SPECIAL ARTICLE

Approaches to Sudden Death from Coronary Heart Disease

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SUMMARY
Sudden cardiac death (SCD) continues unabated. Coronary care units, while effective in lowering hospital mortality, cannot significantly reduce SCD which occurs primarily outside the hospital and accounts for the majority of deaths from coronary heart disease (CHD). In view of the frequent precipitous nature of SCD, only a program which identifies and protects the victim prior to the event can hope to be successful in preventing the majority of SCD. Since it is likely that SCD is due to an arrhythmia, drug prophylaxis might prove effective. In view of the toxicity of currently available agents, it is mandatory to preselect a population at highest risk before embarking on a drug trial. Ventricular premature beats (VPB) may identify subjects susceptible to SCD. Epidemiologic and physiologic information on VPB is reviewed, and proposals are made for studies designed to establish the usefulness of VPB as a risk factor for SCD.

Additional Indexing Words:  Antiarrhythmic drugs  Exercise  Risk factors  Ventricular fibrillation

THE ROMAN Seneca, 2000 years ago, commented that "death is sometimes a punishment, often a gift, and for many a favor." In the case of sudden coronary death, it is neither gift nor favor, for it frequently explodes life in its very prime. The toll from coronary heart disease continues to rise, and has now reached the staggering figure of 625,000 annually.1

Hitherto, the major research direction has been to evolve methods for primary prevention. Epidemiologic studies have shed much light on the factors that predispose to coronary heart disease (CHD).2-5 A number of environmental and biologic risk factors have been identified, but there is no conclusive evidence that alteration of one or more of these factors will reduce sudden death. Yet primary prevention has the stamp of logic and is a mandatory area for increasing research endeavor. Medical history, however, teaches that consequences of disease are frequently controlled before the underlying derangement is fully comprehended and prevented. In medicine great rewards have flowed from partial answers and usually have preceded complete solutions; for example, the coronary care unit (CCU) has significantly lowered hospital death from acute myocardial infarction. A partial solution now also appears possible for sudden coronary death.

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Formulation of the Problem

The thrust of current endeavor has been on the development of CCU's. This has resulted in a 30% reduction in mortality among hospitalized patients with myocardial infarction. However, two-thirds of patients who die from CHD do not reach a hospital.6–11 It follows that even universal availability of CCU’s could not reduce overall mortality by much more than 10%. Nonetheless, the CCU has contributed to a changed zeitgeist which no longer views the problem of sudden death with futility.12–14 The new perspective derives from success in reversing and, more importantly, in preventing unexpected ischemic death in the hospitalized patient with acute myocardial infarction. Three findings account for the effectiveness of the CCU:

1. Sudden death in the patient with acute myocardial infarction is due to electrical derangement in heart rhythm manifesting as ventricular fibrillation.
2. Ventricular premature beats (VPB) precede and identify the patient susceptible to sudden death.
3. Suppression of VPB with antiarrhythmic drugs prevents occurrence of ventricular fibrillation.

These facts generate three hypotheses that are applicable to those who die suddenly outside the hospital. If these hypotheses are validated, a strategy of care can be evolved for these patients.

Mechanism of Sudden Death in Ambulatory Patients

The first hypothesis postulates that ventricular fibrillation is the mechanism of sudden death in the prehospital phase. The very nature of fatality has hitherto precluded acquisition of precise information. The sudden onset and rapid termination suggest an arrhythmia. Already in 1889, the British physiologist MacWilliam suggested that sudden death in man was due to “fibrillar contraction,” the “violent and prolonged turmoil of fruitless activity in the ventricular wall.”15 Coronary care unit experience provides some circumstantial evidence. Ventricular fibrillation is predominantly a complication immediately after inception of the ischemic event. Primary ventricular fibrillation occurred in 5.5% of patients admitted to a CCU within 4 hr after onset of symptoms, as contrasted with an incidence of 0.4% when admission was delayed.16 This tendency is even more strikingly illustrated when patients are reached earlier by means of a mobile care unit.17 Ventricular fibrillation was 25 times more frequent during the initial 4 hr than during the ensuing 24 hr. Furthermore, bradycardia, which enhances ventricular ectopic activity and lowers the threshold to ventricular fibrillation,18,19 also occurs at the very onset of the acute episode. Thus, nearly 61% of patients with inferior myocardial infarction who came under care within 1 hr exhibited bradyarrhythmias.20

These arguments are partially faulted since the model selected is acute myocardial infarction. Indeed, myocardial infarction is not a consistent precondition for sudden death. However, when abrupt asymptomatic cardiac arrest occurs during fortuitous electrocardiographic monitoring of patients with stable coronary heart disease, the mechanism is invariably ventricular fibrillation.14

Ventricular Premature Beats and Sudden Death

The second hypothesis associates the occurrence of ventricular premature beats (VPB) with sudden death. In the Tecumseh study, the incidence of sudden death in patients with VPB in a single electrocardiogram was 61 per 1000, or three times the age-adjusted rate of the population free of ectopic activity.21 Hinkle and coworkers,22 monitoring actively employed men age 55 for 6 hr during ordinary activities, found that the presence of VPB with a frequency greater than 10/1000 cycles identified a group with a ten times greater risk of cardiac death. Data from the prospective epidemiologic studies at Framingham, however, indicate that VPB detected in a routine electrocardiogram seldom herald immediate sudden death in the absence of preexisting evidence of CHD or left ventricular hypertrophy.23 The data from these studies are derived
from small numbers of patients dying suddenly. Furthermore, it is uncertain whether, in the Tecumseh studies or in those of Hinkle and coworkers, the VPB were independent variables not confounded by other evidence of heart disease. Highly pertinent, therefore, are the early findings of the Coronary Drug Project Research Group (J. Stamler, Chairman, Steering Committee, personal communication). After a 2-year follow-up of 2788 men with previous myocardial infarctions, there were 271 deaths in the placebo group, 75% due to CHD, a majority of which were sudden. Patients with frequent VPB on a single electrocardiogram at time of entry had over twice the mortality of those with rare or no ectopic activity. This difference was significant even after correction for other CHD risk factors was made.*

**Antiarrhythmic Drugs**

The third hypothesis now needs to be examined; namely, whether the control of VPB by an antiarrhythmic drug will prevent ventricular fibrillation in the ambulatory patient dying suddenly. It is tempting to try to solve the problem with a prophylactic drug program. Before we can embark on such an effort, however, it is necessary to determine the efficacy and safety of available agents.

A paramount question is whether drugs will protect against ventricular fibrillation occurring at the very onset of an ischemic event. Yenikomshian and coworkers\(^{24}\) studied this question in an animal model. The effect of eight currently employed antiarrhythmic agents was assessed in 157 dogs following coronary artery occlusion. Small inflatable balloons were placed high on the left anterior descending artery. After recovery from operation, animals were randomly allocated to a control or drug treatment group, and received high therapeutic doses of one of the following: procainamide, quinidine, lidocaine, procainamide, bretylium tosylate, d-propranolol, ajmaline, or diphenylhydantoin. Balloons were inflated while the animal was awake. If the animal survived 10 min, the balloon was rapidly deflated.

After coronary occlusion in control animals, there was a consistent pattern of arrhythmia. Ventricular ectopic activity emerged within a mean time of 2.3 min, rapidly increased in frequency and multiformity, and culminated in ventricular tachycardia and ventricular fibrillation. This sequence occurred in 53% of control animals (fig. 1). In the remaining dogs, the arrhythmia abated almost completely within 6 min after occlusion. However, 40% of the surviving animals developed ventricular fibrillation on balloon deflation. Here the sequence was different: there were no prodro- nal VPB; within a mean time of only 7.5 sec, rapid ventricular tachycardia augured the immediately ensuing ventricular fibrillation (fig. 2).

Of the drugs tested, procainamide was associated with the lowest incidence of ventricular fibrillation. Of 18 dogs, only one animal developed ventricular fibrillation on balloon inflation, and two on deflation. By contrast, diphenylhydantoin showed no protection against ventricular fibrillation, with 13 out of 18 animals succumbing to either

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*Includes 22 clinical, electrocardiographic, and biochemical factors possibly related to long-term prognosis exclusive of VPB. Among the electrocardiographic variables are: Q/QS abnormalities, S-T segment depression or elevation, T-wave abnormalities, left ventricular hypertrophy, resting heart rate, and ventricular and A-V conduction defects.
Ten minutes after left anterior descending coronary artery balloon inflation, dog remained in sinus rhythm free of VPB. Within 2.2 sec after deflation, though S-T-segment depression lessened, VTvp began without antecedent VPB. This subsequently deteriorated to ventricular fibrillation.

occlusion or release (fig. 3). A comparison of the eight drugs employed showed a wide range of effectiveness (fig. 4).

Although it is uncertain whether ventricular fibrillation which follows occlusion or release is the better model for sudden death in man, drugs can suppress arrhythmias resulting from either of these manipulations in the experimental animal. If these data are applicable to man, antiarrhythmic drugs have a role in preventing sudden death. Before proposing a clinical trial in high-risk patients, it is essential to define guidelines for effective drug usage, as well as to determine the nature and incidence of adverse drug reactions. Clinical experience with diphenylhydantoin, procainamide, and quinidine emphasizes the limitations of currently available antiarrhythmic measures.

Diphenylhydantoin is a drug with modest side effects and substantial evidence for effectiveness against ventricular arrhythmias.\textsuperscript{25, 26} While it is difficult to determine whether a drug protects against ventricular fibrillation in man, action against paroxysmal ventricular tachycardia is more readily ascertainable. Ten patients with chronic ischemic coronary artery disease with recurring life-threatening ventricular tachycardia were monitored for periods up to 72 hr while receiving diphenylhydantoin.\textsuperscript{27} The drug was given in a loading dose of 1000 to 1500 mg during the first day, followed by large maintenance doses, which resulted in high blood levels and neurologic side effects. Nonetheless, diphenylhydantoin did not protect any of these patients against recurrence of ventricular tachycardia. These animal and human studies suggest that diphenylhydantoin

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\caption{Figure 4}
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Incidence of ventricular fibrillation during inflation and deflation of a balloon on the left anterior descending coronary artery in controls and in animals premedicated with procainamide or diphenylhydantoin. While procainamide significantly decreased the incidence of ventricular fibrillation, diphenylhydantoin did not afford protection during either period.

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is probably unsuitable for any intended prophylactic program against sudden death. Procainamide is perhaps the most effective agent for combating ventricular ectopic activity. Unfortunately, it is also the antiarrhythmic drug most likely to produce toxicity in chronic use. Current studies by our group demonstrate the magnitude of this problem. Patients recovered from acute myocardial infarction and free of major arrhythmias are being randomized into a control and a procainamide group. Of 84 patients enrolled in the study to date, 42 received 0.5 g of procainamide every 8 hr. Serious adverse reactions occurred in 55%. These include arthralgias, fevers, rashes, lupus-like syndrome, disabling myasthenia, and a catalog of other afflictions. Furthermore, this dose of procainamide does not suppress ventricular ectopic activity in ambulatory subjects. For the present, therefore, procainamide is not suitable as a mass prophylactic agent against sudden death.

Medical experience in the use of quinidine now extends over half a century. Its use is also associated with a significant incidence of toxic reactions. In the past 10 years we have employed quinidine to prevent recurrence of atrial fibrillation in 650 patients subjected to cardioversion. The dose varied from 0.8 to 1.2 g daily, and resulted in blood levels ranging from 1.0 to 4.0 μg/ml. Significant untoward effects forced discontinuation of quinidine in 30% of these patients. There was also a 0.5% incidence of sudden deaths, probably related to the drug. Quinidine, therefore, is also an unsuitable drug for pretreating large groups of patients in the hope of preventing sudden death.

This information emphasizes the difficulty in justifying a clinical trial at this time. Patients who have recovered from acute myocardial infarction constitute the group at highest risk from sudden death. In a larger representative group of such patients, one may anticipate an annual mortality of about 6%, with a 3% incidence of sudden death. Assuming that an antiarrhythmic drug was available that could reduce mortality by 30%, then one person per hundred per year could be saved. However, 99 patients would be exposed to the risks of significant toxic reaction, including possible fatality, in the effort to save one individual. Thus, until safe and highly effective measures are developed, prophylactic employment of antiarrhythmic drugs will require more precise identification of potential victims.

Identification of Susceptible Individuals

How then is one to select a population at sufficiently high risk of sudden death to test potentially toxic antiarrhythmic agents? Though 30% of sudden deaths are derived from patients with CHD, the mere presence of CHD does not constitute an adequate risk for an interventive antiarrhythmic drug program. In middle-aged males an additional 40% of sudden deaths comes from a definable population with at least two of the following risk factors: hypertension, hypercholesterolemia, or any cigarette consumption, but these subjects have only one-fifth the risk of sudden death experienced by those with overt disease. Study of risk factors among patients with already established CHD is also unlikely to define groups with significantly greater susceptibility to sudden death. Ventricular fibrillation is superimposed upon a chronic, progressive derangement in coronary circulation, and may be viewed as an electrical accident that is provoked by a complex series of variables, many of which operate but transiently. If this analysis is correct, there is need to examine for the transient alterations in clinical state which precede sudden death.

Prodromes of Sudden Death

A majority of sudden deaths occur before development of the full-blown syndrome of acute myocardial infarction. While prodromal symptoms may be present, their real incidence is unknown. This is not surprising since the only knowledgeable witness is unavailable to provide testimony. If one assumes that the pathophysiology leading to sudden death is

*Statistical estimates generously supplied by Eve Weinblatt, Department of Research and Statistics, Health Insurance Plan of Greater New York.
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similar to that which results in myocardial infarction, a significant occurrence of prodromes is to be anticipated. Warning symptoms are the rule prior to myocardial infarction. Solomon et al. have found that of 100 patients with proven acute infarction, 65 had significant symptoms of heart disease during the 2 months prior to hospitalization. Stowers and Short report, among 180 such patients, that 68% recalled probable cardiac symptoms antedating their acute attack.

An estimate of the possible incidence of prodromal symptoms among patients dying suddenly within the community is provided by the studies of Kuller et al. They observed that 23% of victims of sudden CHD death had seen their physician during the week prior to death. Tibblin and Holmberg noted that one-third of 157 patients dying suddenly in Gothenburg, Sweden, during 1969, had seen their physician within 2 weeks preceding death. The major complaints consisted of changing anginal pattern and unusual fatigue. Fatigue, however, is a ubiquitous state, and anginal discomfort can periodically change with altered life style without dire outcome. Prodromes based on symptoms will probably not prove sufficient for subgrouping a CHD population as regards risk of sudden death.

VPB may constitute a prodrome suitable for defining risk. If the characteristics of VPB that predict fatality are to be identified, extended periods of monitoring of populations highly susceptible to sudden death will be necessary. Patients surviving myocardial infarction form an important reservoir of sudden death victims and are readily available for these studies.

Monitoring for Ventricular Premature Beats

If monitoring is to be employed, what constitutes an appropriate time? It is clear that the longer the duration, the more ectopies will be detected. At some point there must be a cutoff, a compromise between the practicality of the endeavor and the increasing increment of relevant information. In patients with coronary heart disease, a standard electrocardiogram, equivalent to about 1 min of monitoring, will exhibit some ventricular ectopic activity in about 8%. If the period of monitoring is extended to 3 min, about 14% show extrasystoles. The yield from 12 hr of monitoring was recently analyzed in patients 1 to 24 months after acute myocardial infarction. Of the 220 patients studied, 136, or 61.8%, exhibited some ventricular ectopic activity. If monitoring had been limited to 1 hr, about 70% of those showing VPB would have been detected.

Are the VPB a fixed characteristic of these patients with CHD or do they wax and wane? This question was examined in 41 patients who were monitored after coronary care unit discharge while still in the hospital, and again 3 and 6 months later. Twenty-five patients showed no VPB while in hospital; 15 of these had none during ambulatory monitoring. Ten patients not previously shown to have VPB had ectopic activity in the 3- and 6-month sessions. Of these ten, five had complex ventricular arrhythmias; in three the arrhythmia was paroxysmal ventricular tachycardia. Of 16 patients who exhibited arrhythmia during hospital monitoring, four were consistently free of ectopic activity during later follow-up. Thus, 34% of these CHD patients showed a change in ventricular ectopic activity within a 6-month period. Ectopies may also vary with the time of day. In 78 patients monitored during hospital convalescence from myocardial infarction, the incidence of VPB was compared during waking and sleeping hours. Salvos of VPB and paroxysms of ventricular tachycardia were observed in 12 patients, or 15%. It is noteworthy that in eight of these, the major arrhythmia was recorded only while the patient was asleep, and three of these showed no ectopic activity at all during daytime monitoring.

Significance of VPB

The present observations, though based on as yet inadequate data, permit a preliminary conclusion. It would appear that the mere presence of VPB probably has little prognostic implication. This is based on the fact that 62% of CHD patients monitored for 12 hr while awake demonstrated ectopic activity. One
would predict that if monitoring were extended in time, as many as four-fifths of patients with CHD would have exhibited some extra-systole. Obviously, a variable is unlikely to be a powerful discriminator if present in 80% of a population. This conclusion is not inconsistent with what clinicians have long surmised. Ectopic beats may have different clinical implications. VPB are common and occur in healthy young individuals, and do not appear to affect longevity. There are numerous examples of CHD patients who demonstrate frequent ectopic ventricular beats without seeming compromise of survival.

Does this mean that the model of the coronary care unit and the hypothesis that relates occurrence of VPB to ventricular fibrillation are inapplicable to the ambulatory patient with coronary heart disease? It may very well be that the association of ventricular fibrillation is with the pattern of the ectopic beats rather than with their mere occurrence. Examination of the electrophysiology of ventricular fibrillation provides some information as to which type of VPB may be hazardous.

**VPB and Ventricular Fibrillation**

The current widely held view is that ventricular fibrillation is initiated by reentrant depolarization, favored by inhomogeneity in myocardial excitability and refractoriness. This accounts for the ease of induction of ventricular fibrillation by an electrical pulse delivered during a brief phase of relative refractoriness, designated as the vulnerable period. This period exhibits the greatest disparity in the degree of recovery from the refractory state. An impulse discharged during this phase must pursue a tortuous pathway, thereby predisposing to reentrant and self-sustained activity.

The rhythm disorder immediately preceding ventricular fibrillation usually consists of a sequence of rapid, repetitive beats (fig. 1). In the experimental animal, this mechanism can only be elicited from the vulnerable period of the cardiac cycle following coronary artery ligation. The arrhythmia has been designated ventricular tachycardia of the vulnerable period, or VT. About 75% of episodes of VT deteriorate to ventricular fibrillation. Such an arrhythmia also precedes ventricular fibrillation in man. A unique feature of the disorder is that it can be terminated with small electrical discharges or a thump to the chest. Both these maneuvers induce depolarization of a fraction of the reentrant circuitry, thereby terminating the ventricular arrhythmia. Thus, VT is closely allied to ventricular fibrillation in underlying pathophysiology.

Ventricular tachycardia in the patient with coronary heart disease can also be abolished with low discharge energies. Over the past several years we have titrated the energy for cardioversion of patients with ventricular tachycardia. In 27 episodes in 11 patients with previous myocardial infarction, the initial energy employed was 10 w-sec or less. In 25 of these, or 93%, less than 10 w-sec was the effective level of discharge (fig. 5). It is, therefore, likely that ventricular tachycardia due to ischemic heart disease is a reentrant arrhythmia, and therefore related in mechanism to ventricular fibrillation.

Salvos of ventricular ectopic beats may be harbingers of ventricular fibrillation. The production of ventricular fibrillation with a single stimulus in the animal with or without myocardial infarction requires delivery of large electrical energies during the vulnerable period. The energy requirement is reduced by a sequence of ectopic beats. Three or more consecutive extrasystoles lower the threshold for ventricular fibrillation to the level of a propagated diastolic response. In the animal with myocardial infarction, the number of accelerating premature beats required to initiate fibrillation is reduced compared to the normal control.

![Figure 5](http://circ.ahajournals.org/)

**Figure 5**

Ventricular tachycardia in a patient with acute myocardial infarction was restored to a supraventricular mechanism by cardioversion with a 1 ws (watt-second) discharge.
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The distribution of ventricular ectopic activity among the 136 of 220 postmyocardial infarction patients with VPB detected by prolonged monitoring is shown. Twenty-five patients demonstrated grade 4 or 5 arrhythmias.

The interception of the vulnerable period by an ectopic may trigger ventricular fibrillation. Clinicians have long been aware that extrasystoles are hazardous if they interrupt the T wave. Smirk and Palmer have designated such early ectopic beats as the R on T phenomenon, and have emphasized its association with sudden death. These early VPB are rarely encountered except in the presence of acute myocardial infarction or in patients with far-advanced heart disease.

The studies of Chiang et al. and Stamler (Coronary Drug Project Research Group, personal communication) showed a correlation between sudden death and VPB based solely on the less than 1 min of monitoring provided by a routine electrocardiogram. It follows that many of the patients detected by such an abbreviated monitoring interval probably had a high frequency of ectopic activity. This suggests that frequency of VPB may also have prognostic import.

Thus, if monitoring for ventricular premature beats is to be employed for identification of the subject susceptible to sudden death, certain aspects of ectopic activity may be of special pertinence: frequency, couplets, paroxysms of ventricular tachycardia, and early cycle extrasystoles.

Grading of VPB

In the earlier cited study of 220 patients who were monitored after hospital discharge after recovery from acute myocardial infarction, the ectopic beats were graded. The following grading system was employed: * grade 1 denoted less than 10 ventricular premature beats per hour; grade 2, 11 or more VPB per hour; grade 3, multiform VPB; grade 4, couplets; and grade 5, ventricular tachycardia. Classification by grade shows that 20% of the 220 patients experienced frequent, or grade 2, VPB; 7% had couplets; and 4.5% exhibited ventricular tachycardia (fig. 6). If monitoring had been limited to 1 hr, 48.5% of the 136 patients showing ventricular ectopic

*At present the grading system for VPB has been modified:

<table>
<thead>
<tr>
<th>Grade</th>
<th>Observed</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>No ventricular ectopic beats</td>
</tr>
<tr>
<td>1</td>
<td>Occasional, isolated VPB</td>
</tr>
<tr>
<td>2</td>
<td>Frequent VPB (&gt;1/min or 30/hr)</td>
</tr>
<tr>
<td>3</td>
<td>Multiform VPB</td>
</tr>
<tr>
<td>4</td>
<td>Repetitive VPB</td>
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<tr>
<td>(a)</td>
<td>Couplets</td>
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<tr>
<td>(b)</td>
<td>Salvos</td>
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<td>5</td>
<td>Early VPB</td>
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The hour when 136 patients with VPB achieved their maximum grade of arrhythmia is plotted against the duration of monitoring. Although nearly half of the patients achieved their maximum grade in the first hour, less than one-quarter of the patients with grade 4 and 5 arrhythmias were detected during this interval.
activity would have achieved their maximum grade. However, a brief period of monitoring, such as an hour, may not be proper compromise for duration of monitoring. While the first hour is most rewarding as regards the total occurrence of ectopic activity, this is true primarily for grades 1 to 3. In grades 4 and 5, which from the earlier analysis may have the greatest significance, less than 25% were recognized during the first hour, and not many more during the second hour. In fact, monitoring had to extend to about 6 hr before a majority of these forms of ectopic activity were detected (fig. 7). Although 70% of these patients exhibited some VPB during the first hour, 40% of patients with ventricular tachycardia did not even demonstrate a rare VPB. It remains to be determined whether the same holds for early cycle VPB.

Mere cataloging of the type and frequency of VPB, independent of the circumstances under which they occur, may not suffice to define their clinical significance. The data already presented demonstrate that grades 4 and 5 ectopic activity, which augur ventricular fibrillation during the early phases of an acute myocardial infarction, occur frequently in a population with stable CHD. It has long been recognized that VPB occurring during anginal pain indicate a serious prognosis. It may very well be that stresses of diverse source which accentuate the ischemic process are requirements for the development of electrical instability. If this is indeed the case, passive monitoring may be inadequate to identify the individual susceptible to sudden death. It is, therefore, pertinent to examine the ectopic activity that occurs with a potential ischemic stress such as exercise.

Exposure of VPB with Exercise

The effect of exercise was studied in 205 patients with CHD. The incidence of VPB during a 3-min period of monitoring was compared to the results of treadmill exercise. The reason for this short period of monitoring is that ectopic activity generated through exercise occurs during a similar brief interval at peak stress and immediately upon cessation of exercise. Of 205 patients exercised, 158 had sustained acute myocardial infarction 3 to 6 months earlier, and 47 had been experiencing angina pectoris. The respective incidence of ventricular premature beats in the two groups during control monitoring was 22 and 17%. With exercise, the incidence of ectopic activity more than doubled in both groups. Since the rate acceleration accompanying peak exercise may suppress VPB at the time of maximum ischemia, maneuvers that slow the heart rate may reveal electrical instability. This tendency can, at times, be demonstrated by the use of carotid sinus pressure (fig. 8).

In 66 patients who were free of ectopic activity during 3-min monitoring, the results of exercise were compared to a prolonged period of ambulatory monitoring, averaging 10 hr in duration. Exercise again proved advantageous as compared to passive monitoring. In this population, 38% showed ectopies on passive monitoring, and 65% with exercise, a near doubling of incidence. Perhaps more significant is the grade of arrhythmia exposed with exercise. There was a consistent increase in grade with frequent emergence of ventricular tachycardia in patients who were free of these disorders during passive monitoring. Thus, exercise in patients with ischemic heart disease can expose major grades of arrhythmia not observed with monitoring. Whether these maneuvers will permit subgrouping as regards

Figure 8

Patient with CHD with normal electrocardiogram was free of VPB during development of angina pectoris at peak exercise. No VPB occurred until the heart rate was slowed during right carotid sinus massage (Rt. CSP).
magnitudes of risk of sudden coronary death remains to be determined.

**Current Strategies**

Reduction of the toll of sudden death in the community need not await identification of the susceptible. It is already possible to initiate an effective program for the patient with acute myocardial infarction who does not die instantly. The prime objective is to bring the patient under medical care expeditiously. No system of care will prove effective if a call for help is not initiated promptly. The central problem is that of patient delay in seeking help, which accounts for two-thirds of the interval between the onset of symptoms and the patient's arrival at the hospital.50 This is, in part, compounded by misinterpretation of early symptoms and, in part, by psychologic denial.50 An educational program which will enable the patient to appreciate the significance of early symptoms of myocardial infarction is an essential element in dealing with this problem. Such a program can have little effect unless there exists a readily available medical care response system.61

The initial contact of the patient with the care system would probably be either an ambulance or a community screening facility, both of which may be manned solely by allied health personnel.52 At these early stages of myocardial infarction, there is the greatest likelihood of ventricular fibrillation. It follows that at the very inception of a possible ischemic attack, these allied health personnel should use drugs that stabilize heart rhythm.

At present, decisive clinical evidence is lacking that lidocaine is as effective at the onset of an attack as it is later in its course.53 Nevertheless, the safety of the drug and its remarkable effect in reducing fatal arrhythmia in the CCU already justifies its employment by allied health personnel at the very onset of myocardial infarction. When heart rates are above 50 beats/min, lidocaine should be administered in a bolus of 50 mg intravenously and 200 mg intramuscularly. This will assure a blood level of at least 1 μg/ml at the end of an hour, providing adequate time for patient transport. The routine use of atropine by allied health personnel, based on the possible "overdrive" suppression of ectopic activity, has little justification. The patient with infarction is in a hypercatecholamine state and susceptible to serious complications from the undue rate acceleration occasionally produced by vagolytic drugs. However, when bradycardia is present, especially when accompanied by VPB or by evidence of hemodynamic compromise, atropine is a useful drug.52

Intense interest is currently focused on specially equipped ambulances for coronary patient transport.54–60 While some lives will no doubt be saved, it is certain that sparse medical resources can be better allocated. Instead of fractionating coronary care from other acute problems in the community, a generalized community-wide emergency service needs to be constituted, relying on already existing emergency services. Such a program will need to utilize available emergency transport resources, train allied health personnel in early care of patients with heart attacks, and be oriented to monitoring and stabilizing heart rhythm at the very onset of the acute episode.

A substantial inroad into coronary mortality requires a multifaceted precoronary program. To be successful, such a program will necessarily have to provide an integrated system of health care which includes continuous educational programs within the community, a centralized screening switchboard, efficient utilization of existing emergency transport, training of allied health personnel in emergency care of patients with coronary "incidents," and early initiation of monitoring and heart rhythm stabilization.51

**Direction of Further Investigation**

We are presented with the unpleasant paradox of a fatal process that is reversible or even preventable, but a subject who is untreatable. The essential problem revolves around identification of the subject prone to sudden death. There is compelling necessity to answer the following questions: (1) Which type of ventricular premature beats in patients with ischemic heart disease identify a group at
higher risk from sudden death? (2) Is the risk a function of the condition under which ectopic activity develops? (3) If certain VPB have prognostic implication, is this short range or long run? Answers to these questions may provide a rational basis for the prophylactic use of antiarrhythmic drugs.

None of these questions can be answered in a hospital. Such studies can only be conducted in a stable community, whose dimension can already be estimated. Around 10% of coronary heart disease patients have grade 4 or 5 ventricular premature beats. If one hypothesizes that patients with such arrhythmia have a two times higher risk of sudden death than those without arrhythmia, then 60 sudden deaths would constitute an adequate sample size for validation of the hypothesis. This would require following 1100 myocardial infarction survivors for 1 year. It would take 2 years to recruit such a sample from a population of 150,000 males, age 35 to 74 (Eve Weinblatt, personal communication). Such populations are now available. There need not be delay in initiating these pertinent investigations.

A community-wide effort to prevent sudden death must give first priority to the group at highest risk. Patients with definite CHD are the most threatened and constitute about 5% of men age 35 to 74. Once methods for identification of susceptible individuals are evolved and effective prophylactic measures are developed, the program will need to encompass a much larger population. Patients with CHD contribute but one-third of the victims who die suddenly. In order to deal with a majority of potential sudden death victims, the program will have to include, in addition, those patients manifesting various constellations of risk factors for CHD.

Defining the possible is the critical touchstone of progress. For the first time it is now possible to begin to reduce the awesome toll of coronary death. The resources required are available. The challenge should no longer be evaded.

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