The Use of Procaine Amide in Cardiac Arrhythmias

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Procaine amide, a new synthetic analogue of procaine, has marked antiarrhythmic activity and is relatively stable in the body. It is effective when administered orally or intravenously, and has few toxic effects in therapeutic doses. The drug has been used successfully in the suppression of ventricular premature contractions and in the interruption of ventricular tachycardia. Some patients treated successfully with procaine amide had been given quinidine to the point of toxicity without affecting the aberrant rhythm. Procaine amide appears to be less effective in interrupting auricular than ventricular arrhythmias.

PROCaine, administered intravenously, exerts an antiarrhythmic action on the heart. However, its stimulatory effects on the central nervous system limit its application as an antiarrhythmic drug to the anesthetized patient. In addition, procaine is rapidly inactivated by its hydrolysis in the bloodstream to p-aminobenzoic acid and diethylaminoethanol. The latter compound in rather large dosage also exhibits antiarrhythmic action, but with minimal stimulatory effects on the central nervous system. In a previous communication, experiences with diethylaminoethanol and its possible value in ventricular tachycardia were discussed.

A series of derivatives of diethylaminoethanol were synthesized in the hope that the activity of the alcohol could be enhanced without a comparable increase in toxicity and that a compound would be found which would have greater stability than procaine. The compounds were tested for antiarrhythmic activity on the ventricular tachycardia which is induced by injection of epinephrine into dogs anesthetized with cyclopropane. The most promising compound of the series was procaine amide, the amide analogue of procaine. This report is concerned with results obtained in treating various cardiac arrhythmias with procaine amide.

The pharmacologic data on procaine amide has been detailed elsewhere. Briefly, the drug is rapidly and completely absorbed from the gastrointestinal tract, peak blood concentrations being obtained one to two hours after its oral administration. It is relatively stable in the body, not being affected by the enzyme which catalyzes the hydrolysis of procaine. It is slowly excreted by the kidneys, plasma levels declining only about 15 per cent per hour. About 60 per cent of the drug is excreted unchanged in the urine. In patients with normal renal function, plasma levels reach a relative plateau after 36 to 48 hours of repeated oral administration of a constant amount.

The most common arrhythmia available for study was the premature contraction of ventricular origin. The effects of procaine amide were observed in 54 patients with this condition. In some patients, the premature beats were attributable to the administration of digitalis, while in others they were associated with organic, primarily arteriosclerotic heart disease.

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† Supplied as Pronestyl hydrochloride by E. R. Squibb & Co.
In each instance, the drug administered orally or intravenously in doses varying from 0.4 to 1.0 Gm., suppressed the ectopic beats. On intravenous administration the effect occurred during or shortly following the period of injection; after oral administration there was usually a delay of 30 to 60 minutes. After a single intravenous dose, the period of suppression usually varied from three to six hours. The irregularity of the occurrence of extrasystoles makes it difficult, however, to estimate the duration of effect of the drug. In an occasional patient suppression has lasted for less than one hour, and in a few for more than 24 hours. Experience with oral administration has helped in estimating the duration of effect. Following a single oral dose, the usual period of suppression appeared to be the same as with an intravenous dose, namely three to six hours. In 14 cases, the administration of procaine amide at intervals of three to six hours successfully prevented the recurrence of ventricular extrasystoles for many weeks. In one patient, therapy has been continued successfully for four months.

The effect of procaine amide on ventricular tachycardia was studied in 15 patients with this disturbance. In 13 of these, administration of the drug orally, intravenously, or by both routes was successful in that there was reversion to the cardiac rhythm that existed prior to the ventricular tachycardia. (Three examples are shown in figures 1, 2 and 3.) There were two failures. One patient (case 3), who presented an unusually difficult problem, died during intravenous injection of procaine amide. In retrospect, too rapid administration of the drug may have been responsible for the development of ventricular fibrillation. In the other patient (case 9), death due to ventricular fibrillation occurred during administration of procaine amide, but before a significant quantity (150 mg.) had been administered. A resume of the clinical findings and therapy for each of the treated cases is appended.

Analysis of the electrocardiograms obtained

![Fig. 1. Effect of procaine amide on ventricular tachycardia (case 5). A, lead I; B, lead II, and C, lead III: control tracings. Ventricular tachycardia. Rate 190 per minute. D. After injection 600 mg. procaine amide (lead II). E. After injection 1 Gm. procaine amide (lead II). Maintenance oral therapy 1 Gm. every three hours (see case report). F. Four hours later (lead I). Ventricular tachycardia recurred. Dosage increased to 1 Gm. every two hours. G, lead I; H, lead II; and I, lead III: 12 hours later. Normal sinus rhythm. Rate 78.](http://circ.ahajournals.org/).
during intravenous injections indicates that the sequence of events incidental to the interruption of ventricular tachycardia may vary considerably. In some cases, the ventricular tachycardia is abruptly interrupted and a supra-ventricular pacemaker, frequently the A-V node, is established. This occurs with or without preliminary slowing of the ventricular rate. In other patients, the aberrant rhythm does not terminate abruptly; occasional beats of supra-ventricular origin first interrupt the ventricular tachycardia, increase in frequency during a period of several minutes, until the supra-ventricular pacemaker is established. The course of response is not predictable.

The treatment of patients with auricular arrhythmias was much less successful. Auricular premature contractions could be eliminated by intravenous administration of procaine amide, but the effect was of shorter duration than with ventricular premature contractions. Apparently the duration of the abnormal rhythm is of considerable importance. Ten patients with chronic auricular flutter and 14 patients with chronic auricular fibrillation were treated with 1 Gm. of procaine amide injected intravenously over a period of five minutes. In none of these patients was normal sinus rhythm re-established, but an effect on auricular activity was observed in that there was marked slowing of the f waves (fig. 4). In 2 patients with recently established auricular fibrillation, however, normal rhythm appeared during the intravenous administration of 1 Gm. of procaine amide and persisted for several days. Further exploration of the effect of the drug on auricular fibrillation of recent origin seems warranted.

Two patients with nodal tachycardia were treated with procaine amide. One patient reverted to normal rhythm once on oral administration (3 Gm. in divided doses) and twice on
intravenous injection of 1 Gm. (fig. 5). The other patient did not respond to 1 Gm. given intravenously. This patient was not treated further with the drug.

The mechanism of action of procaine amide is not completely understood. The refractory period, as measured by Q-T interval, is prolonged and conduction is apparently slowed. In animal studies, procaine amide has been shown to increase the threshold to electrical stimulation of the ventricle.²

Electrocardiographic changes were noted in approximately one-third of patients receiving procaine amide orally or intravenously.* They have consisted in widening of QRS and Q-T intervals and diminution of voltage of QRS and T waves. The changes are transient in oral therapeutic schedules (6 to 8 Gm. per day). Following the intravenous administration of procaine amide, transient hypotension has occurred in about one-third of patients who did not have ventricular tachycardia. In the group with ventricular tachycardia, in whom hypotension is already frequently present, intravenous administration of procaine amide has usually produced a more marked depression, but this promptly disappeared with the establishment of a supraventricular rhythm. Hypotensive effects have not been

* In animal experiments, the continuous intravenous infusion of procaine amide to fatality produced the following cardiac disturbances: prolongation of P-R interval, widening of the QRS complexes, wandering pacemaker, nodal and ventricular premature contractions, ventricular tachycardia and fibrillation.

Fig. 3. Effect of procaine amide on ventricular tachycardia (case 8). A, lead I; B, lead II; C, lead III; and D, lead CF₁; Control tracings. Ventricular tachycardia. Rate 148 per minute. E, lead I; F, lead II; G, lead III; and H, lead CF₁; Four hours after injection 1 Gm. procaine amide. Normal sinus rhythm. Rate 94.
observed with oral administration even in the nine bouts of ventricular tachycardia successfully treated by this route.

Any dosage schedule based on the limited number of cases so far studied is, naturally, a provisional one. The intravenous route is preferable only in patients who are critically ill or who are unable to take oral medication. The maximal rate of intravenous administration has been 200 mg. per minute until aberrant rhythm has been interrupted or until a total of 1 Gm. has been administered. It is helpful to have an electrocardiogram, preferably recorded with a direct-writing instrument, during the injection. Because blood pressure often falls, it also should be frequently recorded. When the drug is given orally to patients, 1.25 Gm. may be given initially, and if the electrocardiogram reveals no change in one hour, a second dose of 0.75 Gm. Further doses of 0.5 to 1 Gm. may be administered every two hours as required until the aberrant rhythm is eliminated. Maintenance oral therapy may be necessary to prevent recurrence of extrasystoles and paroxysms of ventricular tachycardia. Doses of 0.5 to 1 Gm. administered every three to six hours during the day and night have maintained normal rhythm in patients studied to date. Similar oral schedules are recommended for ventricular premature contractions—requirements have varied from 1.5 to 8 Gm. per day in divided doses. Since the drug is excreted to a large extent by the kidneys, patients with impaired renal function receiving oral maintenance therapy may achieve unusually high plasma levels.

Further investigation is needed to evaluate the place of procaine amide in the treatment of cardiac arrhythmias. It would appear to be a safer and more effective agent than quinidine in the management of ventricular tachycardia and ventricular extrasystoles. Its application to the control of arrhythmias in anesthesia and in cardiac surgery is at present under study. Initial reports indicate that the prophylactic administration of procaine amide materially diminishes the incidence of arrhythmias during intrathoracic surgery.6

Case Reports

Case 1. W. W., a 77 year old male, was admitted in 1947 with acute urinary retention. He had been on maintenance digitalis therapy for congestive heart failure for several years following a myocardial infarction. There was no history of hypertension. In November 1948 he complained of palpitations and an electrocardiogram revealed a supraventricular tachycardia at a rate of 150 per minute. Oral quinidine sulfate and additional digitalis medication slowed the rate to 80, but the rhythm remained that of auricular flutter with a varying block. Seven months later, the patient had sudden precordial pain, dyspnea and palpitation. An electrocardiogram revealed ventricular tachycardia. Procaine amide was given intravenously four hours after the onset; at the end of five minutes (432 mg.), the ventricular tachycardia ceased and the rhythm of auricular flutter was renewed. Thirty-five minutes later the aberrant ventricular rhythm reappeared, and persisted for 25 minutes. The additional injection of 432 mg. over a five minute period again established

![Fig. 4. Effect of procaine amide on auricular flutter (right parasternal lead). A. Control tracing. Auricular rate 300 per minute. Ventricular rate 62. Ventricular premature contractions. B. After injection of 600 mg. procaine amide. Auricular rate 240. Ventricular rate 66. C. After injection 1 Gm. procaine amide. Auricular rate 196. Ventricular rate 82. D. Five minutes later. Auricular rate 187. Ventricular rate 86.](image)

![Fig. 5. The effect of procaine amide on nodal tachycardia. (Lead II retouched). Rate before injection 150 per minute; on completion of injection of 850 mg. (arrow), regular sinus tachycardia 110.](image)
auricular flutter. Subsequent clinical and electrocardiographic findings confirmed the impression of a new myocardial infarction. The patient had an uneventful convalescence, although his rhythm remained that of auricular flutter. Two months later he fell and died within 24 hours of a fractured skull. Postmortem examination was not obtained.

Case 2. M. G., a 60 year old white male, was admitted to the hospital with a diagnosis of acute myocardial infarction. On the fifth hospital day, he developed ventricular tachycardia. During the next 48 hours he was treated with quinidine sulfate orally to toxicity and magnesium sulfate intravenously, but there was no change in the rhythm. Then 0.5 Gm. of procaine amide was injected. At the end of injection (five minutes), occasional beats of sinus origin appeared, but the dominant rhythm remained that of ventricular tachycardia. Twenty minutes later, 0.5 Gm. of procaine amide was again given intravenously, and resulted in the appearance of more beats of sinus origin, which, however, did not persist for long. In the succeeding 48 hours the intravenous injection of quinidine sulfate, atabrine and diethylaminoethanol failed to interrupt the ventricular tachycardia. On the fifth day of the sustained ventricular tachycardia, procaine amide was again tried intravenously. One Gm. given over a 10 minute period had no demonstrable effect; 35 minutes later a second dose of 1 Gm. administered over a five minute period produced frequent sinus beats that established trigeminy. An additional dose of 0.25 Gm. intravenously was given 20 minutes later. The ventricular premature contractions disappeared completely in 40 minutes and the patient had an entirely uneventful hospital convalescence. He was hospitalized again 18 months later because of congestive heart failure. He responded promptly to treatment and was discharged two weeks after admission.

Case 3. S. L., a 45 year old male, was admitted to the hospital with a history of sudden chest pain and palpitation. Two years previously he had sustained a myocardial infarction. During the year prior to the second admission, he had observed increasing angina on effort. On admission, an electrocardiogram revealed ventricular tachycardia. Oral and intravenous therapy with quinidine administered to toxicity, as well as intravenous magnesium sulfate, did not alter the rhythm. On the third hospital day, 1 Gm. procaine amide administered intravenously in five minutes had no effect. An additional Gm. 30 minutes later produced occasional sinus beats (one per six to seven ventricular beats) for about 25 minutes. A third dose of 1 Gm. in three and a half minutes had no effect. That night 0.6 Gm. quinidine lactate was given intravenously, without producing either toxic or therapeutic effect. The next day the patient appeared moribund. An attempt was made to give 2 Gm. procaine amide at a faster rate, that is 400 mg. per minute. After the injection of 1 Gm. in two and a half minutes (one half contemplated dose), the patient developed ventricular fibrillation and died. At autopsy extensive sclerosis of the coronary arteries was found. There was complete occlusion of left coronary artery and a recent thrombus in right coronary artery with fresh necrosis in the papillary muscle of left ventricle. The entire wall of the left ventricle was thin and fibrotic, and at the apex there was an area of calcification.

Case 4. W. M., a 52 year old white male office worker, was admitted to the hospital following collapse on the street. He had been admitted three years before with a diagnosis of myocardial infarction. During the year prior to second admission he had noted polyuria, and had lost 60 pounds. During the weeks just prior to admission, the patient complained of anorexia with nausea and vomiting, polydypsia and increasing retroperitoneal pain on moderate effort. Examination on admission showed an acutely ill, pallid, apprehensive male; his blood pressure was 100/80 and his apical rate was 144 per minute. Examination of the urine showed a specific gravity of 1.032, 4 plus glycosuria and 2 plus acetonuria. After 12 hours of vigorous treatment with insulin and appropriate fluids, the urine became free of glucose and ketone bodies. During this period he was also digitalized with 1.2 mg. of digitoxin because of signs of congestive heart failure. An electrocardiogram taken at the end of this period of therapy revealed ventricular tachycardia. Oral quinidine was administered to toxicity. He was able to tolerate 3 Gm. daily in divided doses for the first five days, and then only 1.5 Gm. daily in divided doses for second five days. No effect on the rhythm was noted, though the QRS interval widened considerably. On the eleventh hospital day procaine amide was given intravenously; at the end of three and a half minutes (042 mg.), the aberrant rhythm was abruptly terminated, and normal sinus rhythm reestablished. The patient had an entirely uneventful convalescence and was discharged at the end of six weeks.

Case 5. E. F., a 65 year old white woman, was known to have had hypertension and diabetes mellitus for the prior 10 years. She was admitted to the hospital with a history of increasing dyspnea on effort and nocturnal orthopnea for two weeks and severe right upper quadrant pain for 24 hours. Physical examination showed an obese cyanotic female, in marked respiratory distress. Pulse rate was 90; blood pressure, 160/90. Examination of the lungs revealed many moist rales bilaterally; there was moderate distention of veins in the neck and a large tender liver extending 4 fingerbreadths below costal margin. Venous pressure was 200 mm. citrate and Decholin circulation time was 35 seconds. An electrocardiogram showed a rate of 90 per minute and changes consistent with posterior wall myocardial infarction. Oxygen, anticoagulants, penicillin...
and digitalis (0.8 mg. digitoxin by mouth in six hours) were administered. The following morning the patient had developed a rapid cardiac rate of 200 per minute, which was shown by electrocardiogram to be ventricular tachycardia (fig. 1A, B, C). The attempted oral administration of 0.9 Gm. of quinidine was unsuccessful because of vomiting. Quinidine lactate, 0.65 Gm., was given intravenously in 250 cc. solution over a period of 75 minutes, and resulted in slowing of the rate from 170 to 140. Three and a half hours later, the administration of 1.4 Gm. procaineamide intravenously in divided doses over 30 minutes, established bigeminal and then trigeminal rhythm (fig. 1D, E). Oral therapy of 1 Gm. every three hours was started, but after the second dose, ventricular tachycardia recurred (fig. 1F).

The dosage schedule was increased to 1 Gm. every two hours, and 12 hours later an electrocardiogram showed normal sinus rhythm at a rate of 72 (fig. 1G, H, I). Dosage was then reduced to 1 Gm. every three hours and the patient maintained normal sinus rhythm. The blood pressure which had been about 90/60 during her tachycardia, rose to 130/80. Twelve hours later the patient suddenly became very dyspneic and expired almost immediately. Permission for postmortem examination was refused.

Case 6. C. O., a 70 year old white female, was known to have had hypertension for 20 years. She had been bedridden for the past 10 years following a left hemiplegia. There was no history of cardiac decompensation. Electrocardiograms obtained during these 10 years of hospitalization had revealed normal sinus rhythm with wandering pacemaker and occasional ventricular premature contractions.

Suddenly, on Jan. 9, 1950, she noticed severe palpitation and an electrocardiogram showed ventricular tachycardia at a rate of 200 per minute. Procaineamide was given intravenously; after 200 mg. had been injected, beats of supraventricular origin appeared. At the end of the injection of 1 Gm., the ectopic ventricular beats had disappeared and the pacemaker appeared to be located in the auriculoventricular node. The electrocardiogram at the termination of injection, showed changes suggestive of fresh myocardial injury, but during the next four hours these abnormalities disappeared and normal sinus rhythm was established. An electrocardiogram on the next day (1/10/50) showed occasional ventricular premature contractions and bursts of ventricular tachycardia. The oral administration of 1 Gm. procaineamide every three hours eliminated these irregularities and the medication was discontinued after five doses. Thirty-eight hours later (1/12/50) ventricular tachycardia recurred. The oral administration of 1.5 Gm. procaineamide established normal sinus rhythm in 45 minutes. Oral maintenance therapy, 1 Gm. every four hours, was continued for four days and during this interval the patient had no aberrant beats. Medication was then discontinued. Three weeks later the patient once again complained of palpitation and an electrocardiogram again showed that ventricular tachycardia had recurred (fig. 2A). Procaineamide was given intravenously and at the end of 200 mg. supraventricular beats were observed to interrupt the ventricular rhythm, and after a total of 400 mg. the ectopic ventricular beats disappeared (fig. 2B, C). The rhythm again became nodal in origin for about two hours and then became normal sinus. An oral maintenance dose of 0.5 Gm. every four hours was given for five months, and during this period the patient remained in normal rhythm. At the end of this period, the medication was discontinued and during the succeeding 10 months there has been no recurrence of the abnormal rhythm.

Case 7. E. R., a 54 year old white male, was admitted on Dec. 25, 1949 with a history of angina on effort for 3 weeks and sudden severe sticking substernal pain for 24 hours prior to admission. There was no history of any previous cardiovascular disease. Physical examination showed a temperature of 101 F.; pulse rate, 96; and blood pressure, 110/80; the patient was not in acute distress and there were no signs of congestive heart failure. Heart sounds were of good quality; no thrills or murmurs were noted. The electrocardiogram showed normal sinus rhythm and changes indicative of acute infarction of the anterior wall of the heart. Therapy included oxygen, sedation, anticoagulants and quinidine, 0.4 Gm. every four hours, as a prophylactic measure. Eight days later (1/2/50), after an entirely uneventful course, the quinidine was discontinued. It was instituted again 24 hours later (1/3/50), when the patient had many ventricular premature contractions (0.4 Gm. administered every four hours four times). The next day (1/4/50), sustained ventricular tachycardia was present and the quinidine was increased to 0.65 Gm. every two hours to a total of 8 Gm. a day. The next day (1/5/50), there was a temporary establishment of normal sinus rhythm but the aberrant rhythm reappeared on 1/6/50 and continued uninterrupted for six days despite daily dosage of 8 Gm. of quinidine. On 1/12/50, a total of 1.5 Gm. of procaineamide was administered intravenously in two doses 35 minutes apart without altering the rhythm. One half hour later an oral dose of 1.5 Gm. was given, and two hours later an additional Gm. was given. An electrocardiogram taken one half hour after the second dose showed that normal sinus rhythm was present. He remained on a maintenance dose of procaineamide, 1 Gm. every four hours (six doses daily) for four days, without any aberrant beats being observed. Medication was then discontinued and the patient had an uneventful convalescence from the myocardial infarction.

Case 8. H. F., a 78 year old white male, was admitted to the hospital on Feb. 6, 1950 with a history of nausea, vomiting and precordial pain.
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for one week. He had been hospitalized previously in 1947 because of anterior wall infarction, and
again in March 1948 because of thrombophlebitis and pulmonary infarction. In October 1948 he
had again been hospitalized because of precordial pain, nausea and vomiting. During four weeks of
observation the findings were insufficient to establish the diagnosis of fresh myocardial infarction. Diagnos-
sis on discharge was arteriosclerotic heart disease, coronary insufficiency and aneurysm of the left
ventricle. For the four months prior to the last admission, the patient continued to receive digitalis
and mercurial diuretics for his congestive heart failure. On admission, an electrocardiogram showed
a ventricular tachycardia at a rate of 150 (fig. 3A, B, C, D). Quinidine sulfate, 0.2 Gm. orally
every hour for sixteen doses (3.2 Gm.), had no effect on the rhythm. On 2/8/50 1 Gm. of procaine
amide was given intravenously in five minutes, and directly after completion of the injection the ven-
tricular tachycardia was abruptly terminated with the establishment of a supraventricular rhythm;
the pacemaker was located first in the auriculo-
ventricular node, and then in the sinoauricular
(fig. 3E, F, G, H). He was given 1 Gm. procaine
amide orally every four hours for maintenance
therapy but could not tolerate this dose because of
nausea. The drug was therefore discontinued after
two days. One week later paroxysmal ventricular
tachycardia reappeared. He was given procaine
amide orally 1 Gm. every hour and after the second
dose was in normal sinus rhythm. Maintenance
therapy (4 Gm. a day) was successfully continued
for five weeks. Clinical findings and serial electro-
cardiograms confirmed the impression of fresh myo-
cardial infarction. Patient was discharged after a
lengthy hospitalization.

Case 9. J. B. was a 61 year old white male with
a history of congestive heart failure controlled
by digitalis and mercurial diuretics for two years.
Though he gave no history of rheumatic fever, he
had evidence of valvular deformities of both the
mitral and aortic valves. Electrocardiograms in this
period had revealed auricular fibrillation. On 3/8/50
digitalis medication was discontinued and in the
next 10 days the patient gained 14 pounds and
got rapidly into acute congestive heart failure.
When examined on 3/18/50, he exhibited signs of
pulmonary edema and a very rapid apical rate.
An electrocardiogram showed the presence of ven-
tricular tachycardia. After receiving 200 mg. pro-
caine amide intravenously the ventricular rhythm
ceased and auricular fibrillation with a ventricular
rate of 130 supervened. The rhythm remained unchanged for the next 30 minutes. At the end of this
period 0.8 mg. lanatoside C was given intravenously
in 10 minutes. An electrocardiogram at the end of
this injection again revealed ventricular tachycardia.
Procaine amide therapy intravenously was again
started but by the time that 150 mg. were injected,
the rhythm changed to ventricular fibrillation and
the patient expired. Postmortem examination re-
vealed extensive rheumatic involvement of the aort-
ic, mitral and tricuspid valves. An area of fresh
pulmonary infarction was found in the left lung.

Case 10. J. W., a 60 year old white male, was
known to have had hypertension for eight years.
On Jan. 2, 1950 he was hospitalized because of
severe precordial pain. Clinical and electrocardio-
graphic findings substantiated the diagnosis of acute
myocardial infarction. His course during three
months of hospitalization and convalescence was
entirely uneventful. One week after discharge, the
patient noted increasing dyspnea on exertion and
ankle edema. A maintenance dose of digitalis was
prescribed and during the next week there was
gradual improvement in the patient's condition.
Suddenly, on the eighth day, the patient noted
palpitation and weakness. Examination revealed a
very rapid cardiac rate, and the patient was hospi-
talized. An electrocardiogram showed a ventricular
tachycardia at a rate of 200. He was given 1 Gm.
of procaine amide intravenously in divided doses,
with the establishment of a nodal rhythm. Subse-
quent electrocardiograms and clinical findings in-
dicated fresh myocardial damage. Ten days later
(5/15/50), the patient again developed ventricular
tachycardia during defecation. On this occasion
400 mg. procaine amide injected intravenously re-
stored normal rhythm. During the succeeding six
months of hospitalization the patient had six bouts
of ventricular tachycardia, each of which was termi-
nated by procaine amide, administered orally, in-
travenously or by both routes. Four of these bouts
appeared to be precipitated by the use of various
digitalis glycosides given because of appearance of
signs of congestive heart failure. Two of these
bouts occurred despite a high maintenance dose
(6 Gm. a day) of procaine amide orally. At present
(12/11/50), the patient is satisfactorily maintained
on this oral maintenance dose, and his congestive
heart failure is controlled by diet and mercurial
diuretics.

Case 11. S. F., a 60 year old white male, was
first admitted to the hospital on Jan. 24, 1950
complaining of left-sided chest pain. He had been
treated for thrombophlebitis of the left leg which had
developed five days prior to admission. He was
hospitalized for pulmonary infarction. Subse-
sequently, both clinical and laboratory findings
indicated hepatitis which prolonged his stay in
hospital for two months. He was discharged on
3/15/50. Two months later he was again hospital-
ized because of recurrent pulmonary infarction.
On admission, an electrocardiogram showed ven-
tricular tachycardia. He was given 1 Gm. procaine
amide intravenously following which normal sinus
rhythm was promptly reestablished. A bilateral
femoral vein ligation was performed the next day and the patient had an uneventful convalescence.

Case 12. W. B., a 65 year old white male with a 10 year history of hypertension and a left hemiplegia sustained in 1947, was admitted to the hospital on May 9, 1950 because of palpitation and syncope. An electrocardiogram revealed a ventricular tachycardia. Quinidine sulfate was given orally, 0.3 Gm. every two hours for six doses, with no change in the rhythm. At the end of this period, 0.8 mg. of lanatoside C was given intravenously every 12 hours for four doses with no effect on the rhythm. Procaine amide (1.2 Gm.) was given intravenously without any change in the rhythm. The patient then received 3 Gm. procaine amide orally in divided doses over a five hour period and the ventricular tachycardia ceased. The initial rhythm established after interruption of the tachycardia was idioventricular with complete auriculoventricular dissociation; subsequently normal sinus rhythm appeared. Evidence of fresh myocardial damage was lacking and the patient was discharged two weeks later.

Case 13. M. F., a 70 year old white woman, was hospitalized since 1947 because of a left hemiplegia and aphasia. On March 22, 1950 the patient complained of difficulty in voiding and was given 1 cc. of prostigmine (1:2000) subcutaneously. One hour later her blood pressure fell to 80/60 and the patient became cold and vomited. An electrocardiogram revealed ventricular tachycardia. The intravenous administration of 0.5 mg. of ouabain had no effect on the rhythm. One hour later the intravenous administration of 500 mg. of procaine amide promptly restored normal sinus rhythm. There has been no subsequent change in her clinical status.

Case 14. E. P., a 70 year old white woman with a history of hypertension for five years and diabetes mellitus for eight months, was hospitalized in 1949 for an acute myocardial infarction. She was admitted to the hospital again on Aug. 22, 1950 because of severe dyspnea. It was difficult to obtain an accurate history, but the patient had received digitalis (0.1 Gm.) for 10 days prior to admission because of increasing dyspnea and edema. On admission an electrocardiogram showed ventricular tachycardia. She was given 0.25 Gm. procaine amide intravenously without effect, but the second injection of the same amount 30 minutes later was followed by a change in rhythm to that of auricular fibrillation with premature ventricular contractions. Oral procaine amide was given, 0.25 Gm. every four hours. The patient was digitalized over the next 24 hours and the ventricular rate slowed to 112, but the auricles continued to fibrillate. Six hours later the patient spontaneously reverted to normal sinus rhythm. Digitalis and procaine amide were discontinued. Dyspnea disappeared and no other signs of congestive failure occurred during her convalescence.

Case 15. D. L., a 53 year old white woman with a history of extensive rheumatoid arthritis for 10 years, was hospitalized in September 1949 because of exacerbation of her arthritis. For five and a half months her clinical course was uneventful; on 3/2/50 her temperature rose suddenly to 104 F., apparently due to an ischiorectal abscess. The heart rate was found to be rapid (136) and an electrocardiogram revealed ventricular tachycardia. Quinidine by mouth for the next two days temporarily interrupted the tachycardia, but the patient became unable to tolerate further medication with quinidine. On the evening of 3/4/50, the injection of 0.5 Gm. of procaine amide intravenously was immediately followed by cessation of the ventricular tachycardia and oral maintenance therapy was started at this time. On the next day, the patient had two bouts of ventricular tachycardia, each controlled by an additional dose of 1 Gm. procaine amide orally. For the next 10 days, the patient received between 8 and 12 Gm. orally each day and maintained normal sinus rhythm with occasional premature ventricular contractions. The daily dose of 12 Gm. appeared to be toxic as evidenced by anorexia, nausea, vomiting and mental confusion. On 3/14/50, the patient again became febrile without obvious explanation and the procaine amide was discontinued. The fever persisted and the patient's condition deteriorated rapidly; she died on 3/17/50. There were no rhythmic abnormalities during the last three days of her life. Postmortem examination revealed old rheumatoid arthritis, extensive diffuse fibrinous pericarditis, and areas of collagen necrosis in the myocardium.

Summary

1. Procaine amide, an analogue of procaine, has been found to be effective in treating arrhythmias of ventricular origin.

2. In 54 patients with premature ventricular contractions, procaine amide administered orally or intravenously effectively suppressed the aberrant beats.

3. In 13 of 15 patients with ventricular tachycardia, the abnormal rhythm was terminated by intravenous or oral administration of procaine amide. Six had previously been treated with quinidine to toxicity without success.

4. Oral rather than intravenous administration is preferable, unless the patient is comatose or vomiting.
5. Procaine amide did not establish normal rhythm in 24 patients with chronic auricular flutter and fibrillation. In 2 cases of recent auricular fibrillation, normal sinus rhythm followed the use of the drug.

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