

Hif2 α indicates that this isoform regulates erythropoietin production in the adult mouse liver.¹ To the best of our knowledge, the corresponding cell-specific deletion experiment for erythropoietin-producing cells of the kidney has not been performed. However, Gruber and colleagues induced acute global deletion of both *Hif1 α* and *Hif2 α* in mice and found that the deletion of *Hif2 α* , but not *Hif1 α* , results in anemia.² If *Hif1 α* were the central isoform or merely a redundant isoform in the kidney, one might expect that *Hif1 α* deletion would result in anemia or, at least, that the *Hif2 α* deletion would not cause anemia. The observation that the *Hif2 α* deletion does cause anemia indicates that this isoform is the critical regulator of erythropoietin. The point regarding the cause of the deep venous thrombosis is well taken and will require further investigation into the question of whether it might be mediated by HIF target genes.

Perrotta and Della Ragione state that they did not find evidence of any *HIF1A* mutation in their patients with erythrocytosis, a finding that is

consistent with the results of a study we reported previously,³ but they did note an additional case of an erythrocytosis-associated mutation in the *HIF2A* gene. This observation is a further indication of the role played by HIF-2 α in regulating erythropoietin in idiopathic erythrocytosis.

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Long-QT Syndrome

TO THE EDITOR: In his discussion of the Clinical Practice vignette involving a fatal arrhythmic event in a child with the long-QT syndrome, Roden (Jan. 10 issue)¹ emphasizes the importance of rigorously screening family members in order to provide an optimal prevention strategy. The author recommends that affected persons not participate in competitive sports; he also mentions the benefit of beta-blocker therapy in these patients and the use of implantable cardiac defibrillators in the highest-risk cases. However, the current recommendations consider “lifestyle modifications,” defined by the contraindication of competitive sports activity and of all drugs known to prolong the QT interval, as a class I recommendation (level of evidence B).² According to such recommendations, education of these patients about the risk associated with certain drugs must be clearly integrated into the strategy of fatal-arrhythmia prevention. All these drugs are listed and regularly updated in the International Registry for Drug-Induced Arrhythmias (www.qtdrugs.org).

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TO THE EDITOR: Effective therapies exist for the long-QT syndrome. The use of beta-blockers should be viewed as the mainstay of therapy, as noted in the Clinical Practice article. Although there is a reduction in cardiovascular events among

patients with the long-QT syndrome who receive beta-blocker therapy, a substantial proportion of patients will have devastating events while receiving beta-blocker therapy.¹ Thus, left cardiac sympathetic denervation (LCSD) should be highlighted as well, not only as a viable therapeutic option but also as one that is distinct from and can be used as an alternative to mere beta-blockade in high-risk patients, including those who do not have a response to traditional beta-blockade. In a study of high-risk patients with the long-QT syndrome, 75% of whom had cardiovascular events despite treatment with beta-blockers, LCSD was associated with a significant reduction in the incidence of aborted cardiac arrest and syncope.² The mean yearly number of cardiovascular events in patients treated with LCSD decreased significantly, by 91%, in this study. The authors concluded that “LCSD should be considered in patients with recurrent syncope despite beta-blockade.”

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THE AUTHOR REPLIES: I agree with the emphasis placed by Marijon et al. on an integrated approach — involving many aspects of lifestyle — to the care of patients and families with the long-

QT syndrome. This includes minimizing exposure to potential triggers such as activity and drugs.

Kapoor notes the potential role of left stellate ganglionectomy in the management of the long-QT syndrome. In their 2004 report, Schwartz et al.¹ described excellent results in high-risk patients, whereas earlier reports had suggested less success.^{2,3} This difference could reflect different patient populations or differences in specific surgical approaches. In my view, ganglionectomy should be considered in patients who have recurrent arrhythmias during conventional therapies; the procedure should be performed in centers that are experienced with the technique in these patients.

Both Marijon et al. and Kapoor address management issues in the long-QT syndrome. It is important to bear in mind that the past decade has seen tremendous advances in our understanding of the fundamental basis of this disease and its subtypes. This information is only now being used in patient care, and the hope is that management guidelines will continue to evolve and improve.

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Medical Mystery: Epigastric Pain — The Answer

TO THE EDITOR: The medical mystery in the March 6 issue¹ involved an 82-year-old woman who presented with respiratory symptoms and then, 6 years later, presented with epigastric pain, nausea, and vomiting. During her first visit, an intrathoracic stomach and an asymptomatic partial gastric volvulus (Panel A, arrows) were diagnosed. The patient refused any intervention at that time. She remained asymptomatic until she presented with the epigastric pain, nausea, and vomiting. An upper endoscopic study showed twisting of gastric folds, and the endoscope could not be advanced beyond 5 cm from the gastroesophageal junction.

A barium study (Panel B) and a computed tomographic scan of the chest and abdomen (Panel C) showed an organoaxial gastric volvulus and an intrathoracic stomach (arrows). The patient continued to refuse surgical intervention, but her symptoms resolved without treatment. At a follow-up visit 12 months later, she remained free of symptoms.

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