Progress in Cardiovascular Diseases

Progress in CARDIOVASCULAR DISEASES

CHARLES K. FRIEDBERG, M.D., *Editor*

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TREATMENT. I.

Atherosclerosis and Myocardial Infarction

THE WM. S. MERRELL COMPANY
announces the availability of

MER/29

(brand of triparanol)

... the first cholesterol-lowering agent to inhibit the formation of excess cholesterol within the body, reducing both serum and tissue cholesterol levels.

... no demonstrable interference with other vital biochemical processes reported to date.

... convenient dosage: one 250 mg. capsule daily

... toleration and absence of toxicity established by 2 years of clinical investigation.

The following pages report the clinical findings of therapy with MER/29 among patients with hypercholesterolemia and conditions thought to be associated with it, such as

coronary artery disease (angina pectoris, postmyocardial infarction)

generalized atherosclerosis

THE FACTS ABOUT MER/29[1-41]

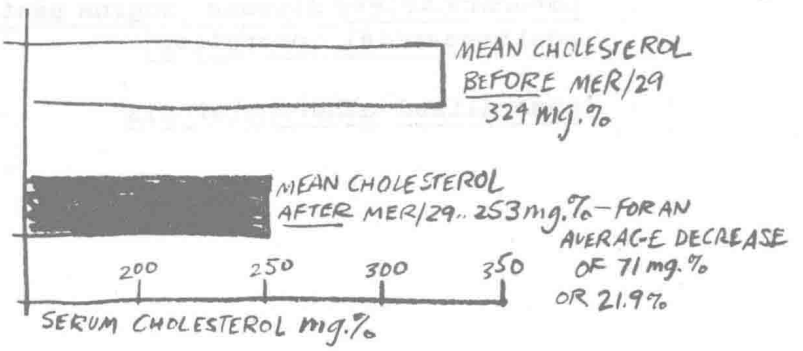
Fundamental differences between MER/29 and other cholesterol-lowering substances

Cholesterol produced within the body by biosynthesis is about three times as great in amount as that obtained from diet. Before MER/29, no practical method of modifying total body cholesterol production was known. Those measures used to lower cholesterol (unsaturated fatty acids or other dietary measures, vitamins, plant sterols, hormones, etc.) succeeded only in modifying exogenous sources of cholesterol or accelerating its metabolism.

MER/29 is fundamentally different, since it inhibits cholesterol biosynthesis. Thus, MER/29 offers for the first time a method of controlling total body cholesterol content.

MER/29 reduces serum cholesterol in 89% of patients, with or without dietary restrictions. Radioisotope studies indicate reduction of tissue cholesterol as well.[4, 5, 7, 30, 31, 34]

High cholesterol levels are generally considered those above 250 mg.%. Here is a tabular summary of preliminary data on MER/29 therapy in 463 patients with hypercholesterolemia (over 250 mg.%).



Clinical studies show that cholesterol reduction usually begins within two weeks. Maximum effect is achieved in five to eight weeks, and is usually maintained as long as therapy is continued. The studies of Hollander, Chobanian and Wilkins and those of Oaks, Lisan and Moyer showed that cholesterol levels were lowered by MER/29 therapy, irrespective of diet.

Reduction of total body "miscible pool" of cholesterol has been confirmed by radioisotope studies. Hollander and Chobanian, for example, found that the apparent miscible pool of cholesterol was reduced from 184 Gm. in the control period to 100 Gm. during MER/29 administration.

Studies in animals on MER/29 have shown the following tissue changes: erythrocyte cholesterol levels reduced 40%; plasma cholesterol reduced 62%; liver reduced 40%; skeletal muscle reduced 27%; lung reduced 33%; aorta reduced 21%. Significantly, brain and adipose tissue remained unaffected during the period of observation.

Safety and toxicity studies[5, 7, 10, 12, 17, 19, 21-24, 30, 32-34]

MER/29 is well tolerated. In a recent analysis of 576 individual case reports, 165 had been treated with MER/29 for continuous periods in excess of a year. A number had received two to four times the daily recommended dose for as long as 14 months. Side effects were seldom seen, and the incidence of those reported (nausea, dermatitis) usually was correlated with dosages greater than those now recommended.

In no case has there been clinical indication of toxic effects on the function of any vital organ or system. It should be noted that excretion of MER/29 or its metabolites may produce a false positive reaction for albuminuria.

THE FACTS ABOUT MER/29

Clinical observations of MER/29 in atherosclerosis[5, 7, 10, 12, 17-19, 21, 23-25, 28-34, 41]

The lowering of high cholesterol levels is regarded by many as a desirable clinical objective. Moreover, a substantial body of medical opinion implicates elevated cholesterol as a contributor to coronary artery disease and generalized atherosclerosis. Since MER/29 lowers total body cholesterol, can it modify atherosclerotic conditions? While the ultimate answer must await the results of long-term clinical experience, preliminary observations were reported at...

The MER/29 Conference at Princeton

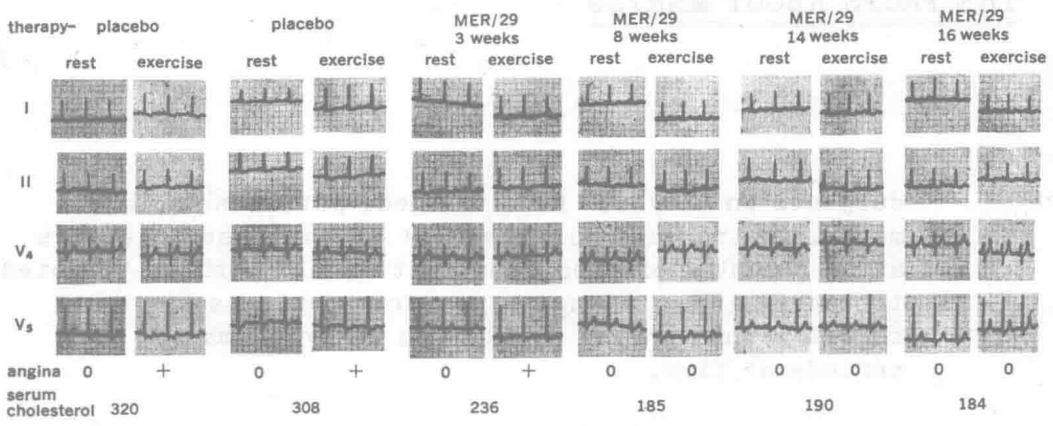
To help find the answer, 18 leading research teams met to discuss the relationship of MER/29 to cholesterol metabolism and atherosclerosis. The conference, moderated by Dr. Irving S. Wright, and summarized by Dr. Konrad E. Bloch, Dr. Robert W. Wilkins, and Dr. Irvine H. Page, was held last December at Princeton, New Jersey.

(The complete transcript of this conference is published as a supplement to the May, 1960, issue of Progress in Cardiovascular Diseases.)

Objective findings

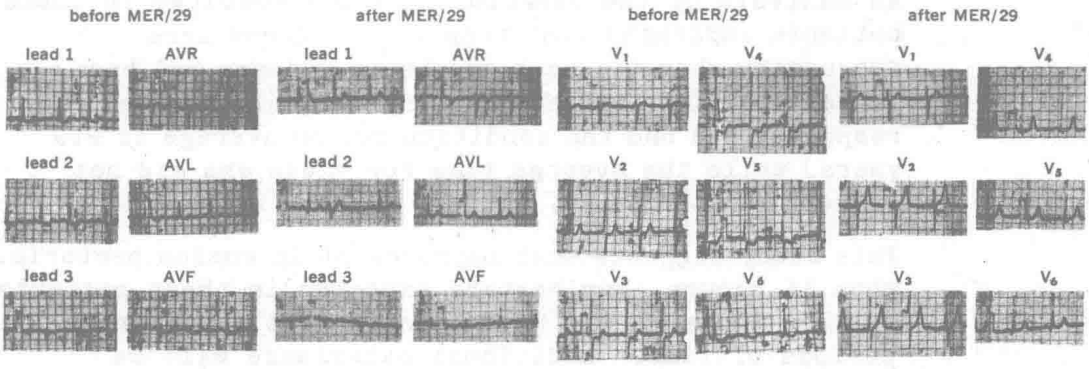
The team of Dr. William Hollander, Dr. Aram V. Chobanian, and Dr. Robert W. Wilkins at Massachusetts Memorial Hospitals presented Fig. 1. It indicates a reversal of exercise-precipitated ECG abnormalities in a patient with angina pectoris during four months of MER/29 therapy. In all, they reported that three of nine patients showed reversal of exercise-induced ECG abnormalities after three months of MER/29 therapy.

Figure 1



Dr. Philip Lisan of Dr. John H. Moyer's group at Hahnemann Hospital presented Fig. 2. It also indicates reversal of ECG abnormalities in a patient with angina pectoris.

Figure 2



Dr. A. C. Corcoran of St. Vincent Charity Hospital, Cleveland, and Dr. Arthur Ruskin of University of Texas reported similar objective findings. Many of these investigators noted that patients offered subjective evidence that they were experiencing a feeling of better health on MER/29 therapy, and that nitroglycerine dependence was diminishing.

Negative data were presented by Dr. Henry I. Russek of Staten Island, N. Y. He reported a study of exercise-electrocardiographic tests in 14 selected

subjects on MER/29. None of these patients had shown more than transient improvement in exercise tolerance after 3 months of treatment. It should perhaps be noted that this group of angina pectoris patients was a select group, having complained of symptoms for long periods of time.

Subjective findings

Dr. Meyer H. Halperin of Lynn, Massachusetts, reported a series of 18 patients with angina pectoris. Nine of this group obtained unequivocal subjective relief of symptoms after various periods of therapy with MER/29. An analysis of the duration of symptomatology in these patients indicated that response occurred more frequently when the ischemic heart disease had been present for shorter periods. Specifically, those who responded had had the condition for an average of 2.9 years, while the average time for those who did not respond was 5.2 years.

This study suggests that improvement in angina pectoris, when it occurs, may best be expected in those patients in whom the symptoms have been present for shorter periods of time. Additional experience will be required to determine whether long-term therapy can reverse long-standing symptomatology.

Dr. William B. Kountz of the Washington University School of Medicine, St. Louis, reported a group of 79 patients with varying degrees of hypertension, angina pectoris, diabetes, atherosclerosis or myocardial infarction. "Clinical improvement was observed and was also reported to us by patients. In some instances the anginal pain improved very much."

Similar subjective findings were also reported by

Dr. Corcoran, eight of whose nine patients noted a feeling of better health, while five demonstrated electrocardiographic improvement on MER/29. In three of these patients, nitroglycerine requirements were dramatically reduced.

IN SUMMARY ... MER/29 does consistently lower total body cholesterol by inhibition of endogenous cholesterol formation. Some patients with coronary artery disease, while on MER/29, have experienced concurrent clinical benefits such as reduction in frequency and severity of anginal attacks, reduction in nitroglycerine dependence, reversal of ECG abnormalities both at rest and following exercise-induced changes, and a sense of improved health and well-being.

The explanation of these clinical benefits is as yet unknown; however, several hypotheses have been advanced. One group speculates that MER/29 "may actually improve the adequacy of coronary circulation." Another investigator suggests that MER/29 exerts a vasodilating action, though pharmacologically MER/29 produces only transient vasodilating effects. Whatever the explanation, observation of these benefits among certain patients has awakened mounting interest in MER/29 as an important new agent in the management of patients with hypercholesterolemia and atherosclerosis.

MER/29 may be given to your patients with hypercholesterolemia and conditions thought to be associated with elevated cholesterol levels, including coronary artery disease (angina pectoris and postmyocardial infarction) and generalized atherosclerosis.

THE WM. S. MERRELL COMPANY
announces the availability of

MER/29

(brand of triparanol)

... the first cholesterol-lowering agent to inhibit the formation of excess cholesterol within the body, reducing both serum and tissue cholesterol levels.

Indications: May be used for patients with hypercholesterolemia and conditions thought to be associated with elevated cholesterol levels, including coronary artery disease (angina pectoris and postmyocardial infarction) and generalized atherosclerosis.

Caution: MER/29 is a new drug which inhibits cholesterol biosynthesis in the body. Since cholesterol plays an important role in the development of the fetus, the drug should not be administered during pregnancy.

Hypercholesterolemia and its associated conditions may require MER/29 therapy over a long period. MER/29 has been shown to be entirely safe in the periods the drug has been studied, but long-term or lifetime effects are unknown. Periodic examination of patients on long-term MER/29 therapy is therefore necessary. While clinical liver damage has not been encountered, periodic liver function tests may be desirable until more long-term safety data are available.

Note: The specific site of action of MER/29 is now known to be between desmosterol (reported to be the last precursor in the synthesis path) and cholesterol. Although greater than normal quantities of desmosterol can be qualitatively shown in the livers and blood of animals and the blood of human beings treated with MER/29, reduction of total sterols suggests little, if any, accumulation. The significance of the presence of this substance is unknown and speculative.

Compatibility with other cardiovascular therapies: MER/29 is not to be considered a substitute for measures ordinarily employed to control anxiety, hypertension, obesity, and other conditions associated with cardiovascular disorders. However, MER/29 is compatible with measures used in these disorders, including anticoagulants, nitroglycerine, and PETN.

Dosage: One capsule daily, before breakfast. Each capsule contains 250 mg. triparanol.

Supplied: In bottles of 30 pearl gray capsules.

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The Management of Arrhythmias in Acute Myocardial Infarction

By E. Grey Dimond, Marvin Dunn and Frank Brosius

THE TREATMENT of cardiac arrhythmias associated with acute myocardial infarction does not differ significantly from the treatment of the same arrhythmias occurring unrelated to an infarction. Medications and dosages are the same. Toxic signs and symptoms are the same. Antidotes are the same. However, all of these gain a new urgency because of the associated jeopardy of the infarcted myocardium. The true issue is not the arrhythmia but the ability of the myocardium to withstand the altered demands of heart rate and coronary flow. For this reason, the arrhythmias of infarction invoke real emergency and the threat of sudden death.

Incidence

Cardiac arrhythmias exclusive of ventricular premature contractions occur in 10 to 20 per cent of all patients with acute myocardial infarction. The incidence is higher in the older age groups. Patients who develop arrhythmias other than ventricular premature contractions have a 7 to 15 per cent higher mortality,[1,2] Woods and Barnes[3] reported 60 deaths in a series of 128 successive unselected patients with myocardal infarctions. Thirty three of these deaths were due to arrhythmia. In a group of 187 cases of acute myocardial infarction, Johnson and Miner reported 31 patients with arrhythmias. Of these 31 patients, 16 had auricular fibrillation, 11 had A-V block, 1 had ventricular tachycardia, 1 had auricular flutter, and 2 had nodal rhythm.

Prevention

The routine use of prophylactic quinidine for the prevention of cardiac arrhythmias during the acute phase of an infarction has been controversial. Levine,[4] a former advocate of its use, indicates his use of quinidine: "At present, I advise administering the drug only when certain cardiac irregularities have already appeared, especially if extrasystoles are noted." Friedberg[5] states simply: "There is no significant basis to justify its routine use for the purpose of preventing these arrhythmias." Similarly, Wood[6] states that: "Quinidine 3 to 5 grains t.i.d. has been given in the hope of preventing ventricular fibrillation and other changes of rhythm, but with little success." Boone and Pappas,[7] however, reported a decreased mortality usng prophylactic quinidine in patients with myocardial infarction. In their series of 190 cases, the mortality of those receiving quinidine was 16 per cent as compared to a mortality of 35 per cent in the untreated group. The incidence of sudden death was 24 per cent in the untreated group as compared with 10 per cent in the group receiving prophylactic quinidine. Although dosage schedules of quinidine were not controlled, the author implied that a dosage

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schedule of 0.2 Gm. every three hours during the waking hours was most effective. Cutts and Rapoport[8] reported a study of 211 cases of acute myocardial infarction consisting of a control group and three treatment groups. In the groups receiving quinidine in doses of 0.4 or 0.6 Gm. every 8 hours there was no significant reduction in over-all mortality, and an actual increase in the incidence of sudden death. However, in the group receiving quinidine 0.2 Gm. q.i.d. there was a reduction both in mortality and in the number of cases of sudden death.

Beck and his co-workers[9] have suggested that the routine use of oxygen following myocardial infarction may increase mortality. Their investigations in dogs with artificially produced myocardial infarction revealed that most sudden deaths had a "mechanistic" origin. They defined mechanistic death as a destruction of the coordinated heart beat occurring in a heart with adequate total coronary inflow and functional myocardium, as opposed to "muscle death," in which the heart becomes hypodynamic and eventually fails. This mechanism death (ventricular fibrillation) depended upon the interrelation of two factors: (1) a vulnerable area of ischemic myocardium; (2) an adequate stimulus, *the current of oxygen differential.* The potential of this current is dependent upon the location of the ischemic area, and on the absolute difference in oxygenation of the ischemic and oxygenated areas. They suggested that the use of oxygen may increase this potential difference, giving rise to a current of oxygen differential provoking ventricular fibrillation.

Ventricular arrhythmias have occurred in digitalized patients with known heart disease after the ingestion of a high carbohydrate meal.[10] This is probably due to a movement of glucose and potassium into the cell with a subsequent decrease in the refractory period and an increase in myocardial irritability. High carbohydrate meals should perhaps therefore be avoided following myocardial infarction to prevent this method of arrhythmia production.

Types of Arrhythmias

Premature Contractions

Premature contractions are common following myocardial infarction. Atrial and nodal prematurities are less common and of less significance than ventricular prematurities.[1] Woods and Barnes[3] found auricular premature contractions in about 3 per cent of their cases surviving an acute myocardial infarction and in 7 per cent of those who did not survive an acute myocardial infarction. The physiologic importance of auricular premature contractions is dependent on their frequency. It has been shown by Corday and coworkers[11] that frequently occurring auricular premature contractions result in a 10 per cent decrease in coronary flow and a decrease in the systemic blood pressure. Infrequent premature supraventricular contractions do not affect coronary flow or systemic blood pressure. However, if such an arrhythmia is occurring frequently (i.e., two to three per minute), in runs, or in a regular pattern, quinidine should be given.

Table 1.—*Method of Quinidine Administration*

I. Conversion of auricular fibrillation to sinus rhythm.
   A. Digitalize patient and maintain on daily maintenance dose.*
   B. Obtain appropriate EKG tracing before each dose of quinidine.
   C. Give quinidine 0.2 Gm. q2h p.o. for 5 doses or until patient converts to sinus rhythm or develops toxicity.†
   D. If the patient does not convert or show signs of toxicity, increase the dosage to 0.4 Gm. q2h on the second day and 0.6 Gm. q2h on the third day until the patient converts to sinus rhythm or develops toxicity.†
   E. After conversion the patient should be maintained on the smallest dose of quinidine which will permit maintenance of regular rhythm. This is usually approximately ⅔ of the amount needed for conversion and is given in divided doses. After 3 or 4 days, the dose can be slowly decreased by decrement to a maintenance dose of 0.2 Gm. q.i.d.

II. Suppression of ventricular premature contractions—quinidine 0.2 Gm. p.o. q.i.d.

III. Conversion of ventricular tachycardia.
   A. 10 ml. of quinidine gluconate solution containing 0.65 Gm. diluted to 50 ml. with 5 per cent glucose in distilled water is administered intravenously at a rate of 2 ml. per minute until conversion or toxicity. Administration should be with continuous EKG monitoring.

*Initial digitalization indicated only if apical rate is above 100.

†Toxic effects which warrant discontinuing quinidine are marked hypotension, a 25 per cent increase in duration of QRS, or extreme ventricular irregularity. An occasional patient may pass from relatively normal QRS complex to cardiac arrest without manifesting these signs of quinidine toxicity. Therefore, caution must be used when administering large doses. A marked prolongation of the Q-T interval should be respected even if the QRS complex has not widened. Diarrhea may force discontinuance of drug. Loose stools are not cause for alarm.

Ventricular Extrasystoles

Ventricular premature contractions occur in about 33 per cent of patients experiencing acute myocardial infarction and may be a forerunner of ventricular tachycardia. Woods and Barnes[3] related the frequency of ventricular premature contractions to mortality. If the frequency of the prematurities was 1 for every 2 to 10 normal beats, the mortality was 82 per cent. When the ventricular premature contractions were less frequent than this, there was a corresponding reduction in the mortality rate. Frequent ventricular premature contractions following myocardial infarction require treatment. Quinidine sulfate is the drug of choice. As demonstrated experimentally,[11] the coronary blood flow may be decreased as much as 25 per cent with frequently occurring ventricular premature contractions.

Paroxysmal Atrial Tachycardia

The development of supraventricular tachycardia in patients with myocardial infarction is associated with an increased mortality. However, Levine and Rosenbaum[1] did not find this arrhythmia once in over 200 cases of pre-

sumed first infarctions. Master et al.[12] reported 9 cases in a series of 300 patients with two deaths. Askey[13] found 5 instances of paroxysmal atrial tachycardia in 1247 cases. All of the patients died, with the arrhythmia persisting until death. All of Askey's cases had longstanding arteriosclerotic heart disease and probably had suffered previous infarcts. All of Master's 9 cases of paroxysmal atrial tachycardia had heart failure and enlarged hearts, but only 2 patients died. This was probably due to the fact that the arrhythmia did not persist for over 24 hours.

Above the rate of 160 to 180 per minute, coronary flow is insufficient to meet the metabolic demands of the myocardium and ischemia occurs.[11] For this reason it is necessary to treat paroxysmal atrial tachycardia promptly. Vagal stimulation induced by carotid sinus massage, eyeball pressure, or Valsalva maneuver may terminate an episode of paroxysmal auricular tachycardia. Pressor amines, which raise the blood pressure and maintain coronary flow, may convert the arrhythmia to regular sinus mechanism or potentiate the effect of vagal stimulation. Should this fail to convert the arrhythmia, the patient should be digitalized. The digitalization should be accomplished fairly rapidly. The greater the evidence of impending shock or failure, the greater the urgency. A useful product is Cedilanid (lanatoside C). The average digitalizing dose with this product is 1.2 to 1.6 mg. (6 to 8 ml.) intravenously. After the digitalis has begun to take effect, vagal stimulation should again be tried; the combination of digitalis and vagal effect may be successful in breaking the arrhythmia.

Table 2.—*Pressor Agents Available for Use in Treatment of Arrhythmias*

Generic name	Trade name	Route	Dose and method of administration	Reference
Norepinephrine	Levophed	I.V. infusion	4–8 ml. (4–8 mg.) in 1 L. of 5% dextrose and water at rate of 10–20 drops/min. Caution: Avoid infiltration.	43
Phenylephrine hydrochloride	Neosynephrine	I.V. injection	0.5 mg. in 10 cc dist. H_2O, injected slowly (30–60 seconds)	44
		I.V. injection	*5 mg., q 10–30 min.	
Methoxamine hydrochloride	Vasoxyl	I.V. injection	5–10 mg., injected slowly	45
		I.V. infusion	*100 mg./L by regulated drip	
Mephentermine	Wyamine	I.V. injection	5–20 mg. slowly	46
		I.M. injection	15–35 mg.	
		I.V. infusion	*30–70 mg. in 500 ml. of 5% glucose D/W	
Ephedrine sulfate		I.M. injection	25 mg.	47
Metaraminol Bitartrate	Aramine	I.V. infusion	50–200 mg. in 1 L. glucose and water at rate sufficient to give desired result (usually 2–6 ml./min.)	48
		I.V. injection	0.5–5.0 mg. injected slowly	
Plasma	Plasma	I.V. infusion	250 ml. rapidly	

*To maintain pressure when patient is in shock.

Note: Epinephrine and Isopropyl Norepinephrine (Isuprel) listed in table 4.

Atrial Fibrillation

Atrial fibrillation occurs in 7 to 12 per cent of patients experiencing acute myocardial infarction.[2,14] The mortality is dependent on whether the arrhythmia is persistent or transient. Askey[15] found that in 29 cases with transient atrial fibrillation the mortality rate was only slightly increased, but in 55 cases with persistent atrial fibrillation the death rate was markedly increased. Rosenbaum and Levine[1] stated that the occurrence of atrial fibrillation did not affect mortality but that over 80 per cent of the patients in their series had only transient fibrillation. Askey found that atrial fibrillation developing after myocardial infarction was less serious and often transient. Cases with atrial fibrillation prior to or concomitant with infarction had a greater mortality and were generally persistent. It is frequently difficult to decide if the infarction of the myocardium occurred as the initial episode, followed by atrial fibrillation, or if the two events occurred simultaneously, or if the atrial fibrillation preceded and actually provoked the infarction. In terms of therapy, the issue is not actually important. First, systemic pressure must be maintained, and second, the apical rate must be controlled. Initially, a vasopressor agent may be needed; and immediately after its administration the arrhythmia may steady, and a normal sinus rhythm established. However, even if the rhythm reverts to normal spontaneously, it is prudent to go ahead with digitalization and maintain the digitalis during the first 2 to 3 weeks after the onset of infarction and fibrillation.

As a general rule, when atrial fibrillation is precipitated by myocardial infarction, it is better to slow the ventricular rate with digitalis and make no attempt to re-establish a regular rhythm during the acute phase of a myocardial infarction. Attempts to convert to a regular sinus rhythm during the acute phase of a myocardial infarction should be limited to those patients who continue to have an uncontrolled ventricular rate even though adequately digitalized. Such persons have a very poor survival rate. In patients who manifest persistent fibrillation following a myocardial infarction, a high incidence of peripheral embolization occurs. Anticoagulants are definitely indicated in this group.

Atrial Flutter

Atrial flutter is uncommon in association with acute myocardial infarction, the incidence varying from 0.5 to 3 per cent.[1,3] If the flutter is associated with a rapid ventricular rate, the patient should be digitalized with a rapidly acting intravenous digitalis preparation. This may result in a regular sinus rhythm, an increase in the block or may convert the rhythm to a controlled auricular fibrillation. It should be emphasized that large amounts of digitalis may be needed to control the ventricular rate or alter the rhythm in patients experiencing atrial flutter. Some patients may require 2 to 3 times the usual digitalizing dose. If the rhythm is converted to a controlled atrial fibrillation, no attempt should be made to convert the fibrillation to regular sinus rhythm during the early weeks of acute infarction.

Ventricular Tachycardia

Ventricular tachycardia is responsible for approximately 30 per cent of the sudden deaths following myocardial infarction. The occurrence of frequent ventricular premature contractions may be a warning of impending ventricular tachycardia. An episode of ventricular tachycardia or frequent ventricular premature contractions may precede electrocardiographic evidence of myocardial infarction. The use of quinidine in the prevention of ventricular tachycardia has already been mentioned. Its value in the treatment of ventricular tachycardia was first stressed by Levine,[16] who reported the successful conversion of ventricular tachycardia to regular sinus rhythm by the use of the amazing dosage of 1.5 Gm. of quinidine sulfate given 5 times daily.

Procaine amide has been found to have an action similar to quinidine and is more useful in the treatment of ventricular tachycardia, since it can be administered intravenously with safety and more predictable results.[17]

Holland[18] has indicated that increased extracellular potassium produces an effect similar to quinidine. The effectiveness of potassium in converting tachycardia to sinus rhythm was demonstrated by Fisch.[19] Its effect is greater when ventricular tachycardia is due to digitalis intoxication.[20]

Corday and his co-workers[11] have stressed the fact that poor coronary artery perfusion may produce an arrhythmia or potentiate an already existing arrhythmia. Increase of central aortic pressure with the subsequent increase in the coronary artery perfusion may be successful in converting ventricular tachycardia or potentiating the effect of other drugs in converting this arrhythmia. Increase in central pressure may be obtained by the use of vasopressor drugs.

Recently, the hydroxyzine derivatives (Vistaril, Atarax) have been found effective in treating certain arrhythmias, especially ventricular premature contraction and ventricular tachycardia.[21] These drugs may be administered orally or parenterally in doses ranging from 25 to 100 mg. every four hours. Dilantin, 250 mg. intravenously, was found to be effective in correcting a case of ventricular tachycardia which was refractory to procaine amide and quinidine.[22]

Occasionally ventricular tachycardia is resistant to all usual forms of therapy, and the patient's condition demands heroic attempts at conversion:

Table 3.—*Method for Procaine Amide Administration*

I. For ventricular premature contractions, procaine amide 250 mg. q.i.d. p.o.*

II. For ventricular tachycardia

A. Procaine amide 500 mg. in 50 ml. of 5% glucose in water administered intravenously at the rate of 50 mg. per minute, with continuous EKG monitoring, until conversion or toxicity.

B. 1.0 Gm. procaine amide in 500 ml. of 5% glucose in distilled water administered over a 30 to 40 minute period by continuous intravenous drip with EKG monitoring until conversion or toxicity occurs.

III. Signs and symptoms of toxicity are similar to quinidine.

*This is an average dose. An individual patient may require a smaller or larger dose.

for example, Sigler[23] reports a case in which it was necessary to give 0.6 mg. of quinidine HCl I.V. as a single dose to effect conversion. This was done after oral quinidine had proved ineffective. Embree and Levine[24] report one case in which it was necessary to give 4.0 Gm. of procaine amide in 36 minutes. In addition, 1 mg. of atropine was given I.V. at the time of maximal cardiac slowing.

Gilson and Schemm[25] first reported the value of digitalization in the treatment of ventricular tachycardia when the arrhythmia was not due to digitalis toxicity. The value of this mode of therapy was recently emphasized by McGee and Tullis.[26] When ventricular tachycardia is complicated by hypotension or heart failure, specific treatment of the complication may be helpful in converting the arrhythmia.

Atrioventricular Block

Disturbances of atrioventricular conduction occur in 3 to 6 per cent of patients with acute myocardial infarction, occurring most frequently in posterior infarctions.[1-3] Although first and second degree block are usually asymptomatic, they are important "alerting arrhythmias," as they may be forerunners of serious third degree block.[14] First and second degree block usually do not require treatment, but Isuprel has been effective in abolishing the block.[27]

Complete A–V dissociation is a serious post-infarction arrhythmia, since it bears a 50 per cent mortality. Stokes–Adams attacks frequently occur with complete A–V dissociation. During the acute phase of myocardial infarction, A–V block may be temporary. At this time, Isuprel sublingually may convert the block to regular sinus rhythm.[27] When sublingual Isuprel is not sufficient to prevent Stokes–Adams attacks, it may be necessary to administer Isuprel or epinephrine intravenously. Phenylephrine (Neosynephrine) and levarteranol (Levophed) may also be administered intravenously but are less effective than Isuprel or epinephrine.[28] Isuprel appears to be the drug of choice since epinephrine has a pressor effect which Isuprel does not exhibit. Both Isuprel and epinephrine have the capacity to induce a ventricular pacemaker, whereas levarteranol and phenylephrine do not. It is frequently necessary to titrate pressor agents intravenously at a rate sufficient to maintain an adequate ventricular rate while avoiding ventricular tachycardia.

Epinephrine may be required in large doses. Larson[29] reports one patient requiring 20 ml. of 1:1000 adrenalin during a 24 hour period. This was administered in a dose of 0.4 ml. subcutaneously every 30 minutes.

Molar sodium lactate is very effective in exciting a ventricular pacemaker and accelerating an already existing idioventricular focus.[30] Although the exact action of lactate is not known, it may act by increasing the rate of influx of sodium which increases the action potential and therefore induces a ventricular contraction.

Prinzmetal[31] has shown that ACTH and cortisone may be helpful in reestablishing a regular sinus rhythm during the immediate post-infarction period in patients with heart block, the rationale being that the steroids reduce the inflammation about the conducting bundle. This method was