tricular volume determinations in children: Normal values and observations with volume or pressure overload. Circulation 47: 144, 1973
16. Ernst RW, Lee YK, Lillehei CW: Cardiac output studies in dogs with normal right ventricle and enlarged right ventricular outflow tract with or without pulmonary insufficiency. Surg Forum 110: 222: 1960

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Potential Role of QT Interval Prolongation in Sudden Infant Death Syndrome

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SUMMARY To investigate the possibility that a genetically transmitted cardiac abnormality is involved in the genesis of the sudden infant death syndrome (SIDS), 42 sets of parents who had at least one infant with SIDS were studied by electrocardiography. Prolongation of the QT interval was present in at least one member of 11 (26%) sets of parents. In families in which QT interval prolongation was found in a parent, prolonged QT interval was also present in 39% of the siblings of infants with SIDS, suggesting an autosomal dominant pattern of inheritance. In addition, an infant with “near-miss” SIDS showed marked prolongation of the QT interval. Thus, our data suggest that prolonged QT interval may play a role in a considerable proportion of sudden and unexpected infant deaths. However, definitive confirmation of the relation between QT interval prolongation and SIDS will require large prospective investigations.

SUDDEN INFANT DEATH SYNDROME (SIDS) is the largest single cause of death between one week and one year of age in the United States, accounting for the deaths of approximately 10,000 apparently well infants annually.1, 2 Although numerous theories have been proposed,3–8 the primary mechanisms responsible for SIDS are still unknown. Recently, many investigators have incriminated respiratory and cardiac mechanisms such as chronic hypoxemia,9 7 prolonged apnea,10 dysfunction of central nervous system reflexes that are responsible for stabilization of cardiac rate,9 or cardiac arrhythmias10, 11 as the cause of SIDS. We have considered the possibility that prolonged QT interval syndrome,11–15 a genetically transmitted cardiac condition known to cause sudden death in children11–15 and in infants,14–21 is related to SIDS. The present study describes our investigation into the possible relation between prolonged QT interval syndrome and sudden, unexplained death in infancy.
Methods

Family Studies

Since prolonged QT interval syndrome may be transmitted as an autosomal dominant trait, we hypothesized that evidence of this disease might be present in parents of infants with SIDS, if this condition was responsible for the infant's death. Therefore, 42 sets of parents who had at least one infant with SIDS (documented by the characteristic clinical and pathologic features of this condition) were studied by electrocardiography. Subjects were selected from organizations (in the Washington, Baltimore and Philadelphia metropolitan areas) of parents who had an infant with SIDS. All parents in these organizations were informed of this investigation and those who volunteered were included in the study. Parents ranged in age from 19 to 59 years (mean 32). Electrocardiograms were also performed on all siblings of infants with SIDS from eight families (23 siblings) in which one parent was shown to have a prolonged QT interval and on all siblings of infants with SIDS from seven other families (18 siblings) in which neither parent had a prolonged QT interval. The siblings ranged in age from 2 to 15 years (mean 8).

Standard 12 lead electrocardiograms were recorded in each subject in the supine position under basal conditions in the waking state. Marquette series 3000-A and Sanborn 100 Viso-Cardette electrocardiograph recorders were used. All electrocardiograms were recorded at a speed of 25 mm/sec. Calibration of the electrocardiographic recorders used in this study demonstrated that the paper speed of each recorder was within 2% of 25 mm/sec. The frequency response of the electrocardiographic recorders was uniform (± 3 dB) from 0.05 Hz to 80 Hz.

Each parent with prolongation of the QT interval (as described below) had normal serum potassium, calcium, sodium, chloride, carbon dioxide and magnesium. No subject was, at the time of study, receiving medications known to alter the QT interval. Furthermore, no subject had evidence of cardiovascular abnormalities known to alter the QT interval such as conduction defect, left ventricular hypertrophy, congestive heart failure, myocardial or valvular disease, pericarditis, cor pulmonale, cerebral disorder, or previous myocardial infarction.

Measurement of QT Interval

QT intervals were measured in standard lead II. The maximal QT interval and an average of QT intervals (derived by measuring six to fourteen consecutive beats) were obtained for each subject. These methods of measurement were employed to permit comparison of our values with those reported in several commonly used studies that define the normal QT interval.

The QT interval was measured from the onset of the Q wave (or from the onset of the R wave if no Q wave was present) to the termination of the T wave (at the point where the downslope of the T wave met the isoelectric baseline). Care was taken to avoid including U or P waves in the measurement of QT intervals. We considered unsatisfactory for measurement any beat in which: 1) the QRS complex was abnormally wide, 2) T waves were notched, bifid, biphasic, flat or inverted, or 3) muscle tremor artifact was present or the baseline was irregular. Furthermore, QT intervals were not measured in premature beats or in areas of the tracing showing marked sinus arrhythmia. Heart rate was calculated over five consecutive beats in the same segment of the tracing that the QT interval was measured.

QT intervals were measured in the majority of tracings on two to four different occasions by the same observer without knowledge of the previous measurements. Only slight deviations (± 0.02 sec) in the duration of the QT interval were noted among the measurements; on no occasion did these slight variations in the measurement of QT interval constitute the difference between a normal or abnormal QT interval.

Because there is no general agreement regarding the standards of normal QT interval, our measured values for adults were compared to two normal populations and our values for children were compared to three normal populations. For adult subjects (18 years of age and older), the maximal measured QT interval in lead II was compared to the normal standards of Simonson et al., the average QT interval in lead II was compared to the normal standards of Ashman and Hull. QT intervals in adults were considered prolonged if the maximal measured QT interval was at or exceeded the 97.5 percentile of Simonson's normal population or if the average QT interval was at or exceeded the 97th percentile of Ashman and Hull's normal population. In addition, the maximal and average QT intervals were corrected for heart rate (QT-c) by dividing the measured QT interval by the square root of the RR interval (a method first described by Bazett).

For children and infants, the maximal QTc was compared to the normal standards of Cammon. The average QT interval was compared to the normal standards of Alimurung et al. and of Fraser et al. QT intervals in children were considered prolonged if the maximal QTc was at or exceeded the 97th percentile of McCammon's normal population, if the average QT interval was at or exceeded the 97th percentile of Alimurung's normal population, or if the average QT interval exceeded the expected value by two standard errors, using the method of Fraser et al. Since the study of McCammon does not provide data for percentiles over the 90th, the 97th percentile was estimated assuming the McCammon results were derived from a normally distributed data base. Where appropriate, data were analyzed statistically using the two-tailed Fisher's exact test.

Infant with "Near-miss" SIDS

We hypothesized that if prolonged QT interval were responsible for some instances of SIDS, then the presence of this electrocardiographic abnormality during life in infants with "near-miss" SIDS would provide some evidence for our hypothesis. Therefore, an apparently normal infant who survived a cardiorespiratory arrest at seven weeks of age was studied. Electrocardiograms obtained in this infant in the waking state were recorded and interpreted in the same manner as described above. Electrocardiograms were also obtained in 18 other members of the infant's family, including her parents and siblings.
TABLE 1. QT Interval Prolongation in Parents of Infants with SIDS

| Subject/ (yrs) | Sex | HR (beats/min) | Maximal QT (sec) | Maximal QT UL* | Average QT (sec) | Average QT UL† | Average QT t‡ | Prolonged§ (Ashman | Prolonged‡ (Ashman  |
|---------------|-----|----------------|------------------|---------------|-----------------|----------------|----------------|-----------------|-------------------|-------------------|
| S.G. / 39 / F |     | 67             | 0.46             | 0.41          | 0.49            | 0.44           | 0.41           | 0.47            |                    | +                 |
| C.M. / 40 / M |     | 95             | 0.38             | 0.39          | 0.48            | 0.36           | 0.35           | 0.45            | 0                 | +                 |
| E.W. / 35 / M |     | 84             | 0.40             | 0.38          | 0.47            | 0.38           | 0.37           | 0.45            | +                 | +                 |
| R.M. / 32 / M |     | 61             | 0.46             | 0.43          | 0.47            | 0.44           | 0.42           | 0.45            | +                 | +                 |
| F.H. / 26 / F |     | 78             | 0.40             | 0.39          | 0.46            | 0.38           | 0.39           | 0.43            | +                 | 0                 |
| C.W. / 34 / F |     | 71             | 0.42             | 0.41          | 0.46            | 0.40           | 0.40           | 0.44            | +                 | +                 |
| A.M. / 31 / F |     | 90             | 0.38             | 0.38          | 0.46            | 0.38           | 0.36           | 0.46            | +                 | +                 |
| R.R. / 59 / M |     | 64             | 0.44             | 0.42          | 0.46            | 0.41           | 0.41           | 0.43            | +                 | +                 |
| S.K. / 26 / F |     | 77             | 0.41             | 0.39          | 0.46            | 0.39           | 0.39           | 0.44            | +                 | +                 |
| D.C. / 36 / M |     | 73             | 0.41             | 0.40          | 0.45            | 0.40           | 0.39           | 0.44            | +                 | +                 |
| P.C. / 20 / F |     | 84             | 0.38             | 0.38          | 0.45            | 0.36           | 0.37           | 0.43            | +                 | 0                 |
| E.K. / 39 / M |     | 73             | 0.40             | 0.40          | 0.44            | 0.39           | 0.39           | 0.43            | +                 | +                 |
| R.L. / 23 / F |     | 69             | 0.41             | 0.41          | 0.44            | 0.39           | 0.41           | 0.42            | +                 | +                 |

Subjects with initials in italics are husband and wife.

*Values given are those for the 97.5 percentile of the normal population of Simonson et al.29
†QT, calculated by dividing the measured QT interval by the square root of the RR interval (method initially described by Bazett34).
‡Values given are those for the 97th percentile of the normal population of Ashman and Hull25 27
§Prolonged QT interval is defined as a value at or beyond the 97.5 percentile.
††Another of two infants with SIDS; all other parents included in the table had one infant with SIDS.
+ = QT interval prolonged; 0 = QT interval normal.
Abbreviations: HR = heart rate (beats per minute); UL = upper limits of normal.

Results

Family Studies

Using the normal standards of Simonson et al.29 for comparison, electrocardiograms showed relatively mild prolongation of the QT interval in one member of ten sets of parents. In one other parental set both members had prolongation of the QT interval (table 1). Maximal QT intervals for all parents are plotted against corresponding R-R intervals in figure 1. While the QT intervals of most parents cluster about the predicted mean (from the linear regression analysis of Simonson29), those considered abnormal appear to stand apart as a separate population.

The symmetrical and relatively close grouping of the normal QT intervals about the predicted mean tends to dispute the possibility that the 12 instances of QT prolongation are due to differences between our technique of QT interval measurement and that of Simonson: 1) a systematically long reading of QT intervals relative to Simonson would displace all QT intervals upward relative to the prediction line, and 2) if our prevalence of prolonged QT interval represented an artifact due to a greater degree of scatter than experienced by Simonson, then we might have expected to show a greater number of shorter as well as longer QT intervals in our study population.

When the relatively small number of 12 individuals in our study group with QT interval prolongation are excluded, the remaining population with normal QT intervals can be com-

![Figure 1. Maximal QT interval (vertical axis) for each of the 84 parents studied is plotted against corresponding R-R interval (horizontal axis). QT interval lengths at or above the 97.5 percentile defined by the data of Simonson et al.29 are designated by unfiled circles while the remaining QT intervals are shown as filled circles. Two subjects with normal QT interval appear to be among the subjects with prolonged QT interval due to the effect of age on normal QT interval. A regression line calculated from Simonson's results in 960 normal subjects29 indicates the predicted mean.](https://example.com/figure1.png)
pared to the published normal population of Simonson et al.\textsuperscript{29} Thus, QT intervals in the apparently normal portion of our population yield a regression line of QT interval related to RR interval (slope = 0.130; intercept = 0.246) that is indistinguishable from a similar line (slope = 0.140; intercept = 0.242) that Simonson et al.\textsuperscript{29} derived from their population of 960 normal adults. Furthermore, the standard error of the estimate was similar for the apparently normal portion of the present study group (0.020) and the normal population of Simonson et al. (0.016).\textsuperscript{29} QT prolongation was not associated with any particular R-R interval length, although subjects with the slowest heart rates tended to exhibit the greatest degree of abnormality. Using the normal standards of Ashman and Hull\textsuperscript{28} for comparison, at least one member of nine sets of parents showed prolonged QT interval, including nine parents identified as abnormal by Simonson's criteria and one parent in whom the QT interval was at the upper limits of normal compared to the standards of Simonson et al.\textsuperscript{29}

Thus, the prevalence of QT interval prolongation in our study population was 12 of 84 subjects (14%) using the standards of Simonson et al.\textsuperscript{29} and ten of 84 subjects (12%) using the standards of Ashman and Hull.\textsuperscript{28, 27} The prevalence of QT interval prolongation, using either standard, differed significantly ($P < 0.001$) from that expected (2.5%) when the 97.5 percentile is employed as the upper limit of normal. Subjects with QT interval prolongation did not differ significantly in age from subjects with normal QT intervals.

Two of the subjects with QT interval prolongation had other electrocardiographic abnormalities, including one subject with left anterior hemiblock and nonspecific ST-segment and T-wave abnormalities and one with nonspecific ST-segment and T-wave abnormalities. Electrocardiograms with QT interval prolongation showed normal sinus rhythm without frequent premature beats or other arrhythmias. In no tracing were T waves abnormally peaked; electrical alternation of the T wave\textsuperscript{29} was not present. One member of three other parental sets (in which QT interval was not prolonged) showed electrocardiographic abnormalities, including one with left anterior hemiblock, one with first degree atrioventricular block, and one with nonspecific ST-segment and T-wave abnormalities. The electrocardiographic findings in the 42 sets of parents who had infants with SIDS are summarized in figure 2.

To investigate further the possible genetic transmission of prolonged QT interval, electrocardiograms were performed in 23 siblings of infants with SIDS; these siblings were members of eight families in which one parent had a prolonged QT interval. Electrocardiograms showed relatively mild QT interval prolongation in nine (39%) of the 23 siblings using the normal standards of McCammon\textsuperscript{28} for comparison (fig. 3). Maximal QTc in these nine children ranged from 0.43 to 0.48 sec (mean 0.45). Children with prolonged QT interval were found in six of the eight families studied. When the normal standards of Fraser et al.\textsuperscript{30, 31} were used for comparison, eight children showed a prolonged QT interval, including six children who were abnormal by McCammon's criteria and two children in whom the QT interval was at the upper limits of normal compared to the standards of McCammon.\textsuperscript{28} When the normal standards of Alimurung et al.\textsuperscript{32} were used, two children showed prolonged QT interval; both of these children also had prolonged QT interval by the criteria of McCammon\textsuperscript{28} or Fraser et al.\textsuperscript{30, 31} The electrocardiograms of children with prolonged QT interval showed normal sinus rhythm without marked sinus arrhythmia, premature beats, or other arrhythmias. In no tracing were the T waves abnormally

\begin{figure}
\centering
\includegraphics[width=\textwidth]{sets_of_parents}
\caption{Diagram summarizing electrocardiographic data in 42 sets of parents who had infants with SIDS. Abn = abnormal; NL = normal; ST-T = nonspecific ST-segment and T-wave abnormalities; 'QT = prolongation of QT interval; LAH = left anterior hemiblock; $1^\circ$ AVB = first degree atrioventricular block. Numbers in circles refer to parental sets in which at least one member had an electrocardiographic abnormality.}
\end{figure}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{dead_of_sids}
\caption{Two family diagrams showing distribution of affected (prolonged QT interval) and unaffected (normal QT interval) members. In the family diagram in the bottom panel, offspring 3 with prolonged QT interval and offspring 4 with SIDS are fraternal twins. Age (in years) of each subject is shown in parentheses; longest QTc for children and average QTc for adults are shown under the age.}
\end{figure}
peaked or markedly inverted. Each electrocardiogram performed on 18 siblings of infants with SIDS from seven families in which neither parent had prolonged QT interval showed normal QT interval. The difference in the prevalence of prolonged QT interval in the siblings from families with an affected parent (9 of 23) compared to the prevalence of prolonged QT interval in siblings from families without affected parents (0 of 18) was significant ($P < 0.01$). QT interval data in siblings of infants with SIDS are summarized in table 2.

None of the adults or children studied had overt clinical evidence of a hearing deficit, nor was a family history of deafness present in other members of their families. In 37 of the 42 families studied no parent or child (other than the infants who were the index cases in this study) had experienced syncope or sudden death. In two families (including one in which QT interval prolongation was present) one sibling of the index case had documented SIDS. In three other families (including two in which QT interval prolongation was present) an infant who was a cousin of the index case died suddenly and unexpectedly (necropsy examination was not performed).

"Near-miss" SIDS

Electrocardiograms from the infant with "near-miss" SIDS showed marked prolongation of the QT interval following a cardiorespiratory arrest with ECG documented asystole at 7 weeks of age (fig. 4); the electrocardiograms were otherwise normal (fig. 5). There was no clinical evidence of heart disease and the patient was not given medications known to prolong the QT interval. The parents of this infant had normal QT intervals (mother's maximal QT$_c$ = 0.41 sec; father's maximal QT$_c$ = 0.38 sec); a mildly

![Figure 4](http://circ.ahajournals.org/)

**Figure 4.** Serial electrocardiographic tracings (standard lead II) from infant with "near-miss" SIDS. Cardiorespiratory arrest occurred on 3-12-73 (7 weeks of age). Five tracings at the top were taken during the subsequent hospitalization. The two tracings at the bottom (6-1-73 and 1-22-75) were taken during outpatient evaluations at four months and two years of age, respectively. Electrocardiographic tracings were retouched for enhanced clarity.

![Figure 5](http://circ.ahajournals.org/)

**Figure 5.** Standard 12 lead electrocardiogram recorded in the infant with "near-miss" SIDS four days after cardiorespiratory arrest. Tracing is normal except for prolongation of the QT interval (longest QT$_c$ in standard lead II = 0.53 second).
prolonged QT interval (maximal QTc = 0.45 sec) was present in only one of 18 family members surveyed, a 10-month-old nephew of the infant. Because of the unique aspects of this case, the clinical features are described.

This female child was the product of a full-term pregnancy complicated by premature rupture of the membranes. Delivery was uncomplicated and the birth weight was 7 lbs. 1 oz. The infant was examined by her pediatrician at six weeks of age and was thought to be in good health. One week later the child was sleeping in a sitting position (in an infant seat) when she was noted by her parents to make "throaty noises" followed by several inspiratory gasps. The child was initially rigid but soon became limp. Her color became ashen gray. At this time, the parents noted that the infant was not breathing and attempted to revive her by mouth-to-mouth resuscitation and external cardiac massage. The infant was taken by ambulance and reached the local hospital emergency room in about 30 minutes. At this time, she was apneic and there were no audible heart sounds. The electrocardiogram revealed asystole. Emergency measures were instituted immediately, including intracardiac epinephrine and intravenous sodium bicarbonate, atropine, lidocaine and isuprel. These therapeutic measures produced ventricular fibrillation within a few minutes. Electrical DC defibrillation restored normal sinus rhythm.

Cardiovascular examination performed two hours after admission with the patient in relatively stable condition showed blood pressure 105/60 mm Hg, heart rate 150/min, respiratory rate 60/min and temperature 99°F. Lung fields were clear to auscultation. First and second heart sounds were normal; no murmurs were audible. There was no evidence of congestive heart failure.

Normal results were obtained from the following laboratory studies: white blood cell count, serum calcium, sodium, chloride, blood urea nitrogen and glucose. Serum potassium ranged from 4.0 to 5.5 mEq/L (normal range 3.5 to 5.3 mEq/L) on seven different determinations. Lumbar puncture was performed; analysis of the cerebrospinal fluid showed no abnormalities. Urinalysis was normal. Chest radiograph showed a normal heart size, normal pulmonary vascular markings and a mild right perihilar infiltrate. Cultures of cerebrospinal fluid, blood, throat and nasopharynx showed no growth of organisms.

Electrocardiographic tracings of standard lead II obtained during the hospitalization and the period of follow-up are shown in figure 4. Maximal QT, ranged from 0.50 to 0.57 second during the period of hospitalization; a trend toward diminishing QT interval with time was apparent. In each instance the QT interval was markedly prolonged compared to normal standards.22, 40, 41 The heart rate during hospitalization ranged from 90 to 160 beats/min (normal range 80 to 180). We cannot exclude the possibility that the prolonged QT interval present in this infant was an effect rather than a cause of the cardiac arrest, since little is known of the effect of cardiac arrest on QT interval. However, an electrocardiogram performed at a follow-up examination at 4 months of age (over two months after the cardiac arrest) (fig. 4) showed persistent prolongation of the QT interval (longest QT, = 0.50 second). Furthermore, none of the electrocardiograms recorded in this infant showed evidence of myocardial ischemia or injury. The patient has remained in good health, exhibited normal developmental landmarks, and has had no overt clinical evidence of a hearing deficit. At 2 years of age she was evaluated at the National Heart and Lung Institute. An echocardiogram was normal with the ventricular septum and posteriorbasal left ventricular wall each 5 mm in thickness. Electrocardiogram (fig. 4) showed a QT interval at the upper limits of normal. Physical examination was normal. There is no family history of sudden death, syncope or deafness in the family.

Discussion

The results of this study suggest that a considerable proportion of first degree relatives of infants with SIDS have prolongation of the QT interval on electrocardiogram. Prolonged QT interval syndrome13, 14, 22, 38, 39 is an inheritable condition that is manifested by cardiac arrhythmias, syncopal spells and sudden death (in addition to an abnormally long QT interval on electrocardiogram). When prolonged QT interval syndrome is associated with congenital bilateral high frequency deafness it is apparently transmitted as an autosomal recessive trait and is known as Jervell and Lange-Nielson syndrome;24 when not associated with deafness prolonged QT interval syndrome is transmitted as an autosomal dominant trait and is referred to as Romano-Ward syndrome.14, 22 The syncopal spells (and presumably sudden death) in prolonged QT interval syndrome are due to arrhythmias (i.e., asystole, ventricular fibrillation or ventricular tachycardia)16, 17, 40 that are probably initiated by premature beats arriving during the lengthened vulnerable period of electrical recovery.17, 41, 42 Most reported sudden deaths in patients with prolonged QT interval syndrome occurred in older children or adults; however, several infants from families with this condition have been reported to die suddenly or experience their initial episode of syncope during the first year of life (i.e., in the SIDS age group).14, 21 Other authors have noted an association of sudden death and prolonged QT interval syndrome in infancy and have postulated a pathogenic link between SIDS and prolonged QT interval syndrome.43 47 Our finding that relatively mild QT interval prolongation is present in parents and siblings of infants with SIDS suggests a relation to the Romano-Ward type of prolonged QT interval syndrome. It should be emphasized, however, that major differences exist between families with infants dying of SIDS and those with Romano-Ward syndrome: 1) unlike families with Romano-Ward syndrome, those with SIDS rarely have members (other than the infant with SIDS) who experience syncope episodes or sudden death; and 2) the magnitude of QT interval prolongation present in asymptomatic first degree relatives of infants with SIDS, as demonstrated in this study, was less than that reported for asymptomatic relatives of patients with Romano-Ward syndrome in some studies.32, 34 However, other studies of the Romano-Ward syndrome have shown that asymptomatic relatives have mild QT interval prolongation12, 46, 47 similar to the values we observed in the relatives of infants with SIDS.

It has been suggested that the QT interval is normally lengthened in infants during sleep.26 However, all electrocardiograms that we obtained in adults, children, and the "near-miss" infant were recorded in the waking state. This excludes the possibility that the QT interval prolongation reported in this study was due to the sleeping state. There are obvious interpretative uncertainties in linking the relatively mild prolongation of the QT interval present in first degree relatives of certain infants with SIDS demonstrated in this study to the mechanism responsible for the infant's death. Obviously, definitive evidence that these conditions are linked requires data obtained directly from the infants during life. However, since infants with SIDS are invariably considered to be healthy prior to their death, electrocardiograms are almost never obtained in these babies.

In this regard, our finding of marked prolongation of the QT interval in an infant with "near-miss" SIDS is confirmatory data that an association between SIDS and prolonged QT interval may exist in some infants. Indeed had this patient died, she most certainly would have been considered an example of SIDS. The absence of QT interval...
prolongation in most members of this infant's family suggests that either the genetic penetrance of QT interval prolongation in this family was incomplete or that the "near-miss" infant demonstrates a nongenetic form of QT interval prolongation. Indeed, there have been reports of families in which one member demonstrated typical QT syndrome, but all other family members were asymptomatic and had normal QT intervals.12, 43

Nevertheless, prospective studies in which electrocardiograms can be obtained in large numbers of apparently normal newborns will be necessary to confirm a causal relation between prolonged QT interval and SIDS. Furthermore, it should be emphasized that it is likely that SIDS is not a single clinicopathologic entity and that several etiologic mechanisms (in addition to prolonged QT interval) may be capable of inducing sudden death during this particularly vulnerable period of infancy.

If prolonged QT interval is an important factor in SIDS, it may operate in the following ways: 1) the abnormally long QT interval may be a primary mechanism causing death in infants with SIDS in much the same way that it does in patients with prolonged QT interval syndrome (i.e., presumably by predisposing to ventricular arrhythmias); 2) prolonged QT interval may convey susceptibility to ventricular arrhythmias or sudden death that is ultimately triggered by an environmental factor (e.g., respiratory infection); 3) prolonged QT interval may be a secondary manifestation of a primary central nervous system abnormality.

It has been demonstrated that the QT interval lengthens in certain cerebral disorders.11, 12, 13, 37, 44, 45, 49 Stimulation of the left stellate ganglion or ablation of the right stellate ganglion in dogs produces prolongation of the QT interval,29 and cooling or ablation of the right stellate ganglion in dogs lowers the ventricular fibrillation threshold.28 The fact that syncopal spells in patients with prolonged QT interval syndrome often are precipitated by excitement, fright or physical exertion suggests that in those patients and conceivably in certain infants with SIDS (who may have QT interval prolongation) ventricular arrhythmias may be induced by sudden sympathetic neural stimulation of the myocardium.44

The analysis of our data is based on the assumption that clear distinctions can be made between normal and abnormal QT intervals. However, it should be emphasized that certain difficulties are associated with measurement and interpretation of the QT interval. In both normal subjects and patients with prolonged QT interval syndrome, the QT interval is relatively labile,11, 23, 28, 48 tends to decrease with age, and appears to be influenced by central nervous and sympathetic neural activity. In addition, the difficulties in exact determination of the beginning and end of the QT interval in a given complex are well recognized.28 Therefore, although the results of this study suggest a role for prolonged QT interval in some instances of SIDS, our conclusions regarding the importance of this association should be considered with these reservations in mind.

In conclusion, we have found that a considerable number of first degree relatives of infants with SIDS, as well as an infant with "near-miss" SIDS, showed prolonged QT interval on electrocardiogram. Although our results are not definitive, they do suggest that cardiac mechanisms related to prolonged QT interval syndrome are causally related to a substantial number of sudden and unexplained infant deaths. Most importantly, these data suggest a potentially important area for future prospective investigations.

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References


PAROXYSMAL SUPRAVENTRICULAR TACHYCARDIA

Is the Atrium a Necessary Link?

MARK E. JOSEPHSON, M.D., AND JOHN A. KASTOR, M.D.

SUMMARY Whether or not the atrium plays an essential role in initiating and/or sustaining atrioventricular (A-V) nodal re-entrant tachycardia was evaluated in eight patients. In all eight patients, the atrium could be rendered refractory to retrograde atrial echoes during the tachycardia without interrupting the arrhythmia. This was accomplished by introducing atrial premature depolarizations prior to the time the atrium would normally be retrogradely depolarized by atrial echoes. In one patient, two atrial premature depolarizations could be introduced, producing A-V dissociation, without terminating the tachycardia. In another patient, the tachycardia could be initiated without an atrial echo. Our data suggest that most, if not all of the atrium is unnecessary for the initiation and maintenance of A-V nodal re-entrant supraventricular tachycardia.

MOST CASES of paroxysmal supraventricular tachycardia are initiated and sustained through re-entry within the atrioventricular (A-V) node.1-3 Whether or not the atria form a portion of the re-entrant pathway remains unsettled. The present investigation of eight patients demonstrated that in each case no portion of the atrium recorded by our electrode catheters was required to sustain A-V nodal re-entrant supraventricular tachycardia and in one the atrium did not play an essential role in initiating the arrhythmia.

Methods, Materials, and Clinical Patient Information

Eight patients were studied in the nonsedated postabsorptive state after informed consent was obtained (table I). All had symptomatic supraventricular tachycardia (SVT), and none demonstrated evidence of pre-excitation. No patient was taking antiarrhythmic drugs at the time of the study.

A quadripolar electrode catheter was introduced percutaneously into an antecubital and/or femoral vein and positioned under fluoroscopic control against the lateral wall of the high right atrium and/or the coronary sinus. The proximal pair of electrodes was used to record a high right atrial or coronary sinus electrogram, while the distal pair was used for atrial stimulation. A bipolar electrode catheter

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