myocardial contractility [2], which could cause exercise-induced left ventricular dysfunction. Because myocardial recruitment is calcium-dependent [2], this abnormality is consistent with an anomalous intracellular signaling mediated by Gq protein, with the consequential abnormality of the intracellular calcium pathway we have reported [3, 4]. This defect contributes to anomalous vascular tone regulation [3, 4] and could be responsible for a generalized defect of vascular reactivity which also includes the myocardium. The presence in Bartter's or Gitelman's syndrome of an anomalous myocardial function reported by us [2], together with the observation of Bettinelli's group [1], may underscore the need to care for a possible anomaly of cardiac function in the clinical evaluation of Bartter's and Gitelman's patients that is generally underestimated.

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Reply from the Authors

Potassium (or magnesium) depletion alters cardiac excitability and prolongs the QT interval on standard electrocardiograms, which might impart an increased risk for development of arrhythmias, culminating in syncope or sudden death. Accordingly, we recently observed that the QT interval is often prolonged in Gitelman's syndrome, the most frequent and benign normotensive-hypokalemic tubulopathy. However, none of the patients had a history of unexplained loss of consciousness [1]. In addition, we reported the history of a 4-year-old boy with a normotensive-hypokalemic tubulopathy and a prolonged QT interval who suddenly died [2]. We were not able to classify the tubulopathy of the patient. In retrospect, we feel that his biochemical features strongly resembled those of a recently reported patient with a normotensive-hypokalemic tubulopathy caused by a gain-of-function mutation in the calcium-sensing receptor [3].

In their stimulating letter, Scognamiglio, Semplicini, and Calò [4] suggest that clinically relevant arrhythmias do not occur in patients with normotensive-hypokalemic tubulopathies. On the contrary, they suggest that chronic potassium and magnesium depletion might cause left ventricular dysfunction.

Recognizing that little is known about the occurrence of dangerous arrhythmias in patients with normotensive-hypokalemic tubulopathies, we recently sent a corresponding questionnaire to a group of pediatric nephrologists with clinical experience in the field of normotensive-hypokalemic tubulopathies. Furthermore, we are currently investigating ambulatory Holter monitoring, exercise testing, and echocardiography in our patients with Gitelman's syndrome.

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Ozonetherapy in a dialyzed patient with calcific uremic arteriolopathy

To the Editor: Some interesting papers on the therapy of calciphylaxis were published in 2002 [1, 2]. Here, we present the first report of successful treatment of calciphylaxis-induced ulcerations with ozonotherapy, a method not mentioned in these articles.

A 25-year-old female with Wegener's granulomatosis, hemodialyzed since 1994, manifested ulcers in her calves, thighs, and abdomen. Skin biopsy revealed calciphylaxis. Therapy, involving hemodialysis with noncalcium dialysate 5 to 6 days a week, antibiotics, and surgical debridement, failed. The patient did not tolerate hyperbaric oxygen therapy. The necrotic ulcerations enlarged and became superinfected. In 2001, we commenced treatment with ozonated autohemotherapy (O3-AHT), the modality used in our center in therapy for intermittent claudi-

cation [3]. The patient received 15 sessions of O3-AHT with ozone concentration of 50 to 70 μg/mL over 3 weeks, accompanied by local wound lavage with ozonated water. Afterwards, we observed healing of necrotic areas with granulation tissue in the abdominal region (area of the largest ulceration); therefore, the patient could undergo successful skin transplantation in this area.

The rationale for the use of O3-AHT is that ozone stimulates synthesis of platelet-derived growth factor (PDGF), transforming growth factor-β1 (TGF-β1), and interleukin 8. Locally, it acts as a potent disinfectant. O3-AHT improves local blood flow in hypoxic regions via increase of endothelial NO synthesis. All of these activities may enhance wound healing [3, 4].

We realize that O3-AHT is a controversial modality that needs better scientific support. However, given the extremely high mortality rate in patients with calciphylaxis and the fact that satisfactory therapy does not exist, the use of ozonotherapy in select serious cases may be warranted.

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