

The therapeutic value of the synthetic estrogen, diethylstilbestrol, is now being investigated. The chief advantages are their relative cheapness and potency by oral route.

Even though this product produces the action simulating the naturally occurring estrogens, still it often produces unpleasant side effects, particularly nausea, vomiting, headache, abdominal distress, annorexia, diarrhea, lassitude, paresthe-

sia, vertigo, thirst acute psychotic reaction and cutaneous rashes. The severity of the toxic effect may be reduced to some extent by coating the pill, limiting the daily dose to 1 mgm. or less and interrupting the treatment with periods of rest. Mac Bryde and his associates (5) recently reported that nausea was the only objectionable symptom and occurred in only 8.6 percent of a group of 150 cases receiving 1 mg. of diethylstilbestrol daily for 2-3 weeks. Dogs (6), rats rabbits may show blood and organ changes, cloudy swelling, congestion and necrosis of the kidney, liver and adrenal glands, but no tissue, liver or blood damage has been demonstrated clinically even with prolonged administration (7) According to Dodds and his associates (8) diethylstilbestrol is at least 5 times as potent as estrone by the oral route. Comparative studies of the potency of diethylstilbestrol by mouth and of estrone by injection have yielded values ranging from 1.5 to 2.1.

Since it is known that estrogens exert a degenerative influence on all male sexual organs Sovran (9) employed diethylstilbestrol as a preventive treatment of orchitis in mumps among soldiers with spectacular success. It is

believed that the same result would be obtained in the treatment of orchitis in bulls and boars.

In the field of veterinary practice, the therapeutic effects of diethylstilbestrol used in animals under various conditions have been investigated and recorded as follows: Gollidge (10) reported the use of stilbestrol in case of hydrops amnii, and Rowson and Sprigg (11) recommended stilbestrol in the treatment of pyometra in cattle, in doses of 20-15 mg. They stated that pus began to discharge twenty-four hours and continued until the uterus was empty. G. R. Moore (12) reported that stilbestrol has marked therapeutic value in the treatment of pyometra following retained fetal membrane in cows. Kendall (13) reported a successful result from the use of stilbestrol in the treatment of acute prostatitis in dogs. Neoplasia in the peritoneal region in dogs responded favorably to the treatment of subcutaneous injection of stilbestrol as stated by Smythe (14). Lewis and Turner (15) have reported that stilbestrol has an effect similar to estrone on the mammary glands of animals. Folley and Young (16) reported that stilbestrol is capable of artificial induction of lactation in some virgin animals. Klein (17) reported that stilbestrol aided in the increased production of milk in dairy cows.

CASE REPORTS AND DISCUSSION

Stilbestrol in the Treatment of Acute Prostatitis in Dogs

Stilbestrol injected intramuscularly in four daily doses in combination with

sulfathiazole was found to give successful results in the treatment of acute prostatitis in dogs. The action of stilbestrol is to inhibit the function of the male sex hormone. This more or less inactivates the prostate gland and allows the body to overcome the aid of sulfathiazole.

Stilbestrol Dipropionate in Canine Neoplasia (19)

About 50 cases of neoplasia in the peritoneal region of dogs have been treated with success by the subcutaneous injection of stilbestrol dipropionate. In old debilitating dogs, prostration, collapse and in rare cases, death may follow full dosage of the drug over a period of several weeks. The weekly dose of stilbestrol should not exceed 5 mg. in senile patients. In bitches small repeated doses produce swelling of the mammary glands with lactation but usually without sign of heat. A large dose (20 mg.) generally causes enlargement of the vulva at about the fourth day with signs of heat and a marked willingness to accept service.

Malignant Neoplasm in a Cow Cured by Stilbestrol (20)

A case was reported in Scotland of a yearling shorthorn heifer suffering from a tumor. Surgical operation to remove the tumor was performed with apparent success. The same animal was later on bred but at calving it was found that the tumor had recurred and appeared to be malignant. It was diffused and occupied the whole vaginal opening. The tumor was considered inoperable and the owner

was advised to dispose of the cow after the lactation.

In the hope to prolong the lactation period with no thought of anti-carcinogenic action, one grain tablet of stilbestrol was implanted in the subcutaneous muscle of the neck.

Three months later the tumor that protruded from the vagina had disappeared and the part inside the vagina was definitely regressing. After 5 months a lump of the size of an orange was all that remained. This was removed with ecraseur under epidura anaesthesia. Microscopical examination of the tumor found it to be a typical cellular fibrocarcinoma. This cow was bred two weeks after the removal of the tumor and became pregnant.

Initiation of Lactation in Heifers by Hormone Administration (21)

Two nulliparous heifers were injected subcutaneously with stilbestrol over periods of 11 and 13 weeks respectively. Dosage consisted of 5 mg. diethylstilbestrol dipropionate twice weekly for 6 and 5 weeks; in the following 5 and 8 weeks the dose injected was progressively increased from 7 mg. twice weekly to 20 mg. twice weekly. The total amounts of stilbestrol used in the two heifers were 163 mg. and 268 mg. respectively; in the heifer receiving the smaller amount, injections were made twice weekly for the first 6 weeks. During the injection periods there was some increase in udder and the teat size, but

there was no distension of the udder with secretion.

Milking was commenced at or shortly after the cessation of the injections, when the secretion was similar to colostrum. Following this, both heifers suckled calves for a time. Approximately 4 and 5 months after the commencement of stilbestrol administration both heifers appeared to be in full milk flow. The peak daily milk production of one heifer was 27.5 lb. and in other 33.7 lb.

The subcutaneous injection of diethylstilbestrol dipropionate stimulated udder and teat growth and initiated and maintained lactation in nulliparous dairy heifers. It is suggested that suckling a calf may aid in bringing about full lactation by hormone administration.

Stilbestrol in Agalactia (22)

According to the report in *Veterinary Extension Quarterly* (No. 101) of University of Pennsylvania on the treatment of 16 heifers for 23 weeks, the milk production varied from $1\frac{1}{2}$ to $30\frac{1}{4}$ lbs. daily with a total production of 5 to 740 gallons. Of the 16 heifers treated, 6 produced enough milk to make the procedure a profitable one.

Symptoms of nymphomania developed in many of the animals treated and in one group, pelvic fracture necessitated slaughter of 20 percent of the animals.

Chemical Caponization of Cockerels (23)

The best age at which to give stilbestrol to cockerels is just as early as the

sexes can be determined or at about 5 weeks of age. Stilbestrol seems to retard the growth of the birds during the first two weeks after the date of administration. They eat less and gain little weight during this period. After two weeks, the treated birds consistently outgain the controls.

They continue to grow and develop without any sign of male characteristics. The only difference between birds from which the testes are removed surgically and those given stilbestrol is that the latter have larger combs. The testes of the treated birds were about the size of a small bean, yellow in color and atrophied.

When the treated birds reach the age of 5 months they start to crow and develop the rooster characteristics. This can be checked by giving two 1 mg. tablets of stilbestrol. Experiments were conducted to compare the advantages between chemical (stilbestrol) and surgical castration. The results were not conclusive but are indicative that the administration of stilbestrol to young birds is profitable. The most significant points to be considered are that there were no slips, no deaths and with possibilities for its use in poultry industry.

Effects of Stilbestrol on Pyometra Following Retained Fetal Membrane (24)

Forty three cows with retained placentae were used in the course of this experimental study. The placentae were removed manually not less than 72 hours

after parturition, and some remained as long as 148 hours before it was taken out. The only treatment given to all these animals was the insertion of 1 oz. gelatin capsule of powdered sulfanilamide deep in each horn of the uterus.

All the animals were kept for examination for a period of two weeks and found to show the evidence of pyometra with the presence of pus in the uterus.

In each case, a single, dose of from 30-50 mg. of stilbestrol, depending on the size of the cow, was administered intramuscularly. Of the 43 cows treated, 14 showed signs of estrus within twenty-four hours after injection, 21 in forty-eight hours, and 5 in seventy-two hours, making a total of 40 (93%) that came in heat within seventy-two hours after an injection of a single dose of stilbestrol. Two required a second injection and one aged cow showed only vague symptoms of heat even after a third injection.

All of the 42 cows coming into heat began discharging pus from the uterus soon after the first symptoms. In from two to seven days from the advent of estrus, all uteri were empty and involution proceeded rapidly. Inspection of cervixes revealed them to be open in all cases.

Forty-two of these cows conceived in from 46-140 days following parturition, 24 conceived at the first service; 10 required two services and the remaining eight conceived on the third service. The results of this experiment showed that stilbestrol gave a very satisfactory

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result in the treatment of pyometra in cows.

DISCUSSION

The use of hormone in veterinary medicine has not progressed as far or as satisfactorily as has the use of this product in human medicine. However, stilbestrol, a synthetic estrogen, has come into wide use in the field of veterinary practice during the past decade. The results shown in these reports indicate its therapeutic value in the treatment of various disorders in farm animals. This material is also used to induce estrus in animals with a high degree of regularity. The use of stilbestrol in stimulation of milk production without intervention of pregnancy is of significance. The chemical caponization by the use of stilbestrol appears to possess considerable economic possibilities.

CONCLUSION

Diethylstilbestrol has a dependable therapeutic effect in the field of veterinary practice not only for treating reproductive disorders in animals but also of use in the dairy and poultry industries.

SUMMARY

1. Diethylstilbestrol can be safely used in the treatment of acute prostatitis and neoplasia in dogs and cows.

2. Lactation in nulliparous heifer can be induced by the subcutaneous injection of diethylstilbestrol.

3. Diethylstilbestrol has a reliable therapeutic value in the treatment of pyometra which follows the manual removal of retained placentas in cows.

4. Caponization of cockerels by the use of stilbestrol has been found to be a very practical and profitable procedure in the poultry industry.

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ตลาดไข่ไก่ในอเมริกา ในขณะนี้ อยู่ในสถานะอันอ่อนแอหนักที่ เนื่องจากไข่
ด้นตลาดราคาไข่ตก.

และนอกจากนี้ยังมีข่าวว่าในสิ้นปีนี้ (๑๙๕๐) ทางการสหรัฐอเมริกาจะเลิกสัม
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เจ้าของฟาร์มไก่ต่างๆ มาแล้วนับสิบ.