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Persistent urinary incontinence in female Golden Retrievers following laser ablation of intramural ectopic ureters may be associated with the presence of historical urinary tract infection

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OBJECTIVE
To identify predictive factors for postoperative continence in female Golden Retrievers following cystoscopic-guided laser ablation of intramural ectopic ureters (CLA-EU).

ANIMALS
41 client-owned female entire Golden Retrievers with uni- or bilateral intramural ectopic ureter(s) were retrospectively enrolled.

METHODS
Patients were diagnosed with ectopic ureters with a combination of ultrasonography and cystoscopy. CLA-EU was performed for all dogs so that each ureteral opening was considered to be in an appropriate position by a single operator. All dogs had short-term follow-up 4 weeks and long-term follow up > 10 weeks after the procedure via telephone, which included urinary continence scoring. Clinical factors and ultrasonographic and cystoscopic findings from initial presentation were evaluated to identify predictive factors for postoperative continence.

RESULTS
Short-term urinary continence was achieved in 46.3% of dogs with no additional medical therapies. Presence of historical urinary tract infections prior to CLA-EU (OR, 0.130; 95% CI, 0.020 to 0.621; *P* = .018) was negatively correlated and ureteral dilatation (OR, 34.260; 95% CI, 1.813 to 2,143; *P* = .043) was positively correlated with likelihood of urinary continence. Long-term urinary continence was achieved in 63.4% of dogs, and presence of historical urinary tract infections was negatively prognostic (OR, 0.173; 95% CI, 0.023 to 0.856; *P* = .048).

CLINICAL RELEVANCE
Female Golden Retrievers undergoing CLA-EU have similar outcomes to those reported for other mixed-breed cohorts with > 30% of dogs failing to regain urinary continence. Historical urinary tract infections were significantly associated with both short- and long-term urinary continence in our population.

Keywords: ectopic ureter, Golden Retriever, incontinence, continence, intramural

Ureteral ectopia is the most common cause of canine juvenile incontinence in female dogs and is a congenital abnormality whereby one or both ureteral orifices are located distal to the bladder trigone. Ectopic ureters can be either extramural or intramural (iEU), with 87% to 99% of canine ureteral ectopia reported to be intramural.[1–4] Numerous breeds have been found to be at higher risk of ureteral ectopia, including the Golden Retriever, Labrador Retriever, Siberian Husky, West Highland White Terrier, Newfoundland, Miniature and Toy Poodle, Entlebucher Mountain Dog, and Soft Coated Wheaten Terrier.[4–9] In these breeds, there is thought to be a heritable basis for the condition. Female dogs commonly present with clinical signs of intermittent or continuous urinary incontinence from a young age, but some dogs may present with clinical signs later in life.[10,11]

Numerous diagnostic imaging modalities have been used to assess ectopic ureters in dogs.[11–13] Abdominal ultrasonography has recently been shown to have a diagnostic accuracy of 95%[12] while also allowing evaluation of the upper urinary tract for the presence of other common concurrent abnormalities such as hydroureter, hydronephrosis, renal hypoplasia, and renal aplasia.[3,11] Cystoscopy has been found to have a 100% sensitivity for diagnosing ureteral ectopia[13,14] and allows for concurrent assessment of the lower urinary tract and treatment of iEU with cystoscopic-guided laser ablation of iEU (CLA-EU), which is the treatment of choice for iEU.[15–18] The success rate (defined broadly as urinary continence) for female dogs undergoing CLA-EU is reported to range from 31% to 80% without additional therapies and 67.7% to 81% with the addition of adjunctive medical or surgical procedures.[15–18]

Previous studies evaluating CLA-EU in female dogs have failed to identify any positive or negative preoperative prognostic factors. These studies have also been limited by variation in breed and age of the dogs at presentation, diagnostic approach, and surgeon performing the procedure, which may have led in part to the lack of identification of any prognostic factors.[3,17,19] Factors proposed for poor outcomes following CLA-EU include other factors related to urinary incontinence in female dogs such as urethral sphincter mechanism incompetence[20,21]; an intrapelvic bladder[22]; a short urethra, lack of a defined bladder neck, and paramesonephric remnants[9,23]; and poor bladder compliance.[19,24] Other factors such as ureteral or renal pelvic dilatation, age at surgery, or preoperative urinary tract infections have been suggested as positive prognostic factors for surgical correction but not CLA of ectopic ureters.[1,25]

Our primary aim was to identify prognostic factors that affect short- and long-term continence scores in female Golden Retrievers undergoing CLA-EU. Our objective was to evaluate a homogenous sample of female Golden Retrievers younger than 24 months, all diagnosed with ectopic ureters using a standard protocol and all treated via cystoscopic laser ablation by the same surgeon to assess for pre- and perioperative prognostic factors associated with short-term (1 month) and long-term urinary continence following cystoscopic laser ablation of ectopic ureters. We hypothesized that both the lack of a defined bladder neck and subjectively reduced bladder compliance would be associated with a lower likelihood of achieving urinary continence following CLA-EU due to the relation of these factors with urinary incontinence in female dogs. The secondary aim was to add to the literature on the efficacy of CLA of ectopic ureters in female Golden Retrievers.

Methods

Forty-two female Golden Retrievers presenting to the Queen's Veterinary School Hospital, University of Cambridge, undergoing CLA of uni- or bilateral ectopic ureters between July 2016 and July 2022 were retrospectively enrolled. All clients had consented to being contacted for the purpose of clinical research. One case was subsequently excluded, as not all relevant clinical data were recorded. Formal institutional approval was granted by the ethics and welfare committee at the Department of Veterinary Medicine, University of Cambridge (CR 494).

Clinical records were reviewed for age at presentation, neuter status, weight, historical urinary tract infections prior to the procedure, and any medications being administered at the time of presentation. Historical urinary tract infections were assessed as present or absent on the basis of review of clinical history from the referring veterinary surgeons, and all cases classified as having historical urinary tract infections had compatible urinalysis results in the history as a minimum. All patients had serum urea and creatinine (but not symmetric dimethylarginine) concentrations assessed either prior to or during referral, and all values were within the reference range of the respective laboratories for all patients; thus, this information was not included in the data analysis. Diagnosis of ectopic ureters prior to cystoscopy was made using abdominal ultrasound. Reports of abdominal ultrasound scans performed by a European College of Veterinary Diagnostic Imaging (ECVDI)–certified veterinary radiologist, or an ECVDI resident under the supervision of an ECVDI-certified veterinary radiologist, were reviewed, and urinary tract abnormalities were recorded. Where ureteral dilation was subjectively described as absent but no specific measurement was recorded, a figure of 1 mm was used. Where the renal pelvis was described as normal but without a specific measurement, a figure of 1 mm was used for statistical analysis. Urinary continence was graded at the time of presentation using a subjective 4-point grading system: 0, completely continent; 1, occasional dripping of urine; 2, intermittent dripping of urine with occasional pooling of urine; and 3, continuous dripping of urine with frequent pooling of urine.

All cystoscopic procedures were performed by a single European College of Veterinary Surgeons (ECVS)–certified specialist in small animal surgery (LJO). Dogs were anesthetized and placed in dorsal recumbency prior to the vulva being clipped and aseptically prepared. All dogs received IV antibiosis at the time of the procedure with cefuroxime (Zinacef). A rigid 2.7- or 4-mm 30° cystoscope (Hopkins telescope; Karl Storz) was inserted retrograde into the vestibule, and assessment of a persistent vestibulovaginal remnant (PVVR) was made prior to advancement into the urethra, with concurrent pressurized irrigation using 0.9% saline solution. Grading of PVVRs was performed by a single operator (LJO) at the time of cystoscopy as follows: grade 0, no PVVR; grade 1, thin band of tissue, commonly broken during the course of the procedure without use of the laser; grade 2, moderate band of tissue requiring use of the laser to transect; and grade 3, thick +/− wide band of tissue preventing access to the vagina with the scope +/− partially dividing the vagina longitudinally. Cystoscopic examination was used to clarify the location of the openings of the ectopic ureter(s). The presence or absence of a distinct bladder neck was assessed subjectively by a single operator (LJO) during cystoscopy. Bladder compliance was also assessed subjectively by the same operator (LJO) on the basis of the volume of fluid required to fill the bladder during cystoscopy. Urodynamics were not performed, and thus the exact volume of fluid required to distend the bladder was not recorded. Ureteral opening location was classified as grade 0 (trigone, nonectopic), grade 1 (bladder neck), grade 2 (proximal urethra), grade 3 (midurethra), or grade 4 (distal urethra or vestibule). For dogs from which it had not been possible to collect a cystocentesis urine sample (on the same day as or the day prior to CLA-EU), a urine sample was collected through the cystoscope operating channel soon after entry prior to administration of IV antibiotics. Urine collected via cystocentesis or cystoscopically was submitted for bacterial culture and sensitivity for all cases. After identification of the ectopic ureteral openings, a 0.025-inch guide wire (Weasel Wire; Infiniti Medical) was advanced into one or both ectopic ureteral orifices prior to the insertion of 4F ureteral catheter(s) (TigerTail ureteral catheter; Becton, Dickinson and Co) over the previously inserted guidewire(s). A 6-μm diode laser fiber (Ceralas Biolitec) at 8W was used through the instrument working channel to ablate the medial wall of the iEU until the new opening was level with the normal ureter (unilateral cases) or until the openings were considered well positioned within the bladder trigone (bilateral cases). All cases were discharged with a 5-day course of amoxicillin clavulanate while awaiting the urine culture and antimicrobial sensitivity results. Additional medication doses and duration were dispensed at the lead clinician's discretion. Patients were discharged the same day, after recovery from the general anesthetic.

All cases were routinely followed up by telephone, and owners were questioned on the degree of urinary continence achieved at 1 month postprocedure, as per hospital policy, using the same scoring system as was used at initial presentation. During this telephone call, owners were also questioned on any additional medication or antibiotic courses that had been prescribed and administered between discharge and the 1-month time point. Urinary continence grade at this initial time point was allocated by one of the authors following a conversation with the owners to minimize variability if owners were allocating this grade without guidance. This information was retrieved for this study via review of the clinical notes and confirmed via a telephone call with the owners by the principal investigator (OLR) at a later time point. Longer term follow-up (> 10 weeks postprocedure) urinary continence scores and medication history were available for all dogs but collected at nonstandardized time points by telephone, email, or follow-up appointments.

Statistical analyses were performed using R version 4.3.0 for Mac (The R Project for Statistical Computing). Significance level was set at 0.05. Descriptive statistics were used to document findings, and nonnormally distributed data were reported as median with range. Categorical variables were reported as numbers and percentages. Continuous variables (age in weeks, weight in kilograms, affected maximal ureteral diameter in millimeters, and affected renal pelvis size in millimeters) were assessed for normality using both a frequency histogram and Shapiro-Wilk test.

Continence at 1 month following the procedure was defined as achievement of grade 0. Univariate logistic regression was initially performed where continence (yes/no) was the dependent variable. Independent variables included for simple logistic regression were as follows: age (weeks), weight (kg), preprocedure continence grade (0 to 3), previous history of urinary tract infections prior to the procedure (yes/no), positive urine culture at the time of the procedure (yes/no), unilateral or bilateral ectopic ureters (unilateral/bilateral), most severely affected ureter location (0 to 4), PVVR severity (0 to 3), presence of a distinct bladder neck (yes/no), reduced bladder compliance (yes/no), affected maximal ureteral diameter (mm), and affected renal pelvis size (mm). For bilateral ectopic ureters, all analysis was performed using the most severely affected ureter. Therefore, the following were used: the grade for the most severely ectopic ureter, maximal measurement of the most severely dilated ureter, and measurement of the most severely dilated renal pelvis. Factors with a *P* value < .25 from the initial univariate logistic regression were selected for multivariant analysis. Multivariant analysis was performed using a backward stepwise logistic regression using Akaike information criterium to achieve the final best-fit model. The same procedure was repeated for the long-term follow-up urinary continence scores, with a continence grade of 0 again selected as representing treatment success.

Results

Forty-one entire female Golden Retrievers were included with a median age of 12 weeks (range, 10 to 80 weeks, with 38 dogs < 52 weeks old) and a median weight of 13.6 kg (range, 8.7 to 35.3 kg). All dogs had serum urea and creatinine measured either during or prior to referral, and the results for all dogs were within the reference range of the respective laboratory. Urinary continence grade at the time of the procedure **(Table 1)** was grade 0 in 0 (0%) dogs, grade 1 in 2 (4.8%) dogs, grade 2 in 23 (56.1%) dogs, and grade 3 in 16 (39.0%) dogs. Twelve (29.3%) dogs had bilateral ectopic ureters, and 29 (70.7%) had unilateral ecto-

Table 1—Total number of animals with each incontinence grade at each time point.

Incontinence grade	Number pre-CLA (%)	Total cases 1 month post-CLA (%)	Total cases long term post-CLA (%)
0	0 (0%)	19 (46.3%)	26 (63.4%)
1	2 (4.8%)	10 (24.3%)	9 (22.0%)
2	23 (56.1%)	9 (22.0%)	4 (9.8%)
3	16 (39%)	3 (7.3%)	2 (4.9%)

CLA = Cystoscopic-guided laser ablation.

pic ureters, of which 22 (53.6%) were left sided and 7 (17.1%) were right sided. The location of the ectopic ureteral orifice was grade 1 in 2 (4.8%) dogs, grade 2 in 7 (17.1%) dogs, grade 3 in 17 (41.5%) dogs, and grade 4 in 15 (36.6%) dogs. Twenty (48.8%) dogs had a history of urinary tract infections, and 17 (41.5%) dogs had a positive urine culture at the time of the procedure. Eight of the 20 dogs that had a history of urinary tract infections also had a positive urine culture at the time of the procedure. Four dogs were receiving antibiotic medication at the time of presentation for CLA-EU, all of whom were classified as having a history of urinary tract infections, and urine culture results were negative in 3 of these dogs.

A persistent PVVR was identified at cystoscopy in 30 (73.2%) dogs, of which 20 (48.8%) were grade 1, 7 (17.1%) were grade 2, and 3 (7.3%) were grade 3. Six (14.6%) dogs were noted as having no distinct bladder neck at surgery, and 10 (24.4%) dogs had subjectively reduced bladder compliance. Ectopic ureters had a median maximal diameter of 3.3 mm (range, 1 to 15 mm), and the renal pelvis on the side of the ectopic ureter had a median diameter of 4 mm (range, 0.6 to 25 mm).

One month after CLA-EU, urinary continence grades (Table 1) were as follows: grade 0 in 19 (46.3%) dogs, grade 1 in 10 (24.4%) dogs, grade 2 in 9 (22.0%) dogs, and grade 3 in 3 (7.3%) dogs. Difference between pre- and postprocedure urinary continence was 0 grades in 8 dogs (19.5%), –1 grade in 14 (34.1%) dogs, –2 grades in 12 (29.2%) dogs, and –3 grades in 7 (17.1%) dogs. No dogs were receiving any form of medical management for urinary incontinence at this time.

Age at the time of CLA, historical urinary tract infections prior to CLA, positive urine culture at the time of CLA, affected maximal ureteral diameter, presence of a discrete bladder neck, and reduced bladder compliance were carried forward into the initial multivariant analysis for short-term outcome. However, only increased age at the time of CLA (*P* = .100), absence of urinary tract infections prior to CLA (*P* = .018), increased maximal diameter of the affected ureter (*P* = .043), and normal bladder compliance (*P* = .054) were carried through into the final model (*P* = .321; **Table 2**). Although the final best-fit model did not significantly correlate pre-/perioperative factors and short-term urinary continence, 2 factors were individually found to be significant. Presence of urinary tract infections prior to CLA was associated with a decreased chance of achieving urinary continence with an estimated OR of 0.130 (95% CI, 0.020 to 0.621). Increased maximal diameter of the affected ureter was associated with an increased chance of achieving urinary continence with an estimated OR of 34.260 (95% CI, 1.813 to 2,143).

At the time of longer term follow-up (median, 92 weeks; range, 10 to 253 weeks), 12 (29.3%) dogs were receiving phenylpropanolamine, 1 (2.5%) dog was receiving oxybutynin, and 3 (7.3%) dogs had undergone surgical placement of an artificial urethral sphincter (AUS). Four (9.8%) dogs had been humanely euthanized, 3 dogs owing to severe recurrent urinary tract infections and 1 dog due to stranguria thought to be due to stricture formation secondary to AUS placement. Long-term follow-up urinary continence grades (Table 1) were as follows: grade 0 in 26 (63.4%) dogs, grade 1 in 10 (24.3%) dogs, grade 2 in 3 (7.3%) dogs, and grade 3 in 2 (4.9%) dogs. Of the 4 dogs that were euthanized, 2 were the continence grade 3 dogs and the other 2 were 2 of 3 dogs to have had an AUS placed. These latter 2 dogs had urinary continence grades of 1 and 2 prior to euthanasia. The difference from short-term to long-term urinary continence grade was as follows: +1 grade in 1 (2.4%) dog, 0 grades in 29 (70.7%) dogs, –1 grade in 7 (17.1%) dogs, –2 grades in 3 (7.3%) dogs, and –3 grades in 1 (2.4%) dog.

For achievement of long-term continence, the following variables were carried into multivariant analysis: historical urinary tract infections prior to CLA (*P* = .048), presence of a discrete bladder neck (*P* = .125), and reduced bladder compliance (*P* = .057). All were carried through into the final best-fit model (*P* = .765; **Table 3**). The best-fit model was not found

Table 2—Logistic regression best-fit model for short-term urinary continence.

Factor	Coefficient (SE)	Z value	Estimated OR (95% CI)	*P* value
Short-term urinary continence	–1.014 (1.022)	–0.992	—	.321
Age at the time of CLA	0.046 (0.028)	1.647	1.047 (0.996–1.118)	.100
Presence of urinary tract infections prior to CLA	–2.042 (0.861)	–2.370	0.130 (0.020–0.621)	.018*
Most severely affected ureter maximal diameter	3.534 (1.748)	2.022	34.260 (1.813–2143)	.043*
Reduced bladder compliance	–1.915 (0.993)	–1.929	0.147 (0.016–0.889)	.054

— = Not applicable.
*Statistically significant.
See Table 1 for remainder of key.

Table 3—Logistic regression best-fit model for long-term urinary continence final best-fit model.

Factor	Coefficient (SE)	Z value	Estimated OR (95% CI)	*P* value
Long-term continence	0.415 (1.388)	0.299	—	.765
Presence of urinary tract infections prior to CLA	–1.752 (0.886)	–1.997	0.173 (0.023–0.856)	.048*
Presence of a normal bladder neck	1.903 (1.240)	1.536	6.71 (0.750–151.6)	.125
Reduced bladder compliance	–1.915 (1.006)	–1.904	0.147 (0.016–0.963)	.057

See Tables 1 and 2 for key.

to correlate significantly with the chance of achieving urinary continence. However, historical urinary tract infections prior to CLA were found to correlate with a reduced chance of achieving urinary continence with an OR of 0.173 (95% CI, 0.023 to 0.856).

Discussion

In our population, CLA-EU led to an improvement in urinary continence scores for the majority of dogs. However, in the initial short-term follow-up at 4 weeks, full urinary continence was achieved in only 46% of dogs. The rate of urinary continence increased to 63% following initiation of additional medical management (most commonly with phenylpropanolamine) or additional surgical procedures. An improvement in urinary continence grade was demonstrated for 80.5% of dogs at short-term follow-up. These rates of urinary continence and improvement in continence scores following CLA-EU match previous studies and add further evidence to these reported rates.[15–18] This also suggests that Golden Retrievers with iEU have a similar prognosis to other breeds following CLA. However, the 37% of cases that never regained urinary continence and the 9.8% of cases that were humanely euthanized due to urinary-associated complications demonstrate that caution is indicated when discussing prognosis in cases of iEU.

One factor proposed to be involved in dogs that fail to regain urinary continence is the presence of concurrent urethral sphincter mechanism incompetence (USMI). USMI can be both congenital or acquired in dogs,[26] is thought to be the most common cause of acquired urinary incontinence in dogs,[27] and is more common in dogs weighing > 15 kg.[28] Definitive diagnosis of USMI can be made by urethral profile profilometry, but a positive response to α-adrenergic medication can also be suggestive of the condition.[29] A number of dogs in this study regained continence following the introduction of phenylpropanolamine, supporting the involvement of concurrent USMI in ongoing incontinence following CLA-EU. Due to their body weight, Golden Retrievers are thought to be more at risk for USMI than smaller-breed dogs. Therefore, it might be expected that Golden Retrievers would be less likely to regain continence following CLA-EU than smaller-breed dogs. However, as stated above, in our study we found Golden Retrievers to have a similar rate of urinary continence following correction of ectopic ureters to the mixed-breed populations described in other studies.[15–18]

We were unable to accept our hypothesis that normal bladder compliance and the presence of a well-defined bladder neck would be associated with an increased chance of achieving urinary continence following CLA-EU. This finding contrasts with previous suggestions that other structural causes of incontinence in female dogs may represent prognostic factors in dogs undergoing CLA-EU.[9,19,22–24] It is possible, however, that rejection of our hypothesis here represents a type II error associated with the small number of cases with reduced bladder compliance (10 [32.3%]) and poorly defined bladder neck (6 [19.34%]). Moreover, due to the subjective nature of both factors and lack of urodynamic studies performed,[29] these conditions may have been inconsistently identified, thus leading to rejection of our hypothesis. Further studies with larger sample sizes and objective assessment criteria for bladder compliance and the presence of a defined bladder neck are warranted.

Presence of a urinary tract infection has previously been found not to be associated with achieving urinary continence following CLA-EU,[3] and this finding was corroborated in our study. Positive urine culture results at the time of the procedure were associated with neither short- nor long-term continence, but this result may have been impacted by false-negative urine culture results due to antibiotic administration at the time of CLA-EU in 4 dogs. However, when the historical presence of urinary tract infections prior to CLA was assessed, this was significantly associated with a reduced chance of achieving both short- and long-term urinary incontinence. This broader assessment of urinary tract infections may have allowed identification of cases highly predisposed to urinary tract infections and may have specifically identified cases with clinical urinary tract infections rather than incidental bacteriuria at the time of CLA-EU, hence explaining the difference in findings. It is possible that these cases are predisposed to urinary tract infections due to anatomical factors other than purely their ectopic ureters[30] and that these anatomical findings also predispose to ongoing incontinence.

Our study found ureteral dilatation to be associated with short-term but not long-term urinary continence. This distinction may explain, at least in part, why there are contrasting reports in the literature over the association between hydroureters and urinary incontinence following correction of ectopic ureters.[3,25] Moreover, this finding is interesting, as previous reports suggesting ureteral dilatation as a positive prognostic factor all involved surgical correction of ectopic ureters[25] rather than CLA-EU. However, due to large CIs associated with this finding and the lack of ultrasonographic follow-up of cases with ureteral dilatation, it is challenging to place too much weight on this finding and further studies are required to explore this further.

The main limitations of this study were the small number of patients predisposing to type II errors, heterogenous long-term follow-up, and inherent subjectivity in assessing the degree of urinary continence. There was also a bias in that more long-term follow-up was available for cases that had less improvement in urinary continence scores. The single short-term follow-up time point was selected to allow postprocedure urinary continence to be graded prior to the initiation of any adjunctive medication. Further limitations included the lack of follow-up imaging to identify ureteral opening location, lack of urodynamic testing, and subjective nature of grading the presence of a distinct bladder neck and bladder compliance. There were a number of limitations related to the retrospective nature of the study. In-clinic reevaluations were not performed (due to financial limitations), which could have allowed repeated ultrasonographic assessment, cystoscopic assessment, and urine bacteriological testing in dogs that were persistently incontinent. The retrospective nature of the study may have led to errors in the clinical information withdrawn from the medical records, issues with medication history or history of urinary tract infections being incorrectly recorded in the original clinical notes, and failures in recall from owners regarding their dog's urinary continence 1 month after the procedure. Finally, the definition of historical urinary tract infections was taken on the basis of reviewing clinical notes and unfortunately urine culture results were not available for all cases prior to CLA-EU.

In conclusion, we have reported the outcomes following CLA-EU of a homogenous group of female entire Golden Retrievers. This study suggests that Golden Retrievers with ectopic ureters have a similar rate of continence following CLA-EU as reported previously for other populations of dogs undergoing correction of iEU. Moreover, this study demonstrates the challenges in identifying pre- or perioperative factors found to give prognostic information regarding achievement of urinary continence. In this population, the only factors found to be significantly associated with both short- and long-term continence were the absence of historical urinary tract infections (short and long term) and increased dilatation of the most severely affected ectopic ureter (short term only). Due to the retrospective nature of this study and the small number of animals, further prospective studies are warranted to assess the prognostic factors identified.

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