Experimental Acute Myocardial Infarction

Characterization and Treatment of the Malignant Premature Ventricular Contraction

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SUMMARY

The majority of deaths from acute myocardial infarction (AMI) occur prior to the arrival of medical aid and appear to be due to ventricular fibrillation (VF). Since the premature ventricular contraction and bradycardia are believed to predispose to VF, it has been suggested that administration of atropine or lidocaine during the prehospital phase of AMI may effectively reduce mortality in AMI. To test the efficacy of these drugs in treating arrhythmias during the acute phase of AMI we studied 72 closed-chest conscious dogs in which AMI was produced by inflating a balloon cuff previously implanted around the left anterior descending coronary artery. Ventricular arrhythmias developed in 52 dogs either during occlusion or within 2 min of release of occlusion. Arrhythmias were treated by (1) atropine, (2) atrial pacing, (3) lidocaine, or (4) atropine plus lidocaine. Of the 18 dogs that developed VF, all had ectopic ventricular beats that followed a preceding beat (R-R_{PVC} interval) by ≤0.43 sec; no dog with a ventricular arrhythmia that exhibited only R-R_{PVC} intervals >0.43 sec developed VF. On this basis arrhythmias were defined as "benign" (R-R_{PVC} > 0.43 sec) or "malignant" (R-R_{PVC} ≤ 0.43 sec). Using this classification, we found that benign arrhythmias were successfully suppressed by atropine (10 of 13 arrhythmias), pacing (nine of 11), and lidocaine (three of five); however, atropine suppressed only two of 18, pacing two of 14, and lidocaine none of six malignant arrhythmias. We conclude that (1) not all ventricular arrhythmias are potentially lethal and (2) while atropine, pacing, and lidocaine successfully suppress most benign arrhythmias, they appear considerably less effective in suppressing those faster arrhythmias that frequently lead to the precipitation of VF.

Additional Indexing Words:
Bradycardia   Atropine   Lidocaine   Pacing   Arrhythmias

T HE MAJORITY of deaths caused by acute myocardial infarction occur within the first few hours after onset of the attack and before the patient receives medical aid.1-3 Although it is believed that ventricular fibrillation is the cause of most such deaths,4 an effective therapeutic approach to this problem is difficult to formulate since those factors leading to ventricular fibrillation shortly after acute myocardial infarction are poorly understood, and since it is difficult to assess the potential efficacy of therapeutic agents under such circumstances in man.

Recent clinical and experimental observations have suggested that the premature ventricular contraction (PVC) is an almost invariable precursor of ventricular fibrillation,6 and that bradycardia, an extremely common complication of the early phase of acute myocardial infarction,6,7 may favor the development of ventricular ectopic beats and increase vulnerability of the myocardium to ventricular fibrillation.6,9 It therefore has been proposed that mortality following acute myocardial infarction might be substantially diminished were the delay between symptom recognition and administration of antiarrhythmic therapy reduced by having the patient self-administer atropine (in the presence of bradycardia) or lidocaine (with heart rates above 60 beats/min) while awaiting the arrival of medical aid.10 Although this therapeutic concept appears theoretically sound, its practical impact is unclear since recent evidence suggests that prophylactic administration of atropine during experimental

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EXPERIMENTAL ACUTE MI

acute myocardial infarction actually tends to increase the incidence of ventricular fibrillation and death, and that lidocaine may not be as effective in the early phase of acute myocardial infarction as it appears to be in the hospitalized patient. Because of the paucity of information concerning arrhythmias and their treatment during the prehospital phase of acute myocardial infarction, we undertook an investigation in the unanesthetized closed-chest dog to define (1) the type of arrhythmias that occur shortly after the onset of acute myocardial infarction, (2) the relation of these arrhythmias to the ultimate development of ventricular fibrillation, and (3) the efficacy of atropine and of lidocaine in controlling these arrhythmias.

Methods

Operative Technic

Coronary occlusion balloon cuffs and atrial pacing wires were implanted in mongrel dogs, weighing between 15 and 24 kg, 1–2 weeks before the definitive investigation. The animals were anesthetized with pentobarbital and respiration was maintained throughout the operative procedure by delivering a mixture of fluorathane, oxygen, and carbon dioxide through an endotracheal tube. The heart was exposed through a left thoracotomy incision, the proximal portion of the left anterior descending coronary artery was dissected free, and an inflatable balloon cuff was sutured around this vessel about 1 cm from its origin and just distal to the first diagonal branch. Care was taken to ensure that vessel patency was not impaired with the cuff deflated. Major collateral vessels between branches of the left anterior descending and other major coronary arteries, if present, were ligated at their midpoint. Pacing wires were sutured to the left atrial appendage; these wires and the silastic tube communicating with the balloon cuff were exteriorized and the thoracotomy incision closed. The operative site was bandaged, and a heavy cloth jacket was placed around the animal’s torso to prevent damage to the tubing and wires.

Experimental Procedure

Seventy-two dogs with uncomplicated postoperative courses were studied 1–2 weeks after surgery, the animals having recovered completely from the effects of operation. Sedation was obtained by intramuscular injection of diazepam, 16 mg, and morphine sulfate, 32–40 mg, depending upon the weight of the animal; within 30 min after the injections each dog became docile and was studied while lying quietly on his side. Diazepam, and occasionally morphine, were administered intermittently by vein to maintain the dogs in a sedated state. A standard limb lead of the electrocardiogram and an atrial lead from one of the implanted pacing wires were recorded continuously and the analog data stored on tape. Baseline recordings were obtained for 5 min after which acute coronary artery occlusion was produced by inflation of the implanted balloon cuff. The pressure within the cuff was measured throughout the course of the experiment with a Statham-23 Db pressure transducer to ensure that leaks were not present.

All dogs were monitored for a period of approximately 4 hours unless ventricular fibrillation supervened. Occlusion was maintained for the 4-hour period in those dogs experiencing persistent ventricular arrhythmias during the first hour of occlusion. In those animals that did not develop persistent PVCs or ventricular tachycardia during the first hour of occlusion, the balloon cuff was quickly released at 1 hour for a period of 2½ min. The balloon was reoccluded either with the appearance of “malignant arrhythmias” (subsequently defined) or at the conclusion of a 2½-min interval. Serial releases were performed at approximately 15-min intervals. Ventricular arrhythmias developing during occlusion of the balloon cuff are referred to as “occlusion arrhythmias”; those occurring following release of the cuff are termed “release arrhythmias.” After the series of release experiments was completed, the cuff was occluded and the animals were monitored for the remainder of the 4-hour study period. In 14 dogs, no drugs were administered prior to release; instead, a total of three to five cycles of release and reocclusion of the balloon cuff was performed at about 15-min intervals to determine whether this technic reproducibly caused ventricular arrhythmias.

Therapeutic Interventions

Atrial Pacing

Atrial pacing at 120 beats/min was initiated 2–5 min following the onset of PVCs or ventricular tachycardia associated with coronary occlusion. Whenever ventricular arrhythmias were suppressed by pacing, pacing was discontinued after 2–4 min in order to determine whether the arrhythmia was still present at the lower heart rate.

In animals in which arrhythmias occurred following release of occlusion, pacing at 120 beats/min was initiated just prior to the subsequent cuff release (performed about 15 min after reocclusion) and maintained for the 2½-min period of release. If no arrhythmias appeared after release of coronary occlusion in the presence of pacing, the artery was reoccluded and pacing discontinued; approximately 15 min later release of occlusion was carried out without pacing to determine whether PVCs or ventricular tachycardia would occur at the control slower heart rate or had spontaneously resolved.

Atropine

In 15 dogs developing frequent PVCs or ventricular tachycardia during coronary occlusion, atropine sulfate was administered in a loading dose of 0.3 mg intravenously and then in 0.1–0.2 mg doses until all ventricular ectopic activity was abolished or until the heart rate increased to approximately 120 beats/min. Those animals in which PVCs or ventricular tachycardia was abolished following atropine were then monitored until the arrhythmias returned or until the heart rates reached control levels.

In 12 animals in which ventricular arrhythmias occurred following release of occlusion, atropine was
given before the next release until a heart rate of approximately 120 beats/min was attained. The cuff was then deflated for 2 min (or less if a ventricular arrhythmia supervened). If no arrhythmias were observed, a third release was performed 20–30 min later after the effects of atropine on heart rate had dissipated in order to determine whether the arrhythmias recurred at the lower heart rates.

Lidocaine

Using a protocol similar to that for atropine, lidocaine was given intravenously in a bolus injection of 2 mg/kg to seven dogs developing ventricular arrhythmias during coronary occlusion. An additional bolus of 2 mg/kg was given to those animals in which suppression of ventricular arrhythmias was unsuccessful.

In four dogs in which release of occlusion had resulted in multiple PVCs or ventricular tachycardia, lidocaine, 2 mg/kg, was administered just before the next release. If no arrhythmias appeared during the release period of 2 min, a third release was performed 30 min later to determine whether the ventricular arrhythmia had recurred.

Atropine and Lidocaine

In 10 animals both atropine and lidocaine were administered either during coronary occlusion or prior to release of occlusion when either drug alone failed to completely suppress the existing arrhythmias. The dose of atropine used was that which was sufficient to increase the heart rate to about 120 beats/min; lidocaine was administered in a bolus injection of 2 mg/kg; with occlusion arrhythmia an equivalent dose was administered 5 min later if no antiarrhythmic effect was observed.

Arrhythmia Analysis

An arrhythmia was considered to be present if four or more ventricular premature contractions occurred during any 1-min period. On the basis of our results, ventricular arrhythmias were divided into two categories: "benign" and "malignant." We defined "malignant" arrhythmia as one in which the R-Rpvc interval or R-R intervals of consecutive ventricular beats were less than or equal to 0.43 sec (corresponding to a heart rate of 140/min or faster), We defined "benign" arrhythmia as one in which the R-Rpvc or R-R intervals were greater than 0.43 sec. Many dogs had both "benign" and "malignant" arrhythmias; in these cases each arrhythmia was analyzed separately. Thus, an intervention in a dog with coexistent malignant and benign PVCs might abolish one type of arrhythmia, but have no effect on the other.

An intervention was judged successful if it reduced the frequency of PVCs to one or less per min. In addition, we attempted to eliminate the inclusion of a spontaneous abatement of arrhythmia as a therapeutic success by considering a therapeutic intervention successful during occlusion arrhythmias only when (1) PVC frequency was reduced to 1 or less per min and (2) when the arrhythmia returned after pacing was discontinued, after heart rate returned to control levels following atropine administration, or within 30 min after the last intravenous dose of lidocaine. In the case of release arrhythmias, the "sandwiching" procedure described above was employed (no intervention-release; intervention-release; no intervention-release); a therapeutic intervention was judged successful only if an arrhythmia, which was present following the first release when no therapeutic intervention was applied, was abolished by the intervention at the second release, and was present at the third release in the absence of any intervention.

We considered it possible that the above requirements for ascertaining the effectiveness of an intervention were too stringent, since an ideal intervention might permanently eliminate any further episodes of arrhythmia. After analysis of the data was completed, however, we found that the results were similar even if those animals that did not satisfy criterion 2 (above) were included in the analysis.

The results were analyzed for statistical significance by the chi-squared test.

Results

Incidence of Ventricular Arrhythmias

A total of 52 of the 72 dogs developed ventricular arrhythmias either during coronary occlusion, within 2 min of release of occlusion, or both (table 1). Eighteen of these animals developed ventricular fibrillation: nine during coronary occlusion and nine following release of the balloon cuff. In a few animals ventricular flutter progressing rapidly to ventricular fibrillation occurred immediately after the first ectopic complex; most manifested premature ventricular contractions or ventricular tachycardia prior to the appearance of ventricular flutter. Regardless of the precise sequence of events, however, all episodes of ventricular fibrillation were preceded by one or more ectopic ventricular beats that followed the preceding normal complex by less than 0.43 sec (fig. 1). Thus, any premature ventricular contraction or ventricular tachycardia having an R-Rpvc or R-R interval equal to or less than 0.43 sec was considered to have a more serious or malignant potential than those with longer intervals.

Table 1

<table>
<thead>
<tr>
<th>Type of arrhythmia</th>
<th>Total no. of dogs with arrhythmias</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>VF</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Malignant†</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Benign*</td>
<td>9</td>
<td></td>
</tr>
</tbody>
</table>

*Includes those dogs which manifest only benign arrhythmia. Those with benign and malignant arrhythmias were considered to have malignant arrhythmias.
†Includes VF.

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**Oclusion Arrhythmias**

Of the 24 dogs that developed occlusion arrhythmias, 17 had onset of ventricular ectopic activity within the first hour of occlusion, the remainder developed arrhythmias later in the study during coronary occlusion, but after one or more releases of the occluding cuff. Heart rates in these 24 dogs with occlusion arrhythmias averaged 87 ± 4 beats/min (range 50–116) in the control preocclusion state, and 91 ± 5 beats/min (range 48–130) at the time of onset of arrhythmias. Table 1 summarizes the data relating to the incidence and type of arrhythmias occurring during coronary occlusion.

**Release Arrhythmias**

In 55 animals that did not have arrhythmias within the first hour of occlusion, sudden release of the balloon cuff resulted in ventricular arrhythmias in 33 animals. The arrhythmias consisted of multiple premature ventricular contractions which often progressed rapidly to a malignant ventricular arrhythmia and, in nine dogs, to ventricular fibrillation (table 1). The reproducibility of the arrhythmic effects of this intervention was demonstrated when successive cycles of release and reocclusion consistently produced ventricular arrhythmias. Thus, of 11 dogs that developed arrhythmias after the first release, each developed arrhythmias after the two succeeding releases. Reocclusion of the cuff after the onset of ventricular premature contractions or ventricular tachycardia (and in one case, ventricular flutter) abolished all arrhythmias within 10–15 sec without exception (fig. 2). Reocclusion had no effect in dogs that developed ventricular fibrillation. Heart rates of the 33 dogs developing release arrhythmias averaged 74 ± 3 beats/min (range 48–100) in the control preocclusion state and 82 ± 4 beats/min (range 56–130) at the time of release.

**Therapeutic Interventions**

Analysis of the effects of pacing and drugs on arrhythmias showed similar trends whether arrhythmias occurred during coronary occlusion or after release of occlusion. Table 2 details the effects of interventions on occlusion and release arrhythmias separately, and figure 3 summarizes the data from both the occlusion and release studies.

**Table 2**

Effects of Interventions on Arrhythmias

<table>
<thead>
<tr>
<th>Type of arrhythmia</th>
<th>Atropine (no.)</th>
<th>Atrial pacing (no.)</th>
<th>Lidocaine (no.)</th>
<th>A + L (no.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oclusion (24 dogs)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benign</td>
<td>10</td>
<td>7</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Suppressed*</td>
<td>9</td>
<td>6</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Malignant</td>
<td>7</td>
<td>5</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Suppressed</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Release arrhythmias (33 dogs)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benign</td>
<td>3</td>
<td>4</td>
<td>—</td>
<td>2</td>
</tr>
<tr>
<td>Suppressed</td>
<td>1</td>
<td>3</td>
<td>—</td>
<td>1</td>
</tr>
<tr>
<td>Malignant</td>
<td>11</td>
<td>9</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Suppressed</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Abbreviations: A + L = atropine and lidocaine.

*Suppressed = frequency of PVCs less than 1/min.
Figure 2

Efficacy of reocclusion in controlling an arrhythmia precipitated by release of coronary artery occlusion.
Ventricular tachycardia occurred shortly after release of occlusion; reocclusion abolishes the arrhythmia and normal sinus rhythm returns.

Atrial Pacing

Atrial pacing at 120 beats/min successfully suppressed nine of 11 benign ventricular arrhythmias. In contrast, it suppressed only two of 14 malignant ventricular arrhythmias. The difference in the effectiveness of pacing in suppressing benign vs malignant arrhythmias was statistically significant (P < 0.02) when the results of occlusion and release arrhythmias are combined. The numbers were too small to achieve statistical significance when the results within each subgroup (i.e., occlusion benign vs occlusion malignant) were analyzed.

Atropine

The heart rate following administration of single or repeated doses of atropine averaged 120 ± 3 beats/min (range 97–130) in the dogs with occlusion arrhythmias and 117 ± 3 beats/min (range 100–125) in the dogs with release arrhythmias. In those animals with benign ventricular arrhythmias 10 of 13 had their arrhythmias suppressed by increasing the heart rate with atropine. However, atropine suppressed malignant ventricular arrhythmias in only two of 18 dogs. The difference in the effectiveness of atropine in suppressing benign vs malignant arrhythmias was statistically significant (P < 0.005).

Figure 3

Suppression of benign and malignant arrhythmias.
when the results of occlusion and release arrhythmias were combined. The lower efficacy of atropine in treating malignant arrhythmias was also significant (P < 0.05) when the effects of atropine on occlusion benign and occlusion malignant arrhythmias were analyzed. The number of dogs in which atropine was given to control release arrhythmias was too small to achieve statistical significance within this subgroup.

If the antiarrhythmic effects of atropine are related solely to its effects on heart rate (and therefore are similar to those achieved by atrial pacing), it would be reasonable to combine the results of atropine and atrial pacing. If this is done, then the numbers of dogs with benign and malignant arrhythmias is sufficiently large for meaningful statistical analyses to be performed on each subgroup (i.e. occlusion and release) separately. Such an analysis indicated that increasing heart rate was less effective in diminishing malignant than benign arrhythmias during either coronary artery occlusion (P < 0.05) or following release of occlusion (P < 0.01).

Lidocaine

Intravenous lidocaine in a bolus of 2 mg/kg suppressed benign ventricular arrhythmias in three of five dogs but in none of six dogs with malignant ventricular arrhythmias. An additional dose of 2 mg/kg of lidocaine also was unsuccessful in suppressing the latter arrhythmias.

Atropine plus Lidocaine

The combination of atropine and lidocaine was no more successful in suppressing malignant ventricular arrhythmias than either drug alone. Two of three benign arrhythmias were abolished by the drug combination whereas only one of seven malignant arrhythmias was suppressed. The differences in the effectiveness of lidocaine, or atropine plus lidocaine, in treating benign vs malignant arrhythmias can only be considered trends since the animals studied were too few for a meaningful statistical analysis to be performed.

Discussion

Several major conclusions regarding the early phase of acute experimental myocardial infarction can be drawn from the results of the present investigation. First, ventricular ectopic beats always precede the development of ventricular fibrillation, although occasionally the first PVC that occurs may be sufficient in itself to precipitate the terminal arrhythmia. These observations confirm earlier investigations. Second, not all ventricular ectopic beats appear to be harbingers of ventricular fibrillation and death. Thus, of the 72 dogs studied during the course of the present investigation, 18 developed ventricular fibrillation. In every instance ventricular fibrillation was preceded by a ventricular arrhythmia in which the R-R PVC interval was 0.43 sec or less. This interval corresponds to a heart rate equal to or greater than 140/min. No animal with only PVCs or ventricular tachycardia with R-R PVC intervals greater than 0.43 sec developed ventricular fibrillation.

When the results of the present investigation are combined with those of another study in our laboratory conducted at the same time and employing an identical preparation, our conclusions are further strengthened. Of the 127 dogs studied in the two investigations, 34 developed ventricular fibrillation; in every instance ventricular fibrillation was preceded by a ventricular arrhythmia in which the R-R PVC interval was 0.43 sec or less. The lethal nature of what we have termed malignant arrhythmias also can be appreciated by the fact that while none of the 21 dogs in the combined series with only benign arrhythmias developed ventricular fibrillation, 42% (34/81) of those animals with malignant arrhythmias did.

The contention that not all types of ventricular ectopic beats predispose to a fatal outcome is supported by several clinical studies. For example, it is commonly recognized that ventricular fibrillation is more likely when a premature ventricular depolarization interrupts the T wave, and a rating system for estimating the relative malignancy of ventricular arrhythmias has been proposed. Furthermore, numerous reports have appeared in the literature indicating that "slow ventricular tachycardia" ("idioventricular rhythm") occurring in patients with acute myocardial infarction is usually "benign" insofar as it rarely leads to a fatal outcome. An example of such an arrhythmia occurring during one of our studies is shown in figure 4. Finally, preliminary clinical evidence has been reported suggesting that during the prehospital phase of acute myocardial infarction, premature ventricular contractions with a short coupling interval represent the only ECG finding of predictive value for determining the subsequent development of serious ventricular arrhythmias.

The observation that not all ventricular ectopic activity is potentially catastrophic forms the basis of the third major conclusion of the present investigation: i.e., that increasing heart rate or infusing
lidocaine are relatively ineffective in suppressing malignant arrhythmias occurring early after the onset of acute myocardial infarction. If the antiarrhythmic efficacy of atropine or lidocaine were judged simply by determining whether or not ventricular arrhythmias in general were abolished, it might have been concluded that these interventions exerted marked salutary effects. However, when their effects on benign and malignant arrhythmias were analyzed separately, very different conclusions emerged. Thus, while increasing heart rate with intravenous atropine successfully suppressed 77% of the benign arrhythmias, suppression occurred in only 11% of the malignant arrhythmias. Increasing heart rate with atrial pacing produced almost identical results; 82% of the benign arrhythmias were suppressed, but only 14% of the malignant. Although the effects of intravenous lidocaine were not studied in as many dogs, and the results can only be considered preliminary, the trend was similar; three of the five benign arrhythmias were suppressed, but none of the six malignant arrhythmias was affected. The combination of atropine and lidocaine also tended to be less effective in the treatment of malignant ventricular arrhythmias.

It must be stressed that our results did not show that increasing heart rate was totally ineffective in suppressing malignant arrhythmias, and it is possible that suppression of 10–15% of malignant arrhythmias may reduce mortality in acute myocardial infarction. It is also possible that increasing heart rate may be more efficacious when baseline rates are extremely slow, as often occurs during acute diaphragmatic infarction in man, or when slow heart rates are associated with severe hypotension. However, it has been demonstrated that during experimental myocardial ischemia deleterious myocardial and electrophysiologic changes occur even when heart rate is increased from slow baseline levels. For example, during experimental coronary occlusion increasing heart rate increases the degree of ischemic injury even when baseline levels of heart rate are as slow as 30 beats/min and increasing rate from a baseline of 50–60/min to 90/min decreases ventricular fibrillation threshold. Thus, the overall effect of increasing heart rate on the course of acute myocardial infarction undoubtedly depends on the net balance of its beneficial and deleterious effects. During experimental acute myocardial infarction in the dog, it would appear that the modest effect of atropine in controlling malignant arrhythmias may be more than counterbalanced by its deleterious myocardial and electrophysiologic effects, since prophylactically administered atropine tends to increase the incidence of malignant arrhythmias and ventricular fibrillation.

Although we must again emphasize that the number of dogs in which lidocaine was administered was small, our results raise the interesting possibility that while lidocaine is extremely effective in abolishing benign arrhythmias occurring during the early phase of experimental acute myocardial infarction, it may be considerably less potent in abolishing malignant arrhythmias. This conclusion might appear to be inconsistent with commonly held clinical impressions; however, it should be pointed out that evidence exists suggesting that lidocaine may not be as reliable as commonly supposed in preventing the occurrence of primary ventricular fibrillation in the hospitalized patient. It is of interest, for example, that Chopra and co-workers studying the effects of lidocaine on arrhythmias occurring in patients admitted to hospital with an acute myocardial infarction, reported results that were virtually identical to ours. These investigators found that lidocaine was extremely effective in abolishing unifocal ventricular premature contractions that occurred late in diastole, but was uniformly ineffective in abolishing ventricular premature

Figure 4

A typical example of ventricular tachycardia characterized as "benign." The rate of the ectopic rhythm is 120/min. Whenever the sinus rate exceeds this, the ventricular arrhythmia is suppressed. The electrocardiogram is being recorded by an atrial lead, and the sharp, small deflections represent P waves.
contractions that were multifocal or were of the "R on T" type. It also has been the clinical impression of the physicians responsible for the Belfast mobile coronary care unit that lidocaine is less effective in the control of ventricular ectopic beats occurring soon after the onset of symptoms of acute myocardial ischemia than it is several hours or days later.6

Finally, although it generally is assumed that arrhythmias leading to sudden death in patients with coronary artery disease occur as a result of coronary occlusion, it is possible that ventricular arrhythmias following sudden release of occlusion, that is, following reperfusion of a previously ischemic portion of myocardium, may be a significant factor in the etiology of sudden death in man. In regard to this concept, Spain and Braden22 showed that the frequency of fresh thrombi in diseased coronary arteries decreased with decreasing intervals between the onset of symptoms of myocardial ischemia and death; only 17% of patients surviving less than 1 hour manifested evidence of recent thrombus formation. Similar findings were reported more recently by Roberts.25 Although by no means definitive, these observations are consistent with the hypothesis that lysis or dislodgement of a fresh clot within a coronary artery may play a role in the precipitation of some fatal ventricular arrhythmias in patients with coronary artery disease.

The occurrence of ventricular fibrillation following the release of a brief period of coronary artery occlusion found in the present investigation confirms the findings of many other workers.15, 16, 34, 35 However, the fact that reocclusion of the coronary artery results in the immediate abolition of the arrhythmia has not been described previously. Knowledge of the potency of reocclusion in abolishing release arrhythmias may be of value to investigators studying experimental acute myocardial infarction and to surgeons performing revascularization procedures in patients with coronary artery disease. Thus, it is possible that refractory ventricular arrhythmias occurring shortly after perfusion of a previously ischemic segment of myocardium by a venous bypass graft may be controlled by reocclusion of the graft and very gradual reinitiation of flow.

In summary, it would appear that ventricular arrhythmias precede the development of ventricular fibrillation during the early phases of experimental acute myocardial infarction and that these arrhythmias can be further defined as to their malignant potential by their R-R/VC interval. Using such an analysis we have demonstrated that while increasing heart rate or infusing lidocaine effectively abolishes benign arrhythmias, these interventions are considerably less effective in abolishing arrhythmias that often are associated with the development of ventricular fibrillation.

We wish to emphasize that although some clinical information is available that is compatible with the data presented in this report, the preceding conclusions are based mainly on our results from the experimental animal and may not be generally applicable to man. Nevertheless, it is clear from this investigation that conclusions regarding the clinical efficacy of antiarrhythmic drugs cannot be based on the assumption that a decrease in arrhythmia incidence is equivalent to a reduction in mortality.

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References


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