Polyuria – Polydypsia in Psittacine Birds

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Introduction

A common presentation in clinical avian practice is polyuria (PU) and/or polydypsia (PD) in psittacine birds. Accurate diagnosis and successful treatment of this problem is often a challenge to the clinician. This paper outlines osmoregulation in birds, discusses differential diagnoses of PU/PD, presents a diagnostic approach, and discusses diagnostic tests.

Osmoregulation

Plasma osmolality in birds, like mammals, is usually 300 mOsm. This is controlled by fluid intake and urinary output. These in turn are controlled by complex interactions between plasma osmolality and volume, osmoreceptors and baroreceptors, the kidney, the hypothalamus, and the pituitary gland.

Fluid intake (thirst) is stimulated by:

a) hyperosmolality of the ECF (due to dehydration or i/v infusion of hypertonic solutions;
b) pain;
c) increased body temperature;
d) hypotension;
e) certain drugs.[2]

Avian kidneys are not as efficient as mammalian in concentrating urine. Unlike mammals, birds have two nephron types: cortical or reptilian nephrons (lacking a Loop of Henle), and medullary or mammalian nephrons (with a Loop of Henle). Cortical nephrons are urecotelic; medullary nephrons produce urine. The more medullary nephrons a bird has, the more efficient it is at conserving water. On average, the medulla comprises 10% of the avian kidney. The urine: plasma osmolar ratio in most birds can only reach 2.0 – 2.5, compared to 25 - 30 in mammals.

Birds will excrete 1% of filtered water, compared to mammals excreting less than 0.1%. This is believed to be, in part, due to the need for water to transport the more viscous uric acid through renal tubules. [12]

Urine production is controlled by arginine vasotocin (AVT), the avian equivalent of anti-diuretic hormone (ADH). Increased plasma osmolality stimulates the hypothalamus to produce AVT. This in turn constricts afferent arterioles of the reptilian nephrons (reducing glomerular filtration rate) and increasing the permeability of the collecting ducts of the mammalian nephrons. The end result is decreased urine production and therefore decreased plasma osmolarity. [10]

Water resorption also occurs in the rectum during retrograde flushing from the cloaca.[1, 9, 12]. According to Lumeij [9], 15% of urine water can be resorbed in this manner, but this is reduced by polyuria and stress-induced defecation. If the urine is too concentrated, a concentration gradient across the rectal mucosa cannot be achieved and so resorption would be limited. But, as urine osmolality increases, birds

are able to gradually increase plasma osmolality, thus preserving the U/P osmolar ratio and allowing water resorption. [1] Birds with functional salt glands can decrease plasma osmolality by excreting salt, but this is not applicable to psittacine birds.

Effective osmoregulation therefore requires:

a) normal plasma osmolalarity;
b) sufficient functional nephrons;
c) normal production of, and response to, AVT; and
d) efficient cloacal water resorption.

If any of these factors are compromised, polyuria can result.

Defining PU/PD as a problem

Polydypsia, defined by Charles [2] as water intake in excess of double the daily maintenance requirements, indicates water intake greater than 100mls/kg/day.

Birds, because of the often high water content of their diet, may normally produce urine in the order of 100 – 200mls/kg/day. Quantifying polyuria would require accurate comparison of urine output with a healthy bird of the same species on the same diet. Subjective assesment of polyuria is usually the norm, and is done by visual examination of the bird's droppings.

PU and PD usually occur concurrently, but owners may not be aware of one or both and often confuse polyuria with diarrhoea. Additionally, PD can occur normally without PU, eg on hot days, or after a lot of flying and PU can be seen without PD where water intake through other sources is high (eg high intake of greens, fruit or nectar mixes, parenteral fluids).

In most cases of PU/PD, however, the polydypsia is secondary to a primary polyuria.

Primary Polydypsia

Psychogenic polydypsia. This is a relatively rare condition, often associated with juvenile hand-reared cockatoos. Stress, excitement and fear may also be contributing factors.

Hepatic disease. Mild hepatoencephalopathy and altered function of portal osmoreceptors can cause polydypsia in mammals [2], and may have a similar effect in birds. Hepatoencephalopathy, due to increased ammonia, has not been proven to occur in birds at this time.

Secondary Nutritional Hyperparathyroidism, due to calcium utilization exceeding its intake, with subsequent stimulation of the parathyroid gland, may have an effect on the thirst centre in the brain, causing polydypsia.[2]

Primary Polyuria

1. Renal.

Renal dysfunction undoubtedly accounts for the majority of cases of PU/PD in birds, as it does in mammals. Causes of renal dysfunction[5] include:

a.   **Inflammatory conditions.**

   i) <u>Infectious</u>

   - viral – adenovirus, circovirus, coronavirus, herpesvirus, orthomyxovirus, polyomavirus, paramyxovirus, poxvirus, retrovirus
   - bacterial – most bacteria, including mycobacteria
   - chlamydial
   - parasitic – coccidia, cryptosporidia, microsporidia, toxoplasma, trichomonas
   - fungal – aspergillus

   ii) <u>non-infectious</u>

   - egg yolk peritonitis
   - visceral gout
   - amyloidosis

i.   **Non-inflammatory conditions**

   - Toxic – acetone, aflotoxin, allopurinol, aminoglycosides, cadmium, ethylene glycol, , hypernatraemia, glycine, lead, oxalic acid, selenium, zinc
   - Nutritional – hypercalcaemia, hypervitaminosis D3, hypovitaminosis A.
   - Metabolic – DIC, haemachromatosis, haemoglobin deposits, lipidosis, nephrogenic diabetes insipidus
   - Genetic / congenital – renal cysts, agenesis, hypoplasia
   - Acquired – dehydration, hypovolaemia
   - Degenerative – renal mineralization, tubular nephrosis
   - Physical – obstipation due to egg-binding, cloacoliths, uroliths
   - Trauma – general trauma, or renal trauma during endoscopy
   - Immune-mediated – membranous glomerulonephropathy
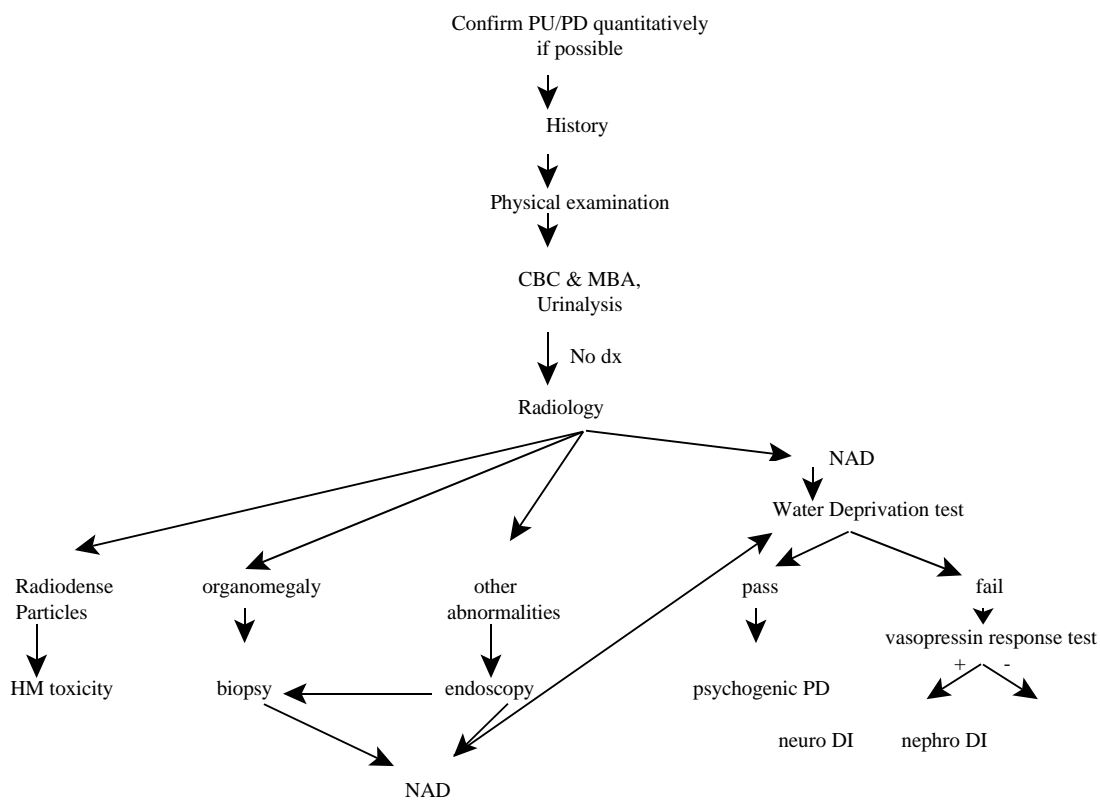
c.   **Neoplasia**

   - Carcinomas
   - Adenocarcinomas
   - Round cell tumours
   - Sarcomas
   - Embryonal nephromas

2. Extra-renal

Conditions arising from outside the kidney, but causing polyuria, include:

i) **liver disease**

ii) **pancreatitis**

iii) **gastrointestinal disease**

iv) **septicaemia**

v) **pituitary or pineal gland neoplasia** is reported as a cause of PU / PD, especially in budgerigars

vi) **diabetes mellitus** is frequently reported in psittacine birds, particularly budgerigars and cockatiels. Unlike mammals, it appears to be due to a glucagon excess, rather than insulin deficiency.

vii) **neurogenic diabetes insipidus,** responsive to ADH administration, has been reported in a budgerigar. (MacWhirter, pers com)

viii) **Hyperadrenocorticism**, due to adrenal neoplasia, has been reported as a cause of PU / PD [3]

ix) **renal phosphate flush** seen in low calcium, high phosphorous diets [15]

DIAGNOSTIC APPROACH

Confirm PU/PD quantitatively
if possible

↓

History

↓

Physical examination

↓

CBC & MBA,
Urinalysis

↓ No dx

Radiology

Radiodense Particles → HM toxicity

organomegaly → biopsy

other abnormalities → endoscopy

NAD → Water Deprivation test

pass → psychogenic PD

fail → vasopressin response test

+ → neuro DI   - → nephro DI

biopsy ← endoscopy

→ NAD

DIAGNOSTIC TESTING

Determination of the cause of PU / PD utilises a range of diagnostic tests, most of which are readily available to veterinarians. These tests include:

1. urinalysis
2. biochemistries
3. imaging
4. water deprivation tests
5. renal biopsy

1. Urinalysis

a. *Physical appearance*

Fresh droppings from a non-stressed bird should be examined visually. Birds that are frightened, stressed or excited are often polyuric due to limited cloacal water re-absorption. These droppings should be ignored. The following warrant closer examination:

i)   persistent polyuria – especially where polydypsia is also evident;

ii)   biliverdinuria – fresh urine that is stained green (as distinct from older droppings where biliverdin has leached from the faeces into the urate / urine) can indicate liver disease.

iii)   haematuria / haemaglobinuria – pink-red urine indicates severe renal damage, and is often considered, in Amazon parrots at least, to be pathognemonic for lead poisoning.

d. *Urine Specific Gravity*

Urine should be collected from a non-absorptive surface and centrifuged. The USG of the supernatant can then be measured with a refractometer. In polyuric birds the USG has been reported as ranging from 1.005 to 1.020. [8] The main value of USG therefore lies in cases with a persistently low USG, and those that fail to increase with water deprivation.

e. *Dipstick evaluation*

The same supernatant collected for USG determination can be used for dipstick evaluation of the urine. Parameters of particular importance include:

i)   pH – normally 6.0 – 7.5. Lower readings in psittacine birds indicates acidosis. Higher values can indicate bacterial metabolism. Care must be taken to ensure that the colour of the urine does not influence the colour readings on the dipstick

ii)   protein – normally only trace amounts are recorded. Higher levels can indicate faecal contamination, renal disease, haemoglobinuria, haematuria, hyperproteinaemia, or sepsis

iii)   glucose – normally zero amounts registered. Glucosuria indicates faecal contamination, diabetes mellitus or renal damage. Glucosuria without hyperglycaemia is, in the author's experience, gives a guarded to poor prognosis.

iv)   Ketones – ketonuria indicates severe catabolism or complicated diabetes mellitus. It is also indicates a poor prognosis.

v)   Blood – haematuria / haemaglobinuria can indicate faecal contamination or severe renal disease, and warrants a sediment exam.

f. *Sediment examination*

Urine sediment should be examined under the microscope, at first unstained, and then stained with methylene blue. The following can be observed:

      i)   desquamated epithelial cells from the cloaca;

      ii)   leucocytes and erythrocytes are rare in normal urine. More than 2 – 3 per high power field should be considered abnormal;

      iii)   casts (granular or cellular) can be seen with renal disease. Haemoglobin casts may account for positive haemoglobin readings seen on dipsticks, and where no erythrocytes are seen;

      iv)   small numbers of gram positive bacteria can originate from the faeces. Large numbers of bacteria should be considered abnormal. Comparison with a faecal gram stain may help to determine origin.

      v)   Uric acid crystals (small & spherical) are normal. Other crystals are occasionally seen, but their significance is unclear. [8]

6. Biochemistries

The biochemistries below are the ones most commonly utilised to assess renal function. Other biochemistries are discussed in most avian texts.

a. *Uric acid*

Uric acid is produced in the liver as the end product of protein metabolism. It is both secreted and filtered by the kidney, forming a non-soluble precipitate. Most of the excretion is through secretion by the kidney, and therefore blood levels of UA are unaffected by the glomerular filtration rate. In conditions of increased plasma osmolality then, the excretion of UA remains unaffected so long as the renal tubules are functional. UA levels will start to rise when there is severe dehydration or significant renal damage. Persistent hyperuricaemia (> 590 – 830 umol/L) after dehydration has been corrected is indicative of renal disease. [5] Clinicians need to be aware however that UA does not rise until there is significant renal damage – normal UA levels do not equate with normal kidneys. [15]

b. *Urea*

Birds only produce small amounts of urea which is then filtered by the kidneys. Reabsorption only occurs with dehydration, and so urea may be useful in determining the hydration status of the patient. [15]

c. *Amylase*

Many birds with renal disease will also have hyperamylasaemia (> 1,000 IU/L). This may be due to concurrent pancreatic disease or decreased renal clearance of amylase. (Speer, pers com)

d. *Phosphorous*

Hyperphosphataemia (> 2 mmol/L), associated with decreased renal excretion due to renal disease, is not commonly noted in birds.

e.   *Glucose*

Birds normally maintain a higher plasma glucose level than mammals (~16.6 mmol/L). Persistent levels over 30 - 50 mmol/L are indicative of diabetes mellitus.

6.   Imaging

Diagnostic imaging currently involves radiology (plain & contrast), ultrasonography and endoscopy.

a.   *Radiology*

Plain view radiographs allow visualization of the size and density of the kidneys. [13] In a lateral view, with both acetabula on the same plane, the normal kidneys lie in the sacral area and do not extend ventrally past the ventral rim of the acetabula. Enlarged kidneys can often be seen below these limits. Radiodense mineralised kidneys can often be seen. Mineralisation is not an indication of chronicity, as it can begin within days of the original insult (Speer, pers com).

Contrast radiology of the kidneys is a field still in its infancy, but holds great promise.

b.   *Ultrasonography*

The normal avian kidney cannot be visualised with ultrasonography, but nephromegaly (eg cysts, neoplasia, infection) can be detected on a ventromedial approach.

c.   *Endoscopy*

The avian kidney is readily visible on endoscopy, but the information gained is usually minimal. Renal gout, mineralisation or physical anomalies can be visualised, but is often of little diagnostic value. Endoscopy does, however, provide for renal biopsy.

4.   Water Deprivation test

Once other possible causes of PU / PD have been eliminated, a water deprivation test can be used to differentiate between psychogenic PD and diabetes insipidus. The rationale behind a WDT is that a bird with the ability to osmoregulate will concentrate urine in response to increased plasma osmolality, due in turn to water deprivation.[2]

A gradual WDT is preferred to an abrupt WDT to overcome the problem of renal medullary washout and cloacal concentration gradients. Water is gradually restricted by 10% per day over 3 – 5 days, and then deprived completely. This process gives the kidneys and the cloaca every chance to respond to gradually increasing plasma osmolality. Close monitoring is mandatory, as severe dehydration can result if the patient is unable to concentrate urine. Plasma proteins, PCV and weight should be monitored closely.

The test should stop when the patient loses 5% – 7% of its bodyweight, or is able to concentrate its urine.

Failure to concentrate urine in the absence of other possible causes indicates diabetes insipidus. A vasopressin response test can then be performed to distinguish between neurogenic and nephrogenic DI. MacWhirter (pers com) recently reported a case of neurogenic DI where a PU / PD budgerigar, unable to concentrate its urine on a WDT, responded to desmopressin acetate (an ADH analogue) within 15 minutes of administration by dramatically reducing the amount of urine produced. This effect

lasted for 3 hours. It should be noted that this bird had a 10% weight loss within 4 hours of being deprived of water.

5. Biopsy

Renal biopsy has been proposed as the single most important tool in the accurate diagnosis of renal disease (Speer, pers com). The kidney can be approached endoscopically [16], via a laparotomy, or via a dorsal approach through the sacrum.[18] The middle or caudal divisions should be biopsied, so as to avoid the cranial renal artery. [15] Haemorrhage is minimal, and the resultant histology (and if appropriate, culture) allows an accurate diagnosis, a more meaningful prognosis, and a more concise treatment plan.

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