Family Practice Grand Rounds

Ventricular Ectopy

Ken Grauer, MD, Larry M. Lopez, PharmD, R. Whitney Curry, MD,
Larry Kravitz, MD, J. Daniel Robinson, PharmD, and Charles R. Sands, PharmD
Gainesville, Florida

DR. CHARLES SANDS *(Second-year Doctor of Pharmacy Resident)*: The presentation today is about the evaluation and management of patients with ventricular ectopy. Following an illustrative case presentation by Dr. Kravitz, we will discuss a number of important clinical and pharmacologic aspects to consider when dealing with this common problem, concentrating on the antiarrhythmic agent procainamide, which was used to manage this patient.

DR. LARRY KRAVITZ *(Assistant Professor, Department of Community Health and Family Medicine)*: J.W., a 70-year-old black man with a history of hypertension, was well until January of last year. At that time, he presented to the Family Practice Center with fatigue, other vague complaints, and chest pain. An electrocardiogram in the office showed ST segment changes suggestive of acute inferior myocardial infarction, and the patient was admitted to the Intensive Care Unit. His hospital course included frequent ventricular ectopy and an episode of transient third-degree heart block that spontaneously resolved. The premature ventricular contractions (PVCs) were initially treated with lidocaine and later with quinidine. The patient progressed satisfactorily through cardiac rehabilitation, but continued to manifest frequent ventricular ectopy. He was discharged on a regimen of sustained-release quinidine sulfate, 600 mg twice daily.

The patient did well until several months later, when he developed a cerebral vascular accident with left hemiparesis for which he was once again hospitalized. During this hospitalization, Holter monitoring demonstrated only infrequent ventricular ectopy. The patient partially recovered function on his left side; he was discharged on the same dose regimen of quinidine and was to be followed at the Family Practice Center. Over the ensuing months, his ventricular ectopy became progressively more frequent. Holter monitoring performed at various times showed up to 200 PVCs per hour with frequent couplets and salvos.

Serum concentrations of quinidine were consistently within the therapeutic range (2 to 5 μg/mL). A serum concentration obtained at the time corresponding to his most worrisome Holter monitor was 4.3 μg/mL. Because of increasing frequency and complexity of J.W.'s ventricular ectopy, despite maintenance of therapeutic quinidine levels, we decided to readmit him in an attempt to reassess his therapeutic regimen. We were also concerned about the possibility that quinidine might be exacerbating the dysrhythmia and considered switching him to another antiarrhythmic agent. We were not comfortable, however, with undertaking this change on an outpatient basis.

DR. KEN GRAUER *(Assistant Professor, Department of Community Health and Family Medicine)*: An interesting facet in the management of this patient is that despite his continuing to manifest very frequent and complex ventricular ectopy, he remained asymptomatic. J.W. was totally unaware of when he was having ectopic beats and had difficulty understanding why his physicians were so concerned about his "irregular heartbeat" when he felt so well. Dr. Curry was attending in the hospital at the time when the patient was admitted.

DR. R. WHITNEY CURRY *(Associate Professor, Department of Community Health and Family Medicine, and Director, Family Practice Residency Program)*: The patient was admitted to our

From the Departments of Community Health and Family Medicine and Pharmacy Practice, University of Florida, Gainesville, Florida. Requests for reprints should be addressed to Dr. Ken Grauer, Family Practice Medical Group, 625 SW Fourth Avenue, Gainesville, FL 32601.

hospital service and monitored continuously via telemetry for several days. A base-line 24-hour Holter monitor was obtained while the patient continued his usual quinidine regimen. Quinidine was then discontinued, and the patient was observed without medication for the next 24 hours. Ventricular ectopy continued unabated during this time. A loading dose of intravenous procainamide was then administered, which was changed to the oral form over the next few days. Although J.W. continued to demonstrate frequent ectopy while receiving procainamide, the number of couplets and salvos decreased dramatically. The patient was discharged a week later on a regimen of sustained-release procainamide, 1.0 g every 6 hours. When seen at his first posthospital appointment by Dr. Grauer, he was feeling well and had therapeutic blood levels of procainamide and N-acetylprocainamide (NAPA).

DR. GRAUER: I will now review some considerations for evaluating and managing patients with ventricular ectopy in an outpatient setting. PVCs are quite common in the general population. Their frequency increases with age, and a majority of middle-aged adults will have some ventricular ectopy during a 24-hour period.[1] The problem facing the physicians is the decision of how far to go in the evaluation of such patients. Consider, for example, a totally asymptomatic 30-year-old woman who comes to the office for a routine physical examination. Imagine that a few ectopic beats are heard on auscultation, and the ventricular origin of these beats is confirmed with an electrocardiogram. How much of a workup is indicated? Would expensive procedures such as echocardiogram, Holter monitor, and an exercise stress test be necessary in this patient? Would evaluation and management be different if, instead of an otherwise healthy asymptomatic young adult, those ectopic beats were heard in a 50-year-old man with several risk factors for coronary heart disease and a history of angina pectoris?

In evaluating patients with ventricular ectopy, the most important question to answer is whether the patient has organic heart disease. In general, patients with PVCs who do not have underlying heart disease tend to have a benign prognosis and usually are not in need of treatment. In the case of the asymptomatic 30-year-old woman who was in for a routine physical examination, the likelihood of her having coronary artery disease would be extremely small considering her age and sex. One would want to look very closely at whether any noncardiac factors might be predisposing her to have PVCs. Specifically, one would want to know whether she was a heavy smoker, drank a lot of coffee or alcohol, or was taking any medications that may be associated with ventricular ectopy. Examples of these medications include anorexics and other sympathomimetics found in many over-the-counter cough and cold remedies. Was she obtaining adequate sleep? Had she been under undue stress of late? All of these factors may play an important role in the genesis of PVCs.

With respect to the physical examination, one should listen closely for the presence of a mid-systolic click or murmur suggestive of mitral valve prolapse. This very common disorder has been estimated to occur in up to 10 percent of the general population and is one of the most frequent causes of PVCs among young adults.[2] Although sudden death has been reported, it is rare, and for the overwhelming majority of patients with mitral valve prolapse, the prognosis is benign.[3]

DR. CURRY: It is important to emphasize that if one hears the characteristic auscultatory findings of mitral valve prolapse, the diagnosis can be made clinically, without the need for echocardiographic confirmation.

DR. SANDS: What about the patient with symptoms?

DR. GRAUER: Here it becomes important to try to correlate the patient's symptoms with the occurrence of the dysrhythmia. This may be accomplished with the Holter monitor by having the patient carefully maintain a diary on the day he is monitored. For example, if the patient had frequent ventricular ectopy throughout the morning but noted symptoms (chest pain, palpitations, etc) only in the evening, when the Holter monitor showed sinus rhythm, one would presume that these symptoms were not cardiac related. On the other hand, if the patient's symptoms did correlate to the occurrence of dysrhythmias, this would suggest that symptoms were causally related to the dysrhythmia, and treatment would be indicated.

DR. SANDS: Which antiarrhythmic agent do you prefer for treatment?

DR. GRAUER: The most commonly used agents for long-term management of ventricular ectopy include the type I antiarrhythmic agents (quinidine, procainamide, disopyramide) and pro-

pranolol. We've gone full circle with quinidine, and many physicians have come back to this agent as their drug of choice for the outpatient management of ventricular ectopy. The principal side effects are gastrointestinal, but often these are idiosyncratic in nature rather than dose related and will decrease with time. Dr. Lopez will discuss the use of procainamide in detail. Popularity of this agent has increased with the advent of sustained-release forms. Disopyramide exerts a quinidine-like action, but because of its anticholinergic side effects, it is probably a second-line agent behind quinidine and procainamide. Propranolol, although not so effective as the other drugs in reducing the frequency of ventricular ectopy, is probably the agent of choice for treatment of mitral valve prolapse, idiopathic hypertrophic subaortic stenosis, and exercise-induced dysrhythmias and for prevention of sudden death in the post-myocardial infarction patient. In addition, it is an excellent adjunctive agent when more than one drug is required to control the dysrhythmia.

DR. KRAVITZ: When would you recommend exercise stress testing in patients with PVCs?

DR. GRAUER: Although the Holter monitor is a much more sensitive diagnostic tool for quantifying ventricular dysrhythmias, the stress test offers two distinct advantages. First, it allows evaluation of PVCs in the presence of activity. PVCs that disappear with exercise tend to be benign, whereas those that are exacerbated by exercise are of much more concern. In addition, the stress test serves as a screen for the presence of coronary artery disease. In the case of the 50-year-old man mentioned previously, PVCs would take on added prognostic significance in the presence of an ischemic response to exercise. Finally, ventricular dysrhythmias such as ventricular tachycardia can sometimes be elicited only with exercise. Thus, exercise testing and Holter monitoring are really complementary procedures in the evaluation of patients with ventricular ectopy.

DR. CURRY: A common source of confusion is what constitutes "frequent" ventricular ectopy.

DR. GRAUER: Frequent ventricular ectopy has been variously defined as between 10 and 30 PVCs per hour over a 24-hour monitoring period or more than 250 PVCs per day.[4-6] In an adult population with underlying coronary artery disease, this frequency has been associated with an increased risk of sudden death. Since 20 to 30 PVCs per hour amount to only 1 PVC every 2 to 3 minutes, it is easy to see how patients with even frequent PVCs may escape electrocardiographic detection.

An important limitation of the Holter monitor is the phenomenon of spontaneous variability in PVC frequency. Studies have shown that there is a tremendous variability in PVC frequency for any particular patient from one day to the next and even from hour to hour within the same day.[4] To achieve a clinically significant change in PVC frequency that accounts for this effect, one must demonstrate at least a 65 percent difference in PVC frequency between two Holter readings.[4] Moreover, in 5 to 10 percent of cases, antiarrhythmic agents have been shown to exert a paradoxical effect and actually exacerbate ventricular arrhythmias.[7-9] Judging the effect of antiarrhythmic therapy may not be so simple as it first appears.

DR. KRAVITZ: Is it known why antiarrhythmic agents may cause an exacerbation of the dysrhythmia?

DR. GRAUER: It is thought that the principal mechanism of ventricular ectopy is re-entry into a terminal portion of the Purkinje fiber network rather than increased automaticity. The effect of the type I antiarrhythmic agents (quinidine, procainamide, disopyramide) is to increase the refractory period of cardiac tissue within the re-entry circuit while decreasing conduction velocity of the impulse. Ideally, the refractory period will be prolonged more than the conduction velocity is slowed. If this occurs, propagation of the impulse within the re-entry circuit will be blocked, and repetitive ventricular ectopy will be presented. It is possible that the conduction velocity may occasionally be slowed to a greater extent than the refractory period is prolonged. If this is the case, propagation of the impulse within the re-entry circuit may take place, and one or more PVCs can occur. The problem becomes more complex when one considers that many micro re-entry circuits are thought to exist in the ventricles. Whereas the antiarrhythmic agent may appropriately prolong the refractory period in one microcircuit, the opposite effect may occur in another. The efficacy of type I antiarrhythmic agents is, thus, somewhat unpredictable. Most of the time an overall beneficial effect occurs, and ventricular ectopy is less-

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ened. However, occasionally there may be a paradoxical exacerbation of frequency and severity of the dysrhythmia.

DR. SANDS: Is this the mechanism of torsade de pointes?

DR. GRAUER: Torsade de pointes is a different phenomenon. Originally described by the French physician Dessertenne in 1966, this dysrhythmia is thought to be triggered by the occurrence of a PVC at a relatively late point during the repolarization process. Paroxysms of ventricular tachycardia with alternating polarity ensue. This dysrhythmia is frequently associated with prolongation of the QT interval. Although it may occur with any of the type I antiarrhythmic agents, quinidine, by far, is the most common precipitating agent.[10-12] The importance of recognizing this dysrhythmia is that it is extremely refractory to treatment for conventional ventricular tachycardia for which it is most often misdiagnosed. Giving the patient additional quinidine or procainamide further lengthens the QT interval and only worsens the situation. Although electrical cardioversion may convert the patient to sinus rhythm, torsade de pointes has a disturbing tendency to recur. Treatment requires recognition and elimination of the precipitating factor. Isoproterenol has been recommended to shorten the QT interval. This agent, however, may itself cause tachydysrhythmias. Definitive treatment is with overdrive pacing.

DR. CURRY: The long QT syndrome occurs more commonly than many physicians realize, and we have seen several cases develop among our own patients on quinidine during the past year. Prolongation of the QT interval may develop early in therapy or sometimes only after a patient has been treated for a long period of time.

DR. SANDS: Does this mean that quinidine should not be used anymore in the treatment of ventricular ectopy?

DR. CURRY: No. It means only that one must monitor patients closely after initiation of treatment with quinidine to check for QT prolongation. If the QT interval becomes progressively more prolonged, one should consider stopping the drug.

DR. GRAUER: I think an important point to make here is that none of the antiarrhythmic agents are totally benign, and they all may be associated with significant incidence of side effects with chronic use. In other words, be sure that the treatment is not worse than the disease.

DR. SANDS: Let's return to the case of J.W. At the time of his discharge from the hospital, treatment with procainamide had greatly decreased the number of couplets and salvos, but the patient was still having frequent ventricular ectopy. Were you satisfied with this result?

DR. GRAUER: To answer this question, one must consider the possible end points of antiarrhythmic therapy. Ideally, ventricular ectopy should be totally abolished. This may not be a realistic goal in patients with frequent and complex PVCs. Myerburg et al[13,14] studied survivors of out-of-hospital cardiac arrest. The overwhelming majority of these patients have frequent and complex ventricular ectopy that places them at very high risk of sudden death. Frequency of PVCs was not significantly decreased even among those patients who were consistently maintained on therapeutic levels of antiarrhythmic drugs. Despite the fact that all of the patients studied still had frequent PVCs, survival was significantly better among those patients in whom antiarrhythmic drug concentrations were consistently maintained within therapeutic range. Although the number of patients studied was small, these findings suggest that when ventricular ectopy cannot be abolished, alternative goals of antiarrhythmic therapy should be to decrease PVC frequency, eliminate the most worrisome forms (ie, multifocal PVCs, couplets, salvos, etc), and maintain therapeutic antiarrhythmic serum levels.[15,16] This is the treatment approach that we used with Mr. J.W.

DR. SANDS: If there are no further comments or questions, Dr. Lopez will now discuss pharmacological aspects of treating ventricular ectopy with procainamide.

DR. LARRY M. LOPEZ *(Assistant Professor of Pharmacy and Medicine)*: Once the decision has been made to use procainamide, it is important that the drug be used appropriately to maximize benefit and minimize risk to the patient. Use of procainamide actually involves administration of two drugs, procainamide and its active metabolite, N-acetyl-procainamide (NAPA). Table 1 summarizes pharmacokinetic parameters and dosing recommendations of both compounds. The indicated loading dose of procainamide is quite variable and is almost exclusively determined by the magnitude of the volume of distribution. Volume of distribu-

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Table 1. Pharmacokinetic Parameters of Procainamide and NAPA[15]

	Procainamide	NAPA
Absorption		
Systemic bioavailability	0.75-0.90	0.85
Distribution		
Volume*	2.0-2.2 L/kg	1.5 L/kg
Protein bound	15-20%	11%
Metabolism/Excretion		
Excreted unchanged	50-60%	85%
Half-life	2.5-4.7 h	6-11 h
Dose		
Loading	10-17 mg/kg slow IV	—
Maintenance	2.8-3.0 mg/kg/h 250 to 1,000 mg orally every 4 to 6 hours	—
Therapeutic Serum Concentrations	4-8 μg/mL**	†

*The volume of distribution of procainamide is calculated on the basis of lean body weight[16]
**Occasionally levels greater than 8 μg/mL may be required for antiarrhythmic control
†The precise therapeutic serum concentration of NAPA is not known. Concentrations of procainamide and NAPA are considered therapeutic if their sum falls between 10 and 30 μg/mL

tion of procainamide was determined from healthy subjects or in patients without evidence of heart or renal disease. In patients with heart failure a 25 percent reduction in the loading dose of procainamide may be necessary as a result of its corresponding reduction in its volume of distribution.[17] For example, Mr. J.W. had a lean body weight of 60 kg, was not felt to be in heart failure, and received a loading dose of 1.0 g (16.7 mg/kg). If evidence of cardiac failure had been present, a reduction in the loading dose to 750 mg (12.5 mg/kg) would have been reasonable. No change in the loading dose is necessary in a patient with moderate renal impairment, and presence of severe renal disease requires only a moderate reduction in the loading dose from 17 mg/kg to 14 mg/kg.[18]

In addition, rapid intravenous infusion of procainamide must be avoided to prevent hypotension or severe cardiac decompensation. Rate of administration of procainamide should never exceed 50 mg/min and should preferably be infused at approximately 25 mg/min.[19] In the case of Mr. J. W., the loading dose was administered as an infusion over a period of 30 minutes. Administration of procainamide could have been extended up to 40 minutes or shortened to not less than 20 minutes. Even if these recommendations are followed, decompensation may nevertheless occur during infusion of the loading dose. Consequently, frequent monitoring of blood pressure and constant monitoring of QRS duration are reasonable precautions to follow until the infusion is complete. At the first sign of toxicity, rate of infusion should be decreased by 50 percent and discontinued altogether if toxic signs persist thereafter.

DR. KRAVITZ: An alternative method of administering procainamide in an emergency setting is to give 100-mg intravenous increments every two to five minutes until one of the following end points is reached: (1) the dysrhythmia is controlled, (2) unacceptable adverse effects occur (QRS widening of greater than 50 percent or hypotension), or (3) a total of 1 g of procainamide is administered. If the drug is tolerated, a constant maintenance infusion should follow administration of the loading dose.

DR. LOPEZ: The usual rate of the maintenance infusion for procainamide is 2.8 to 3.0 mg/kg/h. For Mr. J. W., this comes out to be 2.8 mg/min. In a patient with moderate to severe renal impair-

Table 2. Appropriate Timing of Procainamide and NAPA Serum Concentrations[15]

Rate of Administration	Timing
Intravenous	
Procainamide	Immediately after loading dose
Procainamide	2 hours after initiation of constant infusion
Procainamide and NAPA	24 hours after initiation of constant infusion
Oral	
Procainamide and NAPA	48 hours after first dose

ment, infusion of procainamide should be decreased to 1.0 to 2.0 mg/kg/h or 1.0 to 2.0 mg/min in patients the size of Mr. J.W.[18] It is convenient to remember that recommended maintenance infusion of procainamide is very similar to that of lidocaine.

Whereas size of the loading dose is primarily dependent on volume of distribution, magnitude of the maintenance infusion is dependent on volume of distribution and elimination half-life. Variations in volume of distribution of procainamide in patients are smaller in magnitude than variations in elimination half-life. Consequently, elimination half-life of procainamide becomes the major determinant of its rate of constant infusion.

Two distinct groups of patients have been described with respect to elimination half-life of procainamide based on relative rates at which they convert procainamide to NAPA. Hepatic N-acetyltransferase, the enzyme that acetylates procainamide, is bimodally distributed in humans,[20,21] and patients are either slow or rapid acetylators of the drug. Mean half-life of procainamide in rapid and slow acetylators is 2.7 and 5.2 hours, respectively.[22] Acetylator status can be determined for a particular patient by calculating the NAPA-procainamide ratio from steady-state procainamide and NAPA concentrations. This ratio averages 0.8 and 1.2 in slow and fast acetylators, respectively.[20,21] Usefulness of this ratio in a patient with renal impairment is limited, since NAPA accumulates to a greater extent than procainamide, resulting in a falsely elevated ratio. For example, one would expect a patient with a NAPA level of 9 μg/mL and a procainamide level of 6 μg/mL (NAPA-procainamide ratio = 1.5) to be a fast acetylator provided that renal function was normal.

Phenotypic characterization of a patient with respect to acetylator status is especially important when long-term therapy with procainamide is envisioned. Incidence of procainamide-induced systemic lupus erythematosus (SLE) is considerably higher in slow acetylators than fast acetylators.[23] When SLE is detected in a patient taking procainamide, it is necessary to discontinue the drug immediately and begin alternative antiarrhythmic therapy. Although the syndrome is reversible upon discontinuance of procainamide, up to six months may be necessary for its complete resolution. Periodic determination of titers of antinuclear antibody (ANA) will serve as a useful screening test for SLE.

DR. KRAVITZ: Clinically, the features of procainamide-induced SLE include fever, myalgias, arthritis, pleurisy, and pericarditis. As Dr. Lopez mentioned, the drug-induced form of SLE tends to be reversible when procainamide is stopped. Fortunately, development of the renal vasculitis that is seen with systemic lupus erythematosus does not occur with procainamide-induced SLE. Although many patients on procainamide will develop positive ANA titers with long-term use, clinical manifestations of drug-induced SLE may never occur. Consequently, many physicians choose not to discontinue procainamide unless the patient becomes clinically ill. How frequently to monitor ANA titers is another question. Some physicians obtain these frequently; others obtain them only if the patient develops symptoms.

DR. LOPEZ: Table 2 summarizes general guide-

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lines for timing and interpretation of serum concentrations of procainamide and NAPA. Serum concentrations of procainamide in the sample collected at the end of the loading dose should be higher than the concentration in the sample collected two hours later. In addition, neither sample should contain greater than 15 μg/mL of procainamide. Failure to achieve either of these conditions strongly suggests consideration of a lower maintenance infusion rate. These concentrations are above the accepted therapeutic range of procainamide but are necessary for a short period of time because of delayed appearance of NAPA. This delayed appearance of NAPA also renders unnecessary the measurement of NAPA levels in either of these initial samples.

Normally, steady-state concentrations for both procainamide and NAPA are achieved 24 hours after initiation of the maintenance infusion. At this time, measurement of both serum procainamide and NAPA concentrations is appropriate and can be very informative. Concentrations of procainamide and NAPA are considered therapeutic if their sum falls between 10 and 30 μg/mL.[18] Steady-state levels may not occur for another 24 hours in patients with renal impairment. Consequently, measurement of serum procainamide and NAPA concentrations in these patients should not be determined until at least 48 hours after initiation of the maintenance infusion.

An appropriate oral maintenance dose of procainamide base can be calculated from the product of the maintenance infusion rate and the chosen oral dosing interval. Dose of procainamide base must be corrected for incomplete absorption of oral procainamide (85 percent) and for use of the hydrochloride salt in oral preparations. This correction is easily performed by dividing calculated dose of procainamide base by 0.73.[18] Using Mr. J.W. as an example, the following calculations would serve to illustrate this method:

$$\frac{\text{(Infusion rate)}\ \text{(Dosing interval)}}{0.73} = \text{Dose of procainamide oral}$$

$$\frac{\text{(168 mg/h)}\ \text{(6 hours)}}{0.73} = 1{,}381 \text{ mg}$$

[Note: 2.8 mg/min = 168 mg/h]

Administration of 1,381 mg orally every 6 hours is not practical because of the limited availability of oral dose forms of procainamide. Appropriate use of available oral dose forms of procainamide is a reasonable compromise, but 1.0 g every six hours for Mr. J.W. may have been conservative. It should be pointed out that using these methods of dosing procainamide may result in administration of doses greater than that recommended by the manufacturer.

Mr. J.W. was given a sustained-release form of procainamide upon discharge from the hospital. At present there are two procainamide products available that are formulated in this fashion—Procan SR and Pronestyl-SR. Each of these preparations may be prescribed in three or four daily doses.

DR. CURRY: Previously as many as eight daily doses were required to achieve and maintain therapeutic blood concentrations, which meant that a patient had to set his alarm clock to wake up in the middle of the night in order to follow his medication schedule. As you may imagine, compliance on this regimen was often less than optimal.

DR. J. DANIEL ROBINSON *(Associate Professor of Pharmacy and Medicine)*: It is now clear that previous dosing recommendations for procainamide did not account for the presence or distribution of NAPA. The extended half-life of NAPA suggests that less expensive, conventional formulations of procainamide may also be prescribed in three or four daily doses for certain individuals. Serum drug levels are important for determining the preferred frequency of dosing for the type of formulation that is chosen.

DR. LOPEZ: For patients who begin antiarrhythmic therapy with oral procainamide, initial blood samples for measurement of procainamide and NAPA concentrations are most appropriately obtained when both substances have reached a steady state. Attainment of a steady state normally requires two full days of treatment and longer if there is evidence of renal impairment. Ideally, three samples should be collected during a single dosing interval at a steady state. The first should be collected at the time a dose is given and the others at equally spaced intervals. Collection of blood samples after initial oral doses is unnecessary. If collection of three samples is impractical, at least two samples should be obtained instead. Ideally these two samples should be collected at the end of the dosing interval and two hours fol-

lowing the next dose.

Collection of multiple samples is preferred over use of single-point determination, even if blood is collected at the end of a dosing interval. In some patients values of procainamide and NAPA concentrations obtained at the end of a dosing interval may not reflect a trough level. In up to one third of patients, a concentration obtained at the end of a dosing interval reflects a peak value instead.[18] Multiple sampling techniques will prevent inappropriate interpretation of drug concentrations in these patients.

Once therapeutic concentrations of procainamide and NAPA have been achieved, the need for subsequent analyses will depend upon control of dysrhythmia and occurrence of toxicity. If subsequent determinations of procainamide and NAPA become necessary, multiple sampling techniques would again be preferred.

DR. ROBINSON: It is important to remember that analyses of procainamide and NAPA are separate and distinct procedures in most clinical laboratories. Indeed, some laboratories do not offer analysis of NAPA. A request of analysis of either compound may not automatically result in performance of both assays, and separate requests may be necessary when both procainamide and NAPA concentrations are desired. A check with your clinical laboratory regarding availability of these analyses would be a reasonable precaution.

DR. SANDS: When would you switch from the constant infusion to oral administration?

DR. LOPEZ: That clinical decision can be made at any time. It is best made from a pharmacokinetic point of view when steady-state levels of procainamide and NAPA have been achieved.

DR. KRAVITZ: What's the procedure for switching from quinidine to procainamide in a patient who has received quinidine for a long time?

DR. ROBINSON: No special precautions or procedures are necessary. When the decision is made to switch from quinidine to procainamide, the first dose of procainamide can be administered at the end of the quinidine dosing interval. Although additive cardiovascular toxicity is a possibility in these circumstances, it is unlikely, since concentration of quinidine will decline while procainamide is accumulating.

DR. GRAUER: It has been over a year since Mr. J.W.'s last hospital admission. He has continued on his sustained-release procainamide preparation and has not suffered any adverse effects from either the medication or his ventricular dysrhythmia.

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