WARNING SIGNS Patients with severe hypokalemia suffer from generalized muscle weakness; in cats, cervical ventroflexion may be noted.

INSIGHTS IN ELECTROLYTE DISORDERS

Evaluation and Management of the Hypokalemic Patient

***Audrey Cook**, BVM&S, DACVIM-SAIM, DECVIM-CA, DABVP (Feline), and **Justin Heinz**, DVM, DACVECC*
Texas A&M University College of Veterinary Medicine & Biomedical Sciences

Hypokalemia is defined as a plasma or serum potassium concentration (i.e., [K]) that is below the reference range (usually 3.5 to 5.1 mmol/L). More than 95% of total body potassium is intracellular, where it is the most abundant cation and plays a key role in maintenance of the resting membrane potential.[1] Changes in [K] within the extracellular fluid are therefore a poor reflection of total body potassium content. Healthy animals consuming adequate quantities of a balanced diet ingest abundant amounts of potassium, and the surplus is eliminated in urine. Renal excretion of potassium is primarily determined by aldosterone from the adrenal glands; this hormone triggers the reclamation of filtered sodium in exchange for potassium in the distal convoluted tubules. A primary driver for aldosterone secretion is a decrease in circulating volume; this triggers the release of renin and the generation of angiotensin II, which in turn stimulates aldosterone synthesis. Complex responses within the cells of the zona glomerulosa allow for the release of aldosterone in response to increases in [K]; conversely, hypokalemia blunts aldosterone secretion.[2]

In most instances, hypokalemia reflects potassium loss (via the kidneys or gastrointestinal tract) or the translocation of potassium into the intracellular compartment.[1,4]

Acid–base status also impacts serum [K], as protons are moved across cell membranes in exchange for potassium. Serum [K] is therefore increased by acidosis and lowered by alkalosis. In addition, acid–base disorders significantly impact renal potassium handling, with increased kaliuresis in alkalemic patients.[3] Changes in glycemic status also influence [K], as insulin triggers the intracellular transportation of both glucose and potassium.[3] The administration of insulin to a hyperglycemic patient with borderline hypokalemia may therefore result in a clinically impactful drop in [K].

In most instances, hypokalemia reflects potassium loss (via the kidneys or gastrointestinal tract) or the translocation of potassium into the intracellular compartment.[1,4] Inadequate potassium intake is unlikely to be a primary cause, although acidifying

diets with limited potassium have been associated with clinically impactful potassium depletion in cats.[5] Mild hypokalemia (3 to 3.5 mmol/L) is a common electrolyte derangement and is usually of little clinical consequence, although total body stores may be significantly depleted.[1,4,6] However, serum [K] < 3 mmol/L merits prompt attention, and a value of < 2.5 mmol/L is a medical emergency.

Interested in Learning More?

Readers can find more detail on the physiology of potassium homeostasis in the following reference:

- DiBartola SP, de Morais HA. Disorders of potassium: hypokalemia and hyperkalemia. In: DiBartola SP, ed. *Fluid, Electrolyte, and Acid-Base Disorders in Small Animal Practice*. 4th ed. St. Louis, MO: Saunders Elsevier; 2011:92-119.

CAUSES OF HYPOKALEMIA

Gastrointestinal Loss

Patients with vomiting and diarrhea are often hypokalemic, as significant amounts of potassium are present in digestive fluids. In patients with a gastric outflow obstruction, the loss of hydrochloric acid and subsequent hypochloremic metabolic alkalosis will further decrease serum [K] as protons are moved out of cells in exchange for potassium. In turn, hypokalemia limits the ability of the kidneys to retain protons, which perpetuates the metabolic alkalosis.

Renal Loss

Although surplus dietary potassium is routinely excreted via the kidneys, patients with renal dysfunction or other causes of polyuria may experience excessive kaliuresis. Cats with chronic kidney disease are particularly prone to hypokalemia,[7,8] and life-threatening hypokalemia has been reported in 1 dog with acute leptospirosis.[9] Patients with a postobstructive diuresis may lose substantial amounts of potassium until normal tubular function is restored. Type 1 renal tubular acidosis is also associated with hypokalemia, due to disruption of proton excretion/bicarbonate generation in the distal convoluted tubule.[2] Primary hyperaldosteronism is uncommon in cats and very rare in dogs but will cause sustained kaliuresis and may result in significant clinical compromise.[10]

Iatrogenic

The prolonged administration of fluids with inadequate potassium supplementation is a common cause of hypokalemia; clinicians should routinely add potassium to crystalloids to prevent progressive depletion in anorexic patients. Loop and thiazide diuretics also promote renal potassium loss.[11] Insulin administration will move potassium into the intracellular compartment. The latter is a particular concern in patients with diabetic ketoacidosis because these animals often present with a substantial total body potassium deficit. Serum [K] may be normal at presentation, due to concurrent hyperglycemia and significant metabolic acidosis, but then drop precipitously following fluid and insulin administration.[12]

Toxicity

Albuterol—like all β-adrenergic agonists—triggers the intracellular movement of potassium. This effect is modest at standard therapeutic doses, but inadvertent overdose or the ingestion of an albuterol inhaler can cause significant hypokalemia.[13] Severe hypokalemia has also been reported in a dog following the ingestion of organic barium.[14]

Hereditary

Hypokalemic periodic paralysis/polymyopathy has been reported in European and Australian Burmese cats. Affected cats are less than 12 months of age and present with acute, episodic, cervical ventroflexion, as well as weakness.[15]

Metabolic Alkalosis

An increase in the pH of the extracellular fluid triggers the movement of protons out of cells in exchange for potassium. In addition—and perhaps more importantly—alkalemia promotes urine potassium loss by stimulation of renal sodium transporters and increased kaliuresis.[3] Generous potassium supplementation is therefore necessary in these patients, along with mitigation of the underlying acid–base disturbance.

CONSEQUENCES OF HYPOKALEMIA

As serum [K] decreases, changes in cell excitability result in muscle weakness. In patients with conditions associated with chronic hypokalemia, such as hyperaldosteronism, this may wax and wane depending on dietary potassium intake. As adequate serum [K] is necessary for effective function of antidiuretic hormone receptors in the collecting ducts, hypokalemia results in compromised renal concentrating ability.[16] Affected patients are variably polyuric and polydipsic, and urine specific gravity may fall below 1.008.

Patients with severe hypokalemia (< 2.5 mmol/L) suffer from generalized skeletal muscle weakness caused by instability of muscle cell membranes, resulting in a generalized myopathy. In the cat, a species that lacks a completely developed nuchal ligament, cervical ventroflexion may be noted. Although these findings are not pathognomonic for hypokalemia, potassium status should be determined in any patient with weakness or other evidence of myopathy before administering resuscitative or replacement fluids. Injudicious fluid therapy can quickly drive down serum [K] through simple dilution and lead to further patient deterioration. With progressive hypokalemia, patients will be unable to ventilate due to paralysis of the diaphragm and the other muscles of respiration, resulting in death.

In experimental rodent and feline models, chronic hypokalemia has been associated with changes in renal function, generally attributed to impaired renal angiogenesis.[17,18] However, hypokalemia per se is not recognized as a risk factor for progression in cats with chronic kidney disease.[19]

INITIAL PATIENT ASSESSMENT

It is important to try to establish the cause of hypokalemia with a thorough patient history and physical examination, along with a careful review of other routine laboratory data (e.g., complete blood count, serum biochemical profile, urinalysis). Additional diagnostics, such as measurement of systolic blood pressure, muscle enzyme activities (i.e., creatine kinase, aspartate aminotransferase), blood gas analysis, resting aldosterone concentrations, and abdominal imaging, may be necessary to establish a diagnosis.

See **FIGURE 1** for an algorithm showing evaluation of the hypokalemic patient.

TREATMENT OF HYPOKALEMIA

Serum [K] < 3 mmol/L

Potassium should be administered by continuous rate infusion. As a general rule, the rate of potassium administration should not exceed 0.5 mEq/kg/hr (0.5 mmol/kg/hr); see below for the calculation.

Calculation to determine current rate of potassium administration:

- Determine mEq potassium per mL of fluid = # in bag/volume of bag
- Determine mEq/hr = mEq/mL × patient's current fluid rate
- Determine mEq/kg/hr = mEq/hr/patient's weight in kg

Potassium chloride (KCl; 2 mEq/mL) is the preferred solution; this is extremely hyperosmolar (4000 mOsmol/L) and must be diluted 1:9 before administration into a peripheral vein or 1:4 if given centrally. Faster rates may be given peripherally in exceptional circumstances but require continuous electrocardiogram monitoring for bradycardia. Consultation with a specialist is advisable if a rate in excess of 0.5 mEq/kg/hr is contemplated. If the patient needs concurrent maintenance with or without replacement fluid therapy, it is often easiest to administer potassium through a dedicated catheter using a syringe pump. This potassium-containing line should be clearly identified and should not be flushed or bolused. In small patients, a syringe pump may be used to deliver a single fluid with a robust potassium concentration that can meet all the patient's needs. Concurrent oral potassium supplementation should be provided as soon as the patient is able to swallow.[20] Potassium gluconate is the most appropriate choice and should be dosed at 0.5 mEq potassium/kg (162.5 mg potassium gluconate/kg) PO q6h to q12h. Serum [K] should be checked every 4 to 6 hours and the potassium infusion discontinued when [K] is in the reference range. It is important to note that intracellular deficits will be replaced before the extracellular fluid [K] is restored.

Serum [K] 3 to 3.5 mmol/L

Oral potassium gluconate should be provided to otherwise stable patients that are not receiving fluid therapy at 0.5 mEq potassium/kg PO q12h. If the patient is receiving parenteral fluid therapy, KCl or potassium phosphate should be added to achieve a

potassium concentration of approximately 30 mmol/L.[1] The fluid rate should not exceed 18 mL/kg/hr.

Refractory Hypokalemia

Patients with severe hypokalemia but a poor response to aggressive intravenous supplementation may benefit from concurrent magnesium supplementation. Adequate amounts of intracellular magnesium are necessary to limit potassium loss through the kidneys; magnesium deficiency will therefore result in sustained kaliuresis.[21] As 99% of total body magnesium is contained within the cells, diagnosing hypomagnesemia is difficult; the authors reserve supplementation for patients requiring near-maximum administration of potassium without improvement in serum [K]. Magnesium sulfate can be administered as a constant rate infusion of 1.6 to 2.5 mg/kg/hr.[22] Spironolactone, an aldosterone antagonist, may be very helpful in patients with hyperaldosteronism but should not be administered without sufficient evidence to support this diagnosis.

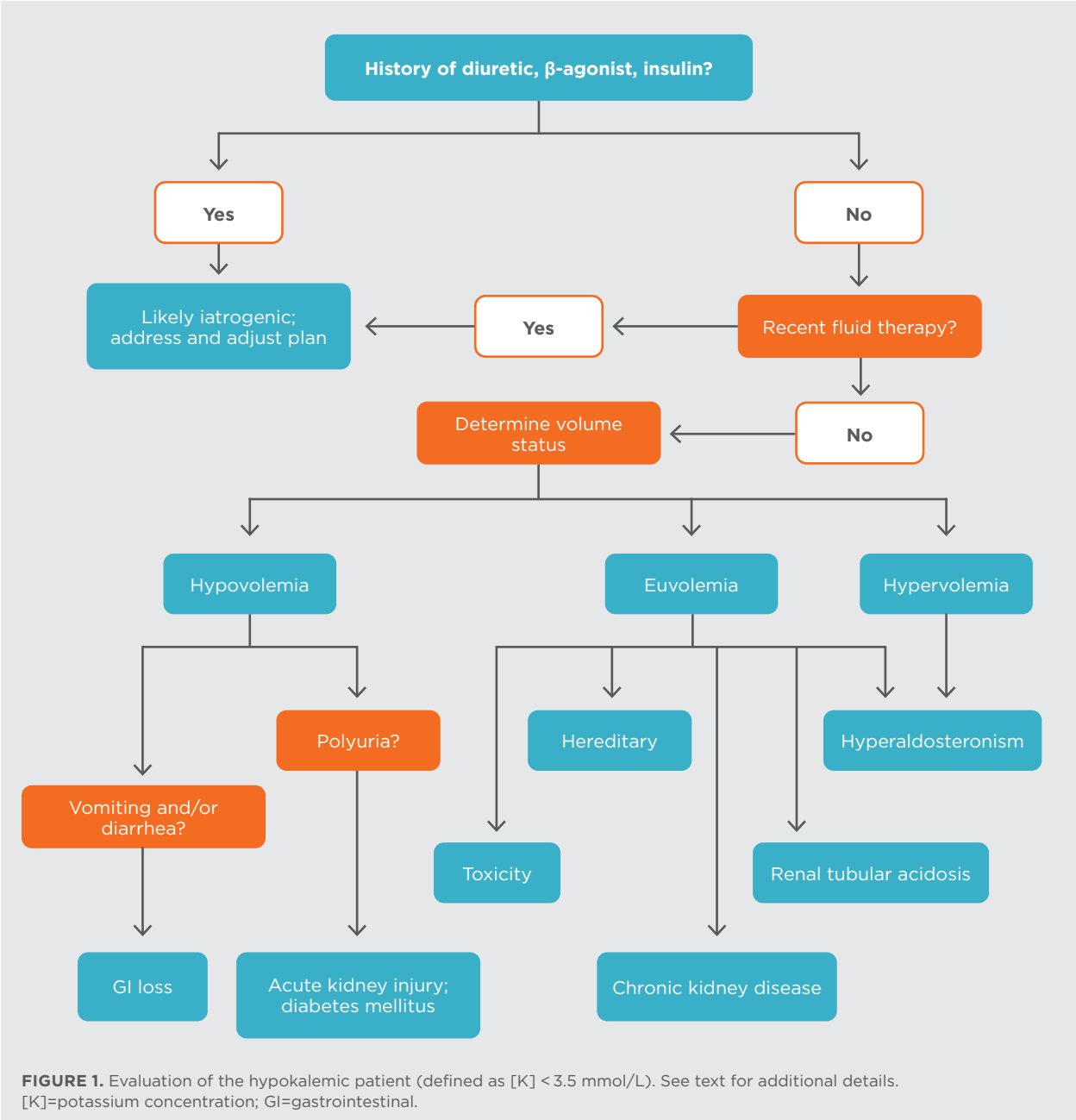

FIGURE 1. Evaluation of the hypokalemic patient (defined as [K] < 3.5 mmol/L). See text for additional details.
[K]=potassium concentration; GI=gastrointestinal.

See **FIGURE 2** for an algorithm of the acute management of the hypokalemic patient.

CASE SCENARIO

History

A 12-year-old neutered male domestic shorthair cat weighing 4.8 kg was presented for weakness. The cat was missing from the home for almost 48 hours and was found under a bush, apparently unable to stand. The owner reported that the cat had difficulty jumping over the past 2 to 3 months; this had been attributed to age-related joint disease. The cat's appetite was unchanged; thirst was questionably increased in recent weeks. The cat had routine access to the outside, so feces and urination were not observed.

On physical examination, the cat was profoundly weak and barely able to support itself. Cervical ventroflexion was evident, with the cat's nose resting on the table. Body temperature was 99.7 °F, heart rate was 220 beats/min, and dehydration was estimated to be 5%. Serum sodium concentration ([Na]) was 157 mmol/L (reference range, 144 to 155 mmol/L); potassium was 2.3 mmol/L (reference range, 3.5 to 5.1 mmol/L). The cat was borderline azotemic (blood urea nitrogen was 33 mg/dL [reference range, 19 to 33 mg/dL]; creatinine

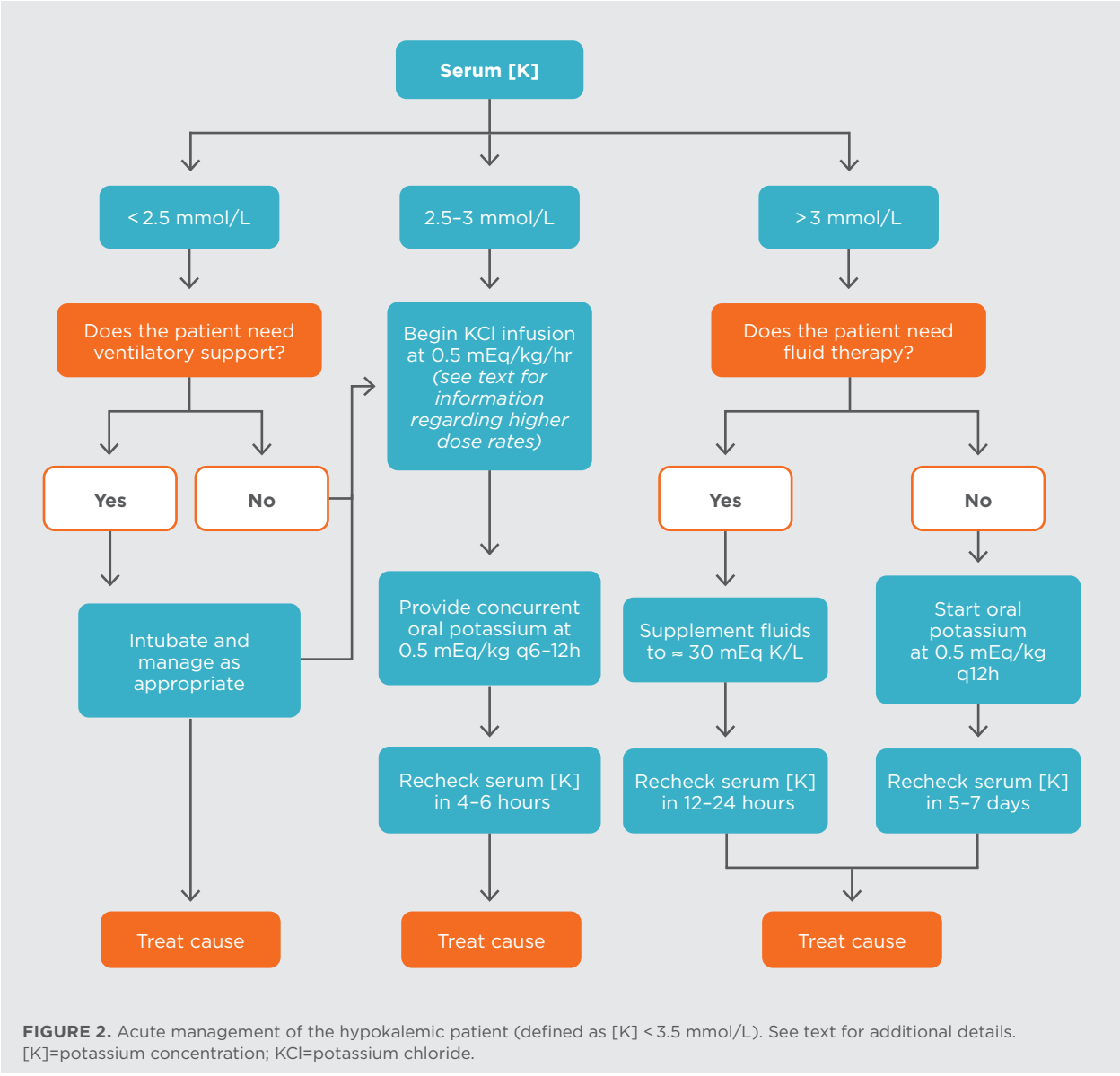

FIGURE 2. Acute management of the hypokalemic patient (defined as [K] < 3.5 mmol/L). See text for additional details. [K]=potassium concentration; KCl=potassium chloride.

was 1.5 mg/dL [reference range, 0.8 to 1.8 mg/dL]), with urine specific gravity of 1.035. Indirect systolic blood pressure was 170 mm Hg. Complete blood count was unremarkable.

Assessment

This patient's weakness can be attributed to the severe hypokalemia. This is likely chronic and explains the historic issues with jumping. Concurrent hypokalemia, hypernatremia, and hypertension (despite volume depletion) are suggestive of primary hyperaldosteronism. This condition is usually caused by a functional adrenal cortical tumor. Bilateral adrenocortical hyperplasia has also been reported in cats with chronic kidney disease.[23] Sustained and inappropriate secretion of aldosterone results in potassium wasting through the kidneys; total body sodium is expected to increase, although concurrent water retention means that serum [Na] usually stays within the reference range. Blood pressure is often increased, due to expansion of the extracellular fluid compartment, and can result in retinal hemorrhage with or without detachment.

The first priority for this patient is to address the hypokalemia. The concurrent mild dehydration should be addressed cautiously, as rapid volume expansion may worsen hypokalemia and compromise the cat's ability to ventilate. In a patient with hyperaldosteronism, total body sodium content is assumed to be increased; this should be taken into consideration when selecting the fluid type.

Calculations

Potassium max (mEq/kg/hr) = 0.5 × 4.8 kg = 2.4 mEq/hr

Determine volume of KCl solution (at 2 Eq/mL) to meet this need = 2.4/2 = 1.2 mL/hr

Volume deficit for 5% dehydration = 0.05 × 4.8 = 240 mL

Target time to replace deficit = 24 hours = 10 mL/hr

Maintenance fluid need = 227 mL/day ≈10 mL/hr

Total fluid rate for first 24 hours = 20 mL/hr

Concurrent hypokalemia, hypernatremia, and hypertension (despite volume depletion) are suggestive of primary hyperaldosteronism.

Plan

Option 1

Withdraw KCl needed for a 3-hour treatment period = 1.2 × 3 = 3.6 mL KCl; place this in a 60 mL syringe

Add enough lactated Ringer's solution (LRS) to complete the volume needed over 3 hours = (20 × 3) – 3.6 = 56.4 mL

(Because the amount of potassium in LRS is only 4 mEq/L, it is acceptable to disregard this amount)

Deliver at 20 mL/hr

Check serum [K] after 4 to 6 hours; adjust supplementation as appropriate

Option 2 (if a syringe pump is not available)

Take a 250 mL bag of LRS

Determine how many hours of fluid therapy this will provide = 250/20 = 12.5 hr

Determine how much potassium needed for this period of time = 12.5 × 2.4 = 30 mEq

Subtract the amount of potassium in the bag of LRS = 30 – 1 = 29 mEq

Add the appropriate amount of KCl to this bag = 29/2 = 14.5 mL (120 mEq/L)

Deliver at 20 mL/hr

Check serum [K] after 4 to 6 hours; adjust fluid plan as appropriate

Additional Considerations

Serum should be collected for measurement of aldosterone concentrations. Oral spironolactone may then be administered to mitigate ongoing kaliuresis. Blood pressure should be monitored and amlodipine added to the treatment plan, if necessary. Abdominal ultrasonography should be performed to assess adrenal size and symmetry.

Note: These calculations are designed to provide an appropriate starting point, but an individual patient's response may differ significantly from the calculated course. Frequent monitoring and adjustments are therefore necessary. Blood pressure should be rechecked frequently on this patient because volume restoration may exacerbate hypertension and specific intervention may be necessary. TVP

Audrey Cook

Dr. Audrey Cook is a graduate of the University of Edinburgh. She completed an internship at NCSU and a residency in internal medicine at UC Davis. She is a diplomate of the American and European Colleges of Veterinary Internal Medicine and is one of the few internists with additional board certification in Feline Practice. After a decade in private referral practice, Dr. Cook joined the faculty at Texas A&M College of Veterinary Medicine. She is currently Professor and Chief of the Internal Medicine Service. Her clinical interests include endocrinology, gastroenterology, and interventional radiology/endoscopy.

Justin Heinz

Dr. Justin Heinz obtained his DVM from Purdue University. He completed an internship at LSU and a residency in emergency and critical care at Texas A&M University. He is a diplomate of the American College of Emergency and Critical Care. After a year in private referral practice, Dr. Heinz joined the faculty at Texas A&M College of Veterinary Medicine. He is currently a Clinical Assistant Professor and Chief of the Emergency and Critical Care Service. His clinical interests include transfusion medicine, sepsis, acute kidney injury, and renal replacement therapies.

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