

Background: Ectopic ureters (EUs) associated with varying combinations of urinary incontinence, hydronephrosis, and urinary tract infection have been identified in related North American Entlebucher Mountain Dogs.

Objectives: To characterize the disease phenotype in affected dogs and evaluate possible modes of inheritance.


Methods: Prospective case series in which 17 dogs were evaluated with excretory urography, ultrasonography, and ureterocystoscopy. Three additional dogs were evaluated by necropsy alone. Clinical and pedigree histories from 165 North American Entlebuchers were compiled for analysis.

Results: Eleven female and 2 male dogs were found to have EUs. Six females and 1 male were continent. Bilateral intravesicular ectopic ureters (IVEUs) were identified in 9 dogs, bilateral extravesicular ectopic ureters (EVEUs) in 3 dogs, and 1 dog had IVEU and EVEU. Hydronephrosis was identified in 5 dogs, 3 of which had bilateral IVEUs. Two necropsied dogs had bilateral hydronephrosis with presumed ureterovesical junction obstruction associated with chronic granulation tissue or lymphoplasmacytic inflammation. Twenty-six dogs with EUs were identified in the pedigree. Because of incomplete penetrance, mode of inheritance could not be determined.

Conclusions and Clinical Importance: Ureteral ectopia is common in North American Entlebucher Mountain Dogs and clinical signs alone could not reliably predict disease phenotype. EVEUs were associated with urinary incontinence and occasionally hydronephrosis. IVEUs were clinically silent or associated with hydronephrosis. Further analyses are necessary to confirm and characterize the hereditary nature of the disorder.

Key words: Hydronephrosis; Interureteral orifice distance; Ureretal obstruction; Urinary tract infection.

Entlebucher Mountain Dogs (Entlebucher Senenhunds) are 1 of 4 Swiss Mountain Dog breeds. Although still relatively uncommon in North America, Entlebuchers have gained popularity and recently have been recognized by the American Kennel Club. Other than presumed inherited eye diseases, few hereditary disorders have been associated with the breed.1 Ectopic ureters (EUs), associated with varying combinations of urinary incontinence, ureteral obstruction, hydronephrosis, and urinary tract infection (UTI), have been identified in related North American Entlebucher Mountain Dogs. In North America, this constellation of abnormalities has been referred to collectively as the “Entlebucher urinary syndrome.” A similar phenomenon has been observed in European Entlebucher Mountain Dogs (Reichler, e-mail communication).

Abbreviations:
EU ectopic ureter
EVEU extravesicular ectopic ureter
IVEU intravesicular ectopic ureter

Congenital EUs are characterized by termination of 1 or both ureters at a site other than the craniolateral aspect of the bladder trigone.2 Large epidemiologic studies in North America and the United Kingdom have identified an increased prevalence of EUs in Border Terriers, Briards, Bulldogs, Fox Terriers, Golden Retrievers, Griffons, Labrador Retrievers, Miniature and Toy Poodles, Newfoundland Dogs, Siberian Huskies, Skye Terriers, and West Highland White Terriers.3,4 The high predilection in these breeds and observation of EUs in a few closely related dogs5,6 strongly suggests a hereditary basis for the disorder. However, the specific mode of inheritance and genetic mutation(s) involved in EUs have not been identified. To our knowledge, this is the first report characterizing congenital EUs in Entlebucher Mountain Dogs. Because accurate phenotyping is essential for future genetic studies, our objectives were to characterize the clinical features of Entlebucher urinary syndrome in affected dogs and evaluate possible modes of inheritance.

Methods and Materials

Study Population

Twenty client-owned Entlebucher Mountain Dogs (13 females and 7 males) were evaluated at the Michigan State University Veterinary Teaching Hospital (MSUVTH) between July 2006 and
respectively. Eight female and 1 male dog had clinical signs of urinary tract disease; 11 dogs were asymptomatic and were screened for Entlebucher urinary syndrome because of their relationships to symptomatic affected dogs. Seventeen dogs were evaluated by history and physical examination, CBC, serum biochemistry profile, urinalysis, quantitative urine culture for aerobic bacteria, excretory urography, ultrasonography, and urethrocytoscop. Buccal mucosal epithelial cells were collected from all dogs and archived for future DNA analyses. Three additional dogs were evaluated by necropsy alone. Clinical and pedigree histories from the 20 dogs evaluated at the MSU VH and those from an additional 145 Entlebucher Mountain Dogs that resided in North America, but were not evaluated at the MSU VH, were obtained from a database maintained by the National Entlebucher Mountain Dog Association. Individual pedigrees were compiled into 1 large pedigree to evaluate relationships among the study dogs, to identify a suspected proband and to gain insight into the possible mode of inheritance. The study was approved by the Michigan State University Institutional Animal Care and Use Committee.

**Diagnostic Imaging**

Abdominal ultrasonography was performed with 5 and 7.5 MHz transducers. Morphology of the ureters, ureterovesical junction, and bladder was further evaluated with either digital fluoroscopic excretory urography in conjunction with pneumocystography (15 dogs), or with helical computed tomographic (CT) excretory urography (3 dogs). Hydronephrosis or hydroureter was diagnosed when the renal pelvis or ureter was >2 or >3 mm in diameter, respectively.5

**Urethrocytoscop**

Anesthetized female dogs were placed in dorsal sacral (lithotomy) position and the vestibule, vagina, urethra, and urinary bladder were examined cystoscopically with a rigid 30° 1.9–2.7-mm telescope and an appropriately-sized operating sheath. Anesthetized male dogs were placed in left lateral position and examined with a flexible fiberoptic or video ureteroscope. Continuous irrigation with sterile saline was used throughout cystoscopy. Positions of the ureteral openings relative to each other and to the bladder neck were assessed when the bladder was distended to a standard-ized pressure of 5 cm H2O. When necessary, the interureteral orifice distance in fresh cadaver urinary bladders prepared from 17 intact female adult Beagle and mixed breed dogs obtained from unrelated studies. Immediately after euthanasia, urinary bladders were removed, emptied of urine, and moderately distended with 5 mL/kg of 10% formalin by transurethral catheterization. The urethra and both ureters were ligated to maintain distention. The bladder then was submerged in formalin and allowed to fix for 48 hours. After fixation, the ventral half of the bladder was removed and the distance between the lateral edges of the ureteral openings (interureteral orifice distance) was measured with an electronic caliper. The mean interureteral orifice distance in female bladders (mean body weight, 13.8 ± 3.0 kg) was 15.6 ± 5.1 mm; the mean interureteral orifice distance in 17 intact male cadavers (mean body weight, 18.8 ± 2.3 kg) was 12.7 ± 3.6 mm. No dog had an interureteral orifice distance <4.5 mm. We defined an abnormal interureteral orifice distance as <4 mm.

**Necropsy Evaluat**

Two asymptomatic female dogs and 1 asymptomatic male dog were evaluated by necropsy. In these dogs, the kidneys, ureters, urinary bladder, and proximal urethra were collected at the time of necropsy. All biopsy and necropsy specimens were fixed in 10% buffered formalin, routinely sectioned and stained with hematoxylin and eosin, and examined by light microscopy.

**Results**

**Population Characteristics and Clinical Signs**

Based on urethrocytoscopic or necropsy findings described below, 13 dogs (11 female and 2 male) were found to have IVEUs or EVEUs and were phenotypically classified as affected dogs (Table 1). Nine of these dogs (8 females and 1 male) had signs of urinary tract disease. Overall, affected dogs ranged in age at the time of

<table>
<thead>
<tr>
<th>Sex</th>
<th>History and Clinical Signs (n)</th>
<th>Ectopic Ureter Opening Position (n)</th>
<th>Other Abnormalities (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female (n = 11)</td>
<td>Urinary incontinence (5)</td>
<td>Bilateral intravesicculara (8)</td>
<td>Bilateral hydrouryter/hydronephrosis (2)</td>
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<td></td>
<td>Abdominal distension (3)</td>
<td>Bilateral extravesiccular (2)</td>
<td>Unilateral hydrouryter/hydronephrosis (3)</td>
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<td>Pollakiuria/dysuria (3)</td>
<td>Intra- and extravesiccular (1)</td>
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<td>Recurrent UTI (3)</td>
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<td>Follicular cystitis (2)</td>
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<td></td>
<td>Chronic renal failure (2)</td>
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<td>Follicular vestibulitis (1)</td>
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<td>Asymptomatic (3)</td>
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<tr>
<td>Male (n = 2)</td>
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<td>Bilateral intravesiccular</td>
<td></td>
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<tr>
<td></td>
<td>Pollakiuria/dysuria (1)</td>
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UTI, urinary tract infection.

aEctopic ureteral openings located within the bladder but positioned in the caudal trigone on midline with ureteral openings spaced <4 mm apart.
evaluation from 2 to 168 months of age (mean, 47.1 ± 53.3 months; median, 21 months). However, most symptomatic dogs developed clinical signs at <1 year of age. Mean body weight of affected dogs was 19.7 ± 7.5 kg. Signs of lower urinary tract disease were not reported in 3 affected females (#8, 10, 11) and 1 affected male (#13). The 1 asymptomatic affected male dog was identified at the time of necropsy after euthanasia for splenic hemangiosarcoma at 14 years of age. The remaining 8 female and 1 male affected dogs were presented with histories of urinary incontinence (n = 6), recurrent UTI (n = 4), polyaikuuria (n = 4), abdominal distention (n = 3), and hydronephrosis and hydroureter (n = 5). Of the 5 female dogs with urinary incontinence, 3 were symptomatic before ovariohysterectomy (#4, 6, 9), whereas 2 dogs developed incontinence after ovariohysterectomy (#7, 12). Urinary incontinence was reported to be intermittent in 3 female dogs. One affected male dog (#5) had lifelong urinary incontinence. Of the 5 dogs with hydroureter and hydronephrosis (#1, 2, 6, 9, 12), only 3 dogs (#6, 9, 12) had urinary incontinence. Two symptomatic affected female dogs with bilateral hydronephrosis were euthanized because of advanced chronic renal failure, 1 at 5 months (#2) and 1 at 124 months of age (#12). The later dog had unilateral nephrectomy performed for hydronephrosis at 4 months of age.

Clinicopathologic Evaluations

In 1 symptomatic affected dog (#6), clinicopathologic findings were consistent with pyelonephritis. Quantitative culture of urine collected by pyelocentesis from that dog yielded 100 CFU/mL of *Staphylococcus intermedius*. Urine cultures from the remaining affected dogs were negative for aerobic bacteria. Urine specific gravity in affected dogs ranged from 1.010 to 1.050 with a mean of 1.030 ± 0.015. Serum creatinine concentrations were within normal limits for all affected dogs evaluated antemortem.

Diagnostic Imaging

Abdominal ultrasonography disclosed unilateral hydronephrosis and hydroureter in 3 affected dogs (#1, 6, 9). When compared with cystoscopic findings, ultrasonography identified 4 of 7 (57%) EVEUs and 0 of 13 (0%) IVEUs in affected dogs. Excretory urograms in the 10 affected dogs were interpreted to be indicative of unilateral EU with ipsilateral hydroureter and hydronephrosis in 3 dogs, unilateral EU in 1 dog, bilateral EUs in 3 dogs, and within normal limits in 3 dogs. When compared with cystoscopic findings, excretory urography identified 6 of 7 (86%) EVEUs and 4 of 13 (31%) IVUEs in affected dogs.

Urethrocystoscopy

With the exception of 1 dog (#6) with polypoid vestibulitis, lesions of the external genitalia, vestibule, and vagina were not identified in affected female dogs by urethrocystoscopy. In all affected dogs, ectopic openings tended to cluster just cranial or caudal to the bladder neck. Bilateral EVEU openings were identified in 2 female (#7, 9) and 1 male (#5) and bilateral IVEU openings were identified in 6 female dogs (#1, 3, 4, 8, 10, 11) examined by urethrocystoscopy (Figs 1–4). In 1 female dog (#6), 1 EU opening was judged to be extravesicular and 1 intravesicular. In dogs with urinary incontinence, EUs were extravesicular in 3 dogs (#5, 7, 9; Figs 1 and 2),
extravesicular and intravesicular in 1 dog (#6), and intravesicular in 1 dog (#4). In 5 continent dogs with IVEU examined cystoscopically, ureteral openings usually were positioned asymmetrically near the midline in the caudal trigone (Figs 3 and 4). In dogs with hydroureter and hydronephrosis, the ipsilateral EU opening appeared stenotic and was extravesicular in 2 dogs (#6, #9; Fig 1) and intravesicular in 1 dog (#1). Multifocal lesions associated with lymphoplasmacytic follicular cystitis were observed in 1 incontinent affected female dog with bilateral IVEUs (#4).

Gross Necropsy and Light Microscopy

Necropsy examination of the urinary tract from a 4-month-old Entlebucher (#2) euthanized because of bilateral hydronephrosis and progressive renal failure identified marked bilateral hydroureter and hydronephrosis as well as severe cortical and medullary parenchymal atrophy, and malformation of the distal trigone characterized by intravesicular malpositioning of both ureteral openings near the bladder neck. Multiple transverse sections through the anomalous ureterovesical junction showed moderate to marked granulation tissue characterized by marked fibrosis of the lamina propria and subepithelial tissue with numerous perpendicular blood vessels, and minimal-to-mild lymphoplasmacytic infiltrates (Fig 5).

Necropsy examination of the urinary tract from a 10-year-old Entlebucher (#12) euthanized because of hydronephrosis and progressive renal failure disclosed marked hydroureter and hydronephrosis, as well as severe cortical and medullary parenchymal atrophy of the right kidney, and an absent left kidney. The left kidney had been removed at 4 months of age because of hydroureter and hydronephrosis. Distal trigone malformation was evident and characterized by intravesicular malpositioning of both ureteral openings near the bladder neck. Histologic examinations showed bilateral moderate lymphoplasmacytic ureteritis, and severe chronic lymphoplasmacytic (follicular) cystitis. In addition, multiple transverse sections through the anomalous bladder neck identified severe lymphoplasmacytic cystourethritis and subepithelial fibrosis (Fig 6).
Necropsy examination of the urinary tract from an asymptomatic affected 14-year-old castrated male Entlebucher (#13) euthanized because of splenic hemangiosarcoma identified distal trigone malformation characterized by intravesicular malpositioning of both ureteral openings. Histologic examination of multiple transverse sections through the anomalous ureterovesicular junction showed disorganized smooth muscle bundles, increased submucosal vascularity, and numerous subepithelial acini lined by transitional epithelium.

Pedigree Analysis

A single large pedigree of 165 related North American Entlebucher Mountain Dogs (94 females, 69 males, 2 unknown sex) was examined in which a putative male founder was located at the beginning of the pedigree. Twenty-seven females and 7 males had been evaluated by contrast radiography, cystoscopy, surgery, or some combination of these procedures. EUs were confirmed in 24 female and 2 male dogs and these cases accounted for 16% of dogs in the pedigree. An additional 5 females and 1 male dog had signs consistent with the syndrome, but were not evaluated. In our series of dogs, affected male #13 was the maternal and paternal great-grandson of the shared common male ancestor. Two affected females (#8, 10) were nonlittermate full siblings and daughters of affected male dog #13. Five additional affected female dogs (#1, 2, 6, 7, 9) were granddaughters of male dog #13. Two of these dogs (#6, 7) were also full siblings.

Because it was evident that some clinically asymptomatic dogs in the pedigree had confirmed EUs when examined at our hospital (dogs #8, 10, 11, and 13), the gene underlying this disorder may be regarded to have a low degree of penetrance with regard to the overt clinical phenotype, but not necessarily with the cystoscopically determined morphologic phenotype. The proportion of females with the clinical phenotype identified in the pedigree was approximately 10 times greater than that of males, suggesting that penetrance of the clinical phenotype in males was considerably lower. However, given the relatively high phenotype frequency in the pedigree, multiple inbreeding loops, and apparent low penetrance, we were unable to ascertain the mode of inheritance.

Discussion

In this study, we describe IVEU and EVEU in 13 closely related continent and incontinent Entlebucher Mountain Dogs. Our observations suggest that the term “Entlebucher urinary syndrome” represents primarily ureteral ectopia and its associated upper and lower urinary tract sequelae. Furthermore, it appears that Entlebuchers cannot be accurately phenotyped by clinical signs alone. Like other affected breeds, EUs in Entlebucher Mountain Dogs may be clinically silent or associated with a variety of clinical presentations depending on specific locations and morphology of anomalous ureteral openings and their adverse effects on continence mechanisms, ureteral function, and host antimicrobial defenses.

Urinary incontinence has been the most common clinical sign associated with EUs in dogs. However, 7 of 13 affected dogs in our series were continent and 4 of these were completely asymptomatic. The other continent affected dogs presented for evaluation of abdominal distension or other lower urinary tract signs (eg, pollakiuria and dysuria). EUs in continent dogs are rare and have been reported in 3 male dogs; all had EUs located in the prostatic urethra that were associated with concomitant hydroureter and hydronephrosis. Uretal ectopia also has been reported in 1 continent 4-year-old female dog, but the site(s) of termination of the EUs and the presence of upper urinary tract abnormalities were not reported. In our series, all continent affected female dogs had bilateral IVEUs, which probably accounts for their lack of urine storage dysfunction.

When compared with cystoscopy, ultrasonography, and fluoroscopic excretory urography correctly identified only 20 and 44% of EUs, respectively, in our series of dogs. Our detection rates were substantially lower than those of previous reports in which ultrasonography detected 91% and fluoroscopic excretory urography detected 64–91% of EUs in dogs compared with cystoscopy, surgery, or necropsy. Other studies have indicated that helical CT excretory urography agrees more closely with cystoscopic, surgical, or postmortem findings than other imaging methods for detecting and localizing EUs. Although helical CT excretory urography correctly identified 2 EVEUs in 1 affected male dog, helical CT excretory urography incorrectly identified an EU in 1 normal male dog (data not shown). Lower rates of detection and localization of EUs by diagnostic imaging in our series are probably related to the relatively high number of IVEUs in affected dogs. In our series, fluoroscopic excretory urography correctly detected 4 of 5 (80%) EVEUs, but only 4 of 13
(31%) IVEUs. More extensive use of helical CT excretory urography or administration of a diuretic during ultrasonography may have improved the sensitivity of diagnostic imaging. Development of less invasive screening methods that are cost-effective and widely available is essential for formulation of rational breeding plans. Although diuretic-enhanced ultrasonography may be useful for this purpose, additional studies are necessary to confirm the diagnostic accuracy of this modality for identifying IVEUs in Entlebucher Mountain Dogs.

Urethrocystoscopy has been used routinely to diagnose EUs in dogs and was the principal method used for phenotypic classification and characterization of lower urinary tract anomalies in our series of affected Entlebuchers. Urethrocystoscopy allowed control of bladder distention, assessment of the ureteral opening position relative to the bladder neck, estimation of interureteral opening distance, and identification of other concurrent genitourinary tract anomalies. Surprisingly, concurrent vaginal anomalies were not identified in affected female Entlebuchers. This is in contrast to previous studies in which nearly all dogs with EUs had vaginovestibular junction abnormalities. IVEU were identified in 10 of 13 affected Entlebuchers and accounted for 73% of EUs. Also, 70% of dogs with IVEUs were continent. Furthermore, hydrourter and hydronephrosis were associated with IVEUs in 2 continent dogs. We speculate that it is likely that most dogs with IVEUs have sufficient urethral pressure to maintain continence, but remain predisposed to hydrourter and hydronephrosis. IVEUs have been reported uncommonly in dogs. In 2 studies of incontinent dogs with EUs evaluated cystoscopically, IVEUs accounted for 2–16% of all EUs. In those studies, EUs were subjectively classified as intravesicular when the ureteral implantation site appeared too caudal or dorsal and too closely apposed despite bladder trigone distention. Diagnosis of IVEU depends on assessing the relative position of the anomalous opening to the bladder neck and the normal position at the cranialolateral angles of the trigone. The ability to identify IVEUs may be confounded by an indistinct bladder-urethral junction, the optical distortion associated with use of rigid cystoscopes with 30° viewing angles, and incomplete bladder distention.

In our experience, IVEU classification was facilitated by estimation of the interureteral orifice distance when the bladder was distended to a standardized pressure. We defined IVEUs as ureters opening within the bladder, but positioned near midline with the interureteral opening distance <4 mm. This relationship reflects the normal embryologic translocation of the ureter openings from the dorsal aspect of distal urogenital sinus (precursor of the urethra) to the cranialolateral angles of the mature bladder trigone. Dyssembryogenesis of the ureteral bud and failure of common excreatory duct apoptosis during ureter transposition results in ectopic openings positioned along the path of ureteral migration (the so-called ectopic pathway). In humans and dogs, the right and left ectopic pathways course along the dorsal urethra near midline until they reach the caudal apex of the bladder trigone; the pathways then diverge and terminate in their respective cranialolateral angles of the trigone. Thus, the closer ureter openings are to each other and to midline, the more likely they are to be ectopic. The interureteral opening distance in a large population of normal dogs has not been reported. Although the mean interureterovesicular junction distance estimated by helical CT excretory urography was reported to be 2.88 cm in dogs, this measurement represented the distance between the points at which the ureters contacted the outer bladder wall and not the actual distance between the luminal ureteral openings. Results of our pilot studies in clinically normal male and female dogs similar in size to Entlebuchers indicated that the mean interureteral opening distance was 13 and 15 mm, respectively, with no measurement being <4.5 mm. Our observations are similar to distances determined from scale anatomic drawings of 2 nondistended canine bladders and to mathematically derived indirect estimates obtained from a study of distended bladders obtained from 60 male and 80 female dogs. However, we caution that the morphology of the trigone and relative ureteral orifice positions may vary by age, sex, breed, body size, and degree of bladder distention. Additional studies are needed to better characterize the normal anatomic relationships of structures in the canine trigone.

Hydronephrosis and hydroureter were observed in 3 of 9 (33%) of Entlebuchers with bilateral IVUEs and 2 of 4 (50%) with unilateral or bilateral EVEUs. In previous studies, hydrourter and hydronephrosis were detected in 17–36% of incontinent dogs with EVEUs. To our knowledge, hydronephrosis has not been reported previously in dogs with IVEUs. Our observations imply that despite their intravesicular location, IVEUs, like their extravesicular counterparts, may be associated with concurrent upper urinary tract sequelae that may result in substantial morbidity or even mortality. Pathogenic factors resulting in hydronephrosis associated with EUs are largely unknown. Hydronephrosis most commonly results from mechanical or functional lesions that interrupt the normal peristaltic flow of urine from the kidney. Possible etiologies in dogs with EUs include congenital or acquired ureteral stenosis, ureteroceles, inflammation or fibrosis of the ureter or ureterovesicular junction, vesicoureteral reflux, adynamic ureter segments, and increased bladder or urethral pressure.

Stenotic ureteral openings have been observed in some dogs with EUs and ipsilateral hydronephrosis. However, ectopic openings in most previous reports of dogs with concomitant hydrourter and hydronephrosis were considered to be normal or increased in size. In our series, the ipsilateral ureteral openings of 3 hydronephrotic kidneys were judged to be smaller than normal when viewed cystoscopically. In 2 dogs with bilateral hydronephrosis that were evaluated by necropsy, histopathology of the ureterovesicular junction identified excessive amounts of granulation tissue in 1 dog and lymphoplasmacytic inflammation in the other. We hypothesize that hydrourter and hydronephrosis in these affected dogs were associated with mechanical obstruction because of
stenosis of the ureteral opening. However, it cannot be determined whether obstruction was the result of congenital ureteral malformation or acquired secondarily to ureterovesical junction inflammation, or both. In addition, we cannot exclude the possibility of concurrent functional causes of obstruction such as an adynamic ureter segment or increased resistance to urine flow because of the position of the ectopic opening in the caudal trigone or bladder neck.2,12,24 Our observations and those of others suggest that EUs should be considered in continent male and female dogs with hydroureter, hydronephrosis, or both.14,15,25

All affected Entlebucher Mountain Dogs included in the pedigree shared a common male ancestor. Although 16% of dogs in the pedigree were affected, this proportion should not be interpreted as the prevalence of EUs in the breed. Litter selection biases and a limited number of phenotyped dogs preclude determination of an actual prevalence rate. Nevertheless, the Entlebucher urinary syndrome is likely to be hereditary, based on the high frequency of incontinent dogs in the breed, occurrence of the disorder in littersmates, and evidence of parent-to-offspring transmission. Interestingly, anecdotal reports suggest that EUs also are common in European Appenzeler Mountain Dogs, another Swiss Mountain Dog breed that is closely related to Entlebucher Mountain Dogs (Reichler, e-mail communication).1 Despite uncertainty regarding the mode of inheritance, it is reasonable to assume that at least 1 necessary gene, identical by descent, must be acting to cause the condition. Oligogenic inheritance without a necessary gene would require an improbable combination of deleterious additive alleles to produce EUs confined to a single breed at a high frequency. However, the specific gene mutation(s) responsible for EUs in Entlebuchers and other high prevalence breeds is (are) unknown. Since 1993, over 400 genes have been identified that are involved in development and maturation of the urinary system.18,28 However, only a few of these genes appear to cause EUs in other species and these will serve as candidate genes for future studies.18 The Entlebucher urinary syndrome is a heritable condition that may provide a useful animal model for future studies of comparative embryogenesis and developmental anomalies of the urinary system in companion animals and humans.

Footnotes

1 Karl Storz Veterinary Endoscopy- America, Goleta, CA
2 AUR-7; Gyrus ACMI, Southborough, MA
3 URF-V; Olympus America Inc, Center Valley, PA
4 Weasel wire, Infinity Medical, Malibu, CA

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