

Chloride: A Quick Reference

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- Chloride constitutes approximately two thirds of the anions in plasma and extracellular fluid, with a much lower intracellular concentration.
- Chloride is the major anion filtered by the glomeruli and reabsorbed in the renal tubules.
- Changes in chloride concentration are associated with metabolic acid-base disorders. Chloride is an important player in renal regulation of acid-base metabolism.

ANALYSIS

- Indications: Serum chloride concentration commonly is measured in systemic diseases characterized by vomiting, diarrhea, dehydration, polyuria, and polydipsia or in patients likely to have metabolic acid-base abnormalities.
- Typical reference range: Chloride concentration must be corrected to account for changes in plasma free water. Primary chloride disorders have abnormal corrected chloride, whereas changes in free water do not (Fig. 1). Corrected chloride can be estimated as follows:

$$[\text{Cl}^-]_{\text{corrected}} = [\text{Cl}^-]_{\text{measured}} \times 146 / [\text{Na}^+]_{\text{measured}}(\text{dogs})$$

$$[\text{Cl}^-]_{\text{corrected}} = [\text{Cl}^-]_{\text{measured}} \times 156 / [\text{Na}^+]_{\text{measured}}(\text{cats})$$

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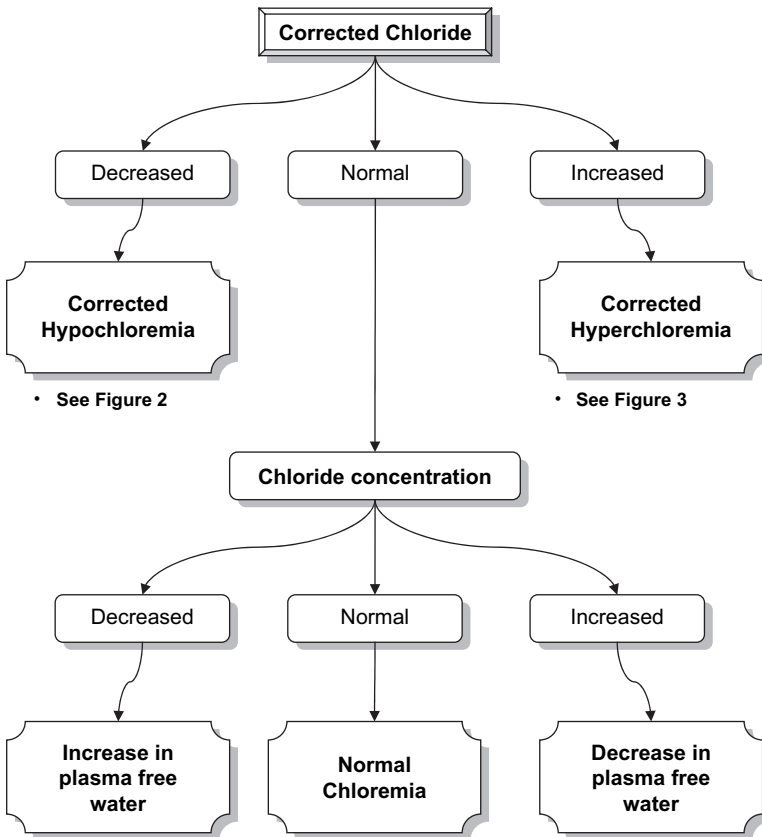


Fig. 1. Algorithm for evaluation of patients with chloride abnormalities. (Adapted from de Morais HSA, Biondo AW. Disorders of chloride: hyperchloremia and hypochloremia. In: DiBartola SP, editor. Fluid, electrolyte, and acid-base disorders. 3rd edition. St. Louis (MO): Elsevier; 2006. p. 84; with permission.)

- Where $[Cl^-]_{\text{measured}}$ and $[Na^+]_{\text{measured}}$, respectively, are the patient's serum chloride and sodium concentrations. The values 146 and 156 reflect the mean values for serum sodium concentration in dogs and cats, respectively. Normal $[Cl^-]_{\text{corrected}}$ is approximately 107 minus 113 mEq/L in dogs and 117 minus 123 mEq/L in cats. These values may vary among laboratories and analyzers.
- Danger values: Unknown. Muscle twitching or seizures in hypochloremic animals are probably attributable to metabolic alkalosis and decreased ionized calcium concentration, whereas clinical signs associated with hyperchloremia are probably attributable to hyperosmolality.
- Artifacts: Pseudohypochloremia results when chloride is measured in markedly lipemic samples by means of techniques that are not ion selective. Halides (eg, bromide, iodide, fluoride) are measured as chloride, falsely

increasing measurements even when ion-selective techniques are used. This is especially important in animals receiving potassium bromide as an anticonvulsant.

- Drug effects: Administration of chloride-containing solutions may increase chloride concentration, whereas loop diuretics and thiazides may cause excessive renal loss of chloride relative to sodium.

CORRECTED HYPOCHLOREMIA

- Causes: Corrected hypochloremia is associated with a tendency toward alkalosis (hypochloremic alkalosis) because of the increase in strong ion difference.
 - Corrected hypochloremia may result from excessive loss of chloride relative to sodium or administration of fluids containing high sodium concentration relative to chloride (Box 1).
 - The most common causes of corrected hypochloremia are chronic vomiting of gastric contents and aggressive diuretic therapy with furosemide or thiazides. Administration of sodium without chloride (eg, sodium bicarbonate) also may cause corrected hypochloremia. Hypochloremia attributable to increased renal chloride excretion is a normal adaptation that is present in chronic respiratory acidosis.
 - Persistent hypochloremia is an indication to determine serum sodium, potassium, and total carbon dioxide (TCO_2) concentrations, preferably with blood gas analysis.

Box 1: Causes of corrected hypochloremia

Excessive loss of chloride relative to sodium

Gastrointestinal loss

Vomiting of stomach contents^a

Gastrointestinal diseases associated with hyperkalemia and hyponatremia in dogs without hypoadrenocorticism (eg, trichuriasis, salmonellosis, perforated duodenal ulcer)

Renal loss

Therapy with thiazides or loop diuretics^a

Chronic respiratory acidosis

Hyperadrenocorticism

Excessive gain of sodium relative to chloride

Sodium bicarbonate

^aMost important causes in small animal practice.

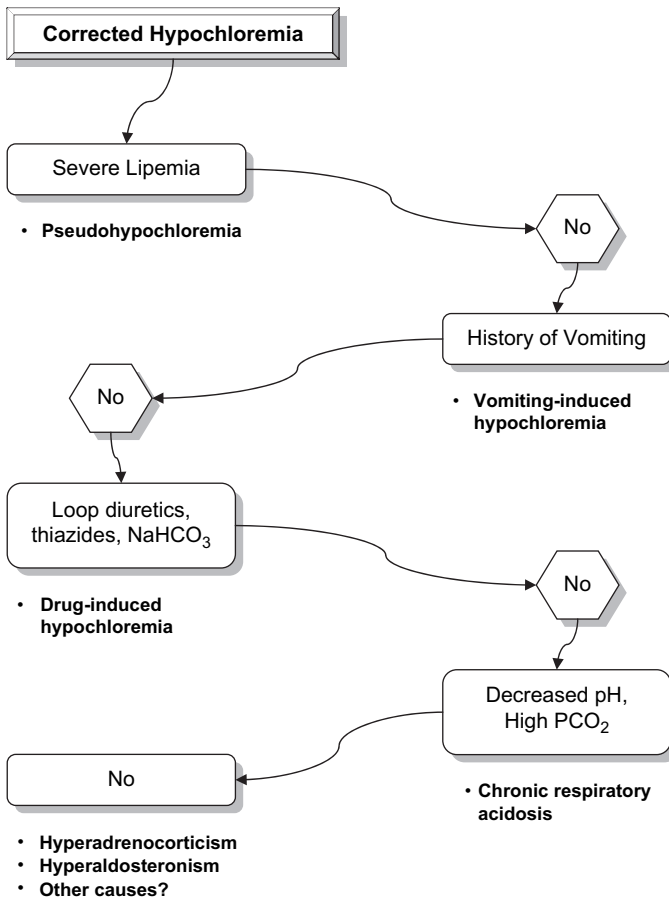


Fig. 2. Algorithm for evaluation of patients that have corrected hypochloremia. (Adapted from de Morais HSA, Biondo AW. Disorders of chloride: hyperchloremia and hypochloremia. In: DiBartola SP, editor. Fluid, electrolyte, and acid-base disorders. 3rd edition. St. Louis (MO): Elsevier; 2006. p. 85; with permission.)

- Signs: Clinical signs associated with pure hypochloremia in dogs and cats have not been described but probably are related to the accompanying metabolic alkalosis.
- Stepwise approach: An algorithm for the differential diagnosis of corrected hypochloremia is presented in Fig. 2.

CORRECTED HYPERCHLOREMIA

- Causes: Corrected hyperchloremia is associated with a tendency toward acidosis (hyperchloremic acidosis) because of the decrease in strong ion difference.

- Corrected hyperchloremia may result from excessive sodium loss relative to chloride, excessive chloride gain relative to sodium, or renal chloride retention (Box 2). Small bowel diarrhea causes hyperchloremic metabolic acidosis because of loss of bicarbonate-rich chloride-poor fluid. Administration of NH_4Cl , potassium chloride (KCl), cationic amino acids (eg, total parenteral nutrition), hypertonic saline, or 0.9% sodium chloride (NaCl) leads to chloride gain.
- The most common causes of corrected hyperchloremia are fluid therapy and diarrhea.
- Hyperchloremia attributable to decreased renal chloride excretion is a normal adaptation that is present in chronic respiratory alkalosis.
- Persistent hyperchloremia is an indication for determining serum sodium, potassium, and TCO_2 concentrations, preferably with blood gas analysis.
- Signs: Specific clinical signs associated with pure hyperchloremia in dogs and cats have not been reported but probably are related to the metabolic acidosis that accompanies hyperchloremia.
- Stepwise approach: An algorithm for the differential diagnosis of corrected hyperchloremia is presented in Fig. 3.

Box 2: Causes of corrected hyperchloremia

Pseudohyperchloremia

Potassium bromide therapy

Excessive loss of sodium relative to chloride

Diarrhea^a

Excessive gain of chloride relative to sodium

Exogenous intake

Fluid therapy (eg, 0.9% NaCl, hypertonic saline, KCl-supplemented fluids)^a

Therapy with chloride salts (NH_4Cl , KCl)

Total parenteral nutrition

Salt poisoning

Renal chloride retention

Renal failure

Renal tubular acidosis

Hypoadrenocorticism

Diabetes mellitus

Chronic respiratory alkalosis

Spirolactone

^aMost important causes in small animal practice.

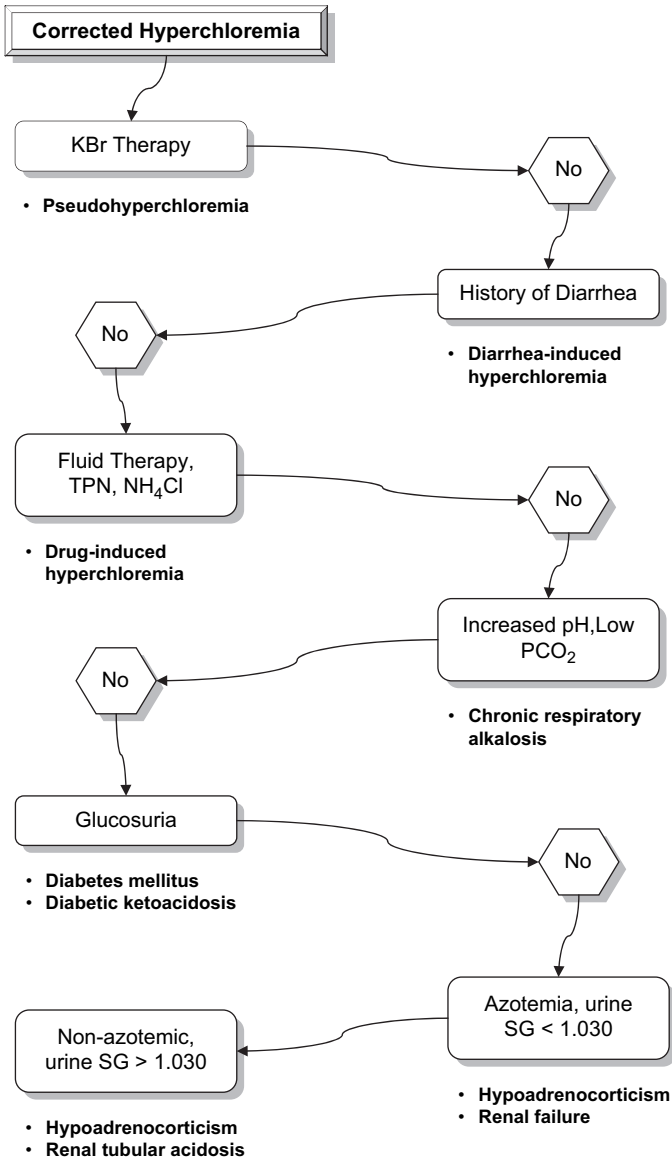


Fig. 3. Algorithm for evaluation of patients that have corrected hyperchloremia. KBr, potassium bromide; SP, specific gravity; TPN, total parenteral nutrition. (Adapted from de Moraes HSA, Biondo AW. Disorders of chloride: hyperchloremia and hypochloremia. In: DiBartola SP, editor. Fluid, electrolyte, and acid-base disorders. 3rd edition. St. Louis (MO): Elsevier; 2006. p. 85; with permission.)

Further Readings

- de Morais HA. Chloride ion in small animal practice: the forgotten ion. *Journal of Veterinary Emergency and Critical Care* 1992;2:11–24.
- de Morais HA, Biondo AW. Disorders of chloride: hyperchloremia and hypochloremia. In: DiBartola SP, editor. *Fluid, electrolyte, and acid-base disorders*. 3rd edition. St. Louis (MO): Elsevier; 2006. p. 80–91.