The Effect of Procaine Amide (Pronestyl) in Clinical Auricular Fibrillation and Flutter

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Procaine amide (Pronestyl) was administered to patients with auricular fibrillation and flutter in an attempt to restore sinus rhythm. Thirteen of 20 patients with auricular fibrillation had sinus rhythm re-established. Several of the patients who were not converted with procaine amide were later restored to sinus rhythm with quinidine.

For many years the restoration of sinus rhythm in patients with auricular fibrillation and auricular flutter has been limited primarily to the use of quinidine and its allies. Other agents have occasionally been used without too satisfactory clinical effects.

In animal experiments, procaine hydrochloride has been shown to exert a markedly depressant action on conduction of the cardiac impulse. Procaine hydrochloride has been employed locally and parenterally in treating cardiac arrhythmias arising during surgical procedures in anesthetized patients and has been tried in various clinical instances of spontaneous cardiac irregularities. While sometimes useful under the former circumstances, its central stimulating effects have precluded its application in the unanesthetized patient.

Recently a procaine derivative, the amide analogue of procaine has been introduced. This agent, procaine amide (Pronestyl), is free of central nervous stimulating effects in the dosages used and is applicable in unanesthetized patients. The experimental data of Newman and Clark demonstrated that procaine amide exerts a slowing effect on conduction and produces a decrease of irritability of auricular muscle of the rabbit and the dog. These observations have led us to explore the sphere of usefulness of the drug in the conversion of auricular fibrillation and flutter to sinus rhythm in clinical instances of these arrhythmias.

Material and Methods

Our material and the therapy used are listed in Table 1. There were 20 patients with auricular fibrillation; of these, 13 had chronic auricular fibrillation. The latter term was arbitrarily applied to those patients who were known to have auricular fibrillation for two weeks or more. Their ages ranged from 37 to 71 years and the duration of the arrhythmia from 16 days to more than three years. Five of these patients had rheumatic heart disease and seven had hypertensive and/or arteriosclerotic heart disease.

Of seven patients with paroxysmal auricular fibrillation, five had hypertensive and/or arteriosclerotic heart disease and one patient (case 2) with no previous evidence of heart disease developed auricular fibrillation one day following an appendectomy.

All three patients with auricular flutter had arteriosclerotic heart disease; in two the auricular flutter was paroxysmal while the duration of the arrhythmia was unknown in the third patient.

Except for five of the patients with paroxysmal auricular fibrillation and one patient with paroxysmal auricular flutter, all were receiving digitalis at the time conversion was attempted. Two of the patients with auricular flutter were partially digitalized. Procaine amide was given orally in the majority of cases, intramuscularly in one case each of paroxysmal and chronic auricular fibrillation, and intravenously in two cases of auricular flutter. Initially there was some variation in the oral doses, but subsequently the following schedule was generally employed: 500 mg. every two hours for five doses on the first day, 750 mg. every two hours for five doses on the second day and similar 250 mg. increments on the following days until toxicity or regular sinus rhythm occurred. The highest single dose was 1500 mg., and the highest dosage in one
### Table 1.—Clinical Data on Twenty-three Patients Treated with Procaine Amide*

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Sex</th>
<th>Clinical Diagnosis†</th>
<th>Auricular Arrhythmia</th>
<th>Duration</th>
<th>Digital-</th>
<th>Maximum Procaine Amide Dosage</th>
<th>Toxicity</th>
<th>Rhythm after Therapy†</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>66</td>
<td>M</td>
<td>H.A.S.H.D.</td>
<td>Parox. aur. fib.</td>
<td>4 days</td>
<td>+</td>
<td>On a q. 2 hr. schedule mg.: 500-500-750-1500-1500-1500</td>
<td>None</td>
<td>SR</td>
</tr>
<tr>
<td>2</td>
<td>60</td>
<td>M</td>
<td>A.S.H.D.(?) postop.</td>
<td>Parox. aur. fib.</td>
<td>2 hrs.</td>
<td>−</td>
<td>1000 mg. followed in 1½ hrs. by 750 mg.</td>
<td>None</td>
<td>SR</td>
</tr>
<tr>
<td>3</td>
<td>57</td>
<td>F</td>
<td>H.A.S.H.D.</td>
<td>Parox. aur. fib.</td>
<td>2 hrs.</td>
<td>−</td>
<td>One dose 500 mg.</td>
<td>None</td>
<td>SR</td>
</tr>
<tr>
<td>4</td>
<td>74</td>
<td>F</td>
<td>A.S.H.D.</td>
<td>Parox. aur. fib.</td>
<td>3 hrs.</td>
<td>−</td>
<td>One dose 1000 mg.</td>
<td>None</td>
<td>SR</td>
</tr>
<tr>
<td>5</td>
<td>62</td>
<td>M</td>
<td>A.S.H.D.</td>
<td>Parox. aur. fib.</td>
<td>14 hrs.</td>
<td>−</td>
<td>1:00 p.m. 500 mg; 6:00 p.m. 500 mg.</td>
<td>None</td>
<td>SR</td>
</tr>
<tr>
<td>6a</td>
<td>55</td>
<td>M</td>
<td>H.A.S.H.D.</td>
<td>Parox. aur. fib.</td>
<td>10 days</td>
<td>+</td>
<td>1000 mg. followed in 3 hrs. by 500 mg.</td>
<td>None</td>
<td>SR</td>
</tr>
<tr>
<td>6b</td>
<td></td>
<td></td>
<td></td>
<td>Recurrence of aur. fib.</td>
<td>4 days</td>
<td>+</td>
<td>1000 mg. q. 3 hrs. × 4</td>
<td>None</td>
<td>SR</td>
</tr>
<tr>
<td>7</td>
<td>70</td>
<td>M</td>
<td>A.S.H.D. postop.</td>
<td>Parox. aur. fib.</td>
<td>1 day</td>
<td>−</td>
<td>750 mg. q. 2 hrs. × 3 (I.M.)</td>
<td>None</td>
<td>SR</td>
</tr>
<tr>
<td>8</td>
<td>63</td>
<td>M</td>
<td>H.A.S.H.D.</td>
<td>Chronic aur. fib.</td>
<td>2½ yrs.</td>
<td>+</td>
<td>On a 2 hr. schedule mg.: 750-1000-1250-1500-1500-1500-1000</td>
<td>Yes</td>
<td>Unchanged</td>
</tr>
<tr>
<td>9</td>
<td>45</td>
<td>F</td>
<td>R.H.D.</td>
<td>Chronic aur. fib.</td>
<td>2 yrs.+</td>
<td>+</td>
<td>1000 mg. q. 2 hrs. × 5</td>
<td>None</td>
<td>Unchanged</td>
</tr>
<tr>
<td>10</td>
<td>51</td>
<td>F</td>
<td>R.H.D.</td>
<td>Chronic aur. fib.</td>
<td>3 yrs.+</td>
<td>+</td>
<td>1000 mg. q. 2 hrs. × 5</td>
<td>Yes</td>
<td>Unchanged</td>
</tr>
<tr>
<td>11</td>
<td>78</td>
<td>M</td>
<td>H.A.S.H.D.</td>
<td>Chronic aur. fib.</td>
<td>years</td>
<td>+</td>
<td>500 mg. q. 4 hrs. × 7</td>
<td>None</td>
<td>SR</td>
</tr>
<tr>
<td>12</td>
<td>71</td>
<td>M</td>
<td>A.S.H.D.</td>
<td>Chronic aur. fib.</td>
<td>1 yr.+</td>
<td>+</td>
<td>1000 mg. q. 4 hrs. × 5</td>
<td>None</td>
<td>Unchanged</td>
</tr>
<tr>
<td>13</td>
<td>50</td>
<td>M</td>
<td>A.S.H.D.</td>
<td>Chronic aur. fib.</td>
<td>16 days+</td>
<td>+</td>
<td>1000 mg. q. 2 hrs. × 4</td>
<td>None</td>
<td>SR</td>
</tr>
<tr>
<td>14</td>
<td>50</td>
<td>M</td>
<td>R.H.D.</td>
<td>Chronic aur. fib.</td>
<td>3 mos.+</td>
<td>+</td>
<td>1000 mg. q. 2 hrs. × 3</td>
<td>Yes</td>
<td>Unchanged</td>
</tr>
<tr>
<td>15</td>
<td>56</td>
<td>M</td>
<td>A.S.H.D.</td>
<td>Chronic aur. fib.</td>
<td>1½ yrs.</td>
<td>+</td>
<td>1250 mg. q. 2 hrs. × 5</td>
<td>Yes</td>
<td>Unchanged</td>
</tr>
<tr>
<td>16</td>
<td>35</td>
<td>F</td>
<td>R.H.D.</td>
<td>Chronic aur. fib.</td>
<td>51 days</td>
<td>+</td>
<td>1000 mg. q. 2 hrs. × 4</td>
<td>Yes</td>
<td>SR</td>
</tr>
<tr>
<td>17</td>
<td>51</td>
<td>M</td>
<td>A.S.H.D.</td>
<td>Chronic aur. fib.</td>
<td>t</td>
<td>+</td>
<td>1250 mg. q. 2 hrs. × 6 followed by 2 doses of 1500 mg. q. 2 hrs.</td>
<td>Yes</td>
<td>SR</td>
</tr>
<tr>
<td>18a</td>
<td>58</td>
<td>M</td>
<td>H.A.S.H.D.</td>
<td>Chronic aur. fib.</td>
<td>at least 16 days: probably months</td>
<td>+</td>
<td>1000 mg. q. 2 hrs. × 5</td>
<td>None</td>
<td>SR</td>
</tr>
<tr>
<td>18b</td>
<td></td>
<td></td>
<td>Recurrence</td>
<td></td>
<td></td>
<td>+</td>
<td>1000 mg. q. 2 hrs. × 5</td>
<td>None</td>
<td>SR</td>
</tr>
<tr>
<td>19</td>
<td>47</td>
<td>M</td>
<td>R.H.D.</td>
<td>Recurrence</td>
<td>1 month+</td>
<td>+</td>
<td>1500 mg. q. 2 hrs. × 6</td>
<td>Nausea</td>
<td>Unchanged</td>
</tr>
</tbody>
</table>
**Results**

All seven patients with eight bouts of paroxysmal auricular fibrillation who received procaine amide were converted to sinus rhythm (tables 1 and 2). The duration of auricular fibrillation prior to therapy ranged from two hours in case 3 to at least 10 days in case 6 (table 1). Cases 3, 4 and 5 returned to sinus rhythm following relatively small doses (500 to 1000 mg.) of the drug and the possibility of spontaneous conversion cannot be excluded. However, larger doses of procaine amide were required for normalization of rhythm in the four other instances. Case 6 was restored to sinus rhythm, but when the maintenance dose of procaine amide was decreased to 500 mg. four times a day auricular fibrillation recurred. Procaine amide was then again used successfully in higher doses to re-establish sinus rhythm. In case 7, sinus rhythm was restored after intramuscular therapy.

Of 13 patients with chronic auricular fibrillation who received procaine amide six returned to sinus rhythm (tables 1 and 2). Except for case 20, there was electrocardiographic evidence of the presence of auricular fibrillation of at least two weeks duration in all patients. The duration of the arrhythmia in case 20 is unknown but it was thought to have been present several months prior to therapy. Of five cases with chronic auricular fibrillation with rheumatic heart disease only one was converted to sinus rhythm with procaine amide although the medication was given in sufficient quantity (table 1) to produce toxic manifestations in three of four failures. In three of the rheumatic patients who were not converted with procaine amide, quinidine sulfate was given later and was successful in restoring sinus rhythm in all (table 3).

Of eight patients in whom chronic auricular fibrillation was associated with arteriosclerotic and/or hypertensive heart disease, sinus rhythm was restored by procaine amide in five. Case 18 was converted a second time when a reduction in his maintenance therapy was followed by a recurrence of auricular fibrillation. All three failures in the hypertensive arteriosclerotic group were subsequently tried briefly on quinidine sulfate (table 3). One patient (case 13) returned to sinus rhythm.

The results of procaine amide treatment in
EFFECT OF PRONESTYL IN AURICULAR FIBRILLATION

the cases of auricular flutter, used intravenously in two cases and orally in one, will be mentioned was diagnosed clinically. In all other patients the auricular mechanism was proved by electro-

Table 2.—Summary of Results of Procaine Amide Treatment

<table>
<thead>
<tr>
<th>Patients</th>
<th>Total Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>Converted to Sinus Rhythm</td>
</tr>
<tr>
<td>Paroxysmal auricular fibrillation</td>
<td>7</td>
</tr>
<tr>
<td>Chronic auricular fibrillation</td>
<td>13</td>
</tr>
<tr>
<td>Auricular flutter</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>23</td>
</tr>
</tbody>
</table>

Table 3.— Patients with Chronic Auricular Fibrillation Who Received Procaine Amide and Quinidine Sulfate on Different Occasions

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Procaine Amide</th>
<th>Quinidine</th>
<th>Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Converted to Sinus Rhythm</td>
<td>Maximum Dosage Received</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>No</td>
<td>1000 mg. q. 2 hrs. × 5</td>
<td>Nausea and dizziness</td>
</tr>
<tr>
<td>12</td>
<td>No</td>
<td>1000 mg. q. 4 hrs. × 5</td>
<td>None</td>
</tr>
<tr>
<td>14</td>
<td>No</td>
<td>1000 mg. q. 2 hrs. × 3</td>
<td>Nausea, vomiting and dizziness</td>
</tr>
<tr>
<td>15</td>
<td>No</td>
<td>1250 mg. q. 2 hrs. × 5</td>
<td>Nausea and dizziness</td>
</tr>
<tr>
<td>8</td>
<td>No</td>
<td>1500 mg. q. 2 hrs. × 5</td>
<td>Dizziness, blurred vision and visual hallucinations</td>
</tr>
<tr>
<td>19</td>
<td>No</td>
<td>1500 mg. q. 2 hrs. × 6</td>
<td>Nausea</td>
</tr>
<tr>
<td>17</td>
<td>Yes</td>
<td>1250 mg. q. 2 hrs. × 6 followed by 2 doses 1500 mg. at 2 hr. intervals</td>
<td>Dizziness, nausea and vomiting</td>
</tr>
</tbody>
</table>

below with the discussion of the electrocardiographic observations.

In one patient (case 1) auricular fibrillation cardiogram prior to therapy. Electrocardiographic changes observed under procaine amide medication consisted in alterations of auricular
rate and rhythm, of the ventricular rate and of the duration of the Q-T interval and are illustrated in figures 1 to 4. The mechanism of conversion to a regular rhythm was observed in eight cases of chronic auricular fibrillation and in two cases of auricular flutter, but only in a single case of paroxysmal auricular fibrillation who developed sinus rhythm with frequent auricular premature systoles (case 3, fig. 1b). In cases of chronic auricular fibrillation procaine amide affected a slowing of the auricular rate five times (fig. 2d) and produced a stage of auricular flutter three times (figs. 1c, 2e). Auricular flutter, both induced and pre-existent, responded to further administration of the drug by slowing of the rate of auricular oscillations before the onset of regular sinus rhythm. Thus it would appear that conversion was prone to occur abruptly in cases with the paroxysmal form of the arrhythmia and more gradually in its chronic manifestation.

In case 23, the auricular arrhythmia was replaced, after a short period of sinus tachycardia, by an ectopic rhythm of nodal origin persisting over several days (fig. 3e). Conversion of auricular fibrillation and flutter to nodal rhythm was observed in the present series in two other instances; in case 14 following quinidine and in case 22 (fig. 4c) after massive digitalization. In both instances procaine amide in doses insufficient for conversion had produced undesired effects (toxicity in case 14 and excessive acceleration of the ventricular rate in case 22).

An untoward increase of ventricular rate under procaine amide medication was observed in 6 instances. Cases 9, 16 (fig. 1c) and 17 (figs. 2d and e) are examples associated with gradual slowing of the rate of auricular oscillations in the course of conversion of chronic auricular fibrillation into sinus rhythm. In two attempts to convert pre-existent auricular
flutter, the ventricular rate became alarmingly high because of transient 1:1 conduction during a stage of slowed auricular flutter (figs. 3 and 4). This marked increase of ventricular rate, which occurred despite preceding digitalization in four cases, may be considered as evidence for the unimpaired A-V conduction during procaine amide therapy.

Fig. 2. Comparison of the effect of quinidine (a and b) and procaine amide (c to f) on the electrocardiogram. Case 17, on maintenance dose (0.2 mg.) of digitoxin.

(a) 1/19/51, lead II: Auricular fibrillation, auricular rate approximately 500, average ventricular rate 66. ST-T configuration typical for digitalis effect. Q-T duration 0.02 second shorter than the expected value.

(b) 1/25/51, lead II: After a total dose of 5.0 Gm. of quinidine sulfate in 2 days: Sinus rhythm, rate 75. Note depression of S-T with prolongation of Q-T to +0.09 second.

(c) 7/2/51, a.m., lead II: Auricular fibrillation, average ventricular rate 62, Q-T duration +0.02 second.

(d) Same day, 9:30 p.m., lead V1: After total of 7.75 Gm. procaine amide. Impure auricular flutter with irregular A-V conduction. Average auricular rate 250, average ventricular rate 85.

(e) Same days as c and d, 11:30 p.m., lead V1: After another 1.0 Gm. of procaine amide. Pure auricular flutter with irregular A-V conduction. Auricular rate 206, average ventricular rate 95.

(f) 7/3/51, lead II: After total dose of 19.25 Gm. Pronestyl. Sinus rhythm with auricular premature systoles, average rate 58. P-R interval 0.22 second. Note S-T depression and Q-T prolongation (+0.06 second). Compare with b.

The Q-T duration before and after medication was evaluated by the method of Hegglin and Holzmann,4 according to which Q-T intervals exceeding the calculated value for the respective heart rate by ±0.04 second are considered abnormal. Prolonged Q-T duration (greater than +0.04 second) was found in eight instances of the procaine amide experiments, a normal Q-T duration (±0.04 second) in 14 instances. The presence or absence of a prolonged Q-T interval did not seem to correlate with the amount of procaine amide used or with clinical signs of procaine amide toxicity. However, it appeared to be influenced by preceding or concomitant digitalization. This was also suggested by the fact, that most instances with normal Q-T duration under procaine amide effect showed the typical "digitalis con-

tour" of ST-T (fig. 1c) while a "pure" procaine amide effect on Q-T could be seen in some undigitalized cases (fig. 1a). In one instance (fig. 1b) a pre-existent abnormal Q-T showed no further prolongation after a small dose of procaine amide.

Toxicity of Procaine Amide. Contrary to its effect after intravenous administration we encountered no significant hypotensive action of orally administered procaine amide. The toxic
Fig. 3. Conversion of paroxysmal auricular flutter to nodal tachycardia. Case 23, no digitalis.
(a) 1/28/51, lead II: Paroxysm of auricular flutter with regular 2:1 conduction. Auricular rate 334, ventricular rate 167, QRS duration 0.10 second. (b-d) were taken at short intervals during and following intravenous injection 0.75 Gm. of Pronestyl in three and one-half minutes.
(b) Lead II: Average ventricular rate 230, QRS duration 0.10 second. Auricular flutter as underlying rhythm can be recognized at the beginning of the strip, where the ventricular rate is slower and irregular due to transitory change of 1:1 to 3:2 A-V conduction. The auricular rate at these times has slowed down to 276.
(c and d) Lead II and III: Auricular flutter with regular 1:1 conduction rate 250. QRS duration 0.16 second. Distinct F waves seen in lead III (right strip). Note similarity to ventricular tachycardia.
(e) Lead II, taken 30 minutes after d. No further therapy. Nodal tachycardia, rate 107. QRS duration 0.06 second.

Fig. 4. Effect of oral procaine amide on auricular flutter. Case 22. On 0.1 mg. digitoxin daily.
(a) 4/28/51, a. m., lead III: Auricular flutter with regular 2:1 A-V conduction. Auricular rate 250, QRS duration 0.11 second. Incomplete right bundle branch system block.
(b) Same day, p. m., lead II: After 1.0 Gm. procaine amide. Auricular flutter with 1:1 conduction. Auricular and ventricular rate 218. QRS duration unchanged. Note similarity to ventricular tachycardia.
(c) Shortly after b, lead II: Auricular flutter with irregular A-V conduction varying between ratios of 4:3 to 3:2. Auricular rate 210, average ventricular rate 148. QRS duration unchanged.
(d) 5/2/51, lead III: Return to a regular 2:1 A-V conduction with auricular flutter persisting, Auricular rate 260.
(e) 5/4/51, lead I: Heavily digitalized. Auricular standstill (due to complete S-A block) and nodal rhythm, rate 65. Electrical alternans due to intermittent complete (QRS 0.18 second), superimposed on a persistent incomplete (QRS 0.11), right bundle branch system block.

manifestations encountered were dizziness, nausea, vomiting, and in one case visual hallucinations. Although in some instances (cases 8 and 19) the amount of procaine amide given
was unusually high and was extended to the point of clinical intolerance, in none was ectopic impulse formation or impairment of intraventricular conduction observed which could be ascribed to the action of the drug. In two instances (cases 16 and 22, figs. 1e and 4) a right sided conduction defect present before medication was started, showed no further impairment. The QRS prolongation seen in case 23 (fig. 3) at the peak of the procaine amide effect, disappeared immediately with conversion to nodal rhythm and may, therefore, be ascribed to the excessively high ventricular rate during auricular flutter.

**Comment**

After screening numerous compounds for possible use in the therapy of cardiac arrhythmia, Mark and co-workers carried out extensive studies with procaine amide.\(^3\)-\(^7\) While these authors advocated its use in arrhythmias of ventricular origin, Newman and Clark subsequently demonstrated that the drug also had a very definite effect on the conduction and irritability of the auricle of the rabbit and dog.\(^4\)\(^-\)\(^5\) Studies with intravenous procaine amide demonstrated a very definite slowing of the fibrillatory rate of the human auricle.\(^5\)\(^-\)\(^7\)\(^-\)\(^4\) The drug has been successfully used by others\(^7\)\(^-\)\(^9\) in cases of paroxysmal auricular fibrillation. The uniformly good success in restoring sinus rhythm in our seven patients with recent onset of auricular fibrillation is in keeping with these findings. However, six of the 13 patients with chronic auricular fibrillation were also restored to sinus rhythm. This result is somewhat better than anticipated since a number of observers\(^5\)\(^-\)\(^7\)\(^-\)\(^8\)\(^-\)\(^13\) have reported the absence of conversions in patients with chronic auricular fibrillation given intravenous procaine amide. It is quite likely that the greater success in more recent investigations using oral procaine amide\(^11\)\(^-\)\(^12\) and in the present study was a result of the higher dosage schedules employed. Reflecting the latter, four of the six patients with chronic auricular fibrillation who were converted had toxic symptoms just prior to, or at the time of, restoration of regular sinus rhythm. Since procaine amide produces its peak blood level approximately one to two hours after each oral dose, we feel that a two hour schedule is to be preferred in attempting conversion. To simplify the observation of all patents receiving procaine amide, we generally omitted night time medication and recommended therapy the following morning at the next higher dose schedule. Procaine amide was not only effectively used orally and intravenously but in two patients, who could not take oral medication, the drug was successfully employed by intramuscular administration.

Although weight for weight quinidine is more potent than procaine amide,\(^14\)\(^-\)\(^16\) this fact in itself does not indicate that it is superior in treating auricular flutter and fibrillation. One must have some idea of the toxic to therapeutic ratio before selecting the desired preparation. Some of our data bears on this point and is shown in table 3. Four patients who failed to convert with procaine amide in spite of the fact that the drug was given to toxicity, subsequently were successfully converted with quinidine. Two of the four patients were converted, without any evidence of quinidine toxicity, while the other two had minor symptoms of quinidine intolerance at the time of conversion. A fifth patient (case 17) who was converted to sinus rhythm with quinidine without toxicity, had a recurrence of auricular fibrillation six weeks later after he failed to take maintenance therapy. He was then successfully treated with procaine amide but had toxic symptoms at the time of conversion. From this preliminary experience it would appear that quinidine can restore sinus rhythm in patients with chronic auricular fibrillation more easily and with fewer toxic manifestations than procaine amide.

Kalmansohn and Sampson have stated\(^17\) that the only serious toxic manifestations of quinidine therapy are ectopic ventricular arrhythmias or marked hypotensive effects. Similar toxic signs, including impairment of A-V and intraventricular conduction, have been said to occur with procaine amide.\(^2\)\(^-\)\(^7\)\(^-\)\(^10\)\(^-\)\(^11\)\(^-\)\(^12\)\(^-\)\(^13\)\(^-\)\(^14\)\(^-\)\(^16\) Although clinical intolerance was reached in several of our cases receiving procaine amide, electrocardiographic signs of toxicity were not observed in the present series. The transient widening of QRS in case 23 is explained by aberration of intraventricular conduction with
the rapid heart rate, due to shortening of diastolic recovery time of the conduction system. It has been pointed out that electrocardiographic patterns like those shown in figures 3b-d and 4b may be mistaken for ventricular tachycardia of ectopic origin and thus may lead to serious therapeutic consequences.

The electrocardiographic alterations found during our procaine amide studies are in accord with previous investigations as far as changes of the auricular mechanism, the auricular and/or ventricular rate and the effect on Q-T duration are concerned. The same discordant effect on auricular and ventricular action (slowing of the former and acceleration of the latter) was seen under procaine amide as was described years ago by Rothberger and Lewis in their studies on the effect of quinidine and quinidine on auricular flutter and fibrillation. This includes the deleterious increase of ventricular rate by production of full A-V conduction as seen in two of our cases with auricular flutter. Prolongation of the Q-T interval was seen in about one third of cases treated orally by procaine amide. The shortening effect on the "electrical systole" of digitalis may explain the lack of appearance of Q-T prolongation in the greater part of our material consisting primarily of cases with chronic auricular fibrillation.

The increase in the ventricular rate may be marked in patients with auricular fibrillation and particularly auricular flutter who receive procaine amide, especially if no digitalis has been given. In view of the danger of prolonged, rapid ventricular rates, particularly in the presence of associated heart disease, it is best to give adequate digitalis therapy prior to an attempt at conversion.

The exact mechanism of the action of procaine amide on the auricular and ventricular myocardium is still obscure and requires further experimental clarification. The striking similarity between quinidine and procaine and its amide in their clinical action and effects upon the electrocardiogram invites speculation upon a possible similar mode of action. Prolongation of the refractory period of the isolated rabbit auricle by procaine amide has been demonstrated, and a similar effect on the ventricular myocardium is suggested by the prolongation of the Q-T interval following clinical application of procaine amide. However, the appearance of persistent nodal rhythm after interruption of experimentally produced auricular fibrillation, as previously reported, as well as its appearance in one of our cases cannot be explained by such a mechanism alone. It is possible that, for unknown reasons, secondary mechanisms may become prevalent in certain instances, like stimulation of subsidiary automatic center and/or a depressing action on impulse transmission in the auricles. The latter mechanism has been especially stressed in recent studies on the action of quinidine in auricular arrhythmias. The similarity to quinidine is further supported by observations of unusually high rates of A-V conduction (276 in case 23), which were ascribed in the case of quinidine to its paralyzing effect upon the vagi.

**Summary and Conclusions**

1. Twenty cases of auricular fibrillation and three cases of auricular flutter were treated with procaine amide (Pronestyl) in an attempt to restore sinus rhythm.

2. The attempt proved successful in all instances of paroxysmal auricular fibrillation, in 6 of 13 cases with chronic auricular fibrillation and in two of three cases of auricular flutter. The dosage used ranged from a single dose of 500 mg. in a case of paroxysmal auricular fibrillation to 11.5 Gm. in a day given to a patient with chronic auricular fibrillation.

3. In no instance were there electrocardiographic manifestations of toxicity in the present series. In two instances slowing of the rate of auricular flutter by procaine amide with transient 1:1 A-V conduction and aberrant intraventricular conduction imitated the electrocardiographic pattern of ventricular tachycardia of ectopic origin.

4. A striking similarity between procaine amide and quinidine was found in their clinical action as well as in their effect upon the electro-

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* Such a complex mechanism was apparently under action and effected by massive digitalization in case 22, figure 4e, and produced complete S-A block, nodal rhythm and electrical alternation.
cardiogram. Although this suggests very strongly a similar mode of action of both drugs, further experimental proof is needed.

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The Effect of Procaine Amide (Pronestyl) in Clinical Auricular Fibrillation and Flutter
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