Electrophysiological Studies with Multiple Drugs in Patients with Atrioventricular Re-entrant Tachycardias Utilizing an Extranodal Pathway

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SUMMARY Eleven patients with recurrent paroxysmal tachycardia (PSVT) underwent electrophysiological studies. In each patient, initial study revealed re-entrant PSVT with antegrade conduction via the normal pathway and retrograde conduction via an extranodal pathway (Kent bundle). A temporary electrode catheter was left at the conclusion of initial study and PSVT induction was performed on subsequent days before and after the following intravenous drugs: ouabain 0.01 mg/kg (OU), propranolol 0.1 mg/kg (PRO), ouabain + propranolol (OU + PRO) and procainamide 750 mg (PA). In all patients, control studies prior to drug administration revealed the ability to induce sustained PSVT. In five patients, OU, PRO, or OU + PRO prevented induction of sustained PSVT by increasing atrioventricular (A-V) nodal refractoriness. In four of the patients, (including one of the above), PA prevented induction of sustained PSVT: in one, by increasing His-Purkinje refractoriness, and in three by increasing refractoriness in the Kent bundle. Oral drug therapy based upon the above studies (8 pts) prevented recurrent sustained PSVT for a mean follow-up period of 9 ± 5 months. In the remaining three patients, all drugs failed to prevent induction of sustained PSVT. These patients were either treated with radio-frequency pacemakers or surgery.

In conclusion, drug responses in patients with recurrent PSVT utilizing a Kent bundle are variable. Antiarrhythmic drugs may interfere with circus movements at the A-V node, His-Purkinje system, or Kent bundle. Chronic oral drug therapy based upon responses to electrophysiological studies with multiple drugs prevents recurrent sustained PSVT over a short-term follow-up period.

All patients had been resistant to at least one prophylactic oral antiarrhythmic drug.

Five had no electrocardiographic evidence of pre-excitation (cases 1, 2, 4, 6, 7), one had previous electrocardiographic pre-excitation (case 10), two had intermittent pre-excitation (cases 5 and 9) and three had constant pre-excitation (cases 3, 8, 11). All 11 patients had electrophysiological demonstration of inducible circus movement tachycardia utilizing a retrogradely conducting anomalous pathway (see below).

Electrophysiological Studies

All antiarrhythmic drugs were discontinued at least three days prior to study. Electrophysiological study was performed in the postabsorptive, non sedated state after obtaining informed written consent. His bundle electrograms were recorded with a bipolar electrode catheter positioned across the tricuspid valve percutaneously via a femoral vein. A second hexapolar catheter was introduced via an antecubital vein and positioned at the right ventricular apex. The distal two electrodes (at the tip) were utilized for ventricular pacing, the middle two electrodes (10 cm from the tip) for atrial pacing and the proximal two electrodes (13.5 cm from the tip) for recording of the high right atrial electrograms. A third bipolar catheter was introduced via another antecubital vein and advanced into the coronary sinus for recording of left atrial electrograms. A third bipolar catheter was introduced via another antecubital vein and advanced into the coronary sinus for recording of left atrial electrograms. Multiple surface and intracardiac electrograms were simultaneously recorded on a multichannel oscilloscopic photographic recorder (Electronics for Medicine DR-16, White Plains, New York) at paper speeds of 100 and 200 mm/sec. Stimuli were approximately twice
diastolic threshold and 2 msec in duration and were provided by a programmable digital stimulator (manufactured by M. Bloom, Philadelphia, Pa.).

The study protocol was as follows: 1) Initial electrophysiological study was performed for definition of mechanisms and reproducibility of PSVT. The study included atrial and ventricular stimulation utilizing incremental pacing and extrastimulus techniques and mapping of retrograde atrial activation sequences (during ventricular pacing and during PSVT). 2) Leaving the hexapolar catheter in place at the right ventricular apex at the conclusion of initial study for atrial and ventricular stimulation and recording on subsequent days. 3) Arrhythmia induction before and after intravenous administration of antiarrhythmic agents on subsequent days. The following drugs and drug combination were utilized intravenously: propranolol 0.1 mg/kg, ouabain 0.01 mg/kg, ouabain 0.01 mg/kg + propranolol 0.1 mg/kg, and procainamide (a total dose of 750 mg). In two patients (cases 9 and 10), intravenous disopyramide phosphate (4 mg/kg) was also utilized, and in one patient (case 9), intravenous aprindine (300 mg) was also administered. 4) If feasible and indicated from results of step 3) of the protocol, arrhythmia induction was repeated on oral drug or drugs. 5) If an effective oral drug or drug combination was delineated from steps 3) and/or 4), the effectiveness of therapy was ascertained by follow-up in a research clinic. Serum digoxin and procainamide blood levels were measured in some of the patients. In patients receiving intravenous procainamide, blood was taken 20 min after infusion.

**Electrophysiological Definitions**

HRA₁, CS₂, H₂ and V₁ were the high right atrial, coronary sinus, low right atrial, His bundle and ventricular electrograms, respectively, of driven beats (S₁). HRA₂, CS₁, A₂, H₃ and V₂ were the high right atrial, coronary sinus, low right atrial, His bundle and ventricular electrograms, respectively, in response to extrastimuli (S₂). Conduction intervals and refractory periods were measured and defined as previously described.³

For the purpose of analysis, sustained PSVT was defined as an induced episode of PSVT lasting longer than two minutes, requiring termination with single or double extrastimuli. A successful response to drug therapy was defined as the total loss of ability to induce or sustain PSVT. If a successful response was demonstrated, the site of action in the circus movement was defined, this being the site in the conduction system at which the drug or drugs prevented induction or sustainment of PSVT.

**Results**

Six of the 11 patients (cases 1, 4, 6, 7, 9 and 10) had no antegrade pre-excitation with incremental atrial pacing at any time. One patient (case 2) had antegrade pre-excitation at initial study only when distal coronary sinus pacing was performed. One patient (case 5) had no antegrade pre-excitation at initial study, but demonstrated antegrade pre-excitation on subsequent studies. Three patients (cases 3, 8 and 11) had antegrade pre-excitation on all studies.

All 11 patients had inducible sustained PSVT under
control conditions (at the time of initial electrophysiological study and on each subsequent day prior to drug administration). PSVT induction was achieved with atrial extrastimulus technique, cessation of rapid atrial pacing, ventricular extrastimulus technique and cessation of rapid ventricular stimulation (table 2). The particular modes of stimulation that were successful varied from patient to patient, some patients having inducible PSVT utilizing multiple types of stimulation patterns and some patients having limited modes of PSVT induction. There was also some variability from day to day in the mode of induction, echo zones (if utilizing extrastimulus induction), or rates for induction (if utilizing cessation of rapid atrial or ventricular pacing).

In all patients, induced PSVT reflected the presence of a retrograderly conducting extranodal anomalous pathway (left-sided in nine and right-sided in two) and an antegrade conducting normal pathway. The criteria for diagnosis of participation of the retrogradely conducting anomalous pathway were as follows: 1) fixed ventriculoatrial conduction time with incremental ventricular pacing (cases 1-11). Abnormal retrograde atrial activation pattern, with coronary sinus atrial electrogram being the earliest (cases 1, 2, 4-7, 9 and 10). Increased ventriculoatrial conduction time with functional bundle branch block ipsilateral to the anomalous pathway occurring during PSVT (cases 1, 3, 4, 6, and 9). Ability to capture the atria during PSVT by a critically timed ventricular extrastimulus at a time when the His bundle was refractory (cases 3, 5, 6, 8 and 11).

The ability to induce sustained PSVT was lost in eight of the patients following one or more of the tested drugs. This reflected drug-related increased refractoriness of the A-V node in five of the patients (cases 1-5), of the His-Purkinje system in one of the patients (case 6), and of the anomalous pathway in three of the patients (cases 3, 7 and 8). In three patients (cases 9, 10 and 11), no drug was found which could prevent induction of sustained PSVT. Examples of the varying responses will be presented below.

### Loss of Ability to Sustain PSVT because of A-V Nodal Refractoriness (cases 1-5)

Case 1 was a 42-year-old female with recurrent PSVT for seven years. Oral therapy with digoxin 0.5 mg/day and propranolol 80 mg per day (separately and combined) had been unsuccessful in preventing recurrent tachycardia. Initial electrophysiological study revealed re-entrant PSVT utilizing a concealed retrogradely conducting extranodal pathway (see above). Susained PSVT could be induced with cessation of rapid atrial pacing, cessation of rapid ventricular pacing (fig. 1A) and with atrial extrastimulus technique. Both intravenous propranolol and intravenous ouabain failed to prevent PSVT induction (figures 1B and C). With intravenous propranolol and intravenous ouabain + propranolol sustained PSVT was induced, despite maintenance of retrograde conduction via the anomalous pathway (fig. 1D).

The failure to induce sustained PSVT reflected the effects of propranolol on refractoriness in the antegrade limb of the circus movement (A-V nodal refractoriness). The effect was also quantitated by noting the effects of drugs on antegrade conduction during rapid atrial pacing, propranolol significantly depressing antegrade conduction so that pacing-induced second degree A-V block occurred at a slower paced rate. The effects of intravenous propranolol on PSVT induction and antegrade conduction were reproduced with oral propranolol in a dose of 160 mg per day (fig. 1E).

Case 2 was an 18-year-old male with recurrent PSVT for six years. Therapy with propranolol 40 mg/day and digoxin 0.125 mg/day had failed to prevent PSVT. Sustained PSVT could be induced with cessation of rapid atrial pacing, cessation of rapid ventricular pacing, atrial extrastimulus testing (fig. 2) and ventricular extrastimulus testing. Sustained PSVT could be induced following intravenous procainamide (serum drug level of 5.4 μg/ml) (fig 2, day 1), intravenous propranolol (fig. 2, day 2) and intravenous ouabain (fig. 2, day 3). With combined intravenous ouabain + propranolol, only short episodes of nonsustained PSVT could be induced (fig. 2, day 6). The loss of the ability to sustain PSVT reflected increased refractoriness of the antegrade limb of the circus movement (A-V node). Oral digoxin (0.25 mg/day) + propranolol (160 mg/day) reproduced the effects of these same drugs intravenously (fig. 2, day 8) with loss of ability to induce sustained PSVT.

Case 3 was a 24-year-old male with type B pre-excitation and recurrent PSVT, refractory to quinidine 800 mg/day, procainamide 1 g/day, diphenylhydantoin 400 mg/day, digoxin 0.25 mg/day, and propranolol 40 mg/day (alone or in combination). Sustained PSVT could be induced with rapid atrial pacing and atrial extrastimulus testing. Intravenous ouabain alone had no effects on induction of

### Table 2. Ability to Induce Sustained PSVT with Drug Testing

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Ouabain</th>
<th>Propranolol</th>
<th>Ouabain + Propranolol</th>
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<th>Disopyramide Phosphate</th>
<th>Aprindine</th>
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</tr>
<tr>
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<td>NT</td>
<td>No (AVN)</td>
<td>No (AP)</td>
<td>NT</td>
<td>NT</td>
</tr>
<tr>
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<td>NT</td>
<td>NT</td>
</tr>
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<td>Yes</td>
<td>No (AVN)</td>
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<td>NT</td>
<td>NT</td>
</tr>
<tr>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No (HPS)</td>
<td>NT</td>
<td>NT</td>
</tr>
<tr>
<td>7</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No (AP)</td>
<td>NT</td>
<td>NT</td>
</tr>
<tr>
<td>8</td>
<td>Yes</td>
<td>NT</td>
<td>Yes</td>
<td>NT (AP)</td>
<td>NT</td>
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<td>11</td>
<td>Yes</td>
<td>Yes</td>
<td>NT</td>
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</tbody>
</table>

*Abbreviations: PSVT = paroxysmal supraventricular tachycardia; Yes = ability to induce sustained PSVT; No = loss of ability to induce sustained PSVT; ( ) = site of action of effective drug; AVN = atrioventricular node; HPS = His-Purkinje system; AP = anomalous pathway; NT = not tested.*
sustained PSVT. A combination of intravenous ouabain and propranolol suppressed induction of sustained PSVT due to increased refractoriness of the antegrade limb of the circus movement (A-V node). In this patient, intravenous procainamide (serum drug level of 6 µg/ml) also prevented induction of sustained PSVT due to increasing refractoriness of the retrograde limb of the circus movement (anomalous pathway). Subsequently, the loss of ability to sustain PSVT was reproduced with a combination of oral digoxin in a dose of 0.375 mg/day (serum drug level of 1.5 µg/ml) and propranolol 80 mg/day. Oral procainamide was not tested.

Cases 4 and 5 will not be presented in detail. Both patients had induced sustained PSVT. In patient 4, intravenous ouabain, intravenous propranolol alone, and both in combination prevented induction of sustained PSVT. In patient 5, only a combination of intravenous ouabain + propranolol prevented induction of sustained PSVT. In both patients, the site of action of the effective drug or drugs was at the A-V node. In both patients, results were replicated with oral drugs (propranolol in case 4 and propranolol + digoxin in case 5).

Loss of Ability to Sustain PSVT because of Refractoriness in the His-Purkinje System

Case 6 was a 12-year-old boy with recurrent PSVT of several years duration. Therapy with propranolol 40 mg/day and quinidine 1.2 g/day had failed to suppress tachycardias. Sustained PSVT could be induced with cessation of rapid atrial pacing, cessation of rapid ventricular pacing (fig. 3A), atrial extrastimulus testing and ventricular extrastimulus testing. Following intravenous procainamide (tested on day 1 of the study), only nonsustained self-terminating PSVT could be induced. Spontaneous conversion of PSVT occurred when an H potential was not followed by a QRS complex, suggesting refractoriness distal
to the His bundle recording site (fig. 3B). On subsequent days, intravenous propranolol alone and intravenous propranolol + ouabain were unsuccessful in preventing induction of sustained PSVT. However, the latter combination was noted to potentiate the conversion of PSVT by simple vagal maneuvers. Oral drugs were not tested in this patient.

Loss of the Ability to Sustain PSVT because of Refractoriness in the Anomalous Pathway (cases 3, 7 and 8)

Three patients had loss of the ability to sustain PSVT because of increased refractoriness in the anomalous pathway following drug administration. Case 3 was already presented above.

Case 7 was a 62-year-old male with angina pectoris and
recurrent PSVT. The patient had been refractory to propranolol 40 mg/day, digoxin 0.25 mg/day, and procainamide 2 g/day. Sustained PSVT could be induced with rapid atrial pacing, rapid ventricular pacing and ventricular extrastimulus testing (fig. 4A). With intravenous procainamide, only nonsustained PSVT could be induced (fig. 4B). This reflected drug-induced refractoriness in the retrograde limb of the circus movement (fig. 4B). This effect was also quantitated by noting the depressant effect of procainamide on retrograde anomalous pathway conduction tested with incremental ventricular pacing (fig. 5A and B). Ouabain alone and ouabain + propranolol had no effects on induction of sustained PSVT (figs. 4C and D). This was consistent with these drugs’ effects on retrograde (anomalous pathway) conduction (fig. 5C and D). The effects of intravenous procainamide were replicated with oral procainamide (serum level of 5.7 μg/ml).

Case 8 was a 47-year-old male with type B pre-excitation and recurrent PSVT. The PSVT was refractory to 160 mg of propranolol/day. Sustained PSVT could be induced with rapid atrial pacing and atrial extrastimulus testing. Intravenous ouabain or a combination of ouabain and propranolol failed to prevent induction of sustained PSVT.

Intravenous procainamide (serum drug level of 3.4 μg/ml) prevented induction of sustained PSVT. This reflected drug-induced refractoriness of the retrograde limb of the circus movement similar to case 7. Termination of PSVT occurred when the QRS was not followed by an atrial response. The ventricular paced cycle length producing retrograde V-A block was increased after procainamide. The effect of intravenous procainamide was reproduced with oral procainamide in a dose of 4 g/day (serum drug level of 4.1 μg/ml).

Lack of Drug Effect on Ability to Induce Sustained PSVT (cases 9–11)

In cases 9, 10, and 11, no drug or drug combination prevented induction of sustained PSVT. An example is shown in figure 6 (from case 9), who was also tested with intravenous disopyramide phosphate and intravenous aprindine. In patient 11, procainamide was not tested because the patient had previously had a hypersensitive reaction to this agent.

Follow-Up

Eight patients were treated with a drug or drug combina-

![Figure 4](http://circ.ahajournals.org/) Recordings from case 7, showing loss of ability to sustain circus movement tachycardia with procainamide. Surface electrocardiographic lead II instead of V1 is shown in panels C and D. Tachycardias were induced with ventricular extrastimulus technique at a driven cycle length of 600 msec. S1 was the driven stimulus and S2 the extrastimulus. Functional left bundle branch block occurred during tachycardia. Panel A shows induction of sustained tachycardia before drug administration. Panel B shows loss of ability to sustain tachycardia after intravenous procainamide. Spontaneous conversion of tachycardia occurred when a QRS was not followed by an atrial response (E), suggesting increased refractoriness in the anomalous pathway (retrograde) after drug administration. Panels C and D show induction of sustained tachycardia after intravenous ouabain or ouabain + propranolol.
tion based upon chronic electrophysiological studies (table 3). In seven of the patients (cases 1–5, 7 and 8), the oral drug or drug combination had been demonstrated to prevent induction of sustained PSVT. In patient 6, digoxin and propranolol were administered; this combination had potentiated PSVT conversion with vagal maneuvers. The combination was used despite the fact that procainamide had eliminated the ability to induce sustained PSVT. This decision was based upon our preference for a drug program that does not usually lead to long-term chronic toxicity.

These eight patients have been followed for a period of one to 14 months (mean 9 ± 5 months). Cases 1, 3, 5, and 8 have been totally free of PSVT. Cases 2 and 4 have had several transient episodes of PSVT (lasting less than five minutes) not necessitating emergency room visits. Case 6 has had several short PSVT episodes that coverted with

**Table 3. Follow-up**

<table>
<thead>
<tr>
<th>Case</th>
<th>Oral therapy delineated by study</th>
<th>Serum drug level</th>
<th>Duration (months)</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>At time of study</td>
<td>During follow-up</td>
<td></td>
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<tr>
<td>1</td>
<td>Propranolol 160 mg/day</td>
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<td>6</td>
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<tr>
<td>2</td>
<td>Digoxin 0.25 mg/day + Propranolol 160 mg/day</td>
<td>1.2 ng/ml</td>
<td>0.8–1.6 ng/ml</td>
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</tr>
<tr>
<td>3</td>
<td>Digoxin 0.375 mg/day + Propranolol 80 mg/day</td>
<td>1.6 ng/ml</td>
<td>1.2 ng/ml</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>Propranolol 80 mg/day</td>
<td>(—)</td>
<td>(—)</td>
<td>12</td>
</tr>
<tr>
<td>5</td>
<td>Digoxin 0.25 mg/day + Propranolol 80 mg/day</td>
<td>(—)</td>
<td>(—)</td>
<td>11</td>
</tr>
<tr>
<td>6</td>
<td>Digoxin 0.25 mg/day + Propranolol 240 mg/day</td>
<td>(—)</td>
<td>0.6–0.8 ng/ml</td>
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<tr>
<td>7</td>
<td>Procainamide 4 g/day</td>
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<td>8</td>
<td>Procainamide 4 g/day</td>
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**Abbreviations:** PSVT = paroxysmal supraventricular tachycardia.
vagal maneuvers, and one episode that necessitated a one-day hospitalization (conversion was spontaneous). In all patients, these responses were in marked contrast to the frequency and severity of PSVT prior to electrophysiological study.

In the three patients in whom a drug could not be defined which prevented induction of sustained PSVT, more invasive therapy was undertaken. Patient 9 was treated surgically with attempted transection of a lateral left anomalous pathway. Patients 10 and 11 were treated with self-activated radiofrequency pacemakers (atrial in patient 10 and ventricular in patient 11), which were totally successful in accomplishing subsequent PSVT conversion. In the latter two patients, chronic electrophysiological study had demonstrated the ability for conversion of PSVT with rapid atrial stimulation in patient 10 and slow ventricular stimulation in patient 11.

**Discussion**

The circus movement allowing PSVT in patients with manifest or concealed pre-excitation usually consists of the normal pathway for antegrade conduction and an anomalous pathway for retrograde conduction. The circus movement thus consists of the following components: the A-V node, His bundle and bundle branches (antegrade limb), the ventricles (final common distal pathway), anomalous pathway (retrograde limb) and the atria (final common proximal pathway).\(^1\) Induction of PSVT depends upon unidirectional block of a premature impulse in one limb and critically slow conduction in the conteralateral limb, allowing the limb with unidirectional block to recover for reciprocal conduction.

In this study, PSVT induction was achieved by one or more of the following means: 1) Achievement of the critical antegrade normal pathway A-V conduction time necessary for reciprocal return to the atrium via the anomalous pathway. This was achieved with either atrial extrastimulus technique or incremental atrial pacing. 2) Achievement of block in the normal pathway with simultaneous retrograde conduction via the anomalous pathway, so that return to the ventricles could occur via the normal pathway. This was achieved with either ventricular extrastimulus technique or incremental ventricular pacing. The pattern of stimulation utilized for PSVT induction on a given day of the study was the simplest mode of stimulation that induced PSVT. In all patients, PSVT could be induced on every day of the study prior to drug administration.

The cycle length of induced PSVT would reflect the sum of conduction times of the components of the circus movement. The sustinament of PSVT would depend upon a cycle length of PSVT shorter than the longest effective refractory period of any component of the circuit. If block were to develop in any component of the circus movement during PSVT, the arrhythmia would terminate.

Drug therapy for prevention of PSVT could be aimed at total elimination of inducing premature beats (atrial and/or

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**Figure 6.** Recordings from case 9, showing lack of effects with multiple drugs on induction of sustained circus movement tachycardia utilizing atrial extrastimulus technique. The driven cycle length was 600 msec. Sustained tachycardias were induced despite administration of procainamide (panel A), ouabain + propranolol (panel B), disopyramide phosphate (panel C) or aprindine (panel D). In panels C and D, the first four beats during tachycardias were conducted with functional left bundle branch block with a longer ventriculo-atrial conduction time and longer cycle length of tachycardia.
ventricular) and/or modification of one or more components of the circus movement, in an attempt to prevent sustainability of the tachycardia. Since even a single critically timed premature beat could initiate PSVT, an effect hard to achieve and difficult to substantiate, the former approach would necessitate almost total suppression of premature beats over a long period of time. The latter approach was tested in the laboratory over a relatively short time span and appeared to be effective in delineating successful therapy (see below).

Procainamide, quinidine and other quinidine-like drugs (disopyramide, aprindine) could prevent circus movement PSVT in patients with retrogradely conducting anomalous pathway by increasing refractoriness of the anomalous pathway, ventricle, atrium or His-Purkinje system. Propranolol and digitalis could prevent sustained PSVT by increasing refractoriness of the A-V node. All of the above drugs could fail to prevent PSVT if effects on refractoriness were minimal, or if the drugs increased conduction times in one or more components of the circus movement, offsetting an increase in absolute refractory period in one of the components. Generally, even with the above knowledge concerning drug effects, the treatment of recurrent PSVT in patients with anomalous pathways has been largely empirical and based upon trial and error.

In the present study with sequential administration of multiple agents, it was demonstrated that the responses to antiarrhythmic drugs in patients with circus movement tachycardia utilizing an anomalous pathway were variable and unpredictable. In five patients, intravenous ouabain and propranolol alone or in combination increased A-V nodal refractoriness so that circus movement tachycardia could not be sustained. In six patients, sustained PSVT could be induced despite administration of ouabain and propranolol. In four patients, the ability to sustain PSVT was lost after procainamide administration. In one, this was due to increased refractoriness in the His-Purkinje system; in three, due to increased refractoriness in the anomalous pathway. In seven patients, sustained PSVT could be induced despite administration of procainamide. The total number of cases studied was small and broad generalizations regarding therapy of individual patients with manifest or concealed pre-excitation cannot be made. Our results do suggest that an oral dose of greater than 40 to 80 mg of propranolol per day may have to be tested before a patient can be defined as refractory to it.

The present study demonstrated that electrophysiological responses to intravenous agents predicted the electrophysiological responses to oral agents. In seven patients, oral therapy predicated upon intravenous drug responses prevented induction of sustained PSVT. This resembled a similar demonstration by Wellens and co-workers, who demonstrated that a beneficial electrophysiological response to ouabain in A-V nodal re-entry predicted a similar response to two weeks of oral digoxin. More importantly, the present study suggested that electrophysiological responses to intravenous and then oral drugs predicted subsequent clinical course. In eight patients, chronic oral drug therapy was predicated based upon electrophysiological studies. Short-term follow-up of these patients demonstrated major clinical improvement with resultant suppression of recurrent episodes of sustained PSVT.

Although in these patients it is possible that identical therapeutic regimens could have been evolved out of trial and error, we feel that the study protocol as described allowed a rapid delineation of a successful oral drug regimen. The ability to induce PSVT at will allowed rapid screening of multiple antiarrhythmic agents.

Serum drug levels were not measured systematically in the present study. This partially reflected inability to measure ouabain and propranolol levels in our institution at the present time. In addition, propranolol levels have been demonstrated to have wide variations, with little reported data concerning the relationship of propranolol to control of arrhythmias. Plasma procainamide levels following intravenous infusion of 750 to 1000 mg have been demonstrated to range from 10.2 ± 3.4 µg/ml (at the end of infusion) to 4.9 ± 3.2 µg/ml (20 min after infusion). These levels could be anticipated to occur with our infusion protocol (cases 2, 3 and 8). Of the five patients (cases 2, 3, 6, 7 and 8) in whom digoxin and procainamide levels were measured at the time of electrophysiological studies and during follow-up, the blood levels were within therapeutic range (table 3). Systematic measurement of appropriate drug blood levels would aid in the interpretation of chronic electrophysiological study.

In three patients, no drug or drug combination could be delineated which prevented induction of sustained PSVT. This type of response was utilized as an indication for more invasive therapeutic modalities. Such therapeutic modalities currently available would include patient-activated radiofrequency pacemakers for PSVT conversion (used in two of the drug-resistant patients) and surgical transection of anomalous pathways (utilized in one of the drug resistant patients). The protocol described in this study is a rapid means of delineating patients who will not be responsive to currently available antiarrhythmic drugs. In the course of daily arrhythmia induction, it was also demonstrated that specific modes of stimulation would be successful in terminating episodes of PSVT. These modes of stimulation were then replicated with patient-activated externally controlled radiofrequency pacemakers.

In summary, the study suggested that chronic electrophysiological study utilizing multiple antiarrhythmic agents, singly and in combination, is a useful means of rapidly delineating successful therapy or the need for more invasive therapeutic modalities in patients with manifest or concealed pre-excitation. A similar type of protocol should be useful in the evaluation of other arrhythmias such as A-V nodal re-entrant PSVT and some cases of ventricular tachycardia that are readily reproduced with cardiac stimulation techniques.

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