Diethylstilbestrol (Veterinary—Systemic)

There are no human- or veterinary-labeled commercial diethystilbestrol products in the United States.

Category: Estrogen.

Indications

Note: The text between [EL]US and [EL] describes uses that are not included in U.S. product labeling. Text between [EL]CAN and [EL] describes uses that are not included in Canadian product labeling.

The [EL]US or [EL]CAN designation may signify a lack of product availability in the country indicated. See the *Dosage Forms* section of this monograph to confirm availability.

See also the *Regulatory Considerations* section below in this monograph.

Classification as *Accepted*, *Potentially effective*, or *Unaccepted* is an evaluation of reasonable use that considers clinical circumstances, including the availability of other therapies. The quality of evidence reviewed for an indication is shown by the evidence rating.

Dogs

Accepted

[EL]US Urethral sphincter mechanism incompetence (treatment): Diethylstilbestrol is used as an aid in the control of urethral sphincter mechanism incompetence (idiopathic incontinence, hormone-responsive incontinence) in dogs (Evidence rating: B-3,5).{R-1-4; 36}

Response to treatment is variable among dogs. The limited evidence available suggests that estrogens may also increase urethral sphincter response to treatment with alpha-adrenergic agonists in some dogs.[EL]{R-3; 4}

Regulatory Considerations

U.S. and Canada—

Commercial diethylstilbestrol products are not available in the United States. **The United States Food and Drug Administration regulations ban diethylstilbestrol from use in animals that are used for food production** (CFR 21 Part 530.41).{R-35} Diethylstilbestrol has demonstrated teratogenic and carcinogenic effects in multiple species.{R-5; 27}

In the United States, diethylstilbestrol must be purchased from an approved source and compounded for veterinary use. Refer to the Animal Medicinal Drug Use Clarification Act, Food and Drug Administration regulations pertaining to compounding (CFR 21 Part 530.13), and the current Food and Drug Administration's Compliance Policy Guide on *Compounding of Drugs for Use in Animals.*{R-10; 34}

Chemistry

Chemical group: Non-steroidal estrogenic stilbene derivative.{R-27}

Source: Synthetic.

Chemical name: (1) Phenol 4,4'-(1,2-diethyl-1,2-ethenediyl)bis-, (*E*)-.{R-31}

Molecular formula: $C_{18}H_{20}O_2$.{R-31}

Molecular weight: 268.35.{R-31}

Description: White, odorless, crystalline powder.{R-30}

Solubility: Practically insoluble in water; soluble in alcohol, in chloroform, in ether, in fatty oils, and in dilute alkali hydroxides.{R-30}

Pharmacology/Pharmacokinetics

Note: There is limited information on the pharmacokinetics of diethylstilbestrol.{R-27} However, synthetic estrogens are believed to readily convert to estrone, an endogenous estrogenic hormone.{R-9}

Mechanism of action/Effect: Estrogen increases the responsiveness of urethral smooth muscle to the hypogastric nerves, thereby increasing muscle tone in the bladder neck and urethral sphincter. This re-establishes the maximal urethral closure pressure, restoring normal urethral function and continence.{R-3; 5}

Evidence ratings

Evidence Quality	
A	Good evidence to support a recommendation for use
B	Moderate evidence to support a recommendation for use
C	Insufficient evidence to support a recommendation for use
D	Moderate evidence to support a recommendation against use
E	Good evidence to support a recommendation against use

Evidence Type	
1	Species-specific evidence from at least one large randomized and controlled trial (RCT) or multiple small RCTs
2	Species-specific evidence from a small RCT, disease models, large case studies, pharmacokinetic studies using surrogate endpoints, or evidence from well-designed trials in a different species that is considered appropriate for comparison
3	Dramatic results from either well-designed, species-specific trials without controls, controlled trials without randomization, or small case studies
4	Pharmacokinetic studies without surrogate endpoints or well designed pharmacodynamic studies in healthy animals
5	*In vitro* studies
6	Opinions of respected authorities on the basis of clinical experience or reports of expert committees

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Additional effects: In *in-vitro* studies, estrogens increased dog urethral sensitivity to alpha-adrenergic agonists, such as phenylephrine.[R-3; 5]

Absorption: Although no information is available on the absorption of diethylstilbestrol in dogs, it is believed to be well absorbed. Despite the poor solubility of diethylstilbestrol, its physical characteristics suggest permeability in the gastrointestinal tract of dogs would be high, which is borne out by evidence of efficacy in the treatment of urinary incontinence. According to the human biopharmaceutics classification system, diethylstilbestrol would be classified as a class 2, poorly soluble and highly permeable substance.[R-5; 24]

Distribution: Diethylstilbestrol is lipid soluble and widely distributed, similar to endogenous estrogens.[R-5]

Protein binding: *Human beings*—50 to 95% of endogenous estrogens are protein bound.[R-9]

Biotransformation: Primarily hepatic. The metabolism of estrogens varies across species.[R-9] Knowledge of diethylstilbestrol's metabolism in dogs is limited to the understanding that excretion of glucuronide metabolites via the bile is relatively common in dogs. The glucoronides may be hydrolyzed in the intestine, reabsorbed, reconjugated in the liver, and re-excreted into the bile.[R-9; 23]

Peak Plasma Concentration: *Dogs*—With a single oral dose of 1.55 mg/kg, a peak of approximately 9 nanograms per mL at one hour after administration.[R-7]

Elimination: *Dogs*—Diethylstilbestrol is metabolized in the liver and distributed into the bile as glucuronides.[R-23] Other routes of elimination have not been defined, although in other species, some elimination occurs in the urine.[R-9]

There appear to be two phases of elimination, perhaps because of enterohepatic recycling:[R-7; 27]

First half-life of elimination—About 1 hour.
Terminal half-life—About 24 hours.

Precautions to Consider

Carcinogenicity

Human beings: Diethylstilbestrol is noted to have carcinogenic effects with either prenatal or adult exposure. Exposure *in utero* is associated with an increased risk of vaginal or cervical cancer in women and testicular cancer in men. Some experimental evidence suggests a second-generation effect, as well.[R-5; 28]

Dogs: In dogs, very high doses of diethylstilbestrol have been shown to cause ovarian neoplasia.[R-5; 15; 17; 25; 26] (See also the *Overdose* section in this monograph.)

Pregnancy

Human beings: In addition to increased risk of cancer in the fetus, diethylstilbestrol can be teratogenic and cause fetal toxicity.[R-28; 22] The Food and Drug Administration assigned it a Pregnancy Category X, meaning there is positive evidence of human fetal risk.[R-22]

Lactation

Human beings: Estrogens are distributed into human breast milk.[R-22]

Pediatrics

Humans beings: Estrogens may accelerate epiphyseal closure in growing bones.[R-9; 22]

Drug interactions and/or related problems

Note: No significant drug interactions have been reported in association with diethylstilbestrol administration to animals.

Human drug interactions and/or related problems [R-22]

The following drug interactions have been reported in human beings*;* these are provided for informational purposes only and may or may not be applicable to the use of diethylstilbestrol in the treatment of animals:

Bromocriptine
(Estrogens may interfere with the effects of bromocriptine in human beings and require dosage adjustment.)

Corticosteroids, glucocorticoid
(Concurrent use with estrogens may alter the metabolism and protein binding of the glucocorticoids, leading to decreased clearance; increased elimination half life, and increased therapeutic and toxic effects of the glucocorticoids in human beings and require dosage adjustment during and following concurrent use.)

Cyclosporine
(Estrogens have been reported to inhibit cyclosporine metabolism in human beings and thereby increase plasma concentrations of cyclosporine, possibly increasing risk of hepatoxicity and nephrotoxicity; concurrent use

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is recommended in people only with great caution and frequent monitoring of blood concentrations and liver and renal function.)

Hepatoxic medications, especially dantrolene and isoniazid

(Concurrent use of these medications with estrogens may increase the risk of hepatotoxicity in human patients and fatal hepatitis has occurred; risk may be further increased with use in older females, prolonged use, or use in patients with a history of liver disease.)

Tamoxifen

(Concurrent use of estrogens in human beings may interfere with the therapeutic effect of tamoxifen.)

Laboratory value alterations

Note: No significant laboratory value alterations have been reported in association with diethylstilbestrol treatment in animals.

Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)—not necessarily inclusive (» = major clinical significance).

Except under special circumstances, this medication should not be used when the following medical problems exist:

A history of hypersensitivity to diethylstilbestrol or estrogen

(Sensitivity to estrogens varies significantly among dogs.)[R-27]

Risk-benefit should be considered when the following medical problems exist:

Severe hepatic dysfunction or disease

(Diethylstilbestrol is believed to be primarily metabolized in the liver.)[R-22]

Patient monitoring

The following may be especially important in patient monitoring (other tests may be warranted in some patients, depending on the condition; » = major clinical significance):

» Complete blood counts (CBCs)

(Periodic CBCs, particularly during prolonged administration, have been recommended for early detection of potential bone marrow toxicity.)

Estrogen-associated risk factors

(Although there is little information about the effects of long-term diethylstilbestrol administration, it may be prudent to monitor for health problems believed to be associated with endogenous estrogen, such as estrogen-sensitive mammary tumors.)

Side/Adverse Effects

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs in parentheses where appropriate)—not necessarily inclusive:

Those indicating need for medical attention

Incidence unknown

Dogs

Alopecia, reversible—reported in dogs treated for several months;[R-14] ***bone marrow toxicity (aplastic pancytopenia)***—reported in dogs given higher doses than is currently recommended to control incontinence; ***thrombocytopenia, reversible*** (bleeding, ecchymoses, epistaxis, gastrointestinal hemorrhage, petechia, regenerative anemia)[R-11; 29]

Note: There are no published reports of *bone marrow suppression* occurring in a dog administered diethylstilbestrol alone at the dosage recommended in this monograph; however, susceptibility to this effect varies among dogs.[R-19] The lowest published diethylstilbestrol dose causing marrow toxicity in a dog was given to a male Corgi, administered a total of 15 mg over 9 days. The dog developed thrombocytopenia, anemia, and leukocytosis followed by leucopenia; and eventually recovered.[R-29] (See also the *Overdose* section of this monograph.)

Thrombocytopenia without bone marrow suppression has been reported in a dog treated with 2.5 mg total dose per week for 3 years. The clinicians believed this to be an hapten-induced, immune-mediated thrombocytopenia and the dog responded to corticosteroid therapy, followed by splenectomy.[R-11]

Those indicating need for medical attention only if they continue or are bothersome

Incidence unknown

Dogs

Attracting male dogs[R-1]

Note: There is one published report of a dog *attracting male dogs* when on a maintenance dose of about 1 mg total dose a week.[R-1]

Overdose

For more information in cases of overdose or unintentional ingestion, **contact the American Society for the Prevention of Cruelty to Animals (ASPCA) National Animal Poison Control Center** (888-426-4435 or 900-443-0000; a fee may be required for consultation) **and/or the drug manufacturer**.

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Lethal dose

LD_{50} {R-20}—

Intraperitoneal administration:

Rats: 34 mg/kg.

Mice: 538mg/kg.

Intravenous administration: *Mice*—300mg/kg.

Oral administration: *Mice* and *rats*— >3000 mg/kg.

Clinical effects of overdose

The following effects have been selected on the basis of their potential clinical significance (possible signs in parentheses where appropriate)—not necessarily inclusive:

Dogs

With a total oral dose of 15 mg administered over 9 days:

Anorexia; bone marrow toxicity (aplastic pancytopenia) (bloody or darkened stool; ecchymoses, epistaxis, pale mucous membranes); ***labored respiration; lethargy; vomiting*** {R-29}

With a total parenteral dose *per dog* of 15 to 75 mg every eight weeks or a total dose *per dog* of 60 to 120 mg a week for eight weeks (formulations intended for slow absorption): {R-15-17; 25; 26}

Alopecia—reversible; ***bone marrow toxicity (aplastic pancytopenia); endometrial hyperplasia progressing to pyometra***—reversible during the course of progression by ending diethylstilbestrol administration; ***ovarian or uterine tissue proliferation; ovarian or uterine tumors***—regressed with withdrawal of diethylstilbestrol therapy; ***death***

Note: A progression of effects occurring with *bone marrow toxicity* in response to high doses of estrogens have been described in dogs: gradual anemia, thrombocytopenia, and rise in leukocyte count for three weeks followed by leucopenia. {R-6; 11-13; 21; 27; 29; 33} The bone marrow changes during this process include an increase in neutrophilic cells, then emigration or destruction of those cells, followed by destruction of erythroid elements, leading to a profound hypocellularity and death. {R-12; 13; 21; 29; 19}

Cats

Note: The following information is provided in the event of accidental overdose.

With a total daily diethylstilbestrol diproprionate dose of 1 to 7.5 mg *per cat* a day: {R-18}

Anorexia; progressive weight loss; jaundice; death

Note: A study demonstrated that a total dose per cat of 1 to 7.5 mg a day is lethal in about 3 to 5 weeks. Inflammation of hepatic bile ducts and other portal structures, myocardial lesions, and pancreatitis were noted on necropsy histopathology, but there was no evidence of bone marrow suppression in these cats.

Treatment of overdose

Treatment may include the following:

- Early induction of emesis
- Supportive therapy
- Monitoring for bone marrow suppression

Client Consultation

In providing consultation, consider emphasizing the following selected information:

Familiarizing clients with signs of potential adverse effects in animals, including depression, intermittent vomiting, labored respiration, severe dehydration, lethargy, and anorexia. Familiarizing clients with how to know when it is necessary to contact their veterinarian.

Familiarizing clients that will be handling these medications with the risk factors for human beings.

Dosing and Dosage Forms

Note: Diethylstilbestrol is not specifically approved for veterinary use. In other USP information monographs, the $^{EL US}$ and $^{EL CAN}$ designations refer to uses that are not included in U.S. and Canadian product labeling; however, in this monograph they reflect the lack of commercial product availability in the countries indicated. See also the *Regulatory Considerations* section in this monograph.

Until dosing studies are performed using diethylstilbestrol prepared by an accepted, standard compounding formula, the most effective dose may depend on how the drug preparation is compounded. Ranges are given based on the information available at this time.

DOSAGES

$^{EL US}$***Dogs***—

For *Diethylstilbestrol Capsules, Veterinary* and *Diethylstilbestrol Tablets USP*

Note: Urinary Incontinence—Because there is not enough information to establish a dose-response relationship, the following dose is administered proportional to the size of the dog and adjusted, based on clinical response: Oral, 0.1 to 1 mg total dose *per dog* every twenty-four hours for five days, then 0.1 to 1 mg total dose *per dog* one to three times a week, as needed to control incontinence. {R-1}

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Note: Splitting tablets or opening capsules should be discouraged.
For some dogs, once incontinence is controlled with the above regimen, diethylstilbestrol may be discontinued for periods of time, as long as possible loss of continence can be tolerated until reinstitution of therapy.

DOSAGE FORMS

Oral

DIETHYLSTILBESTROL TABLETS USP

Strength(s) usually available:

U.S.—
Not commercially available.
Canada—
Veterinary-labeled product(s):
1 mg (Rx) [GENERIC].{R-36}

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), in a well-closed container, unless otherwise specified by the manufacturer.

USP requirements: See the *Diethylstilbestrol Tablets USP* monograph in the *USP-NF*.

DIETHYLSTILBESTROL CAPSULES, VETERINARY

Strength(s) usually available: Diethylstilbestrol capsules are not available as a commercial product in the United States or Canada. Therefore, they must be compounded for veterinary use. Utilizing the services of a qualified compounding pharmacist to formulate this dosage form is recommended.

Caution: Keep out of the reach of children.

Packaging and storage: Pending.

USP requirements: Proposal pending.

Developed: 12/01/08

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Diethylstilbestrol in the treatment of urinary incontinence in dogs

Revision date: July 1, 2008

The following tables are not intended to be in-depth reviews of each article. Instead, they are brief overviews/reviews of the studies, assuming reviewers are already familiar with the cited references. If you would like additional information about these studies, please contact veterinary@usp.org.

Back to the indication.

Study 1 of 4: Nendick PA, Clark WT. Medical therapy of urinary incontinence in ovariectomised bitches: a comparison of the effectiveness of diethylstilboestrol and pseudoephedrine. Australian Veterinary Journal 1987 Apr; 64(4): 117-8.

Design • Retro-spective study with active controls N = 40 cases	**Goal:** This study was conducted to assess the efficacy of the standard medical treatments of urinary incontinence in spayed dogs. **Methods:** • Case records from ovariectomized dogs treated at Murdoch University Veterinary Hospital, Western Australia, for urinary incontinence • Inclusion criteria—A history of "dribbling" incontinence and a normal urinary tract on physical examination • Exclusion criteria—Signs of other urinary tract disease • Owners were contacted to fill in gaps in the records. **Dose:** • The cases were divided into two different treatment groups. Group A—Oral diethylstilbestrol, 1 mg total dose for 3 to 7 days followed by oral diethylstilbestrol, 1 mg total dose, administered once a week as a maintenance dose. If incontinence returned, owners were allowed to increase the frequency of administration. Group B—Dogs with incontinence occurring during the day and weighing >25kg received oral pseudophedrine, 30-mg total dose, administered three times a day. Dogs with incontinence only at night received a single 30-mg total dose, once a day in the evening. Dogs weighing <25kg received oral pseudophedrine, 15-mg total dose three times a day. • Eight dogs in Group A with a poor response were changed to Group B. **Results:** *Diethylstilbestrol Response* Totally effective: 20/31 (64.5%) Partially effective: 7/31 (22.6%) Not effective: 4/31 (12.9%) *Pseudoephedrine Response* Totally effective: 14/17 (82.4%) Partially effective: 0/17 (0.0%) Not effective: 3/17 (17.6%) • One dog treated with diethylstilbestrol was reported to attract male dogs. **Conclusions:** • The results suggest either diethylstilbestrol or pseudoephedrine can produce a satisfactory response in the treatment of urinary incontinence in ovariectomized dogs. • A follow-up survey suggested that once urinary incontinence was controlled and medication ended, dogs sometimes remained continent for many months before clinical signs returned and further treatment was pursued. • Further investigation of concurrent therapy with estrogen and alpha-adrenergic drugs is suggested.	

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Study 2 of 4: Holt PE. Urinary incontinence in the bitch due to sphincter mechanism incompetence: prevalence in referred dogs and retrospective analysis of sixty cases. Journal of Small Animal Practice 1985; 26(4), 181–190.

Design	**Goal:** This study was conducted in order to investigate the frequency of occurrence of urinary sphincter mechanism incontinence (USMI) among all incontinent dogs presented to a teaching hospital and evaluate the clinical aspects of the cases.	**Limitations:**
• Retrospective case series N = 60	**Methods:** • Inclusion criteria: Dogs with incontinence presented to the University of Bristol Department of Veterinary Surgery, Langford, Bristol. • Two groups of cases: Juveniles: Dogs incontinent since birth or since less than 6 months old Adults: Continent dogs as puppies with incontinence developing later in life **Dose:** For the seven controlled dogs—Initial dose was not specified but maintenance dose was stilbestrol [believed to be diethylstilbestrol], 1 to 2 mg total dose per dog, administered once a week **Results:** • The largest subset of incontinent dogs found in this series was females with USMI (60 adult and juvenile dogs). • Although some juvenile dogs were treated with stilbestrol, results were not clearly reported. Seven of these 21 dogs became continent and one significantly improved near the time of first estrus. • Of 39 adult female dogs with USMI, 35 were spayed, most after the first estrus. Incontinence was intermittent in 29 dogs and continuous in 10. Bacteriuria was found in 9 dogs, but the incontinence did not respond to treatment of urinary tract infection. All dogs had estrogen treatment either before after referral. • Of the 39 adult dogs, 23 did not respond to estrogen treatment, 9 responded but relapsed, and 7 spayed females became continent and were maintained on weekly treatment. **Conclusions:** • Urinary incontinence due to sphincter mechanism incompetence is common and is most often seen in spayed females, although the role estrogen and other factors play in the etiology remain unclear. Medium and large dogs appeared to be overrepresented.	• Incidence of cases at this referral hospital may not reflect incidence in general practice. **Comments:** • The dose of diethylstilbestrol was not reported for adult dogs that did not respond to treatment. • Parameters were not well defined, including criteria for diagnosis of sphincter mechanism incompetence.

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Study 3 of 4: Callahan, SM, Creed, KE. The effects of oestrogens on spontaneous activity and responses of phenylephrine of the mammalian utrethra. Journal of Physiology 1985; 358: 35-46.

Design		**Limitations:**
• *In vitro* study and study of effects in healthy animals N = 10	**Goal:** This study was conducted to investigate the effects estrogen has on urethral smooth muscle tissue and determine to what extent phenylephrine and acetylcholine increase the sensitivity of the muscle tissue to estrogen. **Methods:** • The researchers initially looked at urethral pressure measured by transducer in anesthetized female and male rabbits given intravenous medications, but felt technical difficulties prevented accurate measurement of estrogen's effects on other treatments. • The effect of estrogen on urethral tissues were determined by *in vitro* comparison of tissues from ovariectomized rabbits, guinea pigs, wallabies, and dogs to tissues from intact animals or ovariectomized animals treated with estrogens. Estrogen pretreatment apparently was performed in live animals before tissue samples were collected. • The study isolated strips of the lower urinary tract. The animal was killed and the tissue samples removed. Strips were mounted in a "bath" of solution. With the exception of estrogen, drugs were added directly to the bath and the electrical and mechanical responses were recorded. **Dose:** *Dogs—* • Subcutaneous stilbestrol in peanut oil, 33 to 50 mcg per kg a day for seven days before tissue collection. **Results:** • Phenylephrine produced a dose-dependent contraction of urethral strips in all species. • In dog tissues, the mean effective *in vitro* dose (ED_{50}) of phenylephrine to produce contraction was reduced from 4.5×10^{-6} M to 2.6×10^{-6} M when pretreated with estrogen; which was described as probably significant (P = 0.02 to 0.05). **Conclusions:** • These results suggest that estrogens can modify the spontaneous urethral smooth muscle activity and change the response to alpha-adrenergic agonists. • Further study is needed.	• Although this study suggests estrogens modify the response of tissues to phenylephrine, it could not determine the effects of estrogens alone on contractility. • The authors acknowledge that their previous study of dogs (see study 4 of 4 in this table) was a more sensitive test of the effects of estrogen and alpha-adrenergic agonist in dogs. **Comments:** • Tissues were from apparently healthy animals with no consideration of a possible history of incontinence or factors influencing incontinence.

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Study 4 of 4: Creed KE. Effect of hormones on urethral sensitivity to phenylephrine in normal and incontinent dogs. Research in Veterinary Science 1983 Mar; 34(2): 177-81.

Design	**Goal:** This study investigates the effects of phenylephrine on the pressure responses of the urethra and bladder and differences in those effects when dogs are pretreated with stilbestrol or progesterone	**Comments:**
• Estrogen effects in normal versus incontinent dogs. N = 8	**Methods:** • Two groups of spayed dogs were established: Clinically normal animals: Weighing 12 to 38 kg and less than 3 years old Incontinent animals: Weighing 20 to 36 kg, all but one less than 3 years old • Each week, the dogs were anesthetized and bladder and urethral responses to phenylephrine were measured by transducer. No medications were given the first three to four weeks so that control measurements could be taken. • Weekly measurements through the entire regimen could only be done for two incontinent dogs. A single measurement before and another 3 weeks after stilbestrol treatment were done in two dogs. Only control measurements were taken in one dog. **Dose:** During the weekly response test, all dogs received intravenous phenylephrine, in increasing doses from 0.1 to 300 mcg/kg. • Normal dogs—After the three- to four-week control period, oral stilbestrol, 1 mg total dose per dog a day for three weeks. This regimen was followed by either no treatment or oral stilbestrol and progesterone, 10-mg total dose, given every other day. In addition, after a three-week washout, three dogs received intramuscular progesterone. • Incontinent dogs—Oral stilbestrol, 1 mg total dose per dog a day for three weeks. **Results:** Normal dogs— • All but the lowest doses of phenylephrine increased the pressure of the urethra but produced little change in bladder pressure • The increase in the response of the urethra was considerable during the first week of stilbestrol treatment; one-third to one-eighth of the original dose produced the same response. This effect was maintained with no increase in response with ongoing stilbestrol treatment. Incontinent dogs— • The effects varied. Incontinence was controlled in two dogs and improved in one during the initial three-week treatment. Response to stilbestrol was slower than in normal dogs. Two dogs had improved response to phenylephrine during stilbestrol therapy but the urethral pressure increases in these dogs were generally less than normal dogs in response to phenylephrine. • Progesterone did not modify urethral sensitivity in either of the groups. **Conclusions:** • Urethral sensitivity to phenylephrine was increased by pretreatment with stilbestrol. The pressure responses in incontinent dogs did not increase to equal those in the control animals.	• The type of incontinence in these dogs was not specified; histories implied sphincter mechanism incompetence.

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