

Some Clinical Effects of Stilbestrol

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In 1938, Dodds and his co-workers in England published a series of articles on their six year study of synthetic estrogenic hormones related to the stilbenes and diphenylethane. They introduced stilbestrol which produces an even stronger effect in animals than the naturally occurring estrogens. Stilbestrol is the parent substance from which have been developed the other closely related synthetic substances in an attempt to reduce the toxic effects of stilbestrol. The compound 4:4 dihydroxy alpha beta diethylstilbene is referred to in current literature under the name of stilbestrol. It was used experimentally in 1939 and appeared on the American market in 1940.

According to Dodds and the other investigators the potency of stilbestrol is three or four times greater than that of estrone. In addition, stilbestrol has the advantage of being almost as potent orally as parenterally, although Shorr and Papanicolaou say it loses approximately 50 percent of its activity by the oral route.

The actions of stilbestrol are almost identical with those of the natural estrogens. Both the physiological and pathological changes which can be effected with estrone and related compounds can be duplicated by stilbestrol. Stilbestrol has the added advantage of being much cheaper to use.

Effects of Stilbestrol on Pyometra Following Retained Fetal Membranes.

Among the common causes of sterility in cattle are functional abnormalities of the ovaries, uterine infections, retained placenta, and associated metritis and pyometra. A surprising lack of critical research on the proper clinical management of these pathological conditions is evident to anyone who has reviewed the literature. Most of the therapeutic measures advocated for their alleviation are empirical.

It is always difficult to measure the value of any therapeutic measure. This is particularly true of bovine genital disease. The high cost of experimental animals, their slow rate of reproduction, and the expensive equipment necessary to maintain them precludes formal controlled experimentation. Any attempt to evaluate therapeutic measures in this field must rely on clinical observations on animals over which there is not always complete jurisdiction.

During the past five years, many reports of the clinical uses of stilbestrol have appeared in the literature. In a theoretical discussion of the interrelationships between estrogens, progesterone and the pituitary with their effects on the uterus, Brownless (1942) called attention to the fact that when estrogens reach a sufficiently high concentration they cause regression of the corpus luteum and simultaneously sensitize the uterus to the oxytocic principle of the pituitary body.

*Editor's note: Excerpts from available literature compiled by Mr. Anarumo for Dr. Herrick's course in artificial insemination.

Golledge (1942) reported on the use of stilbestrol in a case of hydrops amnii, and Rowson and Spriggs (1942) recommended stilbestrol in the treatment of pyometra of cattle in doses of 20 to 25 mg. They stated that in suitable cases pus began to discharge in 24 hours and continued until the uterus was empty. They presented no data of a critical nature.

Moore selected 43 cows with retained placentae from herds on which breeding records were kept and on which repeated examinations were made. The placentae were removed manually when examination revealed that it was practical to do so. None was removed in less than 24 hours after parturition, and some remained as long as 148 hours before it was considered advisable to remove them. In no case was the uterus irrigated and the only treatment was to place a one oz. gelatin capsule of powdered sulfanilamide deep in each horn of the uterus.

Each case was examined approximately two weeks later. By this time it was found that all symptoms of acute inflammation had subsided, but that in all cases a pyometra was present as evidenced by the presences of pus in the uterus and by retarded involution.

At this time a single dose of from 30 to 50 mg. of stilbestrol, depending on the size of the cow, was administered intramuscularly and the patient was observed daily thereafter until results were noted. If no results were observed in 24 hours the treatment was repeated.

All cows in this experiment were bred at the first estral period after the sixtieth day following parturition and were bred at each succeeding estrus until conception occurred.

Of the 43 cows treated, 14 showed signs of estrus behavior in 24 hours after injection, 21 in 48 hours, and 5 in 72 hours, making a total of 40 (93 percent) that came in heat within 72 hours after the injection of a single dose of from 30 to 50 mg. 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 in heat following the first or second injection be-

gan 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. Rectal examination during the stilbestrol-induced estrus revealed that the tubular genitalia possessed excellent tone and were erectile. Inspection of the cervix through a vaginal speculum revealed them to be open in all cases.

In the cow in which three injections were needed, estral symptoms were never well pronounced. Several examinations were made during the course of treatment. All showed the cervix to be rather tightly closed and the uterus was atonic at all times. Later, a cervical catheter was passed and the uterus irrigated. She came into estrus sixty-five days after parturition. Estral cycles were fairly regular thereafter but after being bred at each of ten heat periods, she was finally discarded as incurably sterile.

Forty-two of these cows conceived in from 60 to 140 days following parturition. None was bred in less than 60 days from calving. The average time required for each conception was 86 1/5 days. Of the 42 that became pregnant, 24 conceived at the first service; 10 required two services, and the remaining 8 conceived on the third service. The average was 1.62 services per conception.

The advent of stilbestrol has placed at the disposal of the veterinarian a wonderful estrogen that can be marketed at a price that makes its use feasible where its effects are beneficial. The treatment of the pyometra which invariably follows the manual removal of retained placentae would seem to be one of these.

Effects of Stilbestrol on Retained Placentae.

Many conflicting reports have appeared in recent years concerning the therapeutic value of stilbestrol as an aid in the expulsion of retained placentae. Those reporting favorably fail to give the results of a pre-treatment examination if one was made, or, in most cases, to report the duration of retention before

treatment with stilbestrol was begun. Early treatment, without examination, leads to highly optimistic results because it includes so many cases that do not need treatment. As a result of studies made on the value of stilbestrol as an aid in the expulsion of retained bovine placentae, the conclusion can be reached that it has little, if any, value. Stilbestrol may sometimes be definitely harmful in cases of retained placentae. Moore (1945) states that 43 cases of bovine retained placentae were treated with doses of stilbestrol ranging from 30 to 50 mg. Of these 43 animals, 4 were benefited, 9 were questionably benefited, 25 received no benefit, and 5 suffered injurious effects. One of this latter group died, 1 was left sterile, and 3 required protracted treatment before recovery was effected.

The straining frequently observed soon after the administration of stilbestrol in these cases seems important. Since mild irritants are known to produce some aphrodisiac effect, it has often been suggested that estrogens in general produce libido either by sensitizing the vaginal mucosa or by producing a mild irritation. Moore (1945) suggests that the estrogenic effect combined with the irritation from the fluid products of placental decomposition resulted in enough stimulus to inaugurate the straining reflex.

Stilbestrol in Anestrus

Stilbestrol has been used as a therapeutic agent in anestrus cattle. Twenty mg. of stilbestrol seems to be an adequate dose. Repeated injections of an excessive dose should not be employed for they may cause cystic ovaries. Anderson (1945) reported that conception was obtained in a number of cases at the first estrus after injection.

Experimental results do not justify the use of hormonal therapy in cows experiencing regular estrous cycles but failing to conceive. Pincus and Kirsch have shown that rabbits can be rendered sterile by injecting estrogen after ovulation. It is doubtful if a cow should be injected with an estrogen when she is in estrus and bred. Under such conditions, the fertilized ova are locked in the Fal-

lopian tubes and do not enter the uterus.

Stilbestrol was used on a 33 month-old barren Jersey heifer. This animal received a total of 273 mg. over a 14-week period. She produced 8,046 lbs. of milk and 383 lbs. of butterfat in 304 days. The results on the initiation and maintenance of lactation are promising yet little is known about the subject.

Use in Stimulating Milk Production

Experiments conducted to date suggest that estrogens should not be used on a heifer to bring her into milk production if you hope to get her with calf at a later date. Indications are that continued estrogenic treatment may cause cystic ovaries. Unless one's purpose is to terminate pregnancy, one should not inject an estrogen into a pregnant animal. More consistent results must be obtained before one is justified in using hormonal therapy for lactational purposes in commercial dairy herds.

Use of Stilbestrol in Cases of Mummified Feti

If the placenta becomes nonfunctional at certain stages of pregnancy, the fetus is retained in the uterus and becomes mummified. The fetus is probably retained because the blood estrogenic level is not high enough to set in motion those factors operating at parturition. If such is the case, estrogenic therapy is indicated. The dose is 25 mg. of stilbestrol given in two injections with a four day interval between. Following the diagnosis of a mummified fetus, one must not inject an estrogen and assume that the fetus will be expelled.

Use of Stilbestrol in Caponizing Cockerels

Chemical caponization of cockerels with stilbestrol has been proven to give good results. Most of the research reports on this subject are on the use of intramuscular injections of stilbestrol.

The best age at which to give stilbestrol to cockerels is just as early as the sexes can be determined by external growth

characteristics or at about five weeks of age. Stilbestrol seems to retard growth of the bird for about two weeks. The chickens develop without any signs of male characteristics. They do not crow or fight. The only difference between birds from which the testes are removed surgically and those given stilbestrol is the latter have the larger combs. The testes of treated birds were about the size of a small bean, yellow and atrophied. There is an improvement in the quality of the meat.

Stilbestrol or any other estrogen will not fulfill its early promise. Estrogens do have the ability to induce estrus in anestrus animals but this in itself serves no purpose. The ovaries must be activated so that they produce mature follicles which will ovulate. It has been proven beyond any doubt that the casual use of stilbestrol can produce more harm and financial loss to a farmer than any gain he might derive from its use at this time.

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Veishea Dog Show

The Veterinary Division sponsored a Veishea exhibit in 1949 which in two years has become a feature of the exposition. Last year, representatives of 33 breeds of dogs were exhibited in the hallway of the Anatomy wing of the Veterinary Quadrangle. A Collie puppy was presented as a door prize as an added attraction. Over 13,000 people viewed

the exhibit, many standing in line an hour and a half awaiting their turn.

The widespread publicity and the unusual attraction of the exhibit encouraged the presentation of a more elaborate exhibit for this year. The armory was secured as a location in order to handle the large number of spectators and accomodate the increased size of the exhibit.

Over 70 breeds of dogs were represented in this years exhibit, including some of the outstanding show dogs in the country. Featured were such dogs as the Briard Ch. Westlawn Defender owned by the Gilbert Kennels of Chicago. This dog has two consecutive Best of Breed placings at the International Dog Show held in Chicago. Another featured dog was the Italian Greyhound Cr. Airo Vana's Phillippe owned by the George Hisers of Grinnell, Iowa. Cr. Phillippe has never been defeated in his breed in over 40 shows.

Demonstrations with Border Collies, retrievers and obedience-trained dogs emphasized the practical aspects of dog ownership. Through the courtesy of the library here at Iowa State College and owners of private collections, a wide variety of books, publications, and periodicals relating to dogs and dog ownership was exhibited.

The exhibit terminated in the drawing for the door prize, a Boxer female puppy, donated by Mr. R. L. Benbow, vice-president of the newly organized Iowa Boxer Club.

Influenza Virus

Dr. George A. Young reports that swine are vulnerable to attack by many of the influenza viruses that attack man. He further states that though these infections may be mild in adult swine, they may assume serious intensity in very young swine. *Vet. Med.* XLV April, 1950.

Dairy farm costs dropped only 5 per cent last year, while milk prices fell almost 2 percent.

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