



It is not always
black or white

Frequently Asked Questions

Short Answers

1. Is there a perfect linear relationship between proteinuria and the USG helping to predict the UPC outcome? **No**
2. Does negative protein on the dipstick mean that the UPC will always be negative? **No**
3. The protein was high on the dipstick but the UPC came back within normal limits. Why? **Interference**
4. There is bacteria in the sediment. Should I run a UPC? **No**
5. There is blood in the urine. Should I run a UPC? **Maybe**
6. It has been three days since I submitted the urine. Can I add an UPC. **Yes**
7. Is a pooled urine sample always better than a single sample better for monitoring in dogs? **No**



Curious on a couple points? Long answers below - Coffee up!

1. Is there a perfect linear relationship between proteinuria and the USG helping to predict the UPC measurement? No

Several studies have shown in dogs and cats that there is not a perfect predictable linear relationship between the amount of protein measured on the dipstick and the USG. An earlier study in dogs suggested that unless the USG was below 1.012 small amounts of proteinuria were unlikely significant. We now know that is not 100 % true, especially in cats. The pathologist comments you receive on a urinalysis will be based on individual experience and the literature. We each have our own biases as to "grey zones". For myself, both cats and dogs with a USG > 1.030 and .3 g/L (2+) protein can, on odd occasion, have a significant UPC elevation. Rarely this occurs with a USG over 1.040. In the aforementioned study, a negative or .1g/L (1+) protein with a USG over 1.030 has a 97.6% negative predictive value (dogs), thus you can feel pretty confident there is no significant proteinuria.

Practical Points: If you are **substaging renal** disease based on IRIS guidelines a UPC performed on a quiet urine sediment is needed to be complete. Cats with negative protein on the dipstick can have a UPC over .2 which is considered significant and may warrant therapy if persistent depending on the clinical concern. If there is **hypoalbuminemia** you need a UPC to rule out renal losses to be complete.

2. A negative protein on the dipstick can have a significant UPC elevation? **Yes**

This could happen very rarely in dogs with dilute urine (below 1.012) as we saw previously since the negative predictive value is not 100% but about 98%. For trace protein between 1.010 and 1.020 you could see borderline proteinuria (UPC .2-.5) and a few UPCs over .5 based on one recent study.

The **concern primarily refers to cats with concurrent CKD** as that is where we see the most cases of consistent borderline proteinuria (UPC of .2-.4) and overt proteinuria (UPC over .4). As an aside, the vast majority of cats with proteinuria have a UPC below 1.0 because of the association with renal disease and chronic tubulointerstitial fibrosis rather than a primary glomerular disease. A UPC over 1.0 is considered severe in a cat. **So what exactly are the stats in cats? How often does this happen?** Possibly 19-24% of the time based on two preliminary studies, (JSAP & Animals). The results were surprising in the latter study given the number of proteinuric cats (UPC >.4) with a negative dipstick (see table below). There were some flaws in both studies but they support the need to substage based on UPC when possible to be complete. Anecdotally we have on occasion seen a UPC over .2 when the dipstick is negative.

Table 2. Association among dipstick results, USG, and distribution of UPCr in 150 urinalysis.

USG	Dipstick Results		
	0	1+	2+ to 4+
<1.012	0 NP/4 P	0 NP/0 P	0 NP/0 P
1.012–1.034	35 NP/27 P	11 NP/10 P	5 NP/12 P
>1.035	13 NP/5 P	11 NP/1 P	8 NP/8 P

NP—Non proteinuric (including borderline cases) according to UPCr; P—Proteinuric according to UPCr.



3. The protein was high on the dipstick but the UPCR came back within normal limits. Why? **Interference**

False positive reactions are possible in highly alkaline urine or when the urine is left for an extensive amount of time on the contact pad. Similarly if the urine was collected off the kennel floor or table and had been in contact with quaternary ammonium compounds and chlorhexidine.

False negative reactions ? Do they happen? Presumably dilute urine or acidic urine contributes to false negative protein reactions on the urine dipstick. Additionally multiple myeloma and associated Bence-Jones proteinuria is associated with false negative urine protein. A dog or cat with a high index of suspicion for multiple myeloma may have negative or only trace protein on the dipstick as it is less sensitive to free light chains of immunoglobulins.

4. There is bacteria in the sediment. Should I run a UPC? **No**

Generally it is not advised to run a UPC on a sediment with bacteria as it can potentially increase the UPC. Bacteria may contribute to an elevated UPC but not always. In a recent study urine samples with 100,000 colony forming units had UPC range of .1 to over 10. About 50% of the dogs had a UPC below .5 and 50% had a UPC above .5.

An abnormal UPC when performed on a sample with bacteria should always be rechecked once the bacteriuria/infection is resolved.



5. There is blood in the urine. Should I run a UPC? **Maybe**

This has been studied better in dogs than cats. It is expected that there will be a somewhat proportional increase in the UPC as the degree of blood contamination increases. Grossly visible blood to any degree is expected to potentially increase the UPC. **Do not run a UPC on slightly pink to red urine.**

Our observations are similar to those of Cornell where they note "Traumatic microscopic hematuria associated with cystocentesis does not usually result in proteinuria (personal observations, Vaden et al 2004) or a UPC >0.5 (based on spiking canine urine with peripheral blood [Vaden et al 2004, Jillings et al 2019]), although there are reports of UPC >0.5 in dogs and >0.4 in cats in dark yellow spiked urine (Vientós-Plotts et al 2017)." This latter study was somewhat difficult to extrapolate into clinical practice given its design.

In a subset of cats with CKD, they may have persistent presumed mild renal hematuria. In such cases, it may be very difficult to obtain a sample that does not have microscopic hematuria assuming all other causes have been ruled out and/or addressed. My personal soft rule for running a UPC is a pale to yellow/clear urine with 2+ or less blood on the dipstick. If there is unavoidably higher amounts of blood and you are trying to determine if there is target organ damage, one may decide to look at individual UPC trends together with blood pressure and a fundic examination. A normal UPC would still be valuable information in those cases with higher than desired blood on the dipstick.



6. It has been three days since I submitted the urine.

Can I add an UPC. **Yes**

A very recent study in cats notes that: "Urine storage at room temperature for 1 day or in the refrigerator for up to 7 days does not clinically affect UPC." How long after submission can a UPC be added on? It is generally advised to run a UPC within three days after submission. This rule of thumb allows for culture results to be obtained and a UPC added if the culture is negative. Up to 5 to 7 days is the maximum amount of time (based on canine & feline studies) that one should consider adding on a UPC knowing that there could be some differences in a subset of patients. In this situation you still may be able to confirm significant proteinuria but you may not be able to rule out significant proteinuria based on normal results in a sample between 4-7 days old. Similarly if the result is between borderline and proteinuric it should be rechecked.



7. Is a pooled urine sample always better than a single sample better for monitoring in dogs? **No.**

Measuring a UPC on a single urine sample, averaging UPCs from 3 consecutive daily urine samples, and pooling 3 consecutive daily urine samples to measure a single UPC all give similar results. There is no strong evidence that any individual method for monitoring the UPC is superior.

Points to consider.

1. When monitoring dogs, it was recommended that the UPC must change by 80% at lower UPC (near 0.5) and by at least 35% at higher UPC (near 12) to be considered clinically relevant. Generally we average this to 50%.
2. Note, based on updated IRIS guidelines for managing proteinuria, the goal is a 50% reduction from baseline if an otherwise lower UPC cannot be achieved safely.
3. Why the evidence was not strong: “In dogs with $UPC \leq 4$, 95% of cases may have a single UPC between 0.38 below and 0.76 above the average UPC result. In dogs with $UPC > 4$, 95% of cases may have a single UPC between 0.40 below and 2.2 above the average UPC result.” The differences would not be considered clinically relevant.

Do UPCs differ between at home or within hospital? Yes this is possible!

They could be higher in hospital for dogs & cats. The authors note for proteinuric dogs, to consider a single, pooled or averaged sample/s obtained at home rather than a sample obtained in the hospital setting. For cats, the authors note home sampling of urine is a valid alternative to cystocentesis in cats but clinically relevant differences in UPC and USG were present in 28% and 18% of cats, respectively. It is advised to use the same collection method for monitoring each cat.



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