Section 5: Pharmacology I: Agents for Arrhythmias

Cardiac Monitoring

Arrhythmias, serious electrical abnormalities of the heart, cause most sudden coronary deaths. Establish ECG monitoring as soon as possible for all patients who collapse suddenly or who have symptoms of coronary ischemia or infarction. To avoid delay, use the “Quick-look paddles” feature available on most conventional defibrillators. For patients with acute myocardial infarction (AMI) or severe ischemia, the greatest risk for serious arrhythmias occurs during the first hour after the start of symptoms. Healthcare professionals must start cardiac monitoring as soon as possible during this critical period.

Arrhythmia Recognition

Interpret all ECG and rhythm information within the context of total patient assessment. Inaccurate diagnoses and inappropriate therapy occur when ACLS providers base their decisions solely on cardiac rhythm and neglect to evaluate the patient’s clinical signs, such as ventilation, oxygenation, heart rate, blood pressure, level of consciousness, and other signs of inadequate organ perfusion. In addition, full diagnosis requires assessment of the patient’s metabolic and acid-base status. In specific clinical settings consider the possibility of proarrhythmic drug effects, adverse drug effects from intentional or unintentional overdose, or drug toxicity occurring with normal dosing patterns.

Providers of ACLS should participate in training and evaluation sessions that will establish their ability to detect and treat serious arrhythmias. After initial training, ACLS providers require regular updates in their rhythm expertise combined with evaluation sessions. Providers of ACLS must know how to use ECG monitoring equipment and be able to troubleshoot the most common technical problems.

Rhythms to Recognize

Professionals at the ACLS level should be able to recognize the following arrhythmias.

Classified as tachycardias

The tachycardias listed above can be classified in a number of ways. One useful system is described below.

- Narrow QRS complex (supraventricular) tachycardias
  - Sinus tachycardia
  - Atrial fibrillation (AF)
  - Atrial flutter
  - Atrial tachycardia (ectopic and reentrant)
  - Multifocal atrial tachycardia (MAT)
  - AV nodal reentry tachycardia (AVNRT)
  - Junctional tachycardia
  - Accessory pathway–mediated tachycardia (see below)
- Wide-QRS complex tachycardias
  - Ventricular tachycardia
  - Ventricular fibrillation
  - Any supraventricular tachycardias (SVT) with aberrancy (bundle-branch block or intraventricular conduction delay)
- Preexcited tachycardias (supraventricular arrhythmias associated with or mediated by the presence of an accessory pathway)
  - Atrial tachycardia with accessory pathway conduction
  - Atrial flutter or AF with accessory pathway conduction
  - AV reentry tachycardia (AVRT)

ACLS providers must be able to distinguish between supraventricular and ventricular rhythms and be aware that most wide-complex (broad-complex) tachycardias are ventricular in origin. If a patient is pulseless, in shock, or in congestive heart failure, such rhythms should always be presumed to be VT. Initial management should proceed under the presumption of VT. Obtain a 12-lead ECG as soon as practicable. An esophageal lead may be helpful if the origin of the arrhythmia remains in doubt. ACLS providers must also be able to identify various artifacts that may mimic arrhythmias and know the clinical significance and appropriate treatment of all common rhythm disorders.

Administration of Medications During Cardiac Arrest: Correct Priorities

The 1992 Guidelines coincided with a reductionist period in cardiac resuscitation in regard to the value of medications. In 1992 evidence review led to recommendations to reduce the indications for calcium chloride, sodium bicarbonate, epinephrine, and isoproterenol. The International Guidelines 2000 continue this pattern. On close evidence review we recognize that few drugs are supported by strong evidence. This includes drugs used for cardiac arrest as well as drugs for prearrest arrhythmias. Therefore, during cardiac arrest, drug

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administration is secondary to other interventions. Rescuers must place primary priorities on basic CPR, defibrillation when indicated, and proper airway management. Once these interventions are initiated, emergency personnel can start an IV infusion and consider which drugs might be useful.

**Central Versus Peripheral Infusions**

If no vein has been cannulated before the arrest, a peripheral vein (antebrachial or external jugular) should be the first choice. Central line access (internal jugular or subclavian) requires interruption of chest compressions. Peak drug concentrations, however, are lower and circulation times are longer when drugs are administered via peripheral sites compared with central sites.\(^1\)\(^-\)\(^3\) When given via a peripheral vein, drugs require 1 to 2 minutes to reach the central circulation, but the delay is appreciably shorter with a central venous route. Peripheral venous cannulation, however, is easier to learn, results in fewer complications, and does not require interruption of CPR. If peripheral venous access is used during resuscitative efforts, administer IV drugs rapidly by bolus injection; follow with a 20-mL bolus of IV fluid and elevate the extremity for 10 to 20 seconds.\(^4\)

If spontaneous circulation does not return after defibrillation and administration of drugs via peripheral vein and experienced providers are available, consider placement of a central line unless there are contraindications. Placement of a central line, however, can produce complications, so consider the risk-benefit ratio.

Central lines may be associated with an increase in the rate of complications for patients who receive fibrinolytic therapy. A punctured central vascular structure or noncompressible vessel—regardless of whether a catheter was inserted—is a relative contraindication for fibrinolytic therapy, although in experienced hands and with no obvious bleeding or hematoma, it is not an absolute contraindication. Avoid attempts at central line placement in patients who are candidates for pharmacological reperfusion.

**Tracheal Drug Administration**

If a tracheal tube has been placed before venous access is achieved, epinephrine,\(^6\)\(^-\)\(^7\) lidocaine, and atropine\(^8\) can be administered via the tracheal tube. Administer all tracheal medications at 2 to 2.5 times the recommended IV dose, diluted in 10 mL of normal saline or distilled water. Tracheal absorption is greater with distilled water as the diluent than with normal saline, but distilled water has a greater adverse effect on PaO\(_2\). Pass a catheter beyond the tip of the tracheal tube, stop chest compressions, spray the drug solution quickly down the tracheal tube, follow immediately with several quick insufflations to create a rapidly absorbed aerosol, then resume chest compressions.\(^6\)

**Arrhythmias and the Drugs Used to Treat Them**

Researchers have gathered important new information since previous resuscitation guidelines. This information has prompted a critical reevaluation of the treatment recommendations for arrhythmias, especially the tachyarrrhythmias. The International Guidelines 2000 experts who performed this reevaluation searched for evidence of clinical efficacy. This has resulted in several new international recommendations for the treatment of common tachyarrrhythmias. As of 2000, arrhythmia specialists and clinical cardiologists advocate a new emphasis on existing hemodynamic instability and on the degree of impaired ventricular function. The experts restricted the evidence evaluation to parenteral medications used during arrest or during the peri-arrest period. Because the guidelines are evidence-based, the experts expanded their search to include all drugs supported by clinical research, not just agents approved and available in each country. In addition, the AHA has dropped references to bretyllium because of its limited utility and availability.

**Hemodynamically Stable Wide-/Broad-Complex Tachycardias**

Wide-/broad-complex tachycardias (see the Tachycardias Overview Algorithm in Part 6, Section 7D) present a diagnostic challenge. When defining tachycardias with a prolonged QRS or QRST interval, “wide” is the common term in the United States, whereas in the United Kingdom “broad” is preferred. A clinician needs to make a specific diagnosis because he or she will treat the different types of wide-complex tachycardias with different interventions. Establish whether a wide-complex tachycardia is stable or unstable. The criteria for hemodynamically stable wide-complex tachycardia are:

- **Regular** tachycardia at a rate greater than the upper limit of sinus tachycardia at rest (>120 bpm)
- **Uniform** (monomorphic) QRS configuration of ≥120 ms in duration
- No signs or symptoms of impaired consciousness or tissue hypoperfusion

The patient must be stable enough to allow time for rhythm diagnosis or transport to a facility more capable of diagnosing the rhythm. The drugs used for most tachycardias lower the blood pressure. Therefore, patients should have blood pressures high enough to permit use of these drugs. Otherwise the drug-induced drop in blood pressure will require immediate electrical cardioversion to end the abnormal rhythm. Table 1 lists the most common forms of wide-complex tachycardia.

### TABLE 1. Classification of Most Common Forms of Wide-Complex Tachycardia

<table>
<thead>
<tr>
<th>Tachycardia</th>
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<tbody>
<tr>
<td>Ventricular tachycardia</td>
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<tr>
<td>Supraventricular tachycardia with aberrancy due to intraventricular conduction delay. These include</td>
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<tr>
<td>Sinus tachycardia</td>
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<tr>
<td>Atrial tachycardia (ectopic or reentrant)</td>
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<tr>
<td>Atrial flutter, with fixed AV block</td>
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<tr>
<td>AV nodal reentry tachycardia</td>
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<tr>
<td>Junctional tachycardia</td>
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<tr>
<td>Preexcited tachycardias (associated with or mediated by an accessory pathway) including</td>
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<tr>
<td>Atrial tachycardia</td>
</tr>
<tr>
<td>Atrial flutter</td>
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<tr>
<td>AV reentry tachycardia</td>
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Treatment of Wide-Complex Tachycardias

Previous treatment recommendations for wide-complex tachycardias in adults listed lidocaine as the treatment of choice. Lidocaine was recommended as well for all wide-complex tachyarrhythmias not known with certainty to be supraventricular in origin. The international Guidelines 2000 Conference, however, focused on the need to establish a rhythm diagnosis before initiating treatment in stable patients. This change in treatment approach is based on new evidence that debunks 2 axioms about wide-complex tachycardias: (1) if the true rhythm is ventricular tachycardia, then only lidocaine will convert the rhythm to a sinus complex; and (2) if the true rhythm is supraventricular tachycardia with aberrancy, then only adenosine will convert the rhythm to a sinus complex. By 2000 most cardiologists who specialize in arrhythmias think that adenosine has been overused for wide-complex tachycardias, certainly in the case of VT unresponsive to lidocaine. This overuse has often delayed more appropriate treatment.

When circumstances and expertise allow, ACLS providers should make a reasonable attempt to distinguish hemodynamically stable VT from SVT with aberrancy. A history of coronary artery disease or other structural heart disease suggests ventricular origin. A history of previous aberrant rhythms, accessory pathways, preexisting bundle-branch block, or rate-dependent bundle-branch blocks suggests supraventricular aberrancy if the QRS matches that observed with the tachycardia.

The 12-lead ECG

Always obtain a 12-lead ECG before and during pharmacological interventions and after conversion to a regular rhythm. If the 12-lead ECG is not diagnostic, an esophageal lead may be helpful if the equipment and experts who can interpret esophageal lead tracings are available.

Adenosine

The principal therapeutic effect of adenosine is to slow AV nodal conduction. Adenosine is not an effective agent for common forms of ventricular arrhythmias or for preexcited atrial arrhythmias such as atrial fibrillation or atrial flutter. Although adenosine has vasodilatory effects that are short-lived, instances of worsened hypotension have been reported in patients with barely compensated blood pressure after inappropriate treatment with adenosine for VT. Adenosine also carries the theoretical risk of causing angina, bronchospasm, proarrhythmia, and acceleration of accessory pathway conduction. Adenosine is used for narrow-complex tachycardias (see The Tachycardia Overview Algorithm, column 2); for narrow-complex supraventricular tachycardia, stable (see the Narrow-Complex Algorithm); and for wide-complex tachycardias that are confirmed as supraventricular in origin (The Tachycardia Overview Algorithm, column 3). These algorithms are in Part 6, Section 7D.

Procainamide

Antiarrhythmic agents such as procainamide have shown efficacy in treating a broad variety of arrhythmias, including supraventricular arrhythmias, with and without aberrancy, and VT. Procainamide is effective at terminating SVT because of its ability to alter conduction across an accessory pathway (Class IIa). Amiodarone also is effective for supraventricular tachycardias because it alters conduction through the accessory pathway (Class IIa if LV function is normal and IIb if rapid VT. The bottom line is to keep it simple and not puzzle over complex rhythm interpretive algorithms.

Lidocaine

Lidocaine is used frequently as a first-line agent to treat wide-complex tachycardias. There is a widely held, albeit incorrect, idea that lidocaine, like adenosine (see below), has diagnostic utility. In fact, lidocaine is not an effective or appropriate treatment for SVT. Evidence does not support the use of lidocaine to discriminate between perfusing VT and wide-complex tachycardia of uncertain origin.

Lidocaine will effectively suppress ventricular arrhythmias associated with acute myocardial ischemia and infarction once they occur. But the prophylactic use of lidocaine to prevent the arrhythmias in the first place causes higher mortality and has been abandoned. Two studies suggest that lidocaine is ineffective for termination of hemodynamically stable sustained VT, and 2 have found lidocaine to be less effective against VT than IV propranolol or IV sotalol.

In summary, lidocaine appears in the algorithm for stable VT, monomorphic or polymorphic (in Part 6, Section 7D). Lidocaine is acceptable for all 4 possible VT scenarios: stable, monomorphic VT with (1) normal cardiac function and (2) with impaired cardiac function; polymorphic VT with either (3) normal baseline QT interval or (4) prolonged QT interval. Note carefully, however, that for all 4 of these indications lidocaine is a second-tier choice. Other drugs are preferred over lidocaine in each VT scenario.

Amiodarone

Amiodarone also is effective for supraventricular tachycardias because it alters conduction through the accessory pathway (Class IIa if LV function is normal and IIb if...
ventricular function is impaired),53–81 (See the Narrow-Complex Tachycardia Algorithm, Part 6, Section 7D.) Note that amiodarone becomes the antiarrhythmic of choice (after failure of adenosine) if the patient’s cardiac function is impaired and the ejection fraction is <40% or there are signs of congestive heart failure.

Amiodarone has not been studied specifically for the pharmacological termination of hemodynamically stable VT, but it is effective in treating hemodynamically unstable VT and VF.78,81–91 Both procainamide and amiodarone have vasodilatory effects and negative inotropic properties, which can destabilize hemodynamic status.87,92,93 These effects seem to depend on the dose given and the rate of administration. IV amiodarone may be better tolerated hemodynamically than procainamide.

Intravenous sotalol, IV propafenone, and IV flecainide are each effective against SVT, including atrial arrhythmias with and without preexcitation. These agents, however, are not available in all countries, nor have they been studied against wide-complex tachycardias. β-blockers (Vaughn-Williams classification) such as flecainide and propafenone are associated with a higher mortality in patients with ischemic heart disease. Avoid using flecainide or propafenone in such patients.

New Concerns From the International Guidelines 2000 Conference: Impaired Hearts and “Proarrhythmic Antiarrhythmics”

The evidence presented at the Guidelines 2000 Conference has dramatically changed the recommended approach to the treatment of tachycardias. The tachycardia algorithm from 1992, complex by necessity, has undergone extensive revisions to accommodate the 2 concerns of proarrhythmias and the effects of antiarrhythmics on impaired hearts.

Proarrhythmias are serious tachyarrhythmias or bradyarrhythmias seemingly generated by antiarrhythmic agents. All antiarrhythmic agents have some degree of proarrhythmic effects. Tachyarrhythmias account for most proarrhythmic events. The rhythm called tachycardia or pointes accounts for the majority of tachycardic proarrhythmic episodes. The interactions between agents are complex. Sequential use of 2 or more antiarrhythmic drugs compounds the adverse effects, particularly for bradycardia, hypotension, and tachycardias. Never use more than 1 agent unless absolutely necessary. In most patients, when an appropriate dose of a single antiarrhythmic medication fails to terminate an arrhythmia, turn to electrical cardioversion rather than a second antiarrhythmic medication. The Stable Ventricular Tachycardia Algorithm implements this conservative approach to VT.

Patients with clinical congestive heart failure or depressed LV function should be treated cautiously with antiarrhythmic therapy. In these patients, many antiarrhythmic agents depress LV function further, often precipitating or worsening congestive heart failure. Amiodarone and lidocaine cause the least additional impairment of LV function. Because of its broad antiarrhythmic spectrum and lesser negative inotropic effect, amiodarone now dominates the management of tachycardias. If amiodarone fails to produce the desired response, the preferred next intervention is to attempt early electrical cardioversion.

Summary: Treatment of Hemodynamically Stable, Wide-Complex Tachycardias

In summary, faced with ECG-confirmed or strongly suspected SVT with aberrancy, treat according to the tachycardia overview and narrow-complex tachycardia algorithms. If a specific rhythm (eg, atrial flutter) is diagnosed, then treat using the tachycardia overview algorithm and rate and rhythm control recommendations for tachycardias (table accompanying the overview algorithm).

Treat confirmed or strongly suspected VT (hemodynamically stable VT) according to the tachycardia overview algorithm and the stable ventricular tachycardia algorithm. DC cardioversion is the definitive therapy, but in some circumstances electrical cardioversion is not possible, desirable, or successful.

In these patients, empirical pharmacological therapy may be necessary for a hemodynamically stable wide-complex tachycardia of unknown origin. (See Tachycardia Overview Algorithm, column 3.) Empirical treatment of wide-complex tachycardia of unknown origin involves broad-spectrum antiarrhythmic agents. Agents such as procainamide, amiodarone, and sotalol possess efficacy against VT, SVT with accessory pathway conduction, and SVT. However, agents that block the AV node (such as adenosine, β-adrenergic receptor blockers, and calcium channel blockers) are hazardous in patients with VT or preexcited atrial arrhythmias. These agents should not be used for the empirical treatment of wide-QRS-complex tachyarrhythmias. Consequently, column 3 of the Tachycardia Overview Algorithm limits the therapeutic options to DC cardioversion, or procainamide or amiodarone.

Hemodynamically Stable (Monomorphic) VT

(See Algorithm)

Consider VT “hemodynamically stable” if there are no symptoms or clinical evidence of tissue hypoperfusion or shock. Hemodynamically unstable VT requires immediate termination with synchronized cardioversion. With clinical stability and adequate blood pressure there is sufficient time to allow pharmacological intervention.

Previous guidelines recommended use of lidocaine followed by procainamide, bretylium, and electrical cardioversion. In cases in which electrical cardioversion is not possible, desirable, or successful, the International Guidelines 2000 now recommend treatment of hemodynamically stable VT with IV procainamide, IV sotalol, IV amiodarone, or IV β-blockers. Each of these is considered preferable to IV lidocaine. The Stable Ventricular Tachycardia Algorithm shows how the specific choice of agent is based on considerations of normal versus impaired cardiac function and long versus short QT intervals. Although lidocaine can be administered rapidly with minimal effect on blood pressure, studies suggest that it is relatively ineffective for termination of VT30,31 and less effective against VT than IV procainamide32 or IV sotalol.33
Polymorphic VT

VT with varying QRS morphology is called polymorphic VT. Polymorphic VT is usually irregular in rate, hemodynamically unstable, and likely to quickly degenerate to VF. It is often associated with ischemic heart events or electrolyte or toxic conditions. A unique form of polymorphic VT is called torsades de pointes, which usually occurs in a setting of bradycardia and prolongation of the QT interval. A continuously changing VT morphology is often described as appearing to rotate or turn around the ECG baseline. Polymorphic VT, including torsades, frequently terminates, but the arrhythmia will recur and seldom remains stable.

There is limited data regarding treatment of polymorphic VT with or without suspected torsades de pointes. The algorithm for stable ventricular tachycardia, monomorphic or polymorphic, displays a reasonably evidence-based approach, supported largely by extrapolation from less-specific studies. Hemodynamically unstable polymorphic VT should be treated using the VF/Pulseless VT Algorithm. These patients and those with hemodynamically stable polymorphic VT are treated according to the presence or absence of torsades de pointes.

Polymorphic VT of the torsades de pointes type should be treated immediately (Stable Ventricular Tachycardia Algorithm) because of the frequent transition to unstable VT. The first step is to stop medications known to prolong the QT interval. Correct electrolyte imbalance and any other acute precipitants.

Other interventions that may be helpful but have not been adequately evaluated in controlled trials include administration of IV magnesium (Class Indeterminate) and temporary atrial or ventricular pacing (“overdrive pacing”) (Class Indeterminate). If patients are free of coronary artery disease, ischemic syndromes, or other contraindications, then isoprotanol (Class Indeterminate) may be administered as an interim measure to accelerate heart rate while temporary pacing is initiated (Class Indeterminate). After pacing has been initiated, β-blockers may be used as adjunctive therapy. Limited studies of lidocaine have shown uncertain efficacy (Class Indeterminate). These recommendations are incorporated into the Stable Ventricular Tachycardia Algorithm.

Polymorphic VTs other than torsades de pointes do not respond to magnesium. For patients in whom polymorphic VT may be precipitated by acute coronary syndromes, use β-blockers (in the absence of bradycardia) and anti-ischemic agents. (See the Stable Ventricular Tachycardia Algorithm.) Lidocaine may be more effective in patients with myocardial ischemia than in patients without ischemia. In other circumstances, effective antiarrhythmic drugs include IV amiodarone (Class Ib), lidocaine (Class Ib), procainamide (Class Ib), IV sotalol (Class Ib), β-blockers (Class Indeterminate), or phenytoin (Class Indeterminate). These agents are recommended only as Class Ib or indeterminate agents because supportive evidence comes only from extrapolation of results from the treatment of hemodynamically stable and unstable monomorphic VT.

VF/Pulseless VT

Efficacy studies of antiarrhythmic drugs in VF/VT arrest have addressed only short-term outcomes. The recommendations for antiarrhythmic agents are based on surrogate, or immediate, or intermediate outcome measures that may not correlate with the preferred outcome of neurologically intact survival for 1 or more years after the cardiac arrest.

The optimal number of defibrillation shocks that should be administered for refractory VF/VT before pharmacological therapy is initiated is also unknown. However, given the established efficacy of early defibrillation (a Class I intervention), it is reasonable to add pharmacological therapy after at least 3 precordial shocks, delivered in rapid sequence, fail to restore a stable perfusing rhythm. In particular, patients in whom a perfusing rhythm can be transiently restored but not successfully maintained between repeated shocks (recurrent VT/VF) are highly appropriate candidates for early treatment with antiarrhythmic medications. In such patients the antiarrhythmics will facilitate and stabilize the return of circulation. Patients with shock-refractory arrhythmias should be considered for pharmacological therapies sooner rather than later, for the likelihood of benefit declines rapidly with the duration of cardiac arrest.

The VF/Pulseless VT Algorithm (Part 6, Section 7C) emphasizes this greater value of defibrillation over pharmacology. The algorithm shows that after 3 unsuccessful defibrillation attempts the rescuers must move quickly to accomplish tracheal intubation and to gain access to the circulation with an intravenous line. Once the IV is established, vasopressors (epinephrine or vasopressin) are administered, followed by another attempt to defibrillate. This fourth shock usually follows a period of many minutes during which the tracheal tube was placed, confirmed, and secured and the intravenous line established. Delivery of the fourth shock is based more on the passage of time than on any requirement that epinephrine or vasopressin must be administered before the fourth shock can be given. In scenarios where an intravenous line is not in place before arrest, long delays to the fourth shock would ensue if rescuers think a specific sequence of medications must be given before further defibrillation attempts. Shocks must not be delayed until an IV line is established and medications have been delivered.

The details of the ARREST study confirm that a mandate that amiodarone (or any antiarrhythmic) must be given before the fourth shock would undoubtedly produce profound delays.
in the fourth shock. The ARREST study observed that the time from medic arrival on the scene to IV access obtained was 4.7 minutes and from arrival to tracheal intubation was 5.2 minutes; however, from arrival of medics to administration of amiodarone took a full 13 minutes. With amiodarone administration requiring so much extra time, it would be unacceptable to require amiodarone before a fourth shock. In addition, an average of 5 shocks were given before amiodarone was administered, and an average of 4 more were given after the amiodarone was given.

The use of lidocaine for ventricular arrhythmias was supported by initial studies in animals\textsuperscript{99–104} and extrapolation from the historical use of the drug to suppress PVCs and prevent VF after acute MI.\textsuperscript{25} Lidocaine improved resuscitation rate and admission alive to the hospital rate in 1 retrospective prehospital study,\textsuperscript{105} but other trials comparing lidocaine and bretylium found no statistically significant differences in outcome.\textsuperscript{106–108} A randomized comparison between amiodarone and lidocaine found a greater likelihood of successful resuscitation with amiodarone.\textsuperscript{109} A randomized comparison between lidocaine and epinephrine showed a higher incidence of asystole with lidocaine use and no difference in return of spontaneous circulation.\textsuperscript{110} Numerous animal studies, as well as a retrospective, uncontrolled trial, suggested that lidocaine reduced short-term resuscitation success.\textsuperscript{111} Some studies have observed an elevated defibrillation threshold after treatment.\textsuperscript{112–115} No benefit and increased morbidity (serious arrhythmias) have been associated with prophylactic administration of lidocaine to patients with acute MI.\textsuperscript{26–29}

Use of procainamide in cardiac arrest is supported by only a retrospective comparison study involving only 20 patients.\textsuperscript{120} Procainamide administration in cardiac arrest is limited by the need for slow infusion and uncertain efficacy in emergent circumstances.

Use of magnesium in torsades de pointes may be beneficial.\textsuperscript{121,122} They are comparably effective in patients with cardiac arrest due to monomorphic, polymorphic, or torsades VT.\textsuperscript{94} Routine administration of magnesium in resuscitation does not affect outcome and may be associated with a higher incidence of hypotension despite a potential for improved neurological outcome in survivors.\textsuperscript{123,124}

In summary, evidence supports the use of IV amiodarone, following epinephrine, to treat shock-refractory cardiac arrest due to VF or pulseless VT (Class IIb).\textsuperscript{125} Amiodarone restored spontaneous circulation and improved early survival to the hospital in adults. However, no pharmacological interventions for cardiac arrest have yet been found to improve survival to hospital discharge. Disadvantages of amiodarone include its side effects (hypotension and bradycardia), its relatively high cost, and difficulties in administration. As currently available, the drug must be drawn up from a 6-mL glass ampule into a syringe and then diluted with 5% dextrose in water to 20 mL before injection. Preloaded syringes are not available because amiodarone adheres to the plastic surface of preloaded syringes.

Lidocaine, an alternative antiarrhythmic of long standing and widespread familiarity, has fewer immediate side effects and lower cost and is available in prefilled syringes. Lidocaine, however, has no proven short- or long-term efficacy in cardiac arrest. Lidocaine and magnesium (for suspected torsades de pointes or hypomagnesemic states) should be considered alternative treatments (Class Indeterminate) on the basis of less supportive evidence for their efficacy.

**Paroxysmal Supraventricular Tachycardia (See the Narrow-Complex Tachycardia Algorithm)**

Paroxysmal SVT (PSVT) is a regular tachycardia exceeding the expected limits of sinus tachycardia at rest (>120 bpm) with or without discernible P waves that is usually of abrupt onset and abrupt termination. The arrhythmia is of known supraventricular origin (QRS complex <100 ms, or if wide [broad], bundle-branch aberrancy is known to be present). PSVT may include AVNRT or AVRT mediated by a concealed or manifest accessory pathway. PSVT can be distinguished from junctional tachycardia (which can also appear “P-less”) or ectopic atrial tachycardia by the relative rarity of such tachycardia in adults and by the often gradual onset (“warm-up”) and termination of automatic tachyarrhythmias (versus the abrupt onset and termination of reentrant PSVT).

Previous guidelines recommended vagal maneuvers to initially attempt termination of PSVT. If the patient was unresponsive, adenosine was given if the patient remained clinically stable. Further treatment was based on the duration of the QRS complex (wide- versus narrow-complex tachycardia) and hemodynamic stability.

New parenteral drugs have completed clinical study and are now available for the treatment of PSVT. New recommendations also include treatment strategies that are modified by the presence of clinical congestive heart failure and the status of LV function, when known.

Initial use of vagal maneuvers and IV adenosine in all patients (without contraindications) with PSVT continues to be recommended. Adenosine can provoke bronchospasm and should be used cautiously in patients with reactive airway disease. Cardiac denervation after cardiac transplantation may render patients hypersensitive to the bradycardic effects of adenosine. Patients treated with methylxanthines (theophylline) may be less sensitive to the effects of adenosine. Use of diprydiamole (Persantine) may enhance sensitivity to adenosine. In patients with preserved LV function, calcium channel blockers (verapamil, diltiazem) and β-blockers (esmolol, metoprolol) remain supported by previous evidence. Digitalis (digoxin) is a time-honored drug for treatment of PSVT, but indirect evidence from treatment of AF and atrial flutter suggests that digitalis has a slower onset of action and lower potency relative to other treatment agents.

In addition to procainamide, newly available parenteral antiarrhythmic agents for treatment of PSVT refractory to vagal maneuvers, adenosine, and AV nodal blocking agents include amiodarone, propafenone, flecainide, and sotalol. Use of IV procainamide for PSVT (in the presence or absence of an accessory pathway) is effective.\textsuperscript{69} IV amiodarone is effective in AVNRT or accessory pathway–mediated AVRT\textsuperscript{53,57,60,63,79} and is comparable to procainamide\textsuperscript{69} and magnesium\textsuperscript{126} but has less efficacy than propafenone.\textsuperscript{58} IV flecainide\textsuperscript{127} and IV sotalol\textsuperscript{128,129} have also been useful in terminating PSVT due to AVNRT.
Primary antiarrhythmic agents (such as amiodarone, procainamide, sotalol, flecainide, propafenone, and disopyramide) require slow administration and can destabilize marginally compensated patients by hypotensive effects. They also have the potential for proarrhythmic effects, including the provocation of life-threatening ventricular arrhythmias. Antiarrhythmic agents should be considered only when AV nodal blocking agents or electrical cardioversion is not feasible, desirable, or successful. 

Serial use of calcium channel blockers, β-blockers, and primary antiarrhythmic agents should be discouraged because of the potential additive hypotensive, bradyarrhythmic, and proarrhythmic effects of these drugs in combination.

In the setting of significantly impaired LV function (clinical evidence of congestive heart failure or moderately to severely reduced LV ejection fraction), caution should be exercised in administering drugs with negative inotropic effects to patients with PSVT. These include verapamil, β-blockers, procainamide, propafenone, flecainide, and sotalol but not digitalis, amiodarone, or perhaps diltiazem. Life-threatening ventricular proarrrhythmias may be higher with primary antiarrhythmic medications in patients with congestive heart failure. In addition, some antiarrhythmic agents have been shown to increase mortality in patients with ischemic heart disease. Thus, flecainide, and perhaps propafenone, should be avoided in patients with documented coronary heart disease.

In summary, in the absence of contraindications, vagal maneuvers or adenosine should be used in an effort to initially terminate PSVT. With preserved LV function, additional treatment options include calcium channel blockers (verapamil or diltiazem; Class I), β-blockers (Class I), or digitalis (Class IIb). Strong consideration should be given to electrical cardioversion when AV nodal agents are unsuccessful in terminating PSVT. When electrical cardioversion is not feasible, desirable, or successful, patients who “fail” AV nodal blocking agents with either persistent or recurrent PSVT may be treated with antiarrhythmic agents, including procainamide (Class Ila), amiodarone (Class Ila), flecainide (Class IIa), propafenone (Class IIa), and sotalol (Class Ila). The proarrhythmic potential of this group of medications makes them less desirable options, however, than AV nodal blocking drugs.

The serial or combined use of parenteral calcium channel blockers, β-adrenergic blockers, and primary antiarrhythmic agents is discouraged. In patients with significantly impaired LV function, verapamil, β-blockers, procainamide, flecainide, propafenone, and sotalol should be avoided in favor of digitalis (Class IIb), amiodarone (Class IIb), or perhaps diltiazem (Class IIb). By itself digitalis is a relatively slow-acting and less effective AV nodal blocking agent. When given in combination with other agents, however, initial use of digitalis may allow for lower doses of subsequently administered agents for rhythm termination or potential blunting of their negative inotropic properties by the positive inotropic effects of digitalis.

Atrial Tachycardia (Ectopic Atrial Tachycardia, MAT)

See the Narrow-Complex Tachycardia Algorithm. Atrial arrhythmias, including ectopic atrial tachycardia and MAT, are the result of increased automaticity of a single or multiple (MAT) atrial focus. Ectopic atrial tachycardia can be distinguished from sinus tachycardia on the 12-lead ECG by the presence of an abnormal P-wave configuration and P-wave axis. It is important to distinguish MAT from AF, because both can result in an irregularly irregular rhythm. MAT is distinguished from AF by the presence of P waves having 3 or more different morphologies preceding QRS complexes. By contrast, atrial activity in AF continuously undulates or is incessant between QRS complexes, without individually identifiable P waves. Automatic arrhythmias such as ectopic atrial tachycardia can be distinguished from reentry-caused PSVT (such as AVNRT or AVRT mediated by an accessory pathway) by their often gradual onset (warm-up) and termination (versus the abrupt onset and termination of reentrant PSVT) and by their continuation even when their conduction is blocked through the AV node.

The 1992 guidelines did not specify treatment for atrial tachycardias, apart from AF and atrial flutter. By 2000 evidence suggests that automatic atrial tachycardias are due to increased automaticity and require a different treatment from the reentrant supraventricular arrhythmias (PSVT, AF, and atrial flutter).

Diagnosis of an atrial tachycardia is made by identifying P-wave morphology on the 12-lead ECG. Vagal maneuvers or adenosine may be used to demonstrate AV block with persistence of the atrial arrhythmia. Automatic rhythms (ectopic atrial tachycardia, MAT, sinus tachycardia), unlike reentry arrhythmias, are not responsive to electrical cardioversion. Many of these arrhythmias are secondary phenomena, requiring supportive measures and treatment of precipitating causes. MAT, for example, typically is seen in patients with decompensated chronic obstructive pulmonary disease. With preserved LV function, β-blockers or calcium channel blockers (verapamil or diltiazem) may provide improved rate control by enhancing AV block or conversion of the arrhythmia to normal sinus rhythm. Digitalis may be effective in slowing heart rate but not in terminating ectopic atrial arrhythmias. Digitalis also has been associated with provoking ectopic atrial tachycardia. Other useful drugs for ectopic atrial tachycardia or MAT include amiodarone, flecainide, and propafenone. Quinidine, procainamide, and phenytoin are not effective. In summary, synchronized electrical cardioversion is ineffective for the treatment of automatic atrial arrhythmias (Class III). In patients with preserved LV function, acceptable treatments include calcium channel blockers (Class IIb), β-blockers (Class IIb), digitalis (Class Indeterminate), amiodarone (Class IIb), intravenous flecainide (Class IIb), and IV propafenone (Class IIb). In patients with impaired LV function, drugs with significant negative inotropic properties (verapamil, β-blockers, flecainide, and propafenone) are contraindicated. In the presence of LV impairment, preferred agents include diltiazem (Class IIb), amiodarone (Class IIb), and digitalis (Class Indeterminate).

Atrial Fibrillation/Flutter

New evidence allows more specific recommendations for acute management of AF and atrial flutter (see The Tachy-
TABLE 2. Management Principles for Atrial Fibrillation/Flutter

| Hemodynamically unstable, rapid-response atrial fibrillation or flutter should be electrically cardioverted immediately, regardless of the duration of the arrhythmia (Class I). | pharmacological rate control is the recommended initial treatment for stable, rapid atrial fibrillation/flutter (≥120 bpm) regardless of its duration. Specific drug treatment depends on the presence or absence of impaired LV function (ejection fraction <40%) |
| Adenosine is an inappropriate drug to use for atrial fibrillation/flutter because of its ultrashort duration of action (Class III). |
| In patients with preserved LV function, β-blockers (Class I), calcium blockers (Class IIa), and digitalis (Class IIIb) are reasonable agents for rate control. |
| In patients with congestive heart failure, digitalis (Class IIb), diltiazem (Class IIb), and amiodarone (Class IIb) are recommended. |
| In patients with preexcited atrial fibrillation/flutter, β-blockers, calcium channel blockers, and digitalis are contraindicated (Class III). If electrical cardioversion is not feasible, desirable, or successful, such patients with preserved LV function may be treated with procainamide (Class IIb) or amiodarone (Class IIb), IV flecainide (Class IIb), propafenone (Class IIb), or sotalol (Class IIb) (not all available in all countries). |
| In patients with congestive heart failure and preexcited atrial fibrillation/flutter, IV amiodarone (Class IIb) is recommended over other drugs. |
| Efforts should be made to minimize the risk of thromboembolic complications that are strongly related to the duration of the arrhythmia before cardioversion (>48 hours). |
| electrical cardioversion is the preferred treatment for restoration of sinus rhythm. |
| Pharmacological cardioversion is recommended if electrical cardioversion is not feasible or desirable or is unsuccessful in maintaining sinus rhythm. |

Major goals in the management of AF are ventricular rate control, assessment of anticoagulation needs, and restoration of sinus rhythm. Reversible and underlying causes of AF should be investigated and corrected, if possible. These include hypoxemia, anemia, hypertension, congestive heart failure, mitral regurgitation, thyrotoxicosis, hypokalemia, hypomagnesemia, and other toxic and metabolic causes. Ischemia is an uncommon cause but may result from AF.

IV verapamil, betablockers, and diltiazem are recommended for rate control in patients with AF or atrial flutter, preserved LV function, and a heart rate ≥120 bpm. Available evidence suggests that digitalis, though effective, is the least potent and has the slowest onset of action of the available pharmacological options for ventricular rate control. In patients with clinical evidence of congestive heart failure, greater caution should be exercised in use of calcium channel and β-blockers because of their recognized negative inotropic properties and because in trials of efficacy, patients with congestive heart failure were usually excluded.

This risk may be less with diltiazem than with verapamil or β-blockers. Digoxin remains the only parenteral AV nodal blocking drug with positive inotropic properties, but its usefulness is limited by its relative impotence and slow onset of action, particularly in high adrenergic states such as congestive heart failure.

New evidence also suggests that IV amiodarone is also effective for rate control in patients resistant to conventional heart rate control measures or in combination with digitalis. Conversion to normal sinus rhythm may occur with amiodarone. Therefore, in patients at risk for systemic emboli, amiodarone is recommended only when other medications for rate control have proved ineffective or are contraindicated and the risk of possible pharmacological cardioversion is felt to be justified. Some studies have found that whereas amiodarone was effective for rate control, conversion to sinus rhythm was no greater with conventional doses of IV amiodarone than placebo or digitalis, particularly in refractory AF and clinical shock. Because of this concern amiodarone should be reserved for use within the first 48 hours of arrhythmia onset or in patients in whom other rate-control measures are ineffective or contraindicated.

In some patients a conduction pathway bypasses the AV node. Such a conduction pathway is called an accessory bypass tract. In a few patients who have downward conduction through this pathway, there is the potential for extremely rapid ventricular responses during AF with degeneration to VF. Digitalis, verapamil, diltiazem, adenosine, and possibly intravenous β-blockers can cause a paradoxical increase in ventricular response rates in these patients with Wolff-Parkinson-White syndrome. If patients are clinically unstable, synchronized electrical cardioversion is indicated. Otherwise, when Wolff-Parkinson-White syndrome is known or suspected, cardiology consultation is indicated for the selection of the most appropriate management strategy. Antiarrhythmic agents that have direct effects on accessory pathway conduction and refractoriness (such as procainamide, propafenone, flecainide, or amiodarone) are more likely to slow ventricular response during preexcited AF or atrial flutter as well as convert the arrhythmia to sinus rhythm.

If AF has been present for >48 hours, a risk of systemic embolization exists with conversion to sinus rhythm unless patients are adequately anticoagulated for at least 3 weeks. Electrical cardioversion and the use of antiarrhythmic agents should be avoided unless the patient is unstable or hemodynamically compromised. In marginal patients, heparinization and cardiology consultation with the use of transesophageal echocardiography to exclude atrial thrombi is indicated to assess the risk and benefits of therapeutic strategies.

Electrical cardioversion is the technique of choice for cardioversion of patients with AF or atrial flutter to sinus rhythm. The recommended initial energy using a damped sinusoidal waveform defibrillator is 100 to 200 J. Atrial flutter and PSVT may require less energy, 50 to 100 J. The optimal AF energy protocol and the efficacy of other shock waveforms for cardioversion of AF and atrial flutter will require additional clinical trials, now ongoing.
Efforts to slow the ventricular rate response or to convert AF to sinus rhythm can lead to profound bradycardia and even asystole, especially in patients with significant underlying conduction system disease or sick sinus syndrome. Consequently, it is advisable to have temporary pacing capability (transcutaneous or transvenous) or pharmacological support (atropine, dopamine, or isoproterenol) available.

After satisfactory rate control and anticoagulation measures (if AF is >48 hours in duration), electrical cardioversion of AF or atrial flutter remains the technique of choice for conversion of patients with either preserved or significantly impaired LV function, particularly in patients with preexcitation. If not feasible, desirable, or successful, a number of pharmacological alternatives are available for cardioversion of patients with preserved LV function, including ibutilide (Class IIa), IV flecainide (Class IIa), IV propafenone (Class IIa), IV procainamide (Class IIa), IV amiodarone (Class IIa), IV sotalol (Class IIb), and IV disopyramide (Class IIb). In patients with impaired LV function, the negative inotropic effects of flecainide, propafenone, sotalol, and procainamide as well as the potential proarrhythmic potential of ibutilide make these agents less desirable. IV amiodarone is a preferable agent in such circumstances (Class IIb). For preexcited AF or atrial flutter, IV propafenone (Class IIb), IV amiodarone (Class IIb), IV flecainide (Class IIb), IV sotalol (Class IIb), and IV procainamide (Class IIb) are acceptable treatments. Preexcited arrhythmias in patients with significantly impaired LV function should be treated preferably with IV amiodarone (Class IIb).

**Junctional Tachycardia**

In adults true junctional tachycardia is rare. Apparent junctional tachycardia is most commonly due to misdiagnosed PSVT and should be treated according to the Narrow-Complex Tachycardia algorithm. True junctional tachycardia in adults is usually a manifestation of digitalis toxicity (best treated by withdrawal of digitalis) or of exogenous catecholamines or theophylline (best treated with reduction or withdrawal of such infusions). If no apparent cause is found, symptomatic junctional tachycardia may respond to IV amiodarone or to β-blockers or calcium channel blockers. This recommendation, however, has no specific human evidence to provide support. Instead, the recommendation is based on rational extrapolations from the known antisymptomatic and nodal effects of β-blockers and calcium channel blockers (Class Indeterminate) or IV amiodarone (Class IIb).

**Antiarrhythmic Drugs and the Arrhythmias They Treat**

**Adenosine**

Adenosine is an endogenous purine nucleoside that depresses AV node and sinus node activity. Most common forms of PSVT involve a reentry pathway including the AV node. Adenosine is effective in terminating these arrhythmias. If the arrhythmias are not due to reentry involving the AV node or sinus node (eg, atrial flutter, AF, atrial or ventricular tachycardias), adenosine will not terminate the arrhythmia but may produce transient AV or retrograde (ventriculoatrial) block that may clarify the diagnosis. Adenosine produces a short-lived pharmacological response because it is rapidly metabolized by enzymatic degradation in blood and peripheral tissue. The half-life of adenosine is <5 seconds. The recommended initial dose is a 6-mg rapid bolus over 1 to 3 seconds. The dose should be followed by a 20-mL saline flush.

If no response is observed within 1 to 2 minutes, a 12-mg repeated dose should be administered in the same manner. Experience with larger doses is limited, but patients taking theophylline are less sensitive to adenosine and may require larger doses. Side effects with adenosine are common but transient; flushing, dyspnea, and chest pain are the most frequently observed. Because of the short half-life of adenosine, PSVT may recur. Repeated episodes may be treated with additional doses of adenosine or with a calcium channel blocker. Adenosine is more likely to precipitate persistent hypotension if the arrhythmia does not terminate.

Adenosine has several important drug interactions. Therapeutic concentrations of theophylline or related methylxanthines (caffeine and theobromine) block the receptor responsible for the electrophysiological and hemodynamic effects of adenosine. Dipyridamole blocks adenosine uptake and potentiates its effects. The effects of adenosine are also prolonged in patients on carbamazepine and in denervated transplanted hearts. Dose adjustment or alternative therapy should be selected in such patients.

Use of adenosine to discriminate VT from SVT with aberrancy in hemodynamically stable wide-complex tachycardia of uncertain origin is controversial, and such a practice should be discouraged. Adenosine should be used only when a supraventricular origin is strongly suspected.

**Amiodarone (IV)**

Intravenous amiodarone is a complex drug with effects on sodium, potassium, and calcium channels as well as α- and β-adrenergic blocking properties. The drug is useful for treatment of atrial and ventricular arrhythmias.

- Amiodarone is also helpful for ventricular rate control of rapid atrial arrhythmias in patients with severely impaired LV function when digitalis has proved ineffective (Class IIb).
- Amiodarone is recommended after defibrillation and epinephrine in cardiac arrest with persistent VT or VF (Class IIb).
- Amiodarone is effective for control of hemodynamically stable VT (Class IIb), polymorphic VT (Class IIb), and wide-complex tachycardia of uncertain origin (Class IIb).
- Amiodarone is an adjunct to electrical cardioversion of refractory PSVTs (Class IIa), atrial tachycardia (Class IIb), and pharmacological cardioversion of AF (Class IIa).
- Amiodarone can control rapid ventricular rate due to accessory pathway conduction in preexcited atrial arrhythmias (Class IIb).

In patients with severely impaired heart function, IV amiodarone is preferable to other antiarrhythmic agents for atrial and ventricular arrhythmias. Amiodarone has both
greater efficacy and a lower incidence of proarrhythmic effects than other antiarrhythmic drugs under similar circumstances. IV amiodarone is administered as 150 mg over 10 minutes, followed by 1 mg/min infusion for 6 hours, and then 0.5 mg/min. Supplementary infusions of 150 mg can be repeated as necessary for recurrent or resistant arrhythmias to a maximum manufacturer-recommended daily dose of 2 g. One study found amiodarone to be effective in patients with AF when administered at relatively high doses of 125 mg/h for 24 hours (total dose 3 g). In cardiac arrest due to pulseless VT or VF, IV amiodarone is initially administered as a 300-mg rapid infusion diluted in a volume of 20 to 30 mL of saline or dextrose in water. Based on extrapolation from studies in patients with hemodynamically unstable VT, supplementary doses of 150 mg by rapid infusion may be administered for recurrent or refractory VT/VF, followed by an infusion of 1 mg/min for 6 hours and then 0.5 mg/min, to a maximum daily dose of 2 g.

The major adverse effects from amiodarone are hypotension and bradycardia, which can be prevented by slowing the rate of drug infusion or can be treated with fluids, pressors, chronotropic agents, or temporary pacing.

Atropine
Atropine sulfate reverses cholinergic-mediated decreases in heart rate, systemic vascular resistance, and blood pressure. Atropine is useful in treating symptomatic sinus bradycardia (Class I). Atropine may be beneficial in the presence of AV block at the nodal level (Class IIa) or ventricular asystole but should not be used when infranodal (Mobitz type II) block is suspected.

The recommended dose of atropine sulfate for asystole and slow pulseless electrical activity is 1.0 mg IV and repeated in 3 to 5 minutes if asystole persists. For bradycardia the dose is 0.5 to 1.0 g IV every 3 to 5 minutes to a total dose of 0.04 mg/kg. A total dose of 3 mg (0.04 mg/kg) results in full vagal blockade in humans. Because atropine increases myocardial oxygen demand and can initiate tachyarrhythmias, the administration of a total vagolytic dose of atropine should be reserved for asystolic cardiac arrest. Doses of atropine sulfate of <0.5 mg may be parasympathomimetic and further slow the cardiac rate. Atropine also is well absorbed through the tracheal route of administration.

Atropine should be used cautiously in the presence of AMI or infarction because excessive increases in rate may worsen ischemia or increase the zone of infarction. Rarely, VF and VT have followed IV administration of atropine. Atropine is not indicated in bradycardia from AV block at the His-Purkinje level (type II AV block and third-degree block with new wide-QRS complexes). In such instances atropine can rarely accelerate sinus rate and AV node conduction.

β-Adrenergic Blockers
β-Adrenergic blockers have potential benefits in patients with acute coronary syndromes, including patients with non-Q-wave MI and unstable angina (Class I). In the absence of contraindications, β-blockers should be given to all patients with suspected AMI and high-risk unstable angina. β-Blockers are also effective antiarrhythmia agents and have been shown to reduce the incidence of VF in studies preceding the reperfusion era. As an adjunctive agent with fibrinolytic therapy, β-blockade may reduce the rate of nonfatal reinfarction and recurrent ischemia. β-Blockers also reduce mortality if administered early to fibrinolytic-ineligible patients.

Atenolol, metoprolol, and propranolol have been shown to reduce the incidence of VF significantly in post-MI patients who did not receive fibrinolytic agents. The recommended dose is 5 mg slow IV (over 5 minutes); wait 10 minutes, then if the first dose was well tolerated, give a second dose of 5 mg slow IV (over 5 minutes). An oral regimen is then initiated at 50 mg every 12 hours. Metoprolol is given in doses of 5 mg by slow IV push at 5-minute intervals to a total of 15 mg. An oral regimen is then initiated 15 minutes after the last IV dose at 50 mg twice daily for 24 hours and increased to 100 mg twice a day, as tolerated. An alternative agent is propranolol (now used uncommonly), to a total dose of 0.1 mg/kg by slow IV push divided into 3 equal doses at 2- to 3-minute intervals. The rate of administration should not exceed 1 mg/min. The oral maintenance regimen is 180 to 320 mg/d, given in divided doses.

IV esmolol is a short-acting (half-life of 2 to 9 minutes) β1-selective β-blocker that is recommended for the acute treatment of supraventricular tachyarrhythmias, including PSVT (Class I), rate control in nonpreexcited AF or atrial flutter (Class I), ectopic atrial tachycardia (Class IIb), inappropriate sinus tachycardia (Class IIb), and polymorphic VT due to torsades de pointes (as adjunctive therapy to cardiac pacing) or myocardial ischemia (Class IIb). It is metabolized by erythrocyte esterases and requires no dose adjustment in patients with renal or hepatic impairment. Esmolol has a complicated dosing regimen and requires an IV infusion pump. Esmolol is administered as an IV loading dose of 0.5 mg/kg over 1 minute, followed by a maintenance infusion of 50 μg/kg per minute for 4 minutes. If the response is inadequate a second bolus of 0.5 mg/kg is infused over 1 minute, with an increase of the maintenance infusion to 100 μg/kg. The bolus dose (0.5 mg/kg) and titration of the infusion dose (addition of 50 μg/kg per minute) can be repeated every 4 minutes to a maximum infusion of 300 μg/kg per minute. Infusions can be maintained for up to 48 hours if necessary. Esmolol 50 to 200 μg/kg per minute IV has an effect equivalent to that of 3 to 6 mg IV propranolol.

Side effects related to β-blockade include bradycardias, AV conduction delays, and hypotension. Cardiovascular decompensation and cardiogenic shock after β-adrenergic blocker therapy are infrequent provided that administration to patients with severe congestive heart failure is avoided and patients with mild and moderate congestive heart failure are monitored closely with appropriate diuresis. β-Blocker therapy should be withheld from patients with absolute contraindications to these agents. Contraindications to the use of β-adrenergic blocking agents include second- or third-degree heart block, hypotension, severe congestive heart failure, and lung disease associated with bronchospasm. β-Adrenergic blocking agents should be used cautiously in patients with preexisting sinus bradycardia and sick sinus syndrome.
Disopyramide
Disopyramide is a Vaughn Williams classification Ia antiarrhythmic agent that acts both to slow conduction velocity and to prolong the effective refractory period, similar to procaainamide. It has potent anticholinergic, negative inotropic, and hypotensive effects that limit its use. IV disopyramide is given as 2 mg/kg over 10 minutes, followed by a continuous infusion of 0.4 mg/kg per hour. IV disopyramide is limited by its need to be infused relatively slowly, which may be impractical and of uncertain efficacy in emergent circumstances, particularly under compromised circulatory conditions.

Bretlyium
tosylate is a quaternary ammonium compound used in the treatment of resistant VT and VF unresponsive to attempts at defibrillation and epinephrine. The cardiovascular actions of bretlyium are complex and include a release of catecholamines initially on injection. Postganglionic adrenergic blocking follows and frequently induces hypotension. In 1999 bretlyium was unavailable from the manufacturer. This stimulated a review of the evidence supporting continued use of bretlyium for VF/VT arrest and the other indications for bretlyium, such as its value as an anti-VF agent in hypothermic cardiac arrest. Subsequently bretlyium has been removed from ACLS treatment algorithms and guidelines because of a high occurrence of side effects, the availability of safer agents at least as efficacious, and the limited supply and availability of the drug.

Calcium Channel Blockers: Verapamil and Diltiazem
Verapamil and diltiazem are calcium channel blocking agents that slow conduction and increase refractoriness in the AV node. These actions may terminate reentrant arrhythmias that require AV nodal conduction for their continuation. Verapamil and diltiazem may also control ventricular response rate in patients with AF, atrial flutter, or MAT. Verapamil and diltiazem may decrease myocardial contractility and may exacerbate congestive heart failure in patients with severe LV dysfunction.

Intravenous verapamil is effective for terminating narrow-complex PSVT and may also be used for rate control in AF. Adenosine, however, is the drug of choice for terminating narrow-complex PSVT. Adenosine has an ultrashort half-life and is not effective for ventricular rate control of AF or atrial flutter. The initial dose of verapamil is 2.5 to 5 mg IV given over 2 minutes. In the absence of a therapeutic response or drug-induced adverse event, repeated doses of 5 to 10 mg may be administered every 15 to 30 minutes to a maximum of 20 mg. Verapamil should be given only to patients with narrow-complex PSVT or arrhythmias known with certainty to be of supraventricular origin. Verapamil should not be given to patients with impaired ventricular function or heart failure.

Diltiazem at a dose of 0.25 mg/kg, followed by a second dose of 0.35 mg/kg, seems to be equivalent in efficacy to verapamil. Diltiazem offers the advantage of producing less myocardial depression than verapamil. Diltiazem may also be used as a maintenance infusion of 5 to 15 mg/h to control the ventricular rate in AF and atrial flutter.

Dopamine hydrochloride is an endogenous catecholamine agent with dose-related dopaminergic and β- and α-adrenergic agonist activity. At doses between 3 and 7.5 μg/kg per minute, dopamine acts as a β-agonist, increasing cardiac output and heart rate. The β-agonist effects of dopamine are less pronounced than those of isoproterenol, and titration is easier. The inotropic effects of dopamine are modest compared with those of dobutamine. Dopamine-induced constriction of pulmonary veins is evidenced by a dose-dependent increase in pulmonary capillary wedge pressure. LV filling pressures are spuriously elevated. As catecholamine stores are depleted, tachyphylaxis to the drug occurs.

Dopamine has been used in low doses (2 μg/kg per minute) as a renal vasodilator. Dopamine, however, has shown no benefit when used in acute oliguric renal failure. Low-dose dopamine is no longer recommended for the management of acute oliguric renal failure.

Flecainide
Flecainide hydrochloride is approved in oral form in the United States (and in intravenous form outside the United States) for ventricular arrhythmias and for supraventricular arrhythmias in patients without structural heart disease. Flecainide is a potent sodium channel blocker with significant conduction-slowing effects (antiarrhythmic Vaughn Williams classification IC agent). IV flecainide (not approved for use in the United States) has been effective for termination of atrial flutter and AF, ectopic atrial tachycardia, AV nodal reentrant tachycardia, and SVTs associated with an accessory pathway (Wolff-Parkinson-White syndrome), including preexcited AF. Because of significant negative inotropic effects, flecainide should be avoided in patients in impaired LV function. It has also been observed to increase mortality in patients who have had MI, and its use should be avoided when coronary artery disease is suspected.

Flecainide is usually administered as 2 mg/kg body weight at 10 mg/min. Reported adverse side effects include bradycardia, hypotension, and neurological symptoms, such as oral paresthesias and visual blurring. Flecainide is limited by its need to be infused relatively slowly, which may be impractical and of uncertain efficacy in emergent circumstances, particularly under compromised circulatory conditions.

Ibutilide
Ibutilide is a short-acting antiarrhythmic, available only in parenteral form. Ibutilide acts by prolonging the action potential duration and increasing the refractory period of cardiac tissue (antiarrhythmic Vaughn Williams classification III effect). Ibutilide is recommended for acute pharmacological conversion of atrial flutter or AF or as an adjunct to electrical cardioversion in patients in whom electrical cardioversion alone has been ineffective. Ibutilide has a relatively short duration of action, making it less effective than other antiarrhythmic agents for maintaining sinus rhythm once
restored. Ibutilide seems most effective for the pharmacological conversion of AF or atrial flutter of relatively brief duration.

For adults weighing ≥60 kg, ibutilide is administered intravenously, diluted or undiluted, as 1 mg (10 mL) over 10 minutes. If that is unsuccessful in terminating the arrhythmia, a second 1-mg dose can be administered at the same rate 10 minutes after the first. In patients weighing <60 kg, an initial dose of 0.01 mg/kg is recommended. Ibutilide has minimal effects on blood pressure and heart rate. Its major limitation is a relatively high incidence of ventricular proarrhythmia (polymorphic VT) including torsades de pointes. Patients receiving ibutilide should be continuously monitored for arrhythmias at the time of its administration and for at least 4 to 6 hours after drug administration (longer in patients with hepatic dysfunction in whom the clearance of ibutilide may be prolonged). Patients with significantly impaired LV function may be at higher risk of ibutilide-induced proarrhythmia.

**Isoproterenol**

Isoproterenol hydrochloride is a pure β-adrenergic agonist with potent inotropic and chronotropic effects. It increases myocardial oxygen consumption, cardiac output, and myocardial work and can exacerbate ischemia and arrhythmias in patients with ischemic heart disease, congestive heart failure, or impaired ventricular function. On the basis of limited evidence, isoproterenol is recommended as a temporizing measure before pacing for torsades de pointes (Class Indeterminate) and immediate temporary control of hemodynamically significant bradyarrhythmia when atropine and dobutamine have failed and transcutaneous and transvenous pacing are not available (Class IIb). Ibutilide is not the treatment of choice for either of these conditions. At low doses the chronotropic effect (increase in heart rate) of isoproterenol raises blood pressure and compensates for its vasodilatory effects. The recommended infusion rate is 2 to 10 μg/min titrated according to the heart rate and rhythm response. An isoproterenol infusion is prepared by adding 1 mg of isoproterenol hydrochloride to 500 mL of D5 W; this produces a concentration of 2 μg/mL. For symptomatic bradycardia isoproterenol should be used, if at all, with extreme caution. Isoproterenol should be administered only in low doses (Class IIb). Higher doses are associated with increased myocardial oxygen consumption, increased infarct size, and malignant ventricular arrhythmias (Class III). Isoproterenol is not indicated in patients with cardiac arrest or hypotension.

**Lidocaine**

Lidocaine is one of a number of antiarrhythmic drugs available for treatment of ventricular ectopy, VT, and VF. Lidocaine seems to be more effective during AMI. In the presence of AMI, prophylactic administration of lidocaine reduces the incidence of primary VF but does not lower mortality. The toxic-to-therapeutic balance is delicate. The routine prophylactic use of lidocaine in patients suspected of having AMI is not recommended. Lidocaine may be used in uncomplicated AMI or ischemia when facilities for defibrillation are not readily available or when circulation is compromised by a high frequency of ventricular premature beats. Such use should be balanced against the potential toxicity of the drug as well as the lack of evidence that prophylactic administration of lidocaine to suppress ventricular premature ectopy reduces mortality. On the basis of established use, historical precedent, and no evidence of significant harm, lidocaine is acceptable for

- VF/pulseless VT that persists after defibrillation and administration of epinephrine (Class Indeterminate)
- Control of hemodynamically compromising PVCs (Class Indeterminate)
- Hemodynamically stable VT (Class IIb)

However, lidocaine remains a second choice behind other alternative agents (amiodarone, procainamide, or sotalol) in many of these circumstances.

In cardiac arrest, an initial bolus of 1.0 to 1.5 mg/kg IV is necessary to rapidly achieve and maintain therapeutic lidocaine levels. For refractory VT/VF an additional bolus of 0.5 to 0.75 mg/kg can be given over 3 to 5 minutes if necessary. Total dose should not exceed 3 mg/kg (or >200 to 300 mg during a 1-hour period). The more aggressive dosing approach (1.5 mg/kg) is recommended in cardiac arrest due to VF or pulseless VT after failure of defibrillation and epinephrine. Only bolus therapy should be used in cardiac arrest. Administering a continuous infusion of (prophylactic) antiarrhythmic agents to maintain circulation after it has been successfully restored is controversial. However, until data is available supporting the prophylactic administration of antiarrhythmic agents after return of circulation, it is reasonable to continue an infusion of the drug associated with the restoration of a stable rhythm (Class Indeterminate). A continuous infusion of lidocaine should be initiated at 1 to 4 mg/min. Reappearance of arrhythmias during a constant infusion of lidocaine should be treated with a small bolus dose (0.5 mg/kg) and an increase in the infusion rate in incremental doses (maximal infusion rate of 4 mg/min).

The half-life of lidocaine increases after 24 to 48 hours as the drug, in effect, inhibits its own hepatic metabolism. With prolonged infusions, the dosage should be reduced after 24 hours or blood levels should be monitored. The dose should be reduced in the presence of decreased cardiac output (eg, in AMI with hypotension or shock, congestive cardiac failure, or poor peripheral perfusion states), in patients older than 70 years, and in those with hepatic dysfunction. These patients should receive the usual bolus dose first, followed by half the normal maintenance infusion. Lidocaine reaches the central circulation after bolus peripheral administration in approximately 2 minutes. Patients should be observed closely for signs of drug efficacy and toxicity. Toxic reactions and side effects include slurred speech, altered consciousness, muscle twitching, seizures, and bradycardia. Lidocaine blood levels may assist in guiding therapy.

**Magnesium**

Severe magnesium deficiency is associated with cardiac arrhythmias, symptoms of cardiac insufficiency, and sudden cardiac death. Hypomagnesemia can precipitate refractory VF and can hinder the replenishment of intracellular potas-
sium. Magnesium deficiency should be corrected if present. In emergent circumstances, magnesium sulfate 1 to 2 g is diluted in 100 mL D_{5}W and administered over 1 to 2 minutes. Rapid administration of magnesium may cause clinically significant hypotension or asystole and should be avoided.

Anecdotal experience suggests that magnesium may be an effective treatment for antiarrhythmic drug-induced torsades de pointes even in the absence of magnesium deficiency. A variety of dosing regimens for magnesium sulfate have been described. Magnesium may be administered as a loading dose of 1 to 2 g (8 to 16 mEq), mixed in 50 to 100 mL D_{5}W, given over 5 to 60 minutes, followed by an infusion of 0.5 to 1.0 g (4 to 8 mEq) per hour. The rate and duration of the infusion should be determined by the clinical situation. The routine prophylactic administration of magnesium in patients with AMI is no longer recommended. Magnesium is not recommended in cardiac arrest except when arrhythmias are suspected to be caused by magnesium deficiency or when the monitor displays torsades de pointes.

**Procainamide**

Procainamide hydrochloride suppresses both atrial and ventricular arrhythmias. Procainamide is acceptable for the pharmacological conversion of supraventricular arrhythmias (particularly AF and atrial flutter) to sinus rhythm (Class IIa), for control of rapid ventricular rate due to accessory pathway conduction in preexcited atrial arrhythmias (Class IIb), and for wide-complex tachycardias that cannot be distinguished as being of supraventricular or ventricular origin (Class IIb). Procainamide hydrochloride may be given in an infusion of 20 mg/min until the arrhythmia is suppressed, hypotension ensues, the QRS complex is prolonged by 50% from its original duration, or a total of 17 mg/kg (1.2 g for a 70-kg patient) of the drug has been given. Bolus administration of the drug can result in toxic concentrations and significant hypotension. Delay resulting from recommendations to infuse procainamide slowly presents the major barrier to its use in life-threatening situations. In urgent situations, up to 50 mg/min may be administered to a total dose of 17 mg/kg. Use of procainamide in pulseless VT/VF is supported by a retrospective comparison study involving only 20 patients and is limited by the need to infuse the agent relatively slowly. The potential hazard of more rapid (bolus) administration during overt cardiac arrest must be balanced against the attendant risks and requires further study. The maintenance infusion rate of procainamide hydrochloride is 1 to 4 mg/min. The maintenance dosage should be reduced in the presence of renal failure. Blood levels should be monitored in patients with renal failure and in patients receiving a constant infusion of more than 3 mg/min for more than 24 hours.

Procainamide should be avoided in patients with preexisting QT prolongation and torsades de pointes. The ECG and blood pressure must be monitored continuously during procainamide administration. Precipitous hypotension may occur if the drug is injected too rapidly.

**Propafenone**

Propafenone hydrochloride, like flecainide, is a Vaughan Williams classification Ic antiarrhythmic agent with significant conduction-slowing and negative inotropic effects. In addition, propafenone has nonselective β-blocking properties. Oral propafenone is approved for use in the United States against ventricular arrhythmias and supraventricular arrhythmias in patients without structural heart disease. Intravenous propafenone (not approved for use in the United States) is used abroad for the same indications as flecainide. Because of significant negative inotropic effects, propafenone, like flecainide, should be avoided in patients with impaired LV function. Propafenone also falls into the same Vaughan Williams classification as flecainide (which has been observed to increase mortality in patients who have had MI), and by extrapolation of this data, its use should also probably be avoided when coronary artery disease is suspected.

Intravenous propafenone is customarily administered as 1 to 2 mg/kg body weight at 10 mg/min. Reported side effects include bradycardia, hypotension, and gastrointestinal upset. Propafenone is limited by its need to be infused relatively slowly, which may be impractical and of uncertain efficacy in emergent circumstances, particularly under compromised circulatory conditions.

**Sotalol**

Sotalol hydrochloride is a Vaughan Williams classification III antiarrhythmic agent that, like amiodarone, prolongs action potential duration and increases cardiac tissue refractoriness. In addition, it has nonselective β-blocking properties. Sotalol is approved in oral form in the United States for ventricular arrhythmias. Sotalol is used orally and intravenously for both ventricular and supraventricular arrhythmias.

**Intravenous** sotalol is usually administered as 1 to 1.5 mg/kg body weight at a rate of 10 mg/min. Side effects include bradycardia, hypotension, and proarrhythmia (torsades de pointes). IV sotalol is limited by its need to be infused relatively slowly. This may be impractical and has uncertain efficacy in emergent circumstances, particularly under compromised circulatory conditions.

**References**

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108. Olson DW, Thompson BM, Darin JC, Milbrath MH. A randomized
109. Kentsch M, Berkel H, Bleifeld W. Intravenose Amiodaron-Applikation bei
110. Babbs CF, Yim GK, Whistler SJ, Tacker WA, Geddes LA. Elevation of
111. van Walraven C, Stiell IG, Wells GA, Hebert PC, Vandemheen K, the
114. Babbs CF, Yim GK, Whistler SJ, Tacker WA, Geddes LA. Elevation of
115. Echt DS, Black JN, Barbey JT, Coxe DR, Cato E. Evaluation of anti-
94. Brady WJ, DeBehnke DJ, Laundrie D. Prevalence, therapeutic response,
97. Assimes TL, Malcolm I. Torsade de pointes with sotalol overdose
95. Tottersen JK, Turto T, Pellinen T. Overdrive pacing as treatment of
89. Copass MK. Effect of epinephrine and lidocaine therapy on outcome
117. Anastasiou-Nana MI, Nanas JN, Nanas SN, Rapti A, Poyadjis A,
119. Anastasiou-Nana MI, Nanas TN, Nanas SN, Rapti A, Poyadjis A,
128. Jordaens L, Gorgels A, Stroobandt R, Temmerman J, the Sotalol Versus
116. Kuck KH, Kunze KP, Schluter M, Duckeck W. Encainide versus fle-
112. Chow MS, Kluger J, Lawrence R, Fieldman A. The effect of lidocaine and
115. Echt DS, Black JN, Barbey JT, Coxe DR, Cato E. Evaluation of anti-
123. Tzivoni D, Keren A, Cohen AM, Loebl H, Zahavi I, Chenzbraun A,
1106 –1117.
116. Kuck KH, Kunze KP, Schluter M, Duckeck W. Encainide versus fle-
125. Alam D, Rouse J, Katzenstein A, Frey RL, Proctor DJ, Redding JS. Ef-
117. Anastasiou-Nana MI, Nanas TN, Nanas SN, Rapti A, Poyadjis A,
119. Anastasiou-Nana MI, Nanas TN, Nanas SN, Rapti A, Poyadjis A,
128. Jordaens L, Gorgels A, Stroobandt R, Temmerman J, the Sotalol Versus
116. Kuck KH, Kunze KP, Schluter M, Duckeck W. Encainide versus fle-
112. Chow MS, Kluger J, Lawrence R, Fieldman A. The effect of lidocaine and
115. Echt DS, Black JN, Barbey JT, Coxe DR, Cato E. Evaluation of anti-
123. Tzivoni D, Keren A, Cohen AM, Loebl H, Zahavi I, Chenzbraun A,
1106 –1117.
116. Kuck KH, Kunze KP, Schluter M, Duckeck W. Encainide versus fle-
112. Chow MS, Kluger J, Lawrence R, Fieldman A. The effect of lidocaine and
115. Echt DS, Black JN, Barbey JT, Coxe DR, Cato E. Evaluation of anti-
123. Tzivoni D, Keren A, Cohen AM, Loebl H, Zahavi I, Chenzbraun A,
1106 –1117.
116. Kuck KH, Kunze KP, Schluter M, Duckeck W. Encainide versus fle-
112. Chow MS, Kluger J, Lawrence R, Fieldman A. The effect of lidocaine and
115. Echt DS, Black JN, Barbey JT, Coxe DR, Cato E. Evaluation of anti-
123. Tzivoni D, Keren A, Cohen AM, Loebl H, Zahavi I, Chenzbraun A,
1106 –1117.
116. Kuck KH, Kunze KP, Schluter M, Duckeck W. Encainide versus fle-
112. Chow MS, Kluger J, Lawrence R, Fieldman A. The effect of lidocaine and
115. Echt DS, Black JN, Barbey JT, Coxe DR, Cato E. Evaluation of anti-
123. Tzivoni D, Keren A, Cohen AM, Loebl H, Zahavi I, Chenzbraun A,
1106 –1117.
116. Kuck KH, Kunze KP, Schluter M, Duckeck W. Encainide versus fle-
112. Chow MS, Kluger J, Lawrence R, Fieldman A. The effect of lidocaine and
115. Echt DS, Black JN, Barbey JT, Coxe DR, Cato E. Evaluation of anti-
123. Tzivoni D, Keren A, Cohen AM, Loebl H, Zahavi I, Chenzbraun A,
1106 –1117.
116. Kuck KH, Kunze KP, Schluter M, Duckeck W. Encainide versus fle-
112. Chow MS, Kluger J, Lawrence R, Fieldman A. The effect of lidocaine and
115. Echt DS, Black JN, Barbey JT, Coxe DR, Cato E. Evaluation of anti-
123. Tzivoni D, Keren A, Cohen AM, Loebl H, Zahavi I, Chenzbraun A,
1106 –1117.
116. Kuck KH, Kunze KP, Schluter M, Duckeck W. Encainide versus fle-
112. Chow MS, Kluger J, Lawrence R, Fieldman A. The effect of lidocaine and
115. Echt DS, Black JN, Barbey JT, Coxe DR, Cato E. Evaluation of anti-
123. Tzivoni D, Keren A, Cohen AM, Loebl H, Zahavi I, Chenzbraun A,
1106 –1117.
116. Kuck KH, Kunze KP, Schluter M, Duckeck W. Encainide versus fle-
112. Chow MS, Kluger J, Lawrence R, Fieldman A. The effect of lidocaine and
115. Echt DS, Black JN, Barbey JT, Coxe DR, Cato E. Evaluation of anti-
123. Tzivoni D, Keren A, Cohen AM, Loebl H, Zahavi I, Chenzbraun A,
1106 –1117.
116. Kuck KH, Kunze KP, Schluter M, Duckeck W. Encainide versus fle-
112. Chow MS, Kluger J, Lawrence R, Fieldman A. The effect of lidocaine and
115. Echt DS, Black JN, Barbey JT, Coxe DR, Cato E. Evaluation of anti-
123. Tzivoni D, Keren A, Cohen AM, Loebl H, Zahavi I, Chenzbraun A,
1106 –1117.
116. Kuck KH, Kunze KP, Schluter M, Duckeck W. Encainide versus fle-
112. Chow MS, Kluger J, Lawrence R, Fieldman A. The effect of lidocaine and
115. Echt DS, Black JN, Barbey JT, Coxe DR, Cato E. Evaluation of anti-
123. Tzivoni D, Keren A, Cohen AM, Loebl H, Zahavi I, Chenzbraun A,
1106 –1117.
116. Kuck KH, Kunze KP, Schluter M, Duckeck W. Encainide versus fle-
112. Chow MS, Kluger J, Lawrence R, Fieldman A. The effect of lidocaine and
115. Echt DS, Black JN, Barbey JT, Coxe DR, Cato E. Evaluation of anti-
123. Tzivoni D, Keren A, Cohen AM, Loebl H, Zahavi I, Chenzbraun A,


