Hematuria and Pigmenturia in the Horse

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Hematuria and Pigmenturia

- Hematuria: Blood in the urine
- Pigmenturia: Presence of a component that gives an abnormal color to urine
- Color of urine → associated with excretion of urochrome
  - Product of the degradation of hemoglobin

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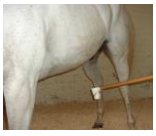
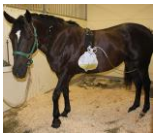
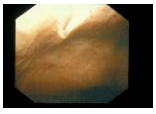
Urine collection

- Free catch
- Catheterization
- Endoscopy
  - Ureter







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Hematuria

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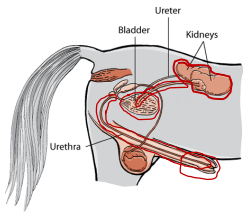
Hematuria

Origin of blood

a) Kidney
b) Bladder
c) Ureter
d) Urethra
e) Reproductive tract



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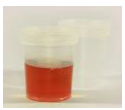
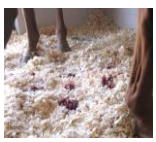
Hematuria

- Macroscopic or microscopic
- Severe cases → voiding of blood clots



History

- Drugs administered
- Type of pasture
- Geographical location
- Recent exercise, abnormal gait



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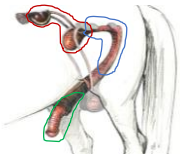
Hematuria

- **Timing of micturition**
  - Beginning to end → renal, ureteral or bladder
  - End → proximal urethra or bladder neck
  - Beginning → distal urethra



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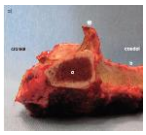
Exercise-induced hematuria

- First void after exercise

a) Cystoliths
b) Bladder trauma against pelvic rim (Concussion)
c) Osteochondroma of the *os pubis*



Hematuria caused by osteochondroma of the os pubis. EVE 24:30-37, 2012

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Urolithiasis

- More often in males
- Hematuria after exercise
- Near the end of urination
- Pollakiuria
- Dysuria
- Dribbling urine
- Prolonged periods of penile protrusion
- Blood-stained pelvic limbs

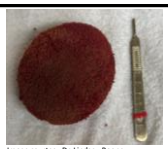

Image courtesy Dr. Lindsey Boone

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Urolithiasis

Nephroliths and ureteroliths

- Partial or complete obstruction
  - If bilateral → chronic renal failure
- Mild recurrent colic
- Microscopic hematuria

Saetra, T., et al. (2018). Equine Vet Educ, 30: 635-639.

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Urolithiasis

Diagnosis

- Rectal palpation
- Ultrasound
- Cystoscopy
- Type 1- yellow to green, spiculated, friable (mainly $CaCO_3$)
  - 90% cases
- Type 2- Smooth, hard and white ($CaCO_3$+phosphate+Mg)

Image courtesy Dr. Lindsey Boone

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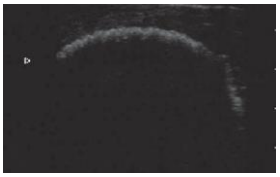
Urolithiasis



Cystolith

Nephrolith

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Cystoscopy

Video courtesy Dr. Erin Groover

Image courtesy Dr. Lindsey Boone

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Urolithiasis - treatment

- Surgical/manual removal
- Laser and shock wave
- Recurrence
  - 46.6%
    - Fragments acting as a nidus remained
    - Undetected calculi
    - Propensity toward stone formation (Ca crystal aggregation)

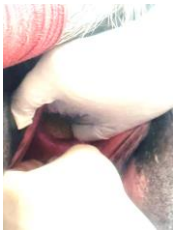

Image courtesy Dr. Lindsey Boone

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Urolithiasis - treatment

- No studies to prove that urine acidification prevents formation
  - Below pH 6.5 calcium carbonate uroliths do not form
  - Prevented new calculi formation in a single case of a horse with recurrent cystic calculi

ment was achieved by feeding a 0.2% calcium oat hay ration and administering 175 mg ammonium sulfate per kg body weight orally twice daily for 7 months which produced a urine pH of 5.0. There was no evidence of metabolic acid/base

Remillard et al. 1984

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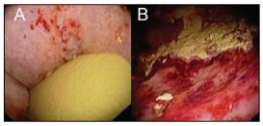
Sabulous cystitis

- Secondary to ventral accumulation of urine sediment
- Associated with bladder dysfunction
- Urinary incontinence
  - Most common presenting complain
- Treatment
  - Bladder lavage
  - Antimicrobials
  - Anti-inflammatories
  - Bethanechol
  - Phenazopyridine



Zakia et al. 2022. JVIM

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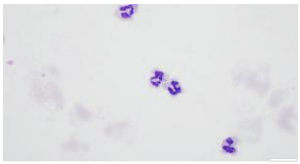
Urinary tract infection and pyelonephritis

- Primary (rare)
- Secondary
  - Paresis or paralysis of the bladder
  - Urocystoliths
- Urinalysis
  - ↑ WBCs
  - Intracellular bacteria
  - Quantitative urine culture (>10,000 CFU/mL)



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Urinary tract infection and pyelonephritis

- Lower urinary tract → Bladder, urethra
  - Multiparous mares
  - Chronic atonic bladders
- Upper urinary tract → kidneys, ureters
  - Pyelonephritis → renal pelvis and parenchyma
    - Associated with nephroliths or ureteroliths
    - Microscopic or macroscopic hematuria
    - Unilateral or bilateral renal hemorrhage

Linton, 2022

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Clinical case

- 12 YO AQH gelding
- Acute hematuria of 3-day duration
- Lethargic 2 weeks prior
- HR 48 bpm, RR 16 brpm, T 100.2F
- Hematuria (frank blood) in the mid-late stream

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Clinical case

RBC	6.37		x 10^6/uL
HGB	10.9		g/dL
HCT	30.9	L	%
MCV	48.4		fL
MCH	17.1		pg
MCHC	35.4		g/dL
RDW	18.9		%
PLATELET COUNT	48	L	x 10^3/uL
MPV	7.6		fL
WBC	10.43		x 10^3/uL

Test	Diff %	Result		Units
SEG	(82%)	8.553	H	x 10^3/uL
BANDS	(0%)	0.000		x 10^3/uL
LYMPH	(13%)	1.356	L	x 10^3/uL
MONO	(3%)	0.313		/uL
EOS	(0%)	0.000		x 10^3/uL
NRBC		0		/100 WBC
PLT EST	BELOW REFERENCE INTERVAL			
Plasma T/S	7.7 g/dL			
Fibrinogen T/S		200		mg/dl

RBC MORPHOLOGY
FEW ECHINOCYTES, MODERATE ROULEAUX

PLATELET MORPHOLOGY
38-50(x10^3/uL)= PLATELET EST

CREATININE	3.4	H	mg/dL	0.0 - 2.0
CALCIUM	12.8		mg/dL	10.5 - 12.9
MAGNESIUM	1.6	L	mg/dL	1.7 - 2.1
BICARBONATE	28.1		mmol/L	21.0 - 30.0
SODIUM	132	L	mmol/L	134 - 150
POTASSIUM	4.3		mmol/L	3.5 - 4.5
CHLORIDE	93	L	mmol/L	97 - 111
ANION GAP	15.2			9.0 - 25.0

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Clinical case

- Diagnosis based on ultrasonographic findings
  - ↑ renal echogenicity
  - Abnormal outline
  - ↓ corticomedullary distinction
  - Debris in the renal pelvis
  - Dilated renal pelvis (pyelectasia)
  - Renal biopsy?

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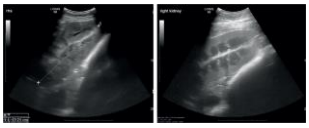
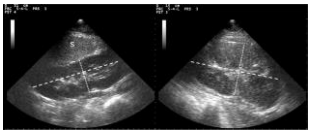


Jocelyn N. Kidney disease in the horse. *Equine Health*. 2020;2020:20-23.



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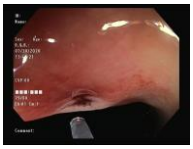
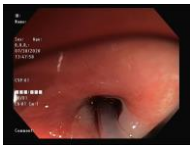
Haboshon-Butcher, J., Bowen, M. and Hallowell, G. (2014), VALIDATION OF A NOVEL TRANSLUMBAR ULTRASOUND TECHNIQUE FOR MEASURING RENAL DIMENSIONS IN HORSES. Journal of Equine Ultrasound, 55: 323-330.

Clinical case





- Unilateral kidney hemorrhage
- Collection of samples for urinalysis, bacterial culture, leptospirosis

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Clinical case

Urine Volume	50.0 ML
Urine Source	VOIDED(FREE-CATCH)
Urine Color	BROWN
Urine Turbidity	CLOUDY
Specific Gravity	1.021
Urine pH	8.5
Urine Protein	97.7 mg/dL
Urine Glucose	NEGATIVE
Urine Ketone	NEGATIVE
Urine Blood	3+
Urine Bilirubin	1+

URINE SEDIMENT EXAM
0-3/hpf WBC, TOO NUMEROUS TO COUNT RBC

CRYSTAL EXAM
MANY CALCIUM CARBONATE CRYSTALS

- IV fluid therapy
- Enrofloxacin IV

- Bacterial culture – No bacterial growth
- Idiopathic renal hematuria?

- <u>Necropsy</u>
  - Bilateral chronic interstitial nephritis and pyelonephritis

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Treatment

- Antibiotic based on culture and sensitivity
- Use an antibiotic eliminated in urine
  - Penicillin (unchanged)
  - Aminoglycosides (unchanged) (nephrotoxic)
  - TMS (mostly—some through the liver)

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Neoplasia

- Clinical signs similar to those of horses with cystic calculi
- Rectal palpation
  - Mass in bladder
  - Enlarged kidney
- Ultrasound
- Cystoscopy
- Urinalysis and cytology
- Nephrectomy → search for metastasis first

Wise et al. 2009. JVIM

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Verminous nephritis

- Halocephalobus gingivalis
  - 1. Brain (mimics EPM)
  - 2. Spinal cord
  - 3. kidney
- Renal granulomas
- Diagnosis
  - Renal ultrasound
  - Nematode in urine sediment
- Treatment
  - Larvicidal antihelmintic
  - No successful medical treatment reported
  - Nephrectomy

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Clinical case

- 13 YO AQH gelding
- Intermittent hematuria of 1 month duration, fever
- Evaluated few weeks prior → unknown origin of hematuria

Physical exam

- HR 74 bpm, RR 20 brpm, T 104.4F
- CRT 3.5 s
- Yellow/cloudy urine with blood at end of urination
- Sabulous material on hind limbs

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Clinical case

- Abdominal ultrasound → Normal kidneys, slightly hypomotile SI
- Rectal → enlarged bladder, normal left kidney
- Abdominocentesis → pale yellow, clear
- Normal coagulation profile
- Urinalysis by catheterization
- CBC and chem

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Clinical case

RBC	7.62	x 10^6/uL	6.00 - 12.00
HGB	13.8	g/dL	10.0 - 18.0
HCT	37.0	%	32.0 - 48.0
MCV	48.5	fL	34.0 - 58.0
MCH	18.1	pg	14.0 - 19.0
MCHC	37.4 H	g/dL	31.0 - 37.0
RDW	18.0	%	17.0 - 20.0
PLATELET COUNT	106	x 10^3/uL	100 - 230
MPV	6.4	fL	5.8 - 11.5
WBC	14.38 H	x 10^3/uL	6.00 - 12.00
Test	Diff % Result	Units	Ref Interval
SEG	(79%) 11.360 H	x 10^3/uL	3.000 - 6.000
BANDS	(3%) 0.431 H	x 10^3/uL	0.000 - 0.100
LYMPH	(16%) 2.301	x 10^3/uL	1.500 - 5.000
MONO	(2%) 0.288	nL	0.000 - 0.600
EOS	(0%) 0.000	x 10^3/uL	0.000 - 0.600
BASO	(0%) 0.000	x 10^3/uL	0.000 - 0.100
OTHER	(0%) 0.000	x 10^3/uL	0.000 - 0.000
NRBC	0	/100 WBC	No Ref Interval
PLT EST	WITHIN REFERENCE INTERVAL		
Plasma T/S	7.2 g/dL		
Fibrinogen T/S	300	mg/dl	100 - 400
RBC MORPHOLOGY			
SLIGHT ROULEAUX			

TOTAL PROTEIN	6.53	g/dL	6.00 - 8.60
ALBUMIN	2.95	g/dL	2.70 - 4.10
GLOBULIN	3.58	g/dL	2.80 - 4.40
ALBUMIN/GLOBULIN RATIO	0.82		0.70 - 1.00
SDH	7.3	U/L	0.5 - 10.0
AST	328	U/L	144 - 350
GGT	17	U/L	2 - 29
TOTAL BILIRUBIN	4.46 H	mg/dL	0.70 - 3.60
CK2	340	U/L	103 - 402
BUN	12.9	mg/dL	9.0 - 24.0
CREATININE	1.1	mg/dL	0.0 - 2.0
CALCIUM	10.3 L	mg/dL	10.5 - 12.9
PHOSPHORUS	1.9 L	mg/dL	2.1 - 4.6
MAGNESIUM	1.2 L	mg/dL	1.7 - 2.1
GLUCOSE	120	mg/dL	81 - 127
BICARBONATE	22.9	mmol/L	21.0 - 30.0
SODIUM	139	mmol/L	134 - 150
POTASSIUM	3.0 L	mmol/L	3.5 - 4.5
CHLORIDE	104	mmol/L	97 - 111
ANION GAP	15.1		9.0 - 25.0
OSMOL(CALC)	275	mOsm/kg	276 - 288
S.IRON	31 L	ug/dL	129 - 173
UIBC	320	ug/dL	123 - 430
TIBC	351	ug/dL	243 - 553

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Clinical case

Urine Volume	23.0 ML
Urine Source	CATHETERIZED
Urine Color	YELLOW
Urine Turbidity	CLEAR
Specific Gravity	1.022
→ Urine pH	>= 9.0
Urine Protein	29.8 mg/dL
Urine Glucose	NEGATIVE
Urine Ketone	NEGATIVE
Urine Blood	NEGATIVE
Urine Bilirubin	NEGATIVE

URINE SEDIMENT EXAM

MANY BACTERIA, 1-5/hpf WBC

CRYSTAL EXAM

→ MANY CALCIUM CARBONATE CRYSTALS

Smear Result: GRAM STAIN - MANY GRAM POSITIVE COCCI IN CHAINS

Culture Description: HEAVY GROWTH

Organism

→ Organism: GROUP D NON-ENTEROCOCCUS

Antibiotic susceptibility Pattern

	GROUP D NON-ENTEROCOCCUS		
	Interpretation	MIC	Test
AMIKACIN	R	>=	
AZITHROMYCIN	R	>=	
CEFAZOLIN	R	>=	
CEFPODOXIME	S	<=	
CEFTIOFUR	S	<=	
CHLORAMPHENICOL	S	<=	
CLARITHROMYCIN	R	>=	
ENROFLOXACIN	S	<=	
GENTAMICIN	S	<=	
PENICILLIN	R	>=	
RIFAMPIN	R	>=	
TETRACYCLINE	S	<=	
→ TRIMETHOPRIM/SULFA	S	<=	

- Treatment with TMS 25 mg/kg q12h
- Flunixin meglumine 1.1 mg/kg q12h

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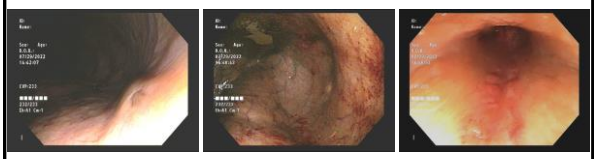
Clinical case

- Cystoscopy



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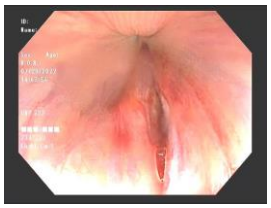
Clinical case



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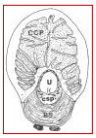
Urethral rents

- Linear defect of the urethral mucosa
- Convex surface of the urethra at the level of the ischial arch
- Communicate with the corpus spongiosum penis (CSP)
- Bulbospongiosus muscle contracts to expel urine from the urethra at the end of urination
  - Increase in pressure within the CSP



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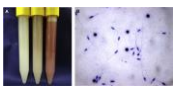
Urethral rents

- Terminal hematuria in geldings
- Hemospermia in stallions
- Baseline pressure within the CSP was not significantly different between geldings and stallions
- Peak urination pressure within the CSP of geldings was significantly increased when compared to stallions (25 vs 14.5 mmHg)



Taintor et al. EVJ. 2004

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Urethral rents

Diagnosis
- Timing of hematuria
- Urinalysis might be normal if caught at the beginning
- +/- mild anemia

Treatment
- Often self resolves
- Perineal urethrotomy or corpus spongiotomy

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Pigmenturia

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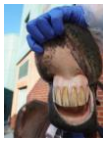
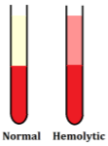
Hemoglobinuria

- Intravascular hemolysis → RBCs release hemoglobin
- Pink/red serum
- Signs of primary disease
- Sample not clear after centrifugation





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Clinical case

- 16 YO AQH mare
- 2-day history of lethargy
- Anemia and urine discoloration
- HR 60 bpm, RR 20 brpm, T 98.8F
- MM: dry, cyanotic, CRT 2 sec
- Dark urine
  - Remained dark after centrifugation

Images courtesy Dr. Lascola and Dr. Ceriotti

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Clinical case

RBC	3.42	L	x 10^6/uL	6.00 - 12.00
HGB	9.4	L	g/dL	10.0 - 18.0
HCT	15.3	L	%	32.0 - 48.0
MCV	44.8		fL	34.0 - 58.0
MCH	27.4	H	pg	14.0 - 19.0
MCHC	61.1	H	g/dL	31.0 - 37.0
RDW	20.0		%	17.0 - 20.0
PLATELET COUNT	624	H	x 10^3/uL	100 - 230
MPV	21.0	H	fL	5.8 - 11.5
WBC	6.68		x 10^3/uL	6.00 - 12.00

Test	Diff %	Result	Units	Ref. Interval
SEG	(77%)	5.144	x 10^3/uL	3.000 - 6.000
BANDS	(0%)	0.000	x 10^3/uL	0.000 - 0.100
LYMPH	(21%)	1.403	L x 10^3/uL	1.500 - 5.000
MONO	(2%)	0.134	/uL	0.000 - 0.600
EOS	(0%)	0.000	x 10^3/uL	0.000 - 0.600
BASO	(0%)	0.000	x 10^3/uL	0.000 - 0.100
OTHER	(0%)	0.000	x 10^3/uL	0.000 - 0.000
NRBC		0	/100 WBC	No Ref Interval
PLT EST	ABOVE REFERENCE INTERVAL			
Plasma T/S	9.5 g/dL			
Fibrinogen T/S		200	mg/dl	100 - 400

TOTAL PROTEIN	7.55		g/dL	6.00 - 8.60
ALBUMIN	2.32	L	g/dL	2.70 - 4.10
GLOBULIN	5.23	H	g/dL	2.60 - 4.40
ALBUMIN/GLOBULIN RATIO	0.44	L		0.70 - 1.00
AST	406	H	U/L	144 - 350
GGT	3		U/L	2 - 29
TOTAL BILIRUBIN	7.97	H	mg/dL	0.70 - 3.60
CK2	851	H	U/L	103 - 402
BUN	32.9	H	mg/dL	9.0 - 24.0
CREATININE	7.9	H	mg/dL	0.0 - 2.0
CALCIUM	10.4	L	mg/dL	10.5 - 12.9
PHOSPHORUS	4.1		mg/dL	2.1 - 4.6
MAGNESIUM	1.6	L	mg/dL	1.7 - 2.1
GLUCOSE	115		mg/dL	81 - 127
BICARBONATE	22.7		mmol/L	21.0 - 30.0
SODIUM	130	L	mmol/L	134 - 150
POTASSIUM	3.6		mmol/L	3.5 - 4.5
CHLORIDE	93	L	mmol/L	97 - 111
ANION GAP	17.9			9.0 - 25.0
OSMOL(CALC)	267	L	mOsm/kg	276 - 288
S.IRON	699	H	ug/dL	129 - 173
UIBC	797		ug/dL	123 - 430
TIBC	1496		ug/dL	243 - 553
LIPEMIA_INDEX	272	H		0 - 14

Marked anemia. Ghost cells indicate intravascular hemolysis. Eccentrocytes are caused by oxidative injury to the erythrocyte membrane. Increased MCHC (hyperchromasia) is likely due to intravascular hemolysis, but can also be seen with lipemia, excess of EDTA, and heinz bodies. Taken together, these findings indicate intravascular hemolysis owing to oxidative damage. Oxidative damage can be caused by toxins (Red Maple toxicosis), drugs, and infectious organisms.

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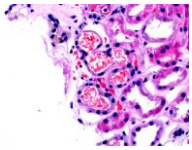
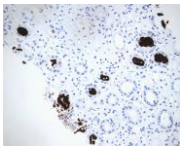
Clinical case

The gross and histological findings of dark red urine, dark red kidneys, and hemoglobin casts are consistent with hemoglobinuria. These findings are supportive of red maple toxicosis, as clinically suspected. The gross and histologic changes observed in the liver are consistent with parasite granulomas. Although no parasites were histologically observed, potential differential diagnoses include *Strongylus* sp. migration, and *Heterobilharzia americana* infection.





Caza T. AJKD. 2022

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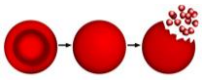
Red maple toxicosis

- Anemia caused by oxidative damage to the erythrocyte cell membrane and hemoglobin
- Summer-fall
- ~60% fatality rate
- Signs observed 12-48 hrs
- Renal failure secondary to hemoglobin deposition in the kidney



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Red maple toxicosis

Management

- Prevent toxic absorption → activated charcoal 1-3 g/kg BW
- Nasal oxygen
- Blood transfusion
- IV fluids
- Judicious use of NSAIDs
- Avoid corticosteroids and DMSO

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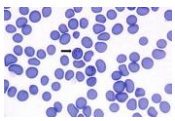
Hemoglobinuria

Common causes of intravascular hemolysis

- Parasitic – piroplasmosis
- Viral – EIA
- Bacterial – C. perfringens type A
- Immune mediated

Toxins
Red maple leaf*
Phenothiazine
Copper
Wild onion



Wise *et al.*, 2013. JVIM

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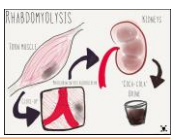
Myoglobinuria

- Secondary to severe muscle injury
  - Exertional rhabdomyolysis
- Leakage of myoglobin from myocytes
- Brown-to-red discolored urine
- Clinical signs of rhabdomyolysis
- Urine discolored after centrifugation



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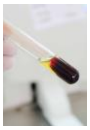
Myoglobinuria

- CK > 2,000 IU
- Serum will be clear
  - Myoglobin has no carrier protein → rapidly cleared
  - Hemoglobin is bound to haptoglobin → not rapidly cleared



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Myoglobinuria

Seasonal pasture/Atypical myopathy

- Non-exertional rhabdomyolisis
- Ingestion of hypoglycin A → disruption of mitochondrial fatty acid metabolism in myocyte
- HGA in seeds of Acer tree
- Onset 12-24 hrs after ingestion
- > fall

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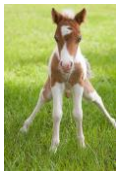
Drugs

- Doxycycline → dark brown or black-colored urine
- Rifampin → red- or orange-colored urine
- Phenazopyridine → red- or orange-colored urine

Plant pigments

- Red clovers → porphyrins → red urine
- Alsike clover → brown urine



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Urinalysis

- Hemorrhage → more than 5-8 RBCs
- Differentiate between hematuria, hemoglobinuria or myoglobinuria
- False results → diluted (<1.006), pH > 8, delayed analysis
  - RBC lysis

	Urine	RBCs
Hematuria	Clear	Precipitated
Hemoglobinuria	Red	
Myoglobinuria	Red	

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Differentiating hemo- and myoglobinuria

- Ammonium sulfate precipitation
  - Hemoglobin precipitates at 80% saturation
  - Myoglobin precipitates at full saturation
- Electrophoresis
- Spectroscopy
- Biochemical results
  - Hemoglobinuria → intravascular hemolysis → Pink serum
- Discoloration with negative strip → plant or drug pigmenturia

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Summary

- Thorough clinical examination
  - Systemic disease
  - Need for blood transfusion
- Differentiate hematuria, hemoglobinuria and myoglobinuria
  - History, bloodwork, serum color, urine color, ultrasound, etc
  - Direct treatment and prognosis
- Acknowledge the risk for renal failure

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Questions

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