Blücare® Granules: A Novel Tool for the Early Detection and Monitoring of Urinary Tract Disorders in Cats

Recommendations from an Expert Panel

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Abstract

Hematuria is an indicator of a number of diseases in cats, predominantly of the lower urinary tract, including urolithiasis, idiopathic cystitis and urinary tract infection. Early detection of hematuria assists in prompt diagnosis and implementation of appropriate management. The available collection methods for urinalysis are all associated with advantages and drawbacks. A novel testing method, Blücare®, has been shown to be a safe, rapid, and noninvasive testing method for the accurate detection of the presence of hematuria in laboratory studies. This review is intended to raise awareness of the significance of early diagnosis of hematuria, present the scientific evidence behind Blücare® technology, and propose its use as an additional tool for the veterinarian and cat owner.

Introduction

Hematuria refers to the presence of red blood cells (RBC) in urine and is classified as microscopic or macroscopic. Any disorder causing damage to the mucosal surface or vasculature of the urogenital tract allows leakage of RBC into urine. Causes of hematuria include uroliths, inflammation, infection, neoplasia, trauma, vascular disease, and coagulopathies. The most common diagnosis in cats with hematuria is feline idiopathic cystitis (FIC), followed by urethral plug or obstruction, urinary tract infection (UTI), and urolithiasis.[1] When bleeding is observed from another organ system, such as petechiation or ecchymoses, a coagulopathy should be suspected.[2] About 0.5 mL blood per liter of urine (approximately 2500 RBC/µL) is necessary for visual macroscopic (gross) detection of hematuria.

A urinalysis is warranted in any cat with abnormal appearing urine or clinical signs of stranguria, periuria (urination outside the litter box), pollakiuria (increased frequency of urination), polyuria, and/or polydipsia, and may also be part of routine health screening.[3] A diagnostic evaluation of cats with hematuria should always be conducted to localize the site of bleeding and identify the underlying causes.[4,5]

A complete urinalysis provides important information about both urinary and non-urinary tract disorders. A number of collection methods – cystocentesis, catheterization, manual expression, and freely voided – are used and each must be interpreted differently. Patient compliance, risk of trauma to the bladder, and technical expertise of the person collecting the sample are factors that can influence the choice of method. All four have advantages and disadvantages and each can impact the cellular composition of the sample:[3]

- Cystocentesis allows collection of uncontaminated urine and is ideal for urinary cultures. A drawback to cystocentesis is that it is not always easy to perform in defensive patients or when only a small amount of urine is present. Iatrogenic microscopic hematuria might be observed, especially if there is pre-existing bladder inflammation; therefore, cystocentesis is not recommended by this expert panel for routine monitoring in cats with recurrent lower urinary tract signs (LUTS).
- Urethral catheterization is not routinely performed because it requires chemical restraint, unless it is also used as treatment, such as for urethral obstructions. Iatrogenic microscopic hematuria might be observed and urethra trauma may occur.
- Samples may be obtained by manual compression of the bladder but are undesirable due to iatrogenic hematuria and discomfort to the cat, especially if there is pre-existing bladder inflammation.
- "Free catch," or voided, samples are useful; however, collecting an adequate sample is difficult for most owners, it requires readiness and cooperation of the cat, and passage through the urethra may contaminate the urine sample.

Considering the limitations of these collection methods and the need for a noninvasive screening test for feline hematuria, a novel tool could be useful for early detection and monitoring of urinary tract disorders in cats (Table 1). Blücare® granules change colour to detect and monitor hematuria. Blücare® is an auxiliary test that can easily be added to litter boxes to monitor daily voiding in the cat's home. Blücare® can be used safely in clinics, shelters, and any household where a litter box is used. Blücare® is not intended to be a replacement for urinalysis; however, it can help to detect at least one clinical

Table 1: Expert panel recommendations for the screening and monitoring of cats predisposed to hematuria

	Without apparent medical issues		With apparent medical issues			
	Not at-risk population	**At-risk population** (History of crystals, stones, plugs, or previous obstruction, or idiopathic cystitis)	**Diagnosis of Urinary Tract Disease**			**Other – Miscellaneous**
Description	Apparently healthy cats	Cat risk factors • Stress • Overweight • Indoor or sedentary lifestyle • Multi-cat household • Male cats • Eating a non-urinary tract diet • Eating a dry food diet • Dehydration prone/poor drinker	Crystalluria, plug, urolithiasis (upper or lower urinary tract)	Idiopathic cystitis	Upper or lower urinary tract infection	• Post-operative hematuria (due to urinary tract surgery) • Urinary tract neoplasia • Toxins: e.g., anticoagulant, ethylene glycol, aminoglycoside • Coagulation disorder • Nephrolithiasis • Polycystic kidney disease • Renovascular abnormalities • Trauma (blunt force, penetrating wounds, and renal biopsy) • Urinary parasites • Polyps (most commonly at the bladder apex) • Stress
Diet Recommendation	Life stage diet	Life stage or condition-specific diet	Specific diet	Stress-reducing, urinary tract diet[a]	Life stage or specific diet	Normal or specific diet
Frequency of Blücare® usage	1–2 times/year[6]	2-4 times/year	**Acute monitoring:** Use Blücare® to monitor resolution of hematuria during treatment for LUTS. Recommendations for recheck frequency:			In discussion with the veterinarian. Lifelong monitoring may be advised.
			10-14 days	5-7 days	10-14 days	
			Continue monitoring for:			
			2 months AND until clinical signs resolve, then:	2 weeks AND until clinical signs resolve, then:	2 months AND until clinical signs resolve, then:	
			4 times/year (lifelong)	When potentially stressful occasions occur	4 times/year (lifelong)	

[a] A cystitis-prevention diet was found to be effective in reducing the incidence of recurrent episodes; however, it was unclear what components were responsible for the benefit.[6]
LUTS: lower urinary tract signs

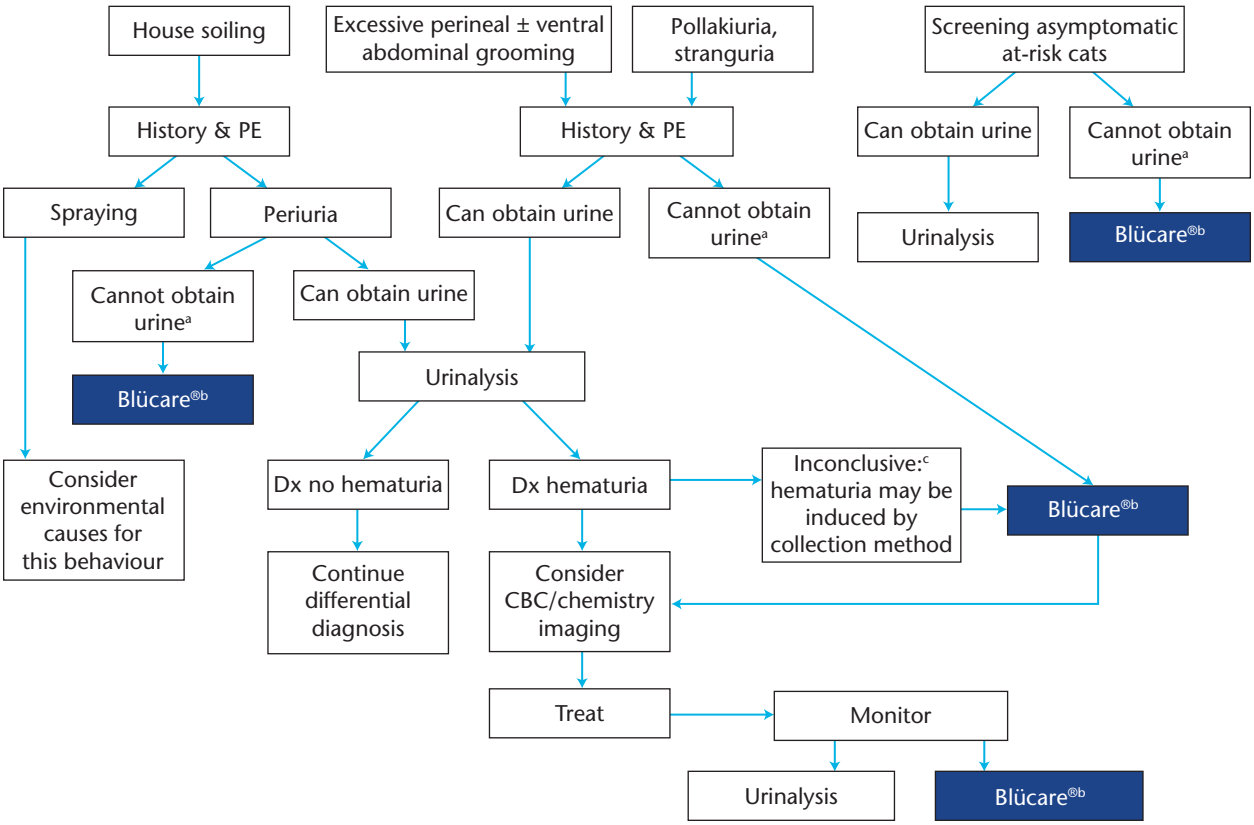
sign and motivate noncompliant owners to seek a complete health check for their cats. The granules are not an endpoint of the diagnostic process, but rather, if they turn blue, the owner will have a clear, visible indication that further complementary examination is indicated. If the granules remain white, owners are instructed to be vigilant for any behavioural change or clinical signs of feline lower urinary tract disorder. Regardless of the presence or absence of a colour change to the Blücare® granules, cats that exhibit clinical signs of a urinary tract disorder should be examined by a veterinarian.

This article and the accompanying algorithm (Figure 1) are intended to guide practitioners through the steps necessary to confirm the presence of hematuria with this new technology and help identify its specific causes.

Feline Urinary Tract Disorders: Etiologies, Pathophysiology, and Clinical Signs

Hematuria is not a clinical sign indicative of a particular disease. While many conditions can result in hematuria, this article will review the main upper and lower urinary tract causes.

Figure 1: Algorithm for the diagnosis and management of cats with clinical signs of low urinary tract disorder



[a] When urine sampling is not an option, for example if the bladder is empty and the owner expresses reluctance to return to the veterinarian's office, or if the owner is not willing to have a complete urinalysis at the time of the consultation.
[b] If a colour change is observed in the Blücare® granules, follow up with the veterinarian is indicated.
[c] Inconclusive is defined as 5-15 RBC/HPF.
CBC, complete blood count; Dx, diagnosis; PE, physical examination

Hematuria, pollakiuria, dysuria, and/or stranguria are common manifestations of lower urinary tract disorders.[7] When signs of systemic disease such as weight loss or fever are present, the source of hematuria is more likely to be the upper urinary tract, and, in some cases, reproductive tract disease.[8]

Causes of chronic LUTS include FIC, urolithiasis, UTI, anatomic, and neurological abnormalities. According to several studies, almost 65% of chronic LUTS result from FIC.[9-13] The 2012 Banfield State of Pet Health Report identified that "cystitis" was diagnosed in approximately 5% of cats older than 3 years of age presented for care of any health problem.[14]

The true prevalence of LUTS might be higher than reported in the literature. For example, LUTS may occur in younger cats and spontaneously resolve without medical intervention.[15]

Feline idiopathic cystitis

Cats with idiopathic cystitis may present with urethral obstruction or with nonobstructive disease. The problem may be acute and self-limiting or chronic in nature. Clinical signs may wax and wane and often follow or are exacerbated by stressful events. Most episodes of acute FIC are self-limiting and of short duration (3–7 days).[16-21] About 50% of cats with acute FIC will have recurrent signs within 1–2 years.[17-21] A small proportion (<15%) of cats will have more frequent recurrences or chronic persistent clinical signs.[20,22]

Cats of any age and sex can be affected, but FIC usually afflicts middle-aged, obese, neutered male cats, that live indoors or with restricted access to the outside, and typically living with other animals.[7,23-25]

Recent studies suggest that FIC is a syndrome that results from complex interactions among the urinary bladder, nervous system, adrenal glands, husbandry practices, environmental conditions, and comorbid disorders.[23] Buffington suggested the term "Pandora Syndrome" to describe cats with an "anxiopathy"; pathology resulting from the effects of chronic anxiety (perception of threat) that can affect any combination of organ systems – including cardiovascular, dermatological, endocrine, gastrointestinal, respiratory, and urinary – as well as the cat's behaviour.[25]

Bladder and neuroendocrine abnormalities are important in the pathophysiology of FIC. Urinary bladder abnormalities have been identified consistently in cats with FIC and have involved alterations in urothelial barrier structure and function, urothelial differentiation and repair, urothelial signaling, eicosanoid biosynthesis, and innate immune and

inflammatory responses.[20,21,27-30] The extent to which urinary bladder changes represent a cause, an effect, or both is not yet understood.[7,28-30]

Alterations in a variety of functions have been identified in cats with FIC.[26] These may provide clues to explain why clinical signs of FIC in cats wax and wane and can be aggravated by stress.[31] However, environment/husbandry and stress alone probably are not enough to cause FIC, which is more likely to occur when susceptible cats are exposed to a "provocative" environment.[18]

Lower and upper tract stone disease (urolithiasis)

Struvite and calcium oxalate (CaOx) are the two most common types of uroliths in cats in many countries and can occur anywhere in the urinary tract. Until 1993, struvite was the most frequent stone type reported in cats; the incidence of CaOx stones subsequently increased. This may be due to dietary modifications (acidification and magnesium restriction) designed to reduce the formation of struvite stones; however, CaOx uroliths increased in dogs without a similar dietary modification.[32,33] In 2010, the proportions of CaOx and struvite stones were similar among cats in many countries. Formation of struvite uroliths is influenced by urine pH, urine concentration, and the concentrations of calculogenic materials. While in dogs, struvite urolith formation may occur as a consequence of UTI with a urease-producing microbe (infection-induced struvite), sterile struvite is the most common form encountered in cats.[34,35] The exact mechanism of CaOx formation is unknown. Cats ranging in age from 7–10 years appear to be more likely to develop CaOx uroliths than younger cats. Male, neutered, long-haired cats (Persian and Himalayan) are also more predisposed.[32,36] In a study of 5,230 uroliths surgically removed from cats and submitted to a diagnostic laboratory in the United States, CaOx stones were found in the bladder (73%), ureter (7%), kidney (4%), and the urethra (13%).[32] Clinical signs of lower urinary tract (LUT) calculi can include any combination of LUTS; however, hematuria alone without concurrent LUTS warrants evaluation for upper urinary tract stones.[37]

Urinary tract infections

UTIs are caused by bacteria through ascending migration of pathogens from the colon, genital tract, and urethra to the bladder, ureters, and kidneys.[38,39] Lower UTIs may be symptomatic or asymptomatic, with the LUTS mentioned earlier.[40] UTI was identified in 18.9% of a German cat population that presented with signs of LUT disease.[41] Pyelonephritis may result in acute (fever, painful kidneys, and/or sepsis) or chronic (progressive azotemia with or without uremia, kidney damage, and kidney failure if untreated) presentation and is normally due to an ascending infection from the urinary bladder. In some cases, the only sign of bacterial pyelonephritis may be hematuria.[42]

Neoplasia

Urinary tumours are rare in cats and account for approximately 1% of all feline tumours. Transitional cell carcinomas are the most frequent type of bladder cancer.[43] Clinical presentation is usually nonspecific but characterized by hematuria, pollakiuria, dysuria and progressive stranguria and, more rarely, lethargy and weight loss.[44,45]

Diagnostic Evaluation

A thorough history and physical examination should be performed in all patients with any abnormal urinary signs or urinalysis findings.[8] Hematuria is a common nonspecific sign for almost every urinary disorder in cats of any age, and the identification of this clinical sign is the first step in a process that may help to localize and determine the diagnosis.

Detecting even macrohematuria is typically difficult for the owner, as it usually requires the identification of discolouration in urine voided on a clear or white surface. A retrospective study of cats with chronic LUTS presented to a German university's small animal clinic reported that microscopically detectable hematuria was present in 91% of 302 recorded cases; however, hematuria was observed by owners in only 42% of the cases.[41]

Cat owners more readily notice behavioural changes in the cat, especially periuria,[46] dysuria, stranguria, and pollakiuria; however, the ability of caregivers to reliably quantify urination behaviours in cats can be compromised by limited direct observation, multiple cats or caregivers, multiple litter boxes, placement of litter boxes in secluded areas, use of covered litter boxes, and secretive or nocturnal voiding habits of some cats. In fact, recent studies have shown that caregivers observed less than one-third of all urinations noted through video recording.[47]

According to a survey conducted on behalf of Groupe Intersand Canada, only 5%–10% of cat owners indicated that they make an appointment immediately upon noticing periuria, and 75% wait for it to become "intolerable."[48] Buffington et al., found that FIC was present in one-half of the cats in whom periuria was the only clinical sign.[49]

Hematuria can be confirmed via urinalysis. In some cases, imaging such as abdominal radiography, ultrasonography, or urethrocystoscopy, and blood tests such as complete blood cell counts and a serum biochemistry panel are necessary to help achieve a diagnosis.[8]

A complete urinalysis includes both a macroscopic and microscopic examination. In addition to determination of the urine specific gravity (USG), the macroscopic examination assesses the physical properties (colour, turbidity, odour, and volume), while the chemical properties of urine (pH, protein, glucose, ketones, bilirubin, urobilinogen, and blood) are assessed through dipstick and pH meter analysis.[3] Blood can only be visually detected when RBC count is greater than ~ 2500 RBC/µL of urine.[50]

The microscopic examination includes evaluation of the urine sediment and urine cytology.[5] Urine sediment examination is especially important for detection and evaluation of red and white blood cells, epithelial cells, crystals, casts, bacteria, yeast cells or hyphae, and parasites.[50] Diagnostic evaluations for microscopic hematuria can lead to

early diagnosis and treatment and supportive care of life-threatening disorders (e.g., neoplasia). Additional evaluations for persistent cases of microhematuria, even in the absence of apparent clinical signs (i.e., subclinical), are still lacking.[2]

Although a urinalysis is an excellent tool for assessing the urinary tract, it can be difficult to obtain a urine sample in cats.

Given the importance of hematuria as a biomarker of common, recurrent, potentially harmful feline illnesses, the development of an efficient, easy-to-use screening test that increases the ability to detect hematuria at home represents a significant benefit for feline patients.

Evaluation of the Blücare® Granules

Blücare® granules work in a similar fashion to a urine dipstick test: a chromogenic enzyme reaction occurs when hemoglobin is detected, turning the white granules blue. A three-phase research project, conducted at the Université de Montréal and approved by their bioethics committee, evaluated the safety and effectiveness of Blücare® granules as a screening test for feline hematuria.[51]

Phases 1 and 2: ex vivo sensitivity and robustness of a novel home-screening test for feline hematuria

Early results of the first phase showed that a prototype of Blücare® granules detected blood in urine at a minimum concentration of 161 RBC/µL of urine (microscopically equivalent to 3-8 RBC/high-power field [HPF] per 1 mL of urine). No relevant safety risks to cats or humans were identified. However, the prototype needed refinements to improve colour stability.

The goals of the two first stages of the study were to determine the lower limit of hematuria detection and colour stability of the final screening product, and to verify its robustness in altered urine composition. The product was initially tested in quadruplicate by pouring 50 µL of pooled feline urine fortified *ex vivo* with feline RBCs. Granule readings were performed at three and 30 minutes, and at 24 and 48 hours after exposure to this fortified urine. The urine samples were centrifuged and subjected to additional blood detection, including dipstick evaluation of the supernatant and microscopy of the sediment.

Next, 12 healthy cats (six male and six female) were randomly assigned in three 4-by-4 Latin squares with distinct treatment sequences (two cats/sex/square), in which they received four lactated Ringer injections by sterile intravenous infusion (10 mL/kg/hour over six hours) containing ammonium chloride (535 mg/L) with and without 7.5% NaCl solution (80:20 volume/volume), and sodium bicarbonate (1620 mg/L) with and without 7.5% NaCl solution (80:20 volume/volume). These solutions caused transient polyuria resulting in changes in USG and pH of the urine. Urine was collected, tested for pH, USG, and protein concentration, and then fortified with RBCs following the protocol from the first experiment.

Colour intensity of the chromogenic reaction was scored visually using an ordinal scale from 0 (none) to 3+ (strong). The investigator consulted a printed visual scale on which each intensity corresponded to a specific colour gradation. The results were statistically analyzed using a generalized linear mixed model for ordinal repeated measures. Fixed factors included urine RBC concentration, specific gravity, pH, protein concentration, sex, and type of fluid administered. Cat-within-sequence was a random factor.

In the first experiment, the lower limit of repeatable colour detection ranged between 100 RBC/µL (with urine at 1.026 g/mL USG) and 851 RBC/µL (at 1.053 g/mL); which corresponds to 15 RBC/HPF and >50 RBC/HPF, respectively. Colour intensity decreased slightly by 30 minutes and remained stable for up to 48 hours. In the second experiment, intravenous fluids affected the USG, pH, and protein concentration. The limit of detection significantly increased with increasing pH (320 RBC/µL at pH ≥ 8.5; P=0.019) and proteinuria (640 RBC/µL at protein ≥15 mg/dL; P=0.0002). Sex and USG had no significant effects on detection (P>0.05). USG was the only between-group variable in the first study; however, the causative effect of parameters other than USG on the detected changes was noted in the second study.

These results show that despite the significant effects of pH and proteinuria, this test still detects microhematuria and shows promise for reliable use in both the clinic and home settings.

Phase 3: reliability assessment of a novel feline hematuria home screening test

It was hypothesized that the metric characteristics of the product are adequate for the clinical monitoring of feline hematuria. The goal of this study was to assess the reliability of the screening test at the veterinary clinic and at home among cats afflicted by a variety of feline health problems.

A multicentre, adaptive clinical trial was conducted, comprising a planned interim statistical analysis to assess and/or revise the experimental plan, using two study arms. In the first arm, six Quebec veterinary clinics tested the product on all sick cats requiring a standardized urinalysis (i.e., centrifugation, dipstick evaluation of supernatant, x400 microscopic analysis of the sediment) as part of their initial urinary tract work-up. In parallel to these tests, two drops of urine were poured on each of four granules and the resulting colour intensity was ranked on an ordinal scale (0, negative; to 3+, dark blue).

In the second study arm, owners of cats at risk of developing hematuria added Blücare® to the cat's litter for one month and brought the cat back to the clinic for urinalysis if a positive colour change was noted. Each participating home was provided with 4 bags (15 g each) of Blücare® granules and 1 bag (12 kg) of clumping litter, and owners were instructed to renew litter and granules weekly. In total, 80 cats were included. For both study arms, hematuria was considered present with a microscopic finding of >5 RBC/HPF (based on interim statistical analysis). The test sensitivity, specificity, and positive and negative predictive values (PPV, NPV) were determined for each level of the colour scale, and response modifiers were assessed with a generalized linear mixed model for ordinal response variables (P=0.05).

Table 2: Examples and expert panel recommendations of clinical situations warranting consideration of Blücare® use

CLINICAL CASES:	
A cat with LUTS (i.e., stranguria, pollakiuria, hematuria, periuria), hematuria on urinalysis, or a diagnosis of uroliths	• During treatment, monitor the cat closely for approximately 2 months. During the first 2 weeks, the colour of the granules should decrease on the colour scale, and should remain white thereafter. If they do not, further veterinary evaluation is warranted. • After treatment, assess the urine regularly with Blücare® (at least 4 times/year); consult with a veterinarian if hematuria is noted.
A cat with recurrent urolithiasis, or a history of urinary tract obstruction	• During treatment, monitor the cat closely for approximately 2 months. During the first 2 weeks, the colour of the granules should decrease on the colour scale, and should remain white thereafter. If they do not, veterinary evaluation is warranted. • After treatment, monitor the cat with Blücare® continuously and for the remainder of its life; consult with a veterinarian if hematuria is noted.
A cat with recurrent FIC and microscopic or gross hematuria	• During treatment, monitor the cat closely for at least 2 weeks. During the first 5 days, the colour of the granules should decrease on the colour scale, and should remain white thereafter. If they do not, veterinary evaluation is warranted. • After treatment, assess the urine regularly with Blücare® when there is concern about the cat's health (e.g., exposure to stressful factors); consult with a veterinarian if hematuria is noted.
To differentiate between behavioural and medical causes of house-soiling[52]	• In the absence of a urinalysis,[a] the use of Blücare® to detect blood in the urine may help to demonstrate to the owner that the soiling includes a medical component. • During environmental and pharmacologic treatment, monitor the cat closely for at least 2 weeks to determine whether hematuria is present. If so, with successful therapy, the colour of the granules should decrease on the colour scale during the first 7-14 days, and should remain white thereafter. If they do not, veterinary evaluation is warranted. • After treatment, assess the urine regularly with Blücare® when there is concern about the cat's health (e.g., exposure to stressful factors); consult with a veterinarian if hematuria is noted.
A cat with a first episode of LUTS and hematuria on urinalysis	• During treatment, monitor the cat closely for approximately 2 months. During the first 2 weeks, the colour of the granules should decrease on the colour scale, and should remain white thereafter. If they do not, veterinary evaluation with urine culture and sensitivity is warranted. • After treatment, assess the urine regularly with Blücare® (at least 4 times/year); consult with a veterinarian if hematuria is noted.
A senior (11-14 years) diabetic cat with a history of recurrent UTI and presence of hematuria during episodes	• During treatment, monitor the cat closely for approximately 2 months. During the first 2 weeks, the colour of the granules should decrease on the colour scale, and should remain white thereafter. If they do not, veterinary evaluation with culture and sensitivity is warranted. • After treatment, monitor the cat with Blücare® lifelong; consult with a veterinarian if hematuria is noted.
CLINICAL SITUATIONS:	
The clinician is unable to collect urine at the clinic	• Blücare® granules can be sent home with the owner to screen for hematuria with or without concurrent urinary signs. • Any clinical signs of urinary tract disease should prompt consultation with a veterinarian regardless of the presence or absence of a colour change with Blücare®.
Annual health screening in cats >8 years and every 6 months in cats >12 years of age[53-55]	• As part of wellness preventive healthcare screening, Blücare® can be used as initial assessment of urinary tract health if urine cannot be obtained.[a]
Inconclusive results due to cystocentesis-induced hematuria	• Colour change in Blücare® granules 3 days after cystocentesis can identify true hematuria as opposed to iatrogenic hematuria.
Monitoring after treatment of any urinary tract disorder with hematuria as the primary presentation	• Blücare® can provide reassurance for clinicians and owners.
Postoperative monitoring further to a bladder, ureteral, or kidney procedure	• Minimum/reasonable immediate postoperative bleeding is normally expected but should decrease/ resolve over time. • Blücare® can be used to monitor/detect further bleeding

[a] When urine sampling is not an option, for example if the bladder is empty and the owner expresses reluctance to return to the veterinarian's office, or if the owner is unwilling to have a complete urinalysis performed at the time.

The final statistical analysis revealed that the number of RBC/HPF, blood estimation from the dipstick, proteinuria, and pH significantly increased the cumulative odds of a positive screening result ($P<0.05$) while increasing proteinuria and pH (i.e., >7.4) slightly decreased the colour intensity of a positive result. For a positive result of 1+ or higher, sensitivity was 91.5%, specificity was 90.9%, and the PPV and NPV were 93.5% and 88.2%, respectively.

Thus, the chromogenic screening product was determined to be a reliable and easy-to-use method to detect feline hematuria. The potentially confounding effect of proteinuria and high (basic) pH should be included in the instructions to users. Further studies are underway to confirm the test reliability on a wider sample of patients and to document the prevalence of hematuria among the North American cat population.

Clinical scenarios and situations in which Blücare® is applicable are presented in Table 2.

Multicat households

Blücare® can be used in households with more than one cat. If one cat is being specifically monitored in a non-emergency situation or if inappropriate elimination or evidence of macrohematuria have been found, the detection of blue granules should prompt the separation of the cats to identify which cat is responsible for the colour change. Blücare® would ideally be added to all litter boxes; however, the owner could choose to add Blücare® to the principal litter box used by the cat suspected of having hematuria.

Conclusion

Blücare® technology offers a new opportunity to improve cat care. This new approach should be beneficial for the pet, the owner, and the veterinarian. When used in the cat's normal environment, Blücare® allows effective and noninvasive detection of the presence of hematuria in cats, encouraging prompt veterinary consultation when necessary.

More rapid assessment allows the veterinarians to improve treatment effectiveness and follow up LUTS. Additionally, this technology has the potential to raise awareness among cat owners of the medical causes of house-soiling behaviour. Veterinarians may feel more confident in their ability to manage their feline patients promptly.

Use of Blücare® may improve the veterinarian-owner relationship, increase the patient's quality of life, avoid development of potentially life-threatening conditions, increase life expectancy, and provide an evaluation method that may prevent the recommendation of often costly therapies that are frequently refused by owners in favour of euthanasia.

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References

1. Forrester SD, Towell TL. Feline idiopathic cystitis. *Vet Clin North Am Small Anim Pract*. 2015;45(4):783-806.
2. Forrester SD. Diagnostic approach to hematuria in dogs and cats. *Vet Clin North Am Small Anim Pract*. 2004;34(4):849-866.
3. Reppas G, Foster SF. Practical urinalysis in the cat: 1: Urine macroscopic examination 'tips and traps'. *J Feline Med Surg*. 2016;18(5):373-385.
4. Lage AL. Diagnostic approach to canine and feline hematuria. *Curr Vet Ther (Small Anim Pract)*. 1989;10:1117-1123.
5. Crow SE. Hematuria: an algorithm for differential diagnosis. *Compend Contin Educ Pract Vet.* 1980;2(12):211-218.
6. Kruger JM, Lulich JP, MacLeay J, Merrills J, Paetau-Robinson I, Brejda J, Osborne CA. A randomized, double-masked, multicenter, clinical trial of two foods for long-term management of acute nonobstructive feline idiopathic cystitis (FIC) *J Am Vet Med Assoc.* 2015; 247(5):508-517.
7. Diez M, Picavet P, Ricci R, et al. Health screening to identify opportunities to improve preventive medicine in cats and dogs. *J Small Anim Pract.* 2015;56(7):463-469.
8. Gunn-Moore DA. Feline lower urinary tract disease. *J Feline Med Surg*. 2003;5(2):133-138.
9. Bowles M. The diagnostic approach to hematuria. *Vet Med.* 2008;103(7).
10. Kruger JM, Osborne CA, Goyal SM, et al. Clinical evaluation of cats with lower urinary tract disease. *J Am Vet Med Assoc*. 1991;199(2):211-216.
11. Osborne CA, Kruger JM, Lulich JP. Feline lower urinary tract disorders: definition of terms and concepts. *Vet Clin North Am Small Anim Pract*. 1996;26(2):169-179.
12. Buffington CA, Chew DJ, Kendall MS, et al. Clinical evaluation of cats with nonobstructive urinary tract diseases. *J Am Vet Med Assoc*. 1997;210(1):46-50.
13. Lekcharoensuk C, Osborne CA, Lulich JP. Epidemiologic study of risk factors for lower urinary tract diseases in cats. *J Am Vet Med Assoc*. 2001;218(9):1429-1435.
14. Gerber B, Boretti FS, Kley S, et al. Evaluation of clinical signs and causes of lower urinary tract disease in European cats. *J Small Anim Pract*. 2005;46(12):571-577.
15. Klausner J. Banfield Pet Hospital State of Pet Health 2012 Report. Banfield Pet Hospital, Portland (OR); 2012.
16. Longstaff L, Gruffydd-Jones TJ, Buffington CT, Casey RA, Murray JK. Owner-reported lower urinary tract signs in a cohort of young cats. *J Feline Med Surg*. 2017;19(6):609-618.
17. Cameron ME, Casey RA, Bradshaw JW, Waran NK, Gunn-Moore DA. A study of environmental and behavioural factors that may be associated with feline idiopathic cystitis. *J Small Anim Pract.* 2004;45(3):144-147.
18. Lund HS, Krontveit RI, Halvorsen I, Eggertsdóttir AV. Evaluation of urinalyses from untreated adult cats with lower urinary tract disease and healthy control cats: predictive abilities and clinical relevance. *J Feline Med Surg*. 2013;15(12):1086-1097.
19. Barsanti JA, Finco DR, Shotts EB, et al. Feline urologic syndrome: further investigation into therapy. *J Am Anim Hosp Assoc* 1982;18:387-390.

20. Defauw PAM, Van de Maele I, Duchateau L, Polis IE, Saunders JH, Daminet S. Risk factors and clinical presentation of cats with feline idiopathic cystitis. *J Feline Med Surg*. 2011;13(12):967-975.
21. Kruger J, Conway T, Kaneene J et al: Randomized controlled trial of the efficacy of short-term amitriptyline administration for treatment of acute-nonobstructive, idiopathic lower urinary tract disease in cats. *J Am Vet Med Assoc* 2003;222(6):749-758.
22. Kruger JM, Osborne CA, Lulich JP: Changing paradigms of feline idiopathic cystitis. *Vet Clin North Am Small Anim Pract* 2009;39(1):15-40.
23. Kruger JM, Lulich JP, MacLeay J, et al. A randomized, double-masked, multicenter, clinical trial of two foods for long-term management of acute nonobstructive feline idiopathic cystitis (FIC). *J Am Vet Med Assoc.* 2015;247(5):508-517.
24. Chew DJ, Buffington CA, Kendall MS, DiBartola SP, Woodworth BE. Amitriptyline treatment for severe recurrent idiopathic cystitis in cats. *J Am Vet Med Assoc*. 1998;213(9):1282-1286.
25. Kim Y, Kim H, Pfeiffer D, Brodbelt D. Epidemiological study of feline idiopathic cystitis in Seoul, South Korea. *J Feline Med Surg.* 2018;20(10):913-921.
26. Buffington CA. Idiopathic cystitis in domestic cats—beyond the lower urinary tract. *J Vet Intern Med.* 2011;25(4):784-796.
27. Parys M, Yuzbasiyan-Gurkan V, Kruger JM. Serum cytokine profiling in cats with acute idiopathic cystitis. *J Vet Intern Med*. 2018;32(1):274-279.
28. Buffington CA, Blaisdell JL, Binns SP Jr, Woodworth BE. Decreased urine glycosaminoglycan excretion in cats with interstitial cystitis. *J Urol*. 1996;155(5):1801-1804.
29. Panchaphanpong J, Asawakarn T, Pusoonthornthum R. Effects of oral administration of N-acetyl-d-glucosamine on plasma and urine concentrations of glycosaminoglycans in cats with idiopathic cystitis. *Am J Vet Res.* 2011;72(6):843-850.
30. Pereira DA, Aguiar JA, Hagiwara MK, Michelacci YM. Changes in cat urinary glycosaminoglycans with age and in feline urologic syndrome. *Biochim Biophys Acta*. 2004;1672(1):1-11.
31. Buffington, CA, Westropp JL, Chew DJ, Bolus RR. Risk factors associated with clinical signs of lower urinary tract disease in indoor-housed cats. *J Am Vet Med Assoc.* 2006;228(5):722-725.
32. Cannon AB, Westropp JL, Ruby AL, Kass PH. Evaluation of trends in urolith composition in cats: 5,230 cases (1985–2004). *J Am Vet Med Assoc.* 2007;231(4):570-576.
33. Palm C, Westropp J. Cats and calcium oxalate strategies of managing lower and upper tract stone disease. 2011 Sep;13(9):651-60. *J Feline Medical Surgery.*
34. Houston DM, Weese HE, Evason MD, et al. A diet with a struvite relative supersaturation less than 1 is effective in dissolving struvite stones in vivo. *Brit J Nutr.* 2011;106:S90-S92.
35. Osborne CA, Lulich JP, Kruger JM, Polzin DJ, Johnston GR, Kroll RA. Medical dissolution of feline struvite urocystoliths. *J Am Vet Med Assoc*. 1990;196(7):1053-1063.
36. Lekcharoensuk C, Lulich JP, Osborne CA, et al. Association between patient-related factors and risk of calcium oxalate and magnesium ammonium phosphate urolithiasis in cats. *J Am Vet Med Assoc.* 2000;217(4):520-525.
37. Palm CA, Westropp JL. Cats and calcium oxalate: strategies for managing lower and upper tract stone disease. *J Feline Med Surg.* 2011;13(9):651-660.
38. Johnson JR, Kaster N, Kuskowski MA, Ling GV. Identification of urovirulence traits in Escherichia coli by comparison of urinary and rectal E. coli isolates from dogs with urinary tract infection. *J Clin Microbiol.* 2003;41(1):337-345.
39. Osborne CA, Caywood DD, Johnston GR, Polzin DJ, Lulich JP, Kruger JM. Perineal urethrostomy versus dietary management in prevention of recurrent lower urinary tract disease. *J Small Anim Pract*. 1991;32(6):296-305.
40. Bartges JW. Diagnosis of urinary tract infections. *Vet Clin North Am Small Anim Pract.* 2004;34(4):923-933.
41. Dorsch R, Remer C, Sauter-Louis C, Hartmann K. Feline lower urinary tract disease in a German cat population. A retrospective analysis of demographic data, causes and clinical signs. *Tierarztl Prax Ausg K Kleintiere Heimtiere.* 2014;42(4):231-239.
42. Olin SJ, Bartges JW. Urinary tract infections: treatment/comparative therapeutics. *Vet Clin North Am Small Anim Pract.* 2015;45(4):721-746.
43. Capasso A, Raiano V, Sontuoso A, Olivero D, Greci V. Fibrosarcoma of the urinary bladder in a cat. *JFMS Open Rep*. 2015;1(1): 2055116915585019.
44. Schwarz PD, Greene RW, Patnaik AK. Urinary bladder tumors in the cat: a review of 27 cases. *J Am Anim Hosp Assoc.* 1985;21:237-245.
45. Beatty JA, Martin P, Kendall K, Malik R. Haematuria in a geriatric cat. *Aust Vet J*. 1999;77(3):160,166-7.
46. Hostutler RA, Chew DJ, DiBartola SP. Recent concepts in feline lower urinary tract disease. *Vet Clin North Am Small Anim Pract.* 2005;35(1):147-170, vii.
47. Dulaney R, Kruger JM, Malinowski R, Hauptman J, Lashbrook B. Quantification of urine elimination behaviors in cats using a video recording system. *J Vet Intern Med.* 2017; 31:486-491.
48. Groupe Intersand Canada. Data on file. 2015.
49. Buffington CA, Chew DJ, Kendall MS, et al. Clinical evaluation of cats with nonobstructive urinary tract diseases. *J Am Vet Med Assoc.* 1997;210(1):46-50.
50. Osborne CA, Stevens JB. Urine sediment: under the microscope. In: *Urinalysis: A Clinical Guide to Compassionate Patient Care.* Leverkusen (Germany): Bayer Corporation; 1999: 125-179.
51. Gara-Boivin C, Khenifar É, del Castillo J. Monitoring feline hematuria at home: assessment of a potential screening test. Presented at the 2016 Annual Meeting of the American College of Veterinary Pathologists. December 3-7, 2016: New Orleans (LA).
52. Carney HC, Sadek TP, Curtis TM, et al; American Association of Feline Practitioners; International Society of Feline Medicine. AAFP and ISFM guidelines for diagnosing and solving house-soiling behavior in cats. *J Feline Med Surg.* 2014;16(7):579-598.
53. Gunn Moore D. Considering older cats. *J Small Anim Pract.* 2006;47(8):430-431.
54. Dowling PM. Geriatric pharmacology. *Vet Clin North Am Small Anim Pract.* 2005;35(3):557-569.
55. Paepe D, Verjans G, Duchateau L, Piron K, Ghys L, Daminet S. Routine health screening: findings in apparently healthy middle-aged and old cats. *J Feline Med Surg*. 2013;15(1):8-19.