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## Recurrent Apneic Episodes in a 6-week-old Infant

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### EDITORS NOTE

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**AUTHOR DISCLOSURE** Drs Feldon, Bahat, Gamsu, Rosenfeld, Bistrizter, and Goldman have disclosed no financial relationships relevant to this article. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.

### CASE PRESENTATION

A 6-week-old infant is brought to the hospital after apparent life-threatening events. She has had three different episodes on three consecutive days that consisted of apnea (lasting between 20 and 30 seconds), cyanosis, and, on one occasion, muscle limpness. The episodes are not directly related to meals. She is exclusively breastfed and experiences food regurgitations. She has no history of abnormal limb movements, vomiting, or diarrhea, and the mother denies use of medication by the infant or herself. Her perinatal history is uneventful. Her weight gain is normal (birthweight was 3.840 kg, weight on admission is 4.870 kg). The parents are of Ashkenazi origin, and no consanguinity is noted. There is a family history of early vascular strokes, kidney failure, and nephrolithiasis.

The baby's vital signs (heart rate 135 beats/min, respiratory rate 40 breaths/min, blood pressure 85/42 mm Hg, and oxygen saturation 100% in room air) and findings on physical examination are normal. She is admitted to the pediatric intensive care unit for monitoring and evaluation.

Results of her laboratory evaluation, including complete blood cell count, electrolytes, renal function tests, liver enzymes, and urinary dipstick testing, are normal. However, an arterial blood gas shows metabolic alkalosis (pH 7.56, bicarbonate 36 mEq/L [36 mmol/L], partial pressure of carbon dioxide 35 mm Hg). Findings on additional tests, including electrocardiography and renal ultrasonography, are normal. One additional test suggests the diagnosis.

### CASE DISCUSSION

Metabolic alkalosis is generally divided into two primary types: chloride-responsive, which is typified by a low urinary chloride that is maintained by volume depletion and corrected by volume repletion; and chloride-resistant, which is characterized by an elevated urinary chloride that does not respond to volume repletion. Chloride-resistant alkalosis typically results from potassium depletion or mineralocorticoid excess and is further divided according to blood pressure elevation (Table).

Metabolic alkalosis in children is most commonly due to emesis or diuretic use. In neonates and young infants, metabolic alkalosis is usually related to an inherited syndrome such as Bartter syndrome or significant emesis from gastrointestinal obstruction, as in hypertrophic pyloric stenosis. Chronic metabolic alkalosis in neonates is typically related to prolonged hypercapnia and respiratory acidosis.

TABLE. Causes of Metabolic Alkalosis

CHLORIDE-RESPONSIVE (URINARY CHLORIDE <15 mEq/L [15 mmol/L])	CHLORIDE-RESISTANT (URINARY CHLORIDE >20 mEq/L [20 mmol/L])	
	ELEVATED BLOOD PRESSURE	NORMAL BLOOD PRESSURE
1. Gastric losses (emesis, nasogastric suction)	1. Adrenal adenoma/hyperplasia	1. Gittelman syndrome
2. Diuretics use	2. Glucocorticoid-remediable aldosteronism	2. Bartter syndrome
3. Cystic fibrosis	3. Renovascular disease	3. Base administration
4. Chloride-losing diarrhea	4. Renin-secreting tumor	4. EAST syndrome
5. Chloride-deficient formula	5. Cushing syndrome	5. Autosomal dominant hypoparathyroidism
6. Posthypercapnia	6. Licorice ingestion	
	7. Liddle syndrome	
	8. 17 $\beta$ -Hydroxylase deficiency	
	9. 11 $\beta$ -Hydroxylase deficiency	
	10. 11 $\beta$ -Hydroxysteroid dehydrogenase deficiency	

This patient was obviously not dehydrated, based on her normal weight, vital signs, physical examination findings, and electrolytes, and she had no history of emesis or diarrhea. Her urinary chloride measured 28 mEq/L (28 mmol/L). Her lack of low potassium concentrations or high blood pressure raised the possibility of base excess (exogenous base).

On repeat questioning, the mother reported treating the infant with gripe water and simethicone drops. Apparently, she gave 10 drops of gripe water every few hours. Testing of the commercial product she used revealed a high concentration of sodium bicarbonate.

### The Condition

Base excess in infants has been reported in cases involving the use of electrolyte-enhanced water in infant formulas and erroneous use of baking soda, but no cases have been reported with over-the-counter food supplements. In the past, most of the observed cases were due to the milk-alkali syndrome, seen when peptic ulcer disease was treated with calcium carbonate and the Sippy diet (a bland diet to treat peptic ulcer disease consisting of milk and other ingredients). The frequency of milk-alkali syndrome decreased dramatically after the introduction of histamine-2 blockers and hydrogen potassium ATPase inhibitors.

Several different studies have shown that metabolic alkalosis can induce apnea in infants and adults after bicarbonate intoxications and acid loss, such as in hypertrophic pyloric stenosis. We believe that the high concentration of bicarbonate in the gripe water combined with the overdosage that the

mother administered to the infant caused the severe metabolic alkalosis, which eventually induced apnea.

### Management

Medical intervention is usually necessary only for children with moderate or severe metabolic alkalosis. The most effective approach is to address the underlying cause. In this case, 2 days after cessation of gripe water use, the infant was symptom-free and repeat blood gas analysis showed normal results. When metabolic alkalosis is due to base excess, terminating the source of the base excess should be sufficient for cure.

### Lessons for the Clinician

- In all cases of chloride-resistant metabolic alkalosis with no signs of potassium depletion or blood pressure abnormalities, the possibility of an external source of base excess should be suspected.
- Ingesting over-the-counter medications, food supplements, and simple household products can result in serious adverse effects when used inappropriately.
- Gripe water is a commonly used product designed to treat infantile colic. Its composition varies according to the country of manufacture. Originally, it was composed from dill seed oil, sodium bicarbonate, and alcohol. In the United States, where it is regarded as a drug, gripe water was banned in 1982.

References for this article are at <http://pedsinreview.aappublications.org/content/36/6/260.full>.

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