Urolithiasis

Cusack, P.M.V.
Australian Livestock Production Services

Aetiology and Pathogenesis: Urolithiasis is very rare in cattle on pasture, but feedlot cattle and lambs are prone to form uroliths and develop urethral obstruction because:

- ⇒ Steers and wethers have a narrow urethra (early castration).
- ⇒ Grain concentrates have a high P content (the most common urolith to form on a high grain diet is struvite ($MgNH_4PO_4$) followed by calcium oxalate and calcium carbonate ($CaCO_3$).
- ⇒ High grain/low roughage diets result in reduced salivation → less P is lost via saliva in faeces and is therefore excreted in the urine.
- ⇒ High concentrate diets produce high concentrations of low molecular weight peptides in the urine which have a strong salt binding potential.

It is important to recognise that there is more to the occurrence of urolithiasis than elevated dietary intake of macrominerals such as P and Mg. There are generally no toxicities from macrominerals per se, with problems arising from negative interactions with other minerals.

Phosphorus (P): There is no known P toxicity *per se* (Ensminger, 1990), however, excess dietary phosphorus can decrease calcium (Ca) absorption. Also, when the dietary P concentration is high relative to Ca, urinary calculi can be formed, especially in ruminants (Ensminger, 1990). Dietary P concentration should not be more than 6 g/kg DM (Jones and Meisner, 2009).

Calcium (Ca): Blood calcium concentration is normally controlled by small intestinal absorption which represents an interaction between dihydroxy-vitamin D3, P and Ca intake. Similar to P, there is no known Ca toxicity *per se*, with the dietary Ca concentration relating primarily to the required Ca:P ratio. Whilst the target of approximately 2:1 is ideal, Ensminger (1990) notes that very broad ratios up to 7:1 are satisfactory for ruminants.

Magnesium (Mg): Spontaneous toxicities for Mg have not been reported (Ensminger, 1990), but excess Mg can interfere with Ca and P metabolism. The NRC (National Research Council, 1985) recommends a maximum dietary Mg concentration of 5 g/kg DM, whilst Jones and Meisner (2009) recommend a maximum Mg concentration of 6 g/kg for the prevention of struvite calculi formation.

If elevated concentrations of macrominerals alone contributed to an increased incidence of urolithiasis, we could expect to see a chronically elevated incidence on grazing lucerne in addition to a range of widely used commercial products (Table 1).

Table 1. Dietary concentrations of macrominerals in commercially available lamb finishing pellets and grazing lucerne.

Product	Concentration (g/kg dry matter)		
	Calcium	Phosphorus	Magnesium
Grazing Lucerne – early vegetative (NSW DPI)	16	4	2.6
Weston Milling Farmyard Finisher Nuts	17 minimum	5 minimum	3.5 minimum
Coprice Sheep Pellets	15 minimum	7.5 minimum	Not quoted
Riverina Lamb Feedlot Pellets	10 minimum	4 minimum	Not quoted
Riverlea Slingshot Lamb Finisher Pellets	11.6	4.2	2.1
Milne EasyOne Pellets	11.5	3.3	2.1

Note that the macromineral concentrations in the commercial pellets manufactured by Weston, Coprice and Riverina are minima, and it can therefore be assumed that the concentrations will frequently be higher than the concentrations in Table 1. The commercially available pellets listed in Table 1 are fed to hundreds of thousands of lambs throughout Australia without reports of problems with urolithiasis (based on outgoing tonnages, approximately 40 000 lambs per annum for Riverina Stockfeeds alone).

Other potential predisposing factors are:

- ⇒ Restricted water intake (urolithiasis is more commonly a problem during winter)
- ⇒ Alkaline water with high mineral concentration (particularly Mg)
- ⇒ The use of feed additives such as $NaHCO_3$ and $CaCO_3$ at high inclusion rates
- ⇒ High dietary inclusion of sorghum which has higher concentrations of the low molecular weight peptides that form the organic matrix to which urinary salts adhere
- ⇒ Vitamin A deficiency due to increased shedding of bladder endothelium.

The short feeding duration of lambs, with most programmes turning lambs off within 6 weeks, likely eliminate most problems due to forming uroliths. The incidence of urolithiasis has been high in lambs fed for prolonged periods due to feedlot placement at low BW and low BCS.

The sequence of events in struvite urolith formation is as follows:

1. Peptides, proteins and mucoproteins aggregate to form an organic matrix.

2. The matrix binds both anions and cations. Mg^{2+} cations and complex $NH_4PO_4^{2-}$ anions are bound (**low dietary Ca increases P absorption**).
3. Crystals form that grow into calculi. These struvite calculi are highly insoluble in alkaline urine.

It has been suggested that negative DCAD could be used to prevent urolithiasis. However, a low or negative DCAD can increase the incidence of calcium oxalate calculi. It is prudent to respond to the occurrence of urinary calculi by acidifying the urine by the addition of dietary ammonium chloride (European Food Safety Authority, 2012; Jones and Meisner, 2009; Jones and Streeter, 2009; Wahlberg and Greiner, 2006). The contribution of chloride ions from ammonium chloride is a potent contributor to a low dietary cation-anion difference (DCAD), where the simplified equation most commonly used (Oetzel, 1998) is

([Na] + [K]) – ([Cl] + [S])

This equation does not include calcium because the research done on the promotion of Ca mobilisation by dairy cows immediately post-partum showed that the incidence of hypocalcaemia could be elevated at both low and high dietary intakes of Ca during the immediate pre-partum period (Oetzel, 1998). Therefore, the effectiveness of the acidaemia induced by the low/negative DCAD occurred independently of the dietary concentration of Ca. This is particularly important in the use of ammonium chloride in response to the occurrence of urinary calculi because the target is acidification of the urine without inducing a sustained acidaemia which mobilises the collagen constituents hydroxyproline and glycine (Holmes et al., 2007; Simsek et al., 2004) concomitantly with the mobilisation of calcium from the skeleton. Circulating hydroxyproline and glycine are then metabolised to oxalate which leads to increased urine concentration of oxalate (Knight et al., 2006), thereby predisposing the animal to the formation of calcium oxalate calculi. Hydroxyproline is a major contributor to endogenous oxalate (Holmes et al., 2007). It is therefore inappropriate to routinely feed elevated dietary concentrations of anionic salts, such as calcium chloride or ammonium chloride, because of their contribution to endogenous oxalate production which can increase the incidence of calcium oxalate calculi. Further, the palatable Ca source, limestone, (calcium carbonate), cannot be replaced by calcium chloride due to the poor palatablity of calcium chloride (Oetzel, 1998), in addition to the capacity for calcium chloride to increase the incidence of calcium oxalate calculi. The importance of endogenous oxalate is greater in ruminants with generous dietary inclusions of Ca and Mg, because both of these bind oxalate in the digestive tract, forming an insoluble, indigestible complex thereby reducing the availability of dietary oxalate to the animal (Leibman and Costa, 2000; Leibman and Chai, 1997; Seawright, 1982).
The target with the strategic inclusion of ammonium chloride to respond to urinary calculi in small ruminants is to achieve acidification of the urine with a compensated acidaemia (Swenson, 1984) to avoid skeletal calcium mobilisation. This effect has been established with a dietary ammonium chloride inclusion of approximately 0.5% to 1%, resulting in a urine pH of 6.0 to 6.5 (Jones et al., 2009).

Clinical Signs: The signs of abdominal discomfort are profound and occur in response to severe stretching of the bladder wall in the hours prior to rupture. The clinical signs include:

- × Possibly crystals on the preputial hairs
- × Twitching of the prepuce may occur at urination

- Signs of abdominal discomfort
    - ⇨ kicking at belly
    - ⇨ increased respiratory rate
    - ⇨ stretching out
    - ⇨ treading with the hind feet
    - ⇨ bruxism (teeth grinding)
    - ⇨ grunting
    - ⇨ and occasionally sternal or lateral recumbency

- Urine may be blood tinged
- Bladder rupture results in rapid development of “water belly” and uraemia, distal urethral rupture results in preputial swelling and necrosis.

Treatment: Surgery, in the form of a perineal urethrostomy, is only economical with high valued cattle such as long-fed Wagyu. Once urolithiasis is diagnosed, it is more cost effective to monitor the affected pens/mobs very closely for early cases for immediate delivery to slaughter while preventative measures are implemented. Cases for slaughter must be idenfied very early, prior to the development of uraemia.

Management and Prevention: The immediate response is to acidify the urine, with the dietary inclusion of 1% NH_4Cl, and to increase water intake with the inclusion of 1% salt. NH_4SO_4 is a cheaper alternative to NH_4Cl, but the sulphate it supplies can induce polioencephalomalacia and therefore I have not used it. Acidification of the urine will dissolve struvite and $CaCO_3$ calculi, but not calcium oxalate calculi, so it is useful to send calculi from post-mortems for laboratory analysis. Based on monitoring of urine pH, it takes approximately one week for urine pH to drop significantly after the inclusion of NH_4Cl.

The single most important factor in the prevention of urolithiasis is the Ca:P ratio. It should always be maintained between 1.5:1 and 2:1.

Don’t forget to address the inclusion rates of $NaHCO_3$ and $CaCO_3$ if these are elevated.

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