

INVESTIGATION OF POLYURIA (PU) AND POLYDIPSIA (PD)

PD in adult horses can be defined as water consumption >100 ml/kg daily (>10% BWT) although under UK management and environmental conditions it is probable when intake is > 70 ml/kg daily (>7% BWT). Typical water intake for horses is 40 - 60 ml/kg daily (4-6% BWT) although it can be as low as 10-15 ml/kg daily (1-1½% BWT) in grazing horses or as high as 80-90 ml/kg daily (8-9% BWT) in lactating mares, horses in hard work and in hot environmental conditions. Smaller breeds tend to drink relatively more per kg BWT than larger breeds due to the effects of metabolic body size.

Physiological Causes of PD:

- Hot weather
- Hard work
- Lactation

PU is usually defined as urine production > 50 ml/kg daily (5% BWT) though in practice it is unlikely to be quantified. Normal urine production is typically between 15 and 30 ml/kg daily (1½ - 3% BWT) and faeces represent the major route of water loss in normal horses.

Physiological Causes of PU & PD:

- Excessive dietary protein
- Excessive salt consumption
- Administration of glucocorticoids or diuretics

Pathophysiological Causes of PU & PD:

- PSYCHOGENIC POLYDIPSIA
- PPID (Cushing's Disease)
- Chronic Renal Failure (CRF)
- Hepatic Insufficiency
- Diabetes Mellitus (DM)
- Diabetes Insipidus (DI)

1. QUANTIFY AND CONFIRM THE PRESENCE OF PD (AND PU?)

Pathophysiologic causes will invariably lead to both PU and PD even though only one and not the other may be recognised and reported by the owner. Therefore it is both easier and diagnostically acceptable to verify and quantify water intake only. Quantification of urine production can be achieved but is less practical. Quantification of water intake should be performed over a full 24 hour period with the horse stabled.

- If water intake is >100 ml/kg/day (>10% BWT) then PD is confirmed and PU is almost inevitable.
- If water intake is <70 ml/kg/day (<7% BWT) then PD is not confirmed.
- If water intake is 70-100 ml/kg/day (7-10% BWT) then PD may be suspected if there are no apparent physiologic causes (see above).

2. INITIAL BLOOD AND URINE TESTS

- i. Anaemia is a common finding with CRF due to effects of uraemia and reduced erythropoietin synthesis. Polycythaemia may arise through dehydration suggesting that PU is the primary problem rather than PD (e.g. DI).
- ii. Neutrophilia may indicate a glucocorticoid response or inflammatory disease.
- iii. Usually urea >15 mmol/L and creatinine >300 mmol/L are seen in CRF cases. More modest increases (eg urea 8-12 mmol/L, creatinine 180-250 mmol/L) more commonly indicate dehydration or acute kidney injury but could also suggest early/mild CRF. Low urea (< 4 mmol/L) and creatinine (<75 mmol/L) may occur in hepatic insufficiency or in cases of primary (psychogenic) polydipsia with washout.
- iv. Persistent hyperglycaemia is occasionally seen in PPID cases.
- v. Hypercalcaemia (total Ca > 3.5 mmol/L, ionised Ca > 1.7 mmol/L) is often seen in CRF. The major differential for hypercalcaemia is paraneoplastic disease
- vi. GGT and AST can be used to rule-out liver disease.

Urinalysis

- SG <1.008 (hyposthenuria) suggests that the kidney is actively excreting water and is typical of primary (psychogenic) PD and DI.
- SG 1.008-1.014 (isosthenuria) suggests that the kidney is neither actively concentrating nor diluting the filtrate and is consistent with (but not diagnostic for) CRF. Although isosthenuria is typical of CRF, other causes of PU/PD might coincidentally happen to fall in the isosthenuric range. Therefore, when isosthenuric samples are obtained, serum urea and creatinine should be checked to rule-in or rule-out possible CRF.
- SG >1.014 (hypersthenuria) indicates that the kidney is actively concentrating urine and CRF is not present.
- Glycosuria indicates diabetes mellitus which is usually caused by PPID although primary DM is a rare possibility. Acute stress and alpha-2 agonists can also cause hyperglycaemia and glycosuria.
- Urine creatinine: serum creatinine ratio is useful in cases with equivocal mild increases in serum creatinine concentration (e.g. 180-250 mmol/L). Mild to moderate increases in serum creatinine due to dehydration will be expected to be matched by high urine creatinine concentrations (>50 x serum concentration) whereas CRF cases will have lower urine creatinine (e.g. <40 x serum creatinine).

3. FURTHER LABORATORY TESTS

On the basis of the above results it should be possible to confirm/rule-out many differential diagnoses including CRF, diabetes mellitus and liver disease. PPID may be apparent from clinical signs or diagnosed by resting ACTH concentration or a TRH stimulation test (see separate notes on endocrinopathies).

The most useful tests to differentiate primary (psychogenic) polydipsia from diabetes insipidus are the water deprivation test, modified water deprivation test, serum ADH concentration and the ADH response test.

Water Deprivation Test

The purpose of this test is to help differentiate primary (psychogenic) polydipsia from diabetes insipidus in subjects found to be producing hyposthenuric urine (urine SG<1.008). This test must not be performed on azotaemic horses suspected to have renal compromise. The object of the test is to establish whether or not the horse can produce concentrated urine (psychogenic polydipsia cases can; diabetes insipidus cases cannot).

Performing a Water Deprivation Test
• Weigh horse (if possible) or make an informed estimate (weigh tape etc)
• Check serum urea and creatinine are normal (if not, don't proceed)
• Take baseline urine sample and measure SG (if > 1.008, don't proceed)
• Keep horse stabled and remove water
• Check serum urea and creatinine and urinary SG at least every 6 hours (and reweigh if possible)
The test is terminated when one of the following occurs:
• 24 hours water deprivation
• 5% reduction in bodyweight
• clinical signs of dehydration
• azotaemia develops
• urinary SG > 1.020

Interpretation

- If SG rises above 1.020 this confirms renal concentrating ability is present and therefore rules-out diabetes insipidus. This indicates psychogenic polydipsia.
- If urine SG stays <1.020 and the horse becomes dehydrated or loses 5% bodyweight this suggests diabetes insipidus (often happens by 12 hours) or 'medullary washout' – perform a modified water deprivation test.
- If urine SG is still low after 24 hours but horse shows no clinical signs of marked dehydration this implies psychogenic polydipsia associated with 'medullary washout', although could be diabetes insipidus - perform a modified water deprivation test.

Modified Water Deprivation Test

This test is used to differentiate equivocal cases of diabetes insipidus from psychogenic polydipsia as described above. However, most DI cases will become rapidly dehydrated within 12 hours of initial water deprivation and therefore this test is really used to confirm the suspected diagnosis of psychogenic polydipsia with medullary washout that has prevented urinary concentration within 24 hours of water deprivation in the standard initial water deprivation test. However, the test can justifiably be used instead of the initial water deprivation test as it may be easier and possibly safer to perform. The test is performed instead of a standard water deprivation test or started immediately following standard water deprivation test (above) if:

- urine SG < 1.020 after 24 hours water deprivation
- < 5% reduction in bodyweight
- no azotaemia
- no clinical signs of dehydration

Performing a Modified Water Deprivation Test	
•	Allow water consumption equivalent to 40 ml/kg BWT daily (4% BWT) offered in several aliquots through the day to avoid immediate consumption of the total daily ration
•	Continue for up to 2-3 days or until one of the criteria above is reached
•	Measure serum urea and creatinine and urinary SG at least every 6 hours

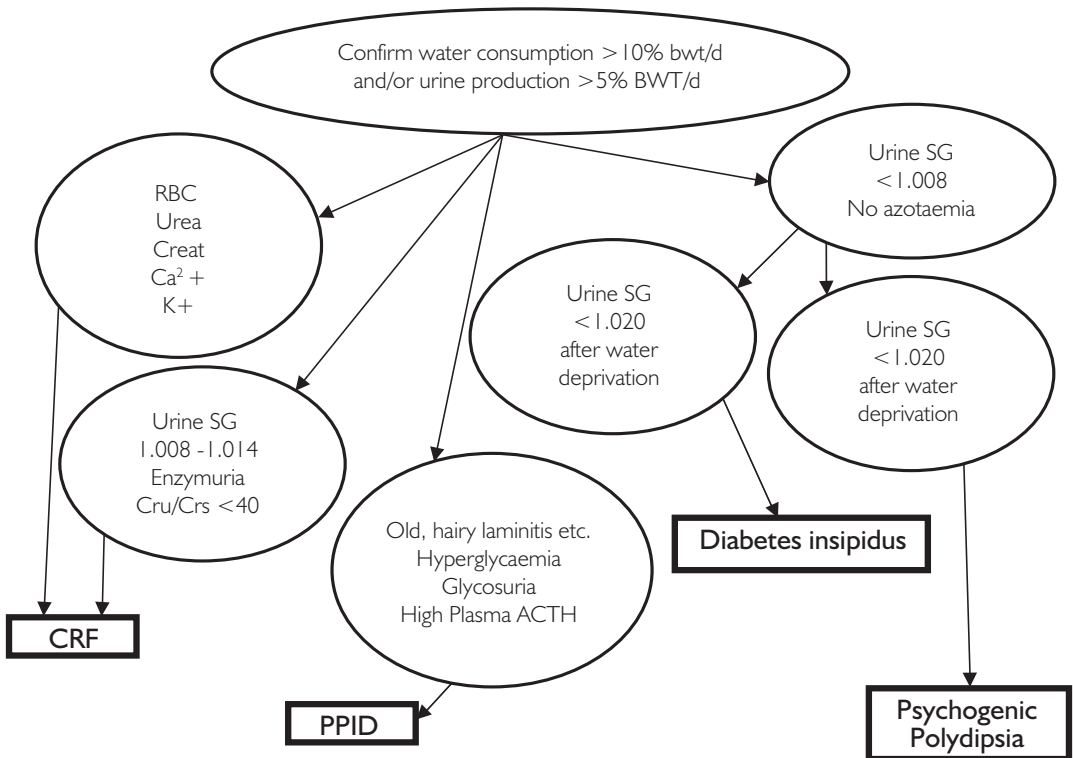
- If urine SG rises above 1.020 this confirms primary (psychogenic) polydipsia.
- Progressive dehydration and continued inability to concentrate urine implies diabetes insipidus.

Serum ADH (vasopressin) concentrations

In normal hydrated horses ADH concentration is reported to be between 1 and 2 pg/mL. In response to 24 hours water deprivation a modest increase to typically between 4 - 8 pg/mL is expected but can be much higher. Low resting ADH concentrations and failure of an increase in response to water deprivation imply central diabetes insipidus. Both primary (psychogenic) polydipsia and nephrogenic diabetes insipidus cases would be expected to have normal ADH concentration and response.

The ADH (vasopressin) response test

This test is indicated when diabetes insipidus is suspected and used to differentiate central from renal forms. Central diabetes insipidus cases will successfully concentrate urine following exogenous ADH administration whereas nephrogenic diabetes insipidus cases shown little to no response to ADH administration.



URINALYSIS

When catheterised urine samples are obtained, consideration of the effects of sedation is important. Alpha-2 agonists have both acute diuretic and hyperglycaemic effects. The diuretic effect is unlikely to alter the properties of the subsequently collected urine sample as a few mLs of most recently produced diuresed urine should not significantly affect the previously accumulated urine in the bladder. However, even a small amount of glycosuria might confuse diagnostic interpretation. Hence acepromazine (5-10 mg/100kg iv) perhaps supplemented by a nose twitch or a small dose of detomidine (0.5 mg/100 kg iv) should be used as necessary in geldings. In mares the use of stocks or a stable door may avoid the need for sedation.

- **Specific gravity**

- **SG <1.008 (hyposthenuria)** suggests that the kidney is actively excreting water and is typical of primary (psychogenic) polydipsia or diabetes insipidus.
- **SG between 1.008-1.014 (isosthenuria)** suggests that the kidney is neither actively concentrating nor diluting the filtrate and is consistent with (but not diagnostic for) CRF. Although isosthenuria is typical of CRF, other causes of PU/PD might coincidentally happen to fall in the isosthenuric range. Therefore, when isosthenuric samples are obtained, serum urea and creatinine should be checked to rule in or rule out possible CRF.
- **SG >1.014 (hypersthenuria)** indicates that the kidney is actively concentrating urine although SG >1.020 is usually regarded as more convincing of good concentrating ability (and therefore absence of CRF).
- **Glycosuria** – if persistent then this indicates diabetes mellitus and usually PPID although primary diabetes mellitus is a rare possibility.
- **Urine creatinine : serum creatinine ratio** is useful in cases with equivocal mild increases in serum creatinine concentration (eg 180-250 mmol/L). Mild to moderate increases in serum creatinine due to dehydration will be expected to be matched by high urine creatinine concentrations (>50 x serum concentration) whereas CRF cases will have lower urine creatinine (eg <40 x serum creatinine).
- **Enzymuria** – urinary GGT, AP and LDH may all be raised in renal failure due to tubular damage (more so in acute renal failure). Urinary GGT is the most commonly assayed urinary enzyme and is usually similar in concentration to serum levels (i.e. <40 iu/L urine). Clearly adjustments should be made for urine concentration and this is done by comparison with urine creatinine concentration (expressed in mmol/L, not μ mol/L):

$$\frac{\text{URINARY GGT (iu/L)}}{\text{URINARY CREATININE (mmol/L)}} < 5.0 \text{ iu/mmol in normal horses}$$

URINARY FRACTIONAL ELECTROLYTE EXCRETION RATES

“CREATININE CLEARANCE RATIOS”

Electrolyte excretion rates require simultaneously collected serum and urine samples. It is vital that serum is separated from the cellular fraction promptly (within hours) as leakage of potassium and phosphate from dying cells will significantly alter serum electrolyte concentrations. For this test it is assumed (slightly incorrectly!) that the sole route of serum creatinine loss is the urine and that it is neither secreted nor absorbed by the kidney. Thus each electrolyte is compared with a substance (creatinine) that is nominally neither secreted nor absorbed to give an impression of the renal handling of each electrolyte. Hence clearance (CL) of a substance, “E” from the plasma is related to its serum (S) and urine (U) concentration, thus:

$$CL_A \times SA = \text{urine output} \times UA \quad \text{or} \quad CL_A = \frac{\text{urine output} \times UA}{SA}$$

Hence, the clearance of any substance (e.g. an electrolyte, “E”) can be compared to creatinine as a fractional excretion rate (or creatinine clearance ratio) thus:

$$\begin{aligned} \text{Fractional electrolyte excretion rate} &= \frac{\text{urine output} \times UE}{SE} \div \frac{\text{urine output} \times UCR}{SCR} \\ &= \frac{UE \times SCR}{UCR \times SE} \end{aligned}$$

A value of 1 (or 100%) suggests similar handling to creatinine – i.e. neither secreted nor absorbed. Values <1 (or <100%) signify active reabsorption of the electrolyte whereas values >1 (or >100%) signify active excretion. Typical normal values comprise:

Na	0.03 – 0.5%	(i.e. 99.5 - 99.97% filtered Na is reabsorbed)
K	15 - 70%	(i.e. 30 - 85% filtered K is reabsorbed)
Cl	0.2 – 1.7%	(i.e. 99.8 - 98.3% filtered Cl is reabsorbed)
Ca	< 7%	(i.e.>93% filtered Ca is reabsorbed)
PO4	<0.5%	(i.e.>99.5% filtered PO4 is reabsorbed)
Mg	< 15%	(i.e.>85% filtered Mg is reabsorbed)

In the context of PU/PD, high values (signifying decreased reabsorption) are consistent with renal tubular failure (especially Na and Cl) although excessive electrolyte consumption should also be considered.