conceivable that residual hypovolemic hyponatremia attenuated the recovery of the plasma Na^+ concentration. Alternatively, attenuated recovery was due to persistent effects of the single dose of DDAVP. Of note, although the plasma half-life of DDAVP is only 1–2 h, pharmacodynamic studies indicate a much more prolonged effect on urine output and/or urine osmolality. One final consideration is the effect of the patient's initial renal dysfunction on the pharmacokinetics and pharmacodynamics of the administered DDAVP, which is renally excreted; DDAVP should be administered with caution for the reinduction of hyponatremia in patients with chronic kidney disease or acute renal dysfunction.

CASE 6

A 44-year-old woman was referred from a local hospital after presenting with flaccid paralysis. Severe hypokalemia was documented (2.0 meq/L), and an infusion containing KCl was initiated.

Laboratory Data	Value	Units
Sodium	140	meq/L
Potassium	2.6	meq/L
Chloride	115	meq/L
Bicarbonate	15	meq/L
Anion gap	10	meq/L
BUN	22	mg/dL
Creatinine	1.4	mg/dL
Arterial Blood Gases		
pH	7.32	U
$Paco_2$	30	mmHg
HCO_3^-	15	meq/L
Additional Laboratory Data		
Rheumatoid factor positive, anti-Ro/SS-A positive, and anti-La/SS-B positive		
Urinalysis		
pH = 6.0, normal sediment without white or red blood cell casts and no bacteria. The urine protein-to-creatinine ratio was 0.150 g/g. Urinary electrolyte values were: Na^+ 35, K^+ 40, Cl^- 18 meq/L. Therefore, the urine anion gap was positive, indicating low urine NH_4^+ excretion.		

APPROACH TO DIAGNOSIS

The diagnosis in this case is classic hypokalemic dRTA from Sjögren's syndrome. This patient presented with a non-AG metabolic acidosis. The urine AG was positive, indicating an abnormally low excretion of ammonium in the face of systemic acidosis. The urine pH was inappropriately alkaline, yet there was no evidence of hypercalciuria, nephrocalcinosis, or bone disease. The patient was subsequently shown to exhibit hyperglobulinemia. These findings, taken together, indicate that the cause of this patient's hypokalemia and non-AG metabolic acidosis was a renal tubular abnormality. The hypokalemia and abnormally low excretion of ammonium, as estimated by the urine AG, in the absence of glycosuria, phosphaturia, or aminoaciduria (Fanconi's syndrome), defines the entity of classic distal renal tubular acidosis (dRTA), also known as type 1 RTA. Because of the hyperglobulinemia, additional serology was obtained, providing evidence for the diagnosis of primary Sjögren's syndrome. Furthermore, additional history indicated a 5-year history of xerostomia and keratoconjunctivitis sicca but without synovitis, arthritis, or rash.

Classic dRTA occurs frequently in patients with Sjögren's syndrome and is a result of an immunologic attack on the collecting tubule, causing failure of the H^+-ATPase to be inserted into the apical membrane of type A intercalated cells. Sjögren's syndrome is one of the best-documented acquired causes of classic dRTA. The loss of H^+-ATPase function also occurs with certain inherited forms of classic dRTA. There was no family history in the present case, and other family members were not affected. A number of autoantibodies have been associated with Sjögren's syndrome; it is likely that these autoantibodies prevent trafficking or function of the H^+-ATPase in the type A intercalated cell of the collecting tubule. Although proximal RTA has also been reported in patients with Sjögren's syndrome, it is much less frequent, and there were no features of proximal tubule dysfunction (Fanconi's syndrome) in this patient. The hypokalemia is due to secondary hyperaldosteronism from volume depletion.

APPROACH TO MANAGEMENT

The long-term renal prognosis for patients with classic dRTA due to Sjögren's syndrome has not been established. Nevertheless, the metabolic acidosis and the hypokalemia respond to alkali replacement with either sodium citrate solution (Shohl's solution) or sodium bicarbonate tablets. Obviously, potassium deficits must be replaced initially, but potassium replacement is usually not required in dRTA patients long term because sodium bicarbonate (or citrate) therapy expands volume and corrects the secondary hyperaldosteronism. A consequence of the interstitial infiltrate seen in patients with Sjögren's syndrome and classic dRTA is progression of chronic kidney disease. Cytotoxic therapy plus glucocorticoids has been the mainstay of therapy in Sjögren's syndrome for many years, although B lymphocyte infiltration in salivary gland tissue subsides and urinary acidification improves after treatment with rituximab.

CASE 7

A 32-year-old man was admitted to the hospital with weakness and hypokalemia. The patient had been very healthy until 2 months previously when he developed intermittent leg weakness. His review of systems was otherwise negative. He denied drug or laxative abuse and was on no medications. Past medical history was unremarkable, with no history of neuromuscular disease. Family history was notable for a sister with thyroid disease. Physical examination was notable only for reduced deep tendon reflexes.

Laboratory Data	Admission	Baseline	Units
Sodium	139	143	meq/L
Potassium	2.0	3.8	meq/L
Chloride	105	107	meq/L
Bicarbonate	26	29	meq/L
BUN	11	16	mg/dL
Creatinine	0.6	1.0	mg/dL
Calcium	8.8	8.8	mg/dL
Phosphate	1.2		mg/dL
Albumin	3.8		mg/dL
Plasma osmolality	290		mOsm/kg
Urine osmolality	590		mOsm/kg
Urine potassium	10		meq/L
TSH 0.08 μIU/L (normal 0.2–5.39)			
Free T_4 41 pmol/L (normal 10–27)			

APPROACH TO DIAGNOSIS

This patient developed hypokalemia due to a redistribution of potassium between the intracellular and extracellular compartments; this pathophysiology was readily apparent following calculation of the TTKG. The TTKG is calculated as $(P_{osmol} \times U_{Potassium})/(P_{Potassium} \times U_{osmol})$. The expected values for the TTKG are <3 in the presence of hypokalemia and >7–8 in the presence of hyperkalemia (see also Case 2 and Case 8). Alternatively, a urinary K^+-to-creatinine ratio of >13 mmol/g creatinine (>1.5 mmol/mmol creatinine) is compatible with excessive renal K^+ excretion. In this case, the calculated TTKG was 2.5, consistent with appropriate renal conservation of K^+ and a nonrenal cause for hypokalemia. In the absence of significant gastrointestinal loss of K^+, the patient was diagnosed with a "redistributive" subtype of hypokalemia.

More than 98% of total-body potassium is intracellular; regulated buffering of extracellular K^+ by this large intracellular pool plays a crucial role in the maintenance of a stable plasma K^+ concentration. Clinically, changes in the exchange and distribution of intra- and