
Preeminence of the Left Stellate Ganglion in the Long Q-T Syndrome

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SUMMARY In seven patients with Romano-Ward syndrome, stellate ganglion block or stimulation and pharmacologic interventions were made to assess their influence on duration of the Q-T interval, electrical alternation of the T wave and ventricular tachydysrhythmias. Left stellate ganglion block and right stellate ganglion stimulation shortened Q-T interval, abolished alternans phenomena and suppressed tachydysrhythmias. Propranolol and phenytoin had a similar effect. In contrast, right stellate ganglion block, left stellate ganglion stimulation and prior administration of quinidine and procainamide had an opposite effect. These responses resemble observations in animal models which suggest that excessive or unopposed activity of the left, or subnormal activity of the right stellate ganglion, or both, account for the pathophysiologic manifestations of the long Q-T syndrome. They are also consistent with clinically correlated, cardiac neuropathologic findings in these patients. An analogous but acquired dysautonomia involving the left stellate ganglion and ischemic left ventricle may precipitate sudden coronary death.

AFTER THE INITIAL RECOGNITION of the long Q-T syndromes,1-3 subsequent clinical observations,4 cardiac neuropathologic correlations,5 experiments in animal models,6, 7 manipulations of the human stellate ganglia,8 and detailed surveys8, 10 have indicated remarkable changes of length in the Q-T interval of the ECG during experimental interventions and in various clinical situations. Experimental reproduction of the long Q-T syndrome in cats7 supported the hypothesis6, 10 that congenitally subnormal activity of the right stellate ganglion combined with reflex overactivity of the left stellate ganglion may cause the prolonged Q-T interval, increased excitability, ectopy and vulnerability to fibrillation of the ventricles of patients with the long Q-T syndrome. The abolition of syncope after excision of the left stellate ganglion in 11 patients unresponsive to medical treatment7, 11 also supports the hypothesis of imbalanced cardiac influences from the stellate ganglia.6, 10 This study examines the responses of the corrected Q-T interval of the ECG, of the phenomena of alternans of the Q-T interval and T wave, and of ventricular ectopy, ventricular tachycardia (VT) and ventricular fibrillation (VF) during interventions which influenced individually or collectively the stellate ganglia in seven patients with the Romano-Ward type of long Q-T syndrome.12

Materials and Methods

Patients

The data on the seven patients are summarized in table 1. All had repetitive syncope in adult life, ventricular ectopy, and periodic spontaneous alternation of the duration of the Q-T interval and of the voltage and duration of the T wave. None had ultrasonic evidence of hypertrophy of the interventricular septum. Case 4 had a normal echocardiogram at presentation, but showed prolapse of the mitral valve 2.5 years later. Cases 2, 3 and 6 had auscultatory signs compatible with mitral prolapse but normal echocardiograms. Syncope and ectopy may have been related to mitral prolapse,13, 14 but it is unlikely, since mitral prolapse is rarely detected in Romano-Ward syndrome.15 All cases met criteria for the Romano-Ward variant.2, 3 None took psychotropic drugs known to cause ectopy or ECG changes.14 Cases 5 and 7 may represent the long Q-T syndrome unmasked by stress. Both had delirium tremens before onset of symptomatic ventricular ectopy. In the absence of acute intoxication and of hypomagnesemia, both had alternation of the Q-T interval and T wave similar to previous description.17
Pharmacologic Experience Before Stellate Ganglion Intervention

To prevent syncope and to suppress VT and VF, six patients received intravenous loading doses of propranolol 0.1 mg/kg and phenytoin 5–10 mg/kg. Since severe asthma and allergy precluded treatment with propranolol in case 3, phenytoin alone was used. After stabilization for several days, either drug was withdrawn to clarify the efficacy of each agent alone. Subsequent increments of these drugs yielded the final therapeutic regimen, using as end points the abolition of syncope, alternation of the T wave, and VT and VF (table 1). Absolute suppression of ventricular ectopy was not required if the preceding end points were achieved. Each patient’s drug regimen at the time of each stellate ganglion study is shown in tables 2–5. When VT and VF were not alleviated by propranolol and phenytoin in case 1, bretylium tosylate was successfully substituted. In case 2, therapy was stopped by the patient without medical consultation, and the stellate ganglion interventions were made before resumption of the treatment. Only in case 5 did syncope and ectopy remain suppressed after withdrawal of phenytoin. This patient underwent left stellate ganglion block 18 hours after a dose of propranolol and 2 weeks after recovery from syncope resulting from repetitive VT and VF.

Before referral, four patients had taken quinidine or procainamide. No patient was deliberately experimentally subjected to either drug. These clinical, ECG and pharmacologic observations were included. In case 7, we could evaluate stellate ganglion intervention during acute exposure to procainamide. After an intravenous loading dose of procainamide 0.6 g to suppress intermittent VT, this dysrhythmia apparently worsened temporally. Left stellate ganglion block was done immediately and 2.5 hours later, after recurrence of VT. When VT recurred 8 hours later, a temporary, transvenous, bipolar, right ventricular endocardial

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**Table 1. Patients with Long Q-T Syndrome**

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (years)</th>
<th>Race</th>
<th>Sex</th>
<th>Q-Tc (sec)</th>
<th>VT</th>
<th>VF</th>
<th>Childhood faint</th>
<th>Audiogram</th>
<th>Familial long Q-Tc</th>
<th>Signs of mitral prolapse</th>
<th>Echocardiogram</th>
<th>Final treatment</th>
<th>24-hour dose (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>22</td>
<td>W</td>
<td>F</td>
<td>0.53</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Bretylium tosylate</td>
</tr>
<tr>
<td>2</td>
<td>38</td>
<td>W</td>
<td>F</td>
<td>0.52</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>NA</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>Phenytoin 0.3</td>
</tr>
<tr>
<td>3</td>
<td>54</td>
<td>W</td>
<td>F</td>
<td>0.69</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>NA</td>
<td>-</td>
<td>Phenytoin 0.4</td>
</tr>
<tr>
<td>4</td>
<td>23</td>
<td>W</td>
<td>F</td>
<td>0.70</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>NA</td>
<td>-</td>
<td>Phenytoin 0.4</td>
</tr>
<tr>
<td>5</td>
<td>29</td>
<td>W</td>
<td>M</td>
<td>0.52</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Propranolol 0.08</td>
</tr>
<tr>
<td>6</td>
<td>46</td>
<td>W</td>
<td>F</td>
<td>0.71</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Propranolol 0.08</td>
</tr>
<tr>
<td>7</td>
<td>47</td>
<td>B</td>
<td>M</td>
<td>0.59</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>NA</td>
<td>NA</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Phenytoin 0.3</td>
</tr>
</tbody>
</table>

Abbreviations: VT = ventricular tachycardia; VF = ventricular fibrillation; W = white; B = black; M = male; F = female; NA = not ascertainable.

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**Table 2. Right Stellate Block and Q-Tc Interval**

<table>
<thead>
<tr>
<th>Case</th>
<th>t test</th>
<th>Block seconds n (mean ± sd)</th>
<th>State of therapy</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>+0.04</td>
<td>10 0.54 ± 0.02</td>
<td>8 hrs after bretylium 0.4 g, 1.2 g daily</td>
<td>Q-T and T alternans; no ecotopy</td>
</tr>
<tr>
<td>2</td>
<td>&lt;0.001</td>
<td>10 0.54 ± 0.03</td>
<td>None</td>
<td>Ectopic beats decreased from 9 to 4/min; Q-T and T alternans continued</td>
</tr>
<tr>
<td>3</td>
<td>&lt;0.05</td>
<td>12 0.50 ± 0.03</td>
<td>None</td>
<td>Ectopic beats increased from 5 to 6/min; Q-T and T alternans increased</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>10 0.58 ± 0.01</td>
<td>Phenytoin 0.4 g daily</td>
<td>No Q-T and T alternans; no ecotopy</td>
</tr>
</tbody>
</table>
pacing electrode was inserted for overdrive suppression. After 88 hours of cardiac pacing and treatment with propranolol and phenytoin as outlined above, ventricular ectopy persisted when the pacemaker was turned off. We then assessed the influence of left stellate ganglion block on the ectopy, the duration of the Q-T interval, and the length of the period of overdrive suppression during interruptions of pacing.

### Techniques

Block of the stellate ganglia was performed by injecting 3–5 ml of a 1–2% solution of lidocaine just medial to the tip of the anterior transverse process of the sixth cervical vertebra. The criteria for successful block of the ganglia to the cardiac level were the appearance of Horner's syndrome with rise of temperature of the thumb or fingers, augmented pulse in the forefinger by plethysmograph and change of galvanic skin response.

Stimulation of the stellate ganglia was done using the 25-gauge needle for subsequent block with lidocaine as the stimulating electrode. Rectangular 1.5-msec pulses at 9–10 Hz came from a Grass S4B stimulator. The initial electrical stimulus was 0.5 V, with gradual increments to 2, 5, 10, 20 and 30 V. The energy level was reduced immediately if it caused discomfort or pain in the arm or neck. Intermittent interruption of the pulses permitted ECG samples without artifact at the higher energy levels.

All patients gave informed consent to the procedures and to the administration of drugs. The cardiac rhythm was monitored by ECG and by plethysmograph. No adverse symptoms or effects appeared, except for introductory pain from the needle prick of the skin during block or stimulation and ipsilateral pain or discomfort in the arm or neck during stimulation; this latter pain disappeared after reduction of stimulating energy.

The clinical 12-lead ECGs and rhythm records were performed at 25 mm/sec and with 1 mV/cm calibration using various single-channel ECG devices and the triple-channel Hewlett Packard 1515B Automatic Cardiograph. Unless otherwise stated, all ECGs before, during and after interventions involving the stellate ganglia and drug treatment were performed at 50 mm/sec and 0.5 mV/cm using the three-channel Hewlett-Packard 1515B and 1517A ECG Terminal recorders.

The conventional 12-lead ECG was obtained before, during and after all interventions. The Q-T interval was considered to start at the earliest deflection of the QRS. Several end points of the Q-T interval were assessed: the notch, if present, between the T and U

### Table 3. Left Stellate Stimulation and Q-Tc Interval

<table>
<thead>
<tr>
<th>Case</th>
<th>Control seconds</th>
<th>t test</th>
<th>Stimulation seconds</th>
<th>State of therapy</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (mean ± sd)</td>
<td>p</td>
<td>n (mean ± sd)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>10 0.51 ± 0.03</td>
<td>0.6</td>
<td>14 0.52 ± 0.03</td>
<td>8 hrs after bretylium 0.4 g, 1.2 g daily</td>
<td>T alternans during needle insertion. Q-T and T alternans at 20 V No ectopy</td>
</tr>
<tr>
<td>2</td>
<td>12 0.48 ± 0.02</td>
<td>0.01</td>
<td>10 0.51 ± 0.03</td>
<td>None</td>
<td>Ectopic beats increased from 9 to 11/min Q-T and T alternans at 2 - 30 V</td>
</tr>
<tr>
<td>3</td>
<td>10 0.58 ± 0.01</td>
<td>0.0002</td>
<td>10 0.61 ± 0.01</td>
<td>Phenytoin 0.4 g daily</td>
<td>No Q-T and T alternans; no ectopy</td>
</tr>
<tr>
<td>5</td>
<td>0.56 ± 0.01</td>
<td>0.02</td>
<td>5 0.58 ± 0.01</td>
<td>Phenytoin 0.4 g daily</td>
<td>No Q-T and T alternans; no ectopy</td>
</tr>
</tbody>
</table>

### Table 4. Right Stellate Stimulation and Q-Tc Interval

<table>
<thead>
<tr>
<th>Case</th>
<th>Control seconds</th>
<th>t test</th>
<th>Stimulation seconds</th>
<th>State of therapy</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (mean ± sd)</td>
<td>p</td>
<td>n (mean ± sd)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>10 0.52 ± 0.02</td>
<td>&lt;0.0001</td>
<td>10 0.46 ± 0.02</td>
<td>8 hrs after bretylium 0.4 g, 1.2 g daily</td>
<td>No Q-T and T alternans; No ectopy</td>
</tr>
<tr>
<td>2</td>
<td>10 0.48 ± 0.02</td>
<td>&lt;0.05</td>
<td>10 0.46 ± 0.02</td>
<td>None</td>
<td>Ectopic beats increased from 7 to 8/min Q-T and T alternans continued</td>
</tr>
<tr>
<td>3</td>
<td>10 0.57 ± 0.01</td>
<td>0.03</td>
<td>10 0.58 ± 0.01</td>
<td>Phenytoin 0.4 g daily</td>
<td>No Q-T and T alternans No ectopy</td>
</tr>
</tbody>
</table>
waves, the one or two breaks of profile, if present, in
the descending limb of the T wave, and the return of
repolarization to the baseline T-P segment. Bazett's
correction of the Q-T interval was used.

Grouped data were recorded as the mean ± SD. Ex-
cept where noted, 10 consecutive sinus beats before,
during and after interventions were compared using
the t test. Samples thus obtained did not differ
significantly from 1- to 2-minute consecutive collec-
tions. The mean ± SD of 10 separate cardiac cycles
randomly chosen during the control, intervention and
postintervention periods likewise did not differ
significantly. These observations also applied in nine
concurrently and identically investigated patients with
sympathetic dystrophy of an arm treated by 19 ipsi-

talateral blocks of the stellate ganglia (Crampton RS,
Carrohn H; unpublished observations). When ectopy
precluded collection of 10 consecutive sinus beats, the
portion of the ECG beginning five sinus beats after the
last ectopic beat was used. We excluded, as much as
possible, the alternans of the Q-T interval and T wave
after episodic ectopy for these routine Q-T mea-
surements related to specific interventions.

Baseline ECG data were collected intermittently
during a 5-20-minute pre-intervention control period
for each of 21 stellate ganglion and 17 drug inter-
ventions. At least three sets of 12-lead ECG record-

ings, each consisting of three simultaneous leads with
at least 12 cardiac cycles per lead, were collected from
3-5, 10-15, and 20-30 minutes after injection of
lidocaine into the neck for stellate ganglion block. The
acute intervention period ranged from 30 seconds to
30 minutes to elicit an ECG response to stimulation or
block of a stellate ganglion with requisite simulta-
nous autonomic changes. Postintervention samples
were recorded for 10 minutes immediately after
stimulation of a stellate ganglion, since that always
sufficed to document return to control values after in-
cremental stimulation from 0.5 to 30 V. More ex-
tended ECG sampling was carried out in block of a
stellate ganglion. After establishment of simulta-
nous changes of Q-Tc interval and ipsilateral peripher-
al autonomic indices in the 30-minute acute study period, further ECG records were made every 15
minutes for 1 hour, every 30 minutes for 2 hours, and
every 1-4 hours thereafter for 24 hours, the longest
time of return to control values detected.

Since these patients may show remarkable vari-
bility of the Q-T interval over time, each of 5
patients underwent assessment during a quiescent
clinical state. Cases 4 and 7 were exceptions, since
they received four urgent blocks of the left stellate
ganglion. Because of life-threatening syncopal attacks
from VT and VF and frequent ectopy in these two pa-
tients, their mean prolonged control Q-Tc intervals,
selected deliberately from brief dysrhythmia-free
periods, were shorter than the paroxysmal further
eelongation preceding or preceding bouts of ectopy,
VT or VF.

Control, intervention and postintervention R-R
and Q-T intervals were measured without knowledge
of the state being examined. The paired antecedent R-R
and Q-T intervals were measured to the nearest tenth
of a millimeter using a magnifier and engineer's
calipers. Vertical comparison with the two simulta-
nous leads was used to minimize error. A techni-
cian then entered these values into a computer pro-
gram which converted millimeters to seconds, then
performed the Bazett correction for rate, and finally
compared by t test the Q-Tc intervals from each con-
trol ECG lead to the same subsequent intervention
and postintervention ECG lead.

### Table 5. Left Stellate Block and Q-Tc Interval

<table>
<thead>
<tr>
<th>Case</th>
<th>Control seconds (mean ± SD)</th>
<th>T-wave break 1 seconds (mean ± SD)</th>
<th>T-wave break 2 seconds (mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>t Test p</td>
<td>n</td>
</tr>
<tr>
<td>1</td>
<td>10</td>
<td>0.51 ± 0.04</td>
<td>10</td>
</tr>
<tr>
<td>2</td>
<td>7</td>
<td>0.51 ± 0.04</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>0.60 ± 0.01</td>
<td>10</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>0.60 ± 0.03</td>
<td>10</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>0.36 ± 0.01</td>
<td>0.9</td>
</tr>
<tr>
<td>7</td>
<td>10</td>
<td>0.69 ± 0.03</td>
<td>0.6</td>
</tr>
</tbody>
</table>

Interval 2.5 hrs

|      | 10                         | 0.85 ± 0.02                        | 0.02                             | 0.46 ± 0.02                        | 0.01                             | 0.02 ± 0.02                        |

Interval 96 hrs

|      | 10                         | 0.50 ± 0.02                        | 0.6                               | 0.49 ± 0.02                        | 0.01                             | 0.02 ± 0.02                        |
| 10    | 0.60 ± 0.02                | 0.01                             | 0.01                             | 0.62 ± 0.02                        | 0.003                            | 0.0003                             |

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The experimental method dictated that at least some intervention ECG samples be recorded during the monitored ipsilateral peripheral autonomic changes. When two stellate ganglion blocks failed to meet these peripheral autonomic criteria, they were rejected. The Q-Tc interval also did not alter during these procedures. The two stellate ganglion blocks were repeated 48 hours later, and peripheral autonomic and Q-T interval changes occurred.

**Results**

In general, the Q-Tc interval lengthened during right stellate ganglion block and left stellate ganglion stimulation and shortened during right stellate ganglion stimulation and left stellate ganglion block (tables 2–6). Heart rates did not change significantly.

The Q-Tc elongated during four right stellate ganglion blocks (table 2). Alternation of the duration of the Q-T interval and of the duration and voltage of the T wave occurred in case 1. In case 2, the frequency of ventricular ectopic beats rose slightly, while the frequency of Q-T and T alternans increased. During another block in the same patient, ectopy declined while the alternans phenomena continued unchanged.

Stimulation of the left stellate ganglion lengthened Q-Tc in three of four attempts (table 3). In case 1, alternans of the T wave appeared during insertion of the needle through the skin, but the Q-Tc interval did not elongate significantly. During left stellate ganglion stimulation, alternation of the Q-T interval and T wave occurred in cases 1 (fig. 1) and 2. Ventricular ectopy increased in case 2. The change of profile of the T wave that lengthened the Q-T interval during block of the right stellate ganglion resembled that seen during stimulation of the left stellate ganglion in the same patient.

Stimulation of the right stellate ganglion abbreviated the Q-Tc interval in two of three cases and elongated it in one (table 4). Alternans of the Q-T interval and T wave continued in case 2.

**Table 5.** (Continued)

<table>
<thead>
<tr>
<th>T-wave Baseline</th>
<th>State of therapy</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>seconds</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n (mean ± sd)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 0.54 ± 0.01</td>
<td>8 hrs after Bretylium 0.4 g, 1.2 g daily</td>
<td>No Q-T and T alternans; no ectopy</td>
</tr>
<tr>
<td>10 0.50 ± 0.02</td>
<td>None</td>
<td>Ectopy and Q-T and T alternans suppressed</td>
</tr>
<tr>
<td>10 0.60 ± 0.01</td>
<td>Phenytoin 0.4 g daily</td>
<td>No Q-T and T alternans; no ectopy</td>
</tr>
<tr>
<td>10 0.55 ± 0.02</td>
<td>After failure of propranolol and phenytoin</td>
<td>Ectopy, Q-T and T alternans, VT, VF suppressed</td>
</tr>
<tr>
<td>—</td>
<td>5 days off phenytoin, 18 hrs after propranolol 20 mg</td>
<td>Q-T alternans suppressed; no ectopy</td>
</tr>
<tr>
<td>10 0.60 ± 0.01</td>
<td>After intravenous procainamide 0.6 g propranolol 4 mg, phenytoin 0.3 g</td>
<td>Ectopy, VT and Q-T and T alternans suppressed for 1.5 hr.</td>
</tr>
<tr>
<td>10 0.83 ± 0.02</td>
<td>See above</td>
<td>Ectopy, Q-T and T alternans suppressed for 1 hr, VT suppressed for 4.5 hr</td>
</tr>
<tr>
<td>—</td>
<td>Phenytoin 0.3 g daily</td>
<td>Ectopy, Q-T and T alternans suppressed</td>
</tr>
<tr>
<td>—</td>
<td>propranolol 0.32 daily</td>
<td>Increased duration of pacer overdrive suppression from 1-3 to 8 min (63–88%)</td>
</tr>
</tbody>
</table>

**Table 6.** Response of Q-Tc Interval

<table>
<thead>
<tr>
<th>Stellate ganglion intervention</th>
<th>Right n</th>
<th>Left n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Block</td>
<td>14</td>
<td>7</td>
</tr>
<tr>
<td>Stimulation</td>
<td>12</td>
<td>12</td>
</tr>
</tbody>
</table>

**Figure 1.** Simultaneous record of leads V1, V2 and V3 from top to bottom. During left stellate ganglion stimulation with 1.5 msec, 20 V, 9.5 Hz DC pulse, T-wave alternans from 0.38-0.51 mV appeared in case 1. Q-T did not elongate. ECG speed 50 mm/sec, 1 mV = 2 cm.
Block of the left stellate ganglion shortened the Q-Tc interval in seven of eight attempts (table 5). In case 7, only the first of three left stellate ganglion blocks did not shorten the Q-Tc interval significantly. This block was performed immediately after an intravenous load of procainamide. However, ventricular	

![Figure 2. Top: Alternation of T-wave voltage in case 7. Center: 15 minutes after left stellate ganglion block, T-wave alternans disappeared. Bottom: 45 minutes later, alternation reappeared. Ventricular tachycardia, twice suppressed simultaneously with T alternans by left stellate ganglion block, also recurred. Bipolar precordial ECG; paper speed 25 mm/sec.](image)

![Figure 3. Simultaneous record of leads V1, V6, and Vb from top to bottom. After left stellate ganglion block the Q-Tc intervals ending at the first two breaks of profile after the nadir of the T wave significantly shortened. The Q-Tc did not change if return to T-P baseline was used as end point. ECG speed 50 mm/sec; 1 mV = 2 cm.](image)

**Table 7. Effects of Stellate and Pharmacologic Interventions on Alternans of Q-T and T**

<table>
<thead>
<tr>
<th>Case</th>
<th>Right stellate</th>
<th>Left stellate</th>
<th>Drug influence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Block</td>
<td>Stimulation</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Evoked</td>
<td>Not observed</td>
<td>Not observed</td>
</tr>
<tr>
<td>2</td>
<td>Evoked</td>
<td>Not observed</td>
<td>Evoked</td>
</tr>
<tr>
<td>3</td>
<td>Not observed</td>
<td>Not observed</td>
<td>Not observed</td>
</tr>
<tr>
<td>4</td>
<td>—</td>
<td>—</td>
<td>Suppressed</td>
</tr>
<tr>
<td>5</td>
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1. 1.5, 1 and 18 hrs later
ectopy, VT and Q-T and T alternans disappeared for 1.5 hours. During six left blocks in four patients, alternans of the Q-T interval and T wave and recurrent ventricular ectopy, VT and VF disappeared (fig. 2, tables 5 and 7). With clinical loss of block, the alternans phenomena recurred in three patients (fig. 2, table 7) and ectopy reappeared in case 7. Left stellate ganglion block also augmented the duration of overdrive suppression of ventricular ectopy during cardiac pacing in case 7 (table 5). The Q-T interval of the paced beats did not change.

During left stellate ganglion block, cases 1–3, 5 and 7 had changes of profile of the T wave which suggested a shift of the bulk of the T wave earlier in time (figs. 3 and 4). In cases 1 and 2, a single break of T profile, not seen in the control state, appeared during left stellate ganglion block. The use of this change of T wave contour as the end point of the Q-T interval revealed a shortened Q-Tc (table 5). Two breaks in profile of the T wave after its apex were seen in cases 3, 5 and 7 (figs. 3 and 4). In case 3, these changes of T profile were not present in the control state. During left stellate ganglion block, use of either change in the T profile as Q-T end point indicated shortening of the Q-Tc (table 5). Cases 5 and 7 had similar breaks in the repolarization waveform before and after a left stellate ganglion block. Each successive break in T profile was used as a Q-T end point (fig. 4). During left stellate ganglion block, the first break of T contour shifted earlier in time in case 5, but not in case 7. The second T contour change did not shift in case 5 and appeared later in case 7. In both patients, the return of repolarization to the baseline shifted earlier. If only the return to baseline defined the Q-T end point, rather than new changes in T profile or shifts of extant breaks in T contour, the prolonged control Q-Tc significantly extended in case 1, did not alter in case 3, became insignificantly shorter in case 2, and shortened significantly in cases 4, 5 and 7 (table 5). Instead of seven of eight Q-Tc intervals shortened with one unchanged during left stellate ganglion block, the results were four shortened, three unchanged and one elongated Q-Tc intervals (table 5).

The responses of alternation of the duration of the Q-T interval and of duration and voltage of the T wave to stimulation and block of the stellate ganglia were compared with responses during pharmacologic treatment (table 7). Except for case 1, phenytoin and propranolol, alone or in combination, terminated the syncope, the alternans of the Q-T interval and of the T wave, and the VT or VF (fig. 5, table 1). In case 1, bretylium tosylate subsequently prevented all but sporadic trivial ventricular ectopy.18 In case 4, who took quinidine, and in cases 1, 4, 6 and 7, who took
procainamide before referral, the frequency of ventricular ectopy, VT and VF increased. Administration of these drugs enhanced the alternans of the Q-T interval and T wave in all but case 1 (table 7). This response resembled the observations during right stellate ganglion block and left stellate ganglion stimulation (tables 2, 3 and 7). In case 7, left stellate ganglion block was done twice, 2.5 hours apart after a 0.6 g intravenous load of procainamide had been given. During the first block, the Q-Tc interval did not decrease significantly. During both blocks, the alternans of the Q-T interval and T wave, ventricular ectopy and VT disappeared. After clinical evidence of recession of the criteria for left stellate ganglion block, the alternans phenomena (fig. 2), ventricular ectopy and VT recurred (tables 5 and 7).

The Q-Tc interval returned to control values within 1.5–24 hours after block of either stellate ganglion. The shortest duration of Q-T effects occurred in the acutely ill cases 4 and 7 after left stellate block. In cases 1–3, both ganglia were individually blocked and stimulated. The time of return to the control Q-Tc interval was always longer after right (range 2.5–24 hours) compared with left (range 1.5–6.5 hours) stellate ganglion block when each patient served as his own control. After stimulation of each ganglion, the Q-Tc interval returned to control within 5–10 minutes without significant time differences between left and right.

Discussion

Block of the stellate ganglion is a blind procedure.19 The moment, extent and duration of diffusion of lidocaine to the ganglion affecting the cardiac cycle are not known, despite attention to simultaneous ophthalmologic and peripheral autonomic activity via that ganglion. Similar criticisms apply to the technique of electrical stimulation of the ganglion. Initiating either procedure might frighten the patient and result in sympathetic overactivity. Although prospectively sought for, no change of heart rate or Q-Tc interval attended introduction of the needle or injection of lidocaine. However, case 1 had transient alternans of the T wave once during introduction of the needle (table 3). The presumably therapeutic or sub-therapeutic amounts of antisypathetic and other drugs (tables 2–5 and 7) recently given all but case 2 may have influenced responses of the Q-Tc interval and T wave, rate, rhythm and alternans phenomena to an unknown degree.

The variation in the amount and time course of diffusion of lidocaine to and from each ganglion was unquantifiable. From the longer time to return to control values of the Q-T interval after right as opposed to left stellate ganglion block, one might argue that this response affirmed the postulated relatively weaker activity of the right stellate ganglion in the long Q-T syndrome.4 However, no confirmatory reciprocal time of return of Q-Tc values to control distinguished right from left ganglion after stimulation. Other influences that might augment or mask lateralization of time course of return to control include heterogeneous influences upon sympathetic nerve traffic23–24 and inhomogeneous neural disease in the hearts of patients with the long Q-T syndrome.5 The latter might facilitate unanticipated and variable responses to drugs and procedures influencing the stellate ganglia and cardiac sympathetic nerves.5

In an earlier study, block of the left and right stellate ganglia each shortened the Q-Tc interval in two persons.8 Stimulation of the right stellate ganglion elongated the Q-Tc in one and did not alter it in the other. Left stellate ganglion stimulation did not change the Q-Tc interval. In contrast, four blocks of the right stellate ganglion lengthened the Q-Tc in the present study (tables 2 and 6). Stimulation of the left stellate ganglion elongated the Q-Tc in two and evoked alternans of the Q-T interval and T wave in a third (tables 3 and 7). However, the Q-T interval did not change during stimulation in the earlier report.9 The reasons for the variation in responses to stellate interventions in these two studies are not immediately apparent. The present observations (tables 2–7) resemble the responses and predictions drawn from experiments in animals.6, 7, 11, 20, 21 Although the techniques and criteria of interventions to influence the stellate ganglia were similar,8 the present study used higher levels of energy during stimulation and presumptive evidence beyond the appearance of Horner’s syndrome that the stellate block descended sufficiently to involve the level of the autonomic innervation of the heart. During each block, autonomically modulated changes in the forearm, hand and fingers occurred.

Variations of behavior of the Q-T interval during block of the stellate ganglia and drug treatment have been reviewed.5, 9, 10 Clinicopathologic examination of eight patients with the long Q-T syndrome showed random distribution of cardiac neural lesions.8 These abnormalities imply altered reception of sympathetic neural traffic which might manifest as a changed sequence of ventricular recovery and account for the variability of response to left stellate ganglion block and other invasive and pharmacologic interventions affecting the Q-T interval and cardiac rhythm.5 The antisympathetic effects of phenytoin, propranolol, and bretylium tosylate27–29 might alter neural traffic to the heart and hence the Q-T interval. Their direct electrophysiologic influence upon the myocardial cell membrane might also affect the Q-T interval. Such reasoning applies to treatment with phenytoin, an agent very effective in prior experience8 and in most of the patients in this study. Earlier6, 9, 10 and present observations (table 5) also indicate that left stellate ganglion block may reduce ectopy in the absence or presence of shortening of the Q-Tc interval. Onset of stabilized length of Q-Tc may therefore indicate beneficial influence of interventions.

In patients with the long Q-T syndrome, alternans of the T wave during physical or emotional stress often precedes VT and VF.4 Stimulation of the left
stellite ganglion evoked T-wave alternans in animal experiments.\textsuperscript{4} Alternans of both Q-T interval and T wave appeared in cases 1 and 2 (table 3, fig. 1) during stimulation of the left stellite ganglion. Likewise, block of the right stellite ganglion lengthened the Q-T interval and precipitated alternans of the Q-T interval and T wave in cases 1 and 2 (table 2). Block of the left stellite ganglion suppressed the alternans phenomena and ventricular ectopy in cases 2, 4 and 7 (table 5, fig. 2). Stimulation of the left stellite ganglion had the opposite effect (table 3).

The left stellite ganglion profoundly influences the Q-T interval\textsuperscript{4-8} and cardiac arrhythmias\textsuperscript{9} in animals. One patient with pharmacologically resistant VT due to long Q-T syndrome responded with VT upon repetitive mechanical stimulation of the left stellite ganglion before its extirpation.\textsuperscript{80} Thus, left stellite ganglion stimulation elicited VT,\textsuperscript{80} elongated the Q-Tc interval experimentally\textsuperscript{4} and in cases 1–3 (table 3), and evoked alternans of Q-T interval and T wave in cases 1 (fig. 1) and 2. These responses are compatible with a major influence of the left stellite ganglion on vulnerability to ventricular ectopy, VT and VF, and also the important ECG precursors of these ventricular dysrhythmias, elongation of the Q-T interval and the alternans phenomena.\textsuperscript{4} The suppression of alternans of the Q-T interval and T wave and of ventricular ectopy by block of the left stellite ganglion in cases 2, 4 and 7 (table 5, fig. 2) also suggest dominance of the left stellite ganglion as a cause of ventricular ectopy, VT and VF. Moreover, abolition of syncpoe, VT, VF and sudden death attended surgical removal of the left stellite ganglion in 11 cases.\textsuperscript{7, 11, 80}

Major fluctuations of heart rate did not appear during stellite stimulation and block in this study. However, three patients with Romano-Ward syndrome showed both a blunted response of heart rate to atropine treatment and a subnormal response of heart rate to exercise during propranolol treatment.\textsuperscript{31} Moreover, one person had alternans of the Q-T interval and T-U wave limited to the period of lowest rate of infusion of isoproterenol and disappearing at higher doses.\textsuperscript{31} In vagotomized cats, left stellite stimulation both lengthened the Q-T and evoked alternans of the Q-T interval and T wave.\textsuperscript{4} In hypocalcemic patients without hereditary long Q-T syndrome, the alternans phenomena disappeared as heart rate changed suddenly after stimulation of the carotid sinus or after a vagolytic drug.\textsuperscript{32} These observations are compatible with an intrinsic cardiac defect beyond isolated subnormal adrenergic activity and with an exquisite, possibly asymmetric cardiac sensitivity to infused epinephrine and isoproterenol which reflect heterogeneous neural lesions of the heart.\textsuperscript{8} The role of hypocalcemia remains unclear, but like hypokalemia and hypomagnesemia, the resulting abnormalities of repolarization are occasionally associated with the alternans phenomena and ventricular dysrhythmias.\textsuperscript{32}

Efficacious therapeutic results from propranolol, phenytoin and bretylium confirmed the beneficial anti-sympathetic influence of these drugs in the long Q-T syndrome.\textsuperscript{9, 10, 18, 27-29} (table 7, fig. 5). Like block of the left stellite ganglion, propranolol and phenytoin averted syncpe, suppressed alternans of the Q-T interval and T wave, and diminished or abolished ventricular ectopy, VT and VF (table 7, figs. 2 and 5).\textsuperscript{12} In otherwise normal hearts, these drugs suppress idiopathic ventricular tachycardia.\textsuperscript{30} Furthermore, the abolition of Q-T and T alternans, ventricular ectopy and VT during block of the left stellite ganglion closely resembled the response to intravenous treatment with phenytoin (tables 5 and 7, figs. 2 and 4). In contrast, the effects of block of the right stellite ganglion or stimulation of the left stellite ganglion (tables 2, 3 and 7, fig. 1) resembled effects of exposure to quinidine and procainamide, drugs which elongate the Q-T interval (table 7). Both drugs aggravated alternans of the Q-T interval and T wave and ventricular ectopy in cases 4, 6 and 7 (table 7), confirming their potentially dangerous effects in the long Q-T syndrome.\textsuperscript{4}

Persons with the long Q-T syndromes experience autonomic mediated dysrhythmias, syncope and sudden death after psychologic or physical stress.\textsuperscript{4-8, 9, 10} However, only recently have similar mechanisms been elucidated in sudden coronary death. Not only does dysautonomia often precede VF in myocardial infarction,\textsuperscript{33} but also the Q-Tc interval acutely lengthens for several days.\textsuperscript{34} After recovery, sudden death occurs almost exclusively in patients left with a prolonged Q-Tc interval.\textsuperscript{35} Coronary patients who survive VF have an increased incidence of ventricular ectopy and of elongated Q-T intervals.\textsuperscript{36} Finally, the longer the Q-T interval, the greater the chance of sudden coronary death.\textsuperscript{37}

Several experiments in animal models deserve scrutiny in view of these apparent similarities between the long Q-T syndromes and sudden coronary death. Myocardial ischemia is known to excite myelinated\textsuperscript{22} and unmyelinated\textsuperscript{40} afferent sympathetic fibers to activate a cardio-cardiac sympathetic reflex.\textsuperscript{34} Resultant ventricular dysrhythmias are ameliorated after section of the thoracic dorsal roots,\textsuperscript{42} the main sensory input to the spinal cord from the heart. The cardiac sympathetic nerves participate in the genesis of dysrhythmias after experimental coronary occlusion\textsuperscript{23} and their heterogeneous distribution partially accounts for these dysrhythmias.\textsuperscript{23} Nonuniform traffic appears in the cardiac sympathetic nerves after coronary occlusion and heralds VT and VF.\textsuperscript{24} Finally, left stelllectomy abolishes the ventricular dysrhythmias of experimental coronary occlusion presumably by interruption of cardiac sympathetic fibers.\textsuperscript{25} Among other possible mechanisms, more extensive ischemic damage of the right adrenergic terminals, compared with left, might permit dominance of the left stellite ganglion, heighten the susceptibility of the injured left ventricle to deleteriously increased left sympathetic traffic, elongate the Q-T interval, evoke VT and VF, and thereby predispose to sudden coronary death in a manner analogous to the hereditary long Q-T syndromes.
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