To those of us who were practicing cardiology in the early 1960s, the reports from Jervell and Lange-Nielsen,1 Romano and colleagues,2 and Ward3 were welcome enlightenment for a few of our patients with alarming episodes of syncope and a family history of sudden death. Although Ward reported that one of his original patients responded to β-blockade and that form of therapy remains central to medical management of the long QT syndrome, it is clear that β-blockade has not been uniformly successful. Subsequently, left stellate ganglionectomy was recommended by Moss and McDonald4 for medically unresponsive cases. But symptoms and deaths have continued, with and without medical and surgical treatment,5 and most of us have concluded that we are dealing with a disease that remains enigmatic, serious, and difficult to treat effectively over a long period.

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The problem appeared to expand in 1976 when Peter Schwartz6 proposed that sudden infant death syndrome was a result of a developmental form of the long QT syndrome.6 Although this was a brilliant concept, the absence of arrhythmias in most of the infants at risk for sudden infant death syndrome provided no support for his theory of a cardiovascular etiology of sudden infant death syndrome. That is not to deny that there were occasional well-documented cases of infant death with long QT syndrome in addition to a larger number of older children and adults with that diagnosis. The clinical characteristics of these older patients have been recently described from an ongoing study by Moss, Schwartz, and colleagues.7

The report in this issue of Circulation8 by a distinguished international group of pediatric electrophysiologists is a welcome addition to our knowledge of the long QT syndrome. This report is based on the experience with 287 infants, children, and young adults, some of whom were included in the study group of Moss et al.7 Although the average age at presentation in the current study was 7 years, 20% presented at under 1 month of age. The latter group had a substantially greater rate of sudden death; 16% compared with 7% for infants who presented after age 1 month.

For the entire group, 9% presented with “cardiac arrest.” Details are lacking as to how a child with this event could be diagnosed as having long QT syndrome; a reasonable presumption is that either they were resuscitated and then diagnosed by the usual clinical criteria or the diagnosis was made retrospectively on the basis of individual and family history. Overall, the family history was positive for the long QT syndrome in 39% and for sudden death in 31%.

Garson and colleagues8 included subjects with a normal corrected QT (QS) (defined as <0.44) in their study on the basis of a positive family history for the long QT syndrome and a history in the patient of unexplained syncope, seizure, or cardiac arrest associated with inciting events typical for the syndrome (exercise or extreme emotion). Considering the variability of the QTc over time, these inclusions appear to be appropriate.

Of concern, however, is their diagnosis of long QT syndrome on the basis of a QTc only slightly >0.44 without symptoms or a positive family history. Moss and Robinson9 found that as many as 1% of a normal population 1–15 years old had a QTc of >0.46. A total of 24 of Garson et al’s patients had a QTc of <0.46. This becomes important when we consider their recommendations for prophylactic treatment of asymptomatic children.

Garson et al’s recommendation for routine prophylaxis with β-blockade, even if the patient is asymptomatic, is based on the 9% of their patients who presented with cardiac arrest as the first symptom; what they have not established is whether these patients would have survived if treated. In fact, they report that 5% of their “effectively treated” patients had sudden death. Of even more concern is the consideration that of all of their cases of sudden death, 83% occurred on treatment, and only 17% occurred on no treatment!

In addition to the socioeconomic disadvantages of β-blockade for life, there is a possibility that the treatment might be dangerous to some patients with long QT syndrome, particularly those with sinus or atrioventricular nodal disorders; Moss et al7 found that bradycardia was one of the most important risk factors for the syndrome. In the present study, bradycardia was present on routine ECG in 20% of all subjects, and with treadmill testing, 36% had maximal heart rates below normal. An additional 5% of their patients had second- or third-degree atrioventricular block. Questions occur, then, as to whether binodal disease is a significant part of the long QT syndrome and whether β-blockade, particularly with large doses of propranolol, might worsen the chances of having syncope or death. In considering treatment of asymptomatic individuals, it

The opinions expressed in this editorial comment are not necessarily those of the editors or of the American Heart Association.

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should be remembered that none of the therapies of β-blockade, ganglionectomy, or pacemaker implantation showed a significant beneficial effect in either univariate or multivariate analysis in the study by Moss and colleagues.  

One of the more useful aspects of this report is the characterizations of high- and low-risk groups with long QT syndrome. Low risk is found for asymptomatic children with a normal QT, and a positive family history, as might be predicted from Mendelian inheritance because 50% of these children will not have the disorder. Although there were three patients who developed serious symptoms or death who initially had a normal QTc, all three developed a QTc of >0.46 on follow-up. None of the 14 who continued to demonstrate a QTc of <0.44 developed symptoms or death. It is therefore difficult to see the logic of starting life-long β-blockade on an asymptomatic patient with a normal QTc, as favored by the authors.

The high-risk group was found to have a QTc of >0.60, bradycardia for age, and “propranolol failure.” (It would be difficult to determine if the latter was a cause or an effect of the disease status.)

Assuredly, almost all cardiologists would recommend treatment with β-blockade for symptomatic patients with long QT syndrome. However, moderate doses may be safer than large doses by lessening the trend toward bradycardia. No data exist, to my knowledge, demonstrating that large doses are more effective. Although the risk of death for asymptomatic children is 4%, there is no evidence that treatment is effective in preventing death; for the answer to that question, we need a randomized clinical trial.

Finally, we probably all can agree that long QT syndrome, taken as a whole, is a serious disease at any age and that treatment is, at best, only partly effective. Let us hope for further elucidation of the basic mechanism and a more specific and effective treatment. In the meantime, “first, do no harm” seems particularly pertinent for this disorder.

References

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Long QT syndrome in children.
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