2005 Changes to the American Heart Association Guidelines for Cardiopulmonary Resuscitation
by Heather Bockheim, Pharm.D.

The concept of resuscitation was first documented in 1740, when the Paris Academy of Sciences recommended mouth-to-mouth resuscitation for drowning victims.\(^1\) Almost 200 years later, in 1903, Dr. George W. Crile, co-founder of the Cleveland Clinic, reported the first successful use of external chest compressions in human resuscitation.\(^1\) In 1957, the United States military adopted the use of mouth-to-mouth resuscitation to aid in the revival of unresponsive patients.\(^1\) Finally, in 1960, closed chest cardiopulmonary resuscitation (CPR) was developed. Shortly thereafter, the American Heart Association (AHA) began developing training programs for both physicians and the public (See Figure 1).\(^1\)

In the United States, sudden cardiac arrest (SCA) accounts for 250,000 out-of-hospital deaths each year.\(^2\) Despite enormous labors to encourage public awareness and education, cardiopulmonary arrest remains a significant public health challenge worldwide. The survival rate for out-of-hospital SCA remains dismal with 94% of victims dying prior to hospital arrival worldwide.\(^2\)

The revised AHA guidelines for CPR and emergency cardiovascular care (ECC) were updated and published in December 2005.\(^3\) The recommendations are based on the review of evidence from the 2005 International Consensus Conference on CPR and ECC.\(^4\) The International Liaison Committee on Resuscitation (ILCOR) was formed in 1993 and is composed of representatives of multiple resuscitation councils from around the world.\(^3\) ILCOR was charged with the responsibility of reviewing international resuscitation literature and lending their expertise about CPR and ECC in order to create consensus treatment recommendations.\(^3\) The culmination of these efforts are the 2005 Adult AHA Guidelines for CPR and ECC.

The focus of this paper is to highlight the major changes to the 2005 Adult AHA Guidelines for CPR and ECC, but is not all inclusive. This review will include the following changes to the Guidelines: 1) a renewed emphasis on the delivery of effective chest compressions, 2) modified treatment of ventricular fibrillation/pulseless ventricular tachycardia (VF/VT), and 3) modified treatment of asystole/pulseless electrical activity.\(^5\) The reader is encouraged to refer to the Guidelines for a detailed review of all aspects of CPR and ECC.

The evidence classification system utilized is the same as that used by the American Heart Association-American College of Cardiology collaboration on
Figure 1: Resuscitation Timeline

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>1740</td>
<td>Paris Academy of Sciences: mouth-to-mouth resuscitation for drowning victims</td>
</tr>
<tr>
<td>1903</td>
<td>Dr. George W. Crile reports successful use of external chest compressions</td>
</tr>
<tr>
<td>1957</td>
<td>United States military adopts mouth-to-mouth resuscitation</td>
</tr>
<tr>
<td>1960</td>
<td>CPR was developed: AHA becomes forerunner of CPR training for public</td>
</tr>
<tr>
<td>1963</td>
<td>Dr. Leonard Scherlis establishes the AHA’s CPR committee</td>
</tr>
<tr>
<td>1972</td>
<td>Dr. Leonard Cobb holds first mass citizen CPR training in Seattle, WA</td>
</tr>
<tr>
<td>1981</td>
<td>Dispatcher-assisted CPR</td>
</tr>
</tbody>
</table>

Evidence-based guidelines (Table 1). Class I recommendations have high-level prospective studies to support the treatment and the risk substantially outweighs the harm. Class IIa recommendations are those in which most of the evidence supports the intervention, and the treatment is considered acceptable and useful. Class IIb recommendations are those for which the intervention has only been documented as beneficial in the short-term, or when positive outcomes were reported with lower levels of evidence. Class III recommendations are treatments that should not be administered as they may be harmful. The Guidelines cannot recommend for or against interventions labeled as Class Indeterminate.

Due to the low survival rate from out-of-hospital cardiac arrest, few resuscitation trials have the power to detect a difference in long-term outcomes among study populations. When investigators attempt to conduct research involving victims of SCA, multiple other considerations and constraints may affect the design and successful completion of studies with the primary outcome being that of “identification of interventions that improve neurologically intact survival to hospital discharge.” Subsequently, there are few Class I recommendations represented in the 2005 Guidelines and thus many recommendations were made by consensus, taking into consideration the clinical and laboratory evidence available for evaluation.

Effective Chest Compressions

The first major change to the 2005 Guidelines is a stronger emphasis on the importance of delivering effective chest compressions (Class I). Rescuers should use a chest compression to ventilation ratio of 30:2 for all adult victims. The rescuer should compress the chest, pushing hard and fast, to a depth of about 1½ to 2 inches. The chest should be allowed to recoil back to the normal position after each compression, thereby allowing blood to fill the heart. Chest compressions should be delivered at a rate of 100 per minute. An effort should be made to minimize interruptions in the delivery of effective chest compressions. Effective chest compressions are the component of CPR that deliver some blood flow to vital organs such as the heart and brain. By optimizing chest compression technique and minimizing interruptions, more blood may be delivered to vital organs, providing a better chance for survival. Previous literature has demonstrated that the quality of chest compressions, even when delivered by trained emergency medical services personnel (EMS), may be less than optimal. In one study of EMS personnel with an average of 6.4 ± 4.2 years of experience, it was found that incomplete chest wall decompression was observed at some point during CPR in 6 of 13 (46%) cardiac arrests. It is hoped that the renewed emphasis on the delivery of effective chest compressions with minimal interruptions will encourage retention of basic cardiac life support sequence by rescuers.

VF/VT

The second change to the 2005 Guidelines is to the algorithm for the treatment of ventricular fibrillation/pulseless ventricular tachycardia (VF/VT) (See Figure 2). Ventricular fibrillation is the presenting arrhythmia in 60 to 80% of SCA, with a survival rate of 4 to 33%. The major change to the VF/VT algorithm is the defibrillation and chest compression sequence. The current recommendation for patients with a shockable rhythm, VF/VT, is to deliver 1 shock followed immediately by a period of CPR, beginning with 5 cycles of chest compressions lasting 2 minutes in duration (Class IIa). This is opposed to the previous recommendation of delivering 3 stacked shocks in sequence. This new recommendation was made in light of a transition to the utilization of biphasic defibrillators that have a much higher rate of first-shock dysrhythmia termination. In addition, rhythm analysis by currently available automated external defibrillators may carry a delay of up to 37 seconds before delivery of the first post-compression shock. This delay may jeopardize the small but critical amount of oxygen that is delivered to the myocardium and brain produced during chest compressions. This change in sequence also recognizes that even when a shock terminates VF, many patients remain in a non-perfusing rhythm. Delivering chest compressions after a successful shock allows time for the heart to return to a
normal perfusing rhythm, while the chest compressions deliver oxygen to the myocardium.\textsuperscript{5} According to the AHA, there is no evidence that performing chest compressions subsequent to defibrillation will induce a recurrence of VF.\textsuperscript{5}

When treating a patient with VF/VT, the rescuer should continue to provide 5 cycles of CPR for approximately 2 minutes, then evaluate for rhythm and/or presence or absence of pulse. The current recommended dose for initial and subsequent shocks is 360 J for a monophasic waveform, 150 to 200 J for a biphasic truncated exponential waveform, and 120 J for a rectangular biphasic waveform.\textsuperscript{7} The dose that has been proven efficacious for elimination of VF should be listed on the defibrillator device. If the rescuer is unable to locate this information, a dose of 200 J should be administered.\textsuperscript{7}

If VF/VT persists despite delivery of 1 to 2 shocks and CPR, epinephrine 1 mg IV push may be administered during CPR without disruption of chest compressions and subsequently every 3 to 5 minutes (Class IIb).\textsuperscript{7} A single dose of vasopressin 40 international units IV may replace the first or second dose of epinephrine (Class Indeterminate).\textsuperscript{7} Drugs should be administered as soon as possible after the rhythm check, however, recognize that the Guidelines state that the timing of medication administration is of less importance than the minimization of chest compression interruptions.\textsuperscript{7} If VF/VT persists after 2 to 3 shocks, an antiarrhythmic agent may be considered. No antiarrhythmic drug administered during cardiac arrest increases survival to hospital discharge.\textsuperscript{5} Amiodarone 300 mg IV once, followed by an additional 150 mg delivered IV in 3 to 5 minutes may be administered (Class IIb).\textsuperscript{7} The maximum cumulative dose of amiodarone is 2.2 grams IV in 24 hours. Lidocaine may be considered if amiodarone is unavailable (Class IIb), using an initial dose of 1 to 1.5 mg/kg IV, with additional doses of 0.5 to 0.75 mg/kg IV administered at 10 to 15 minute intervals for persistent VF/VT to a maximum of 3 mg/kg. Magnesium 1 to 2 grams IV push over 5 to 20 minutes may be administered for torsades de pointes associated with a long QT interval (Class IIa for torsades).

### Asystole/Pulseless Electrical Activity

Asystole and pulseless electrical activity (PEA) account for 20 to 40% and 10% of all presenting arrhythmias, respectively. Survival from a PEA cardiac arrest is only 1 to 4%, and survival from an asystolic arrest is rare. Because the management of these two arrhythmias is so similar, the treatment algorithms have been combined in the new 2005 Advanced Cardiac Life Support (ACLS) Guidelines (See Figure 2). Keeping in mind that these patients will not benefit from defibrillation, the emphasis of treating patients in asystole or PEA is providing CPR and identifying and reversing the cause of the cardiac arrest (See Table 2).\textsuperscript{8} Pulseless electrical activity is often the result of a reversible condition such as those referred to as the five H’s and five T’s.\textsuperscript{8} Such conditions include: hypovolemia, hypoxia, hydrogen ion (acidosis), hypo- or hyperkalemia, hypoglycemia, hypothermia, toxis, cardiac tamponade, tension pneumothorax, thrombosis (coronary or pulmonary), and trauma.\textsuperscript{8} Cardiopulmonary resuscitation should be administered for 5 cycles and epinephrine 1 mg IV administered every 3 to 5 minutes as necessary.\textsuperscript{8} The provider may choose to administer one dose of vasopressin 40 international units IV once in place of the first or second dose of epinephrine.\textsuperscript{8} Cardiopulmonary resuscitation should not be interrupted to administer vasopressor agents and medications should be given as soon as possible after a rhythm check.\textsuperscript{8} Atropine may be considered for patients in asystole or slow PEA at a dose of 1 mg which can be repeated every 3 to 5 minutes up to a maximum of 3 mg.\textsuperscript{8} After the vasopressor agent has been administered and 2 minutes of CPR have been performed, the rhythm should be rechecked. If
This paper highlights the major changes to the Adult AHA Guidelines for CPR and ECC. The 2005 Guidelines place a renewed emphasis on importance of delivering effective chest compressions (Class I). Rescuers should use a chest compression to ventilation ratio of 30:2 for all adult victims. To be effective, chest compressions should be delivered at a rate of 100 per minute, and to a depth of about 1½ to 2 inches. The second major change to the 2005 Guidelines is that when treating VF/VT, the provider should deliver 1 shock followed immediately by a period of CPR, beginning with 5 cycles of chest compressions lasting 2 minutes in duration (Class IIa). The major changes to the treatment algorithm for Asystole/PEA is that CPR should not be interrupted to adminster vasopressor agents and medications should be given as soon as possible after a rhythm check. In addition, the provider may choose to administer one dose of vasopressin 40 international units IV once in place of the first or second dose of epinephrine. Finally, note that drug doses did not change in the 2005 Guidelines, with one exception noted in the management of symptomatic bradycardia. When utilized, atropine should be administered as 0.5 mg IV, repeated every 3 to 5 minutes to a total dose of 3 mg (Class IIa). This is different from the previously recommended dose range of 0.5 to 1 mg IV.

With SCA, the number one cause of death in both the United States and Canada, a concerted effort is needed to increase the quality and consistency of CPR efforts of both lay persons and trained providers of advanced cardiac life support. It is hoped that consistent implementation of the above recommendations from the AHA Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care will increase the proportion of successful resuscitation efforts.

Table 2. Reversible Causes/Complicating Factors

<table>
<thead>
<tr>
<th>Hypovolemia</th>
<th>Toxins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoxia</td>
<td>Tamponade</td>
</tr>
<tr>
<td>Hydrogen ion</td>
<td>Tension pneumothorax</td>
</tr>
<tr>
<td>Hypo / Hyperkalemia</td>
<td>Thrombosis</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>Trauma</td>
</tr>
<tr>
<td>Hypothermia</td>
<td></td>
</tr>
</tbody>
</table>

As adapted from: Circulation 2005;112:IV-59.

References:

Pulseless Arrest

VF / VT

Shockable Rhythm? Yes

Asystole / PEA

Shockable Rhythm? No

CPR

Shockable Rhythm? No

If asystole or PEA, refer to appropriate algorithm
If pulse present, begin post-resuscitation care

Shockable Rhythm? Yes

CPR

Shockable Rhythm? No

CPR

Shockable Rhythm? Yes

Epinephrine 1 mg IV every 3 to 5 minutes
Or
Vasopressin 40 IU IV to replace 1st or 2nd dose of epinephrine (1 dose)

Rhythm Check

Shockable Rhythm? Yes

For asystole or slow PEA: Consider atropine 1 mg IV every 3 to 5 minutes (up to 3 doses)

Shockable Rhythm? No

CPR

Shockable Rhythm? Yes

Epinephrine 1 mg IV every 3 to 5 minutes
Or
Vasopressin 40 IU IV to replace 1st or 2nd dose of epinephrine (1 dose)

Rhythm Check

Shockable Rhythm? No

If shockable, go to VF / VT algorithm
Not shockable, but pulse present, begin post-resuscitation care
Not shockable, and asystole or PEA, return to algorithm

CPR

= 5 cycles or 2 mins of CPR

= CPR while defibrillator charging; then shock
Orlistat Recommended for Over-the-Counter (OTC) Status
by Sarah Boone, Pharm.D. Candidate

In February 2006, the Food and Drug Administration (FDA) Nonprescription Drugs and Endocrine and Metabolic Drugs Advisory Boards recommended to approve orlistat for OTC status.¹ Orlistat was approved for prescription use in 1999 under the brand name Xenical® and has been marketed by Roche Pharmaceuticals. Xenical® is approved for weight loss in patients with either a Body Mass Index (BMI) ≥ 30 or ≥ 27 when accompanied by co-morbid risk factors such as diabetes or hypertension.²

GlaxoSmithKline purchased the rights to market an OTC version of orlistat and has been conducting trials for the past 5 years.³ The manufacturer plans to name the OTC version Alli (pronounced a-lí) to reinforce that the product is intended to be an “ally” to diet and exercise.⁴ Alli will be available as 60 mg capsules (compared to the 120 mg prescription strength). It is indicated for adults that are overweight (BMI 25 to 29.9) or obese (BMI ≥ 30) for a treatment duration of 6 months. Alli will be packaged with a program starter guide, a handbook on how to use the product in conjunction with diet and exercise, a healthy eating and shopping guide, a fat and calorie counter, a daily food journal, and a free customizable online support program. GlaxoSmithKline completed three clinical trials to evaluate safety and efficacy in addition to labeling and packaging comprehension studies.¹³

The three clinical trials, which studied a total of 1,371 patients included the BMI14149 (European 2-year study), NM14161 (US 2-year study), and NM17247 (US lower BMI study). The European 2-year study and the US 2-year study were placebo-controlled, double-blind, randomized, multi-center trials. All of the participants in these two trials were classified by BMI as obese. There was a 4-week run-in period during which participants were placed on a hypocaloric diet and one of three treatments: placebo three times a day, orlistat 60 mg three times a day, or orlistat 120 mg three times a day. In the European study, participants received intensive dietary intervention with a monthly food diary review and diet modification performed by a dietitian. Participants were also advised to exercise. The US study was conducted in a primary care setting and did not involve personalized dietary interventions. Instead, participants received written materials (similar to the materials provided in the proposed OTC packaging) and videos about diet and exercise to be used at the participant’s discretion. In the US lower BMI study, which was performed at the request of the FDA, participants were classified as overweight, but not obese. The duration of the trial was 16 weeks, and there was no run-in period. Participants were randomized to receive either placebo three times a day or orlistat 60 mg three times a day and were provided with reading materials about healthy lifestyles and eating habits.¹³

The primary outcome in the trials was a 5% weight loss at 6 months (16 weeks in the US lower BMI study) compared to baseline. Secondary outcomes included waist and hip circumference, lipid panels, blood glucose, and blood pressure. Despite the differences in dietary intervention, weight loss was similar among patients in the trials and significantly greater than placebo. Most of the weight loss occurred by 6 months in the extended studies and a significant number of participants reached at least a 5% weight loss by 16 weeks in the US lower BMI study. Efficacy was comparable between the 60 mg and 120 mg study groups. In addition, the US 2-year study and the US lower BMI study both had positive effects on systolic and diastolic blood pressure, total cholesterol, and LDL.¹³

There are safety data available from the initial clinical trials, case reports, and the new trials. Because orlistat is minimally absorbed, there are no expected systemic side effects or direct drug interactions. Unlike stimulant diet medications, there are no cardiovascular effects.³ Initial concerns about the absorption of fat soluble vitamins have not been clinically significant, but it is recommended that all patients take a multivitamin in conjunction with orlistat and that they are separated by at least 2 hours. Most of the side effects are gastrointestinal and either subside after several weeks or can be managed by adhering to the recommended low-fat diet. Side effects were generally lower in the participants receiving 60 mg three times a day.³ Despite adverse events that include fecal urgency (18.8% and 23.4% for 60- and 120-mg, respectively), fecal incontinence (4.7% and 7.8%, respectively), oily spotting (17.7% and 21.7%, respectively), and flatulence (18.6% and 18.0%, respectively), there have been consistently low withdrawal rates among study participants. There have been several reports of overdose with no adverse effects, and no abuse/misuse potential has been reported. Because orlistat is not centrally acting, no abuse potential would be expected, unlike with stimulant diet drugs.³ There are only two defined drug interactions with orlistat: cyclosporine and warfarin. Orlistat decreases cyclosporine absorption, in turn decreasing serum cyclosporine concentrations by about 30%; however, there are several reports of concomitant use and no organ rejections or adverse organ events have occurred despite a decrease in the serum concentration of cyclosporine.²³ While the product labeling for Xenical® instructs patients taking cyclosporine to separate the medications by at least 2 hours, Alli’s product labeling will advise transplant patients not to take the product. There are several reports of increased International Normalized Ratios (INRs) in patients receiving orlistat and warfarin concurrently. Orlistat may decrease vitamin K levels, which could increase the INR in a warfarin patient.²³ Alli’s labeling will advise patients receiving warfarin therapy to...
talk to their doctor or pharmacist before taking orlistat. One additional concern includes patients with diabetes. While there are no direct drug interactions with diabetes medications, diabetics who lose weight may have a decreased need for medications and may need to have their medications adjusted to prevent hypoglycemia. Several concerns were raised during the FDA Advisory Board proceedings about OTC orlistat including: side effects, drug interactions, the potential to enable poor eating habits, misuse by patients who are not overweight or obese (e.g., anorexics), and the fact that a 6-month treatment duration is not realistic for a long-term condition. However, many of these concerns have been addressed by the manufacturer, who has proven that not only is orlistat safe and effective for people to use on their own, but the company is dedicating resources to encourage lifestyle modifications both during medication use and continuing past the 6-month duration of therapy. The cost of Alli is expected to be approximately $0.60/capsule. Finally, the FDA Advisory Board believes that placing an FDA-approved weight loss medication OTC will enable consumers to choose a safer alternative to the unapproved weight loss dietary supplements currently available.

References:

Formulary Update

The Cleveland Clinic Pharmacy and Therapeutics Committee met on Tuesday, April 4, 2006, and the following decisions were made:

**Formulary Additions:**

1.) **Nepafenac (Nevanac®)** 0.1% Ophthalmic Suspension: Nepafenac is a non-steroidal anti-inflammatory drug (NSAID) FDA-approved for the treatment of pain and inflammation associated with cataract surgery. Nepafenac has better penetration into the posterior segments of the eye compared to other ophthalmic NSAIDs. Common adverse effects include decreased visual acuity, increased ocular pressure, and foreign body sensation. Nepafenac is available in 3-mL bottles. It should be dosed three times daily beginning 1 day prior to surgery, continued on the day of surgery, and through the first 2 weeks postoperatively.

2.) **Abatacept (Orencia™):** Abatacept is the first member of a new class of drugs for treating rheumatoid arthritis (RA). It is a selective T-cell co-stimulation modulator indicated for reducing the signs and symptoms of RA, slowing the progression of structural damage, and improving physical function in adult patients with moderate-to-severe RA who have had an inadequate response to one or more disease modifying anti-rheumatic drug (DMARD), including methotrexate or TNF-α antagonists (i.e., etanercept [Enbrel®] or infliximab [Remicade®]). The most frequently occurring adverse reactions include headache, nasopharyngitis, dizziness, and cough. Drug interactions include live vaccines, TNF-α antagonists, and anakinra (Kineret®). Dosing is weight based (~10 mg/kg of actual body weight; specific dosing recommendations and number of vials to use based on weight are described in the product labeling). Abatacept is administered as an IV infusion over 30 minutes at 2 and 4 weeks after the initial infusion, and then every 4 weeks thereafter. Abatacept must be reconstituted and transferred from vial to infusion bag using only the silicone-free disposable syringe provided with each 250 mg vial and an 18-21 gauge needle. The solution should be administered within 24 hours of reconstitution using a 0.2 to 1.2 micron filter. The solution should not be delivered via the pneumatic tube system. Abatacept use is restricted to staff physicians in the Department of Rheumatic and Immunologic Disease and adult outpatients who have had an inadequate response to one or more DMARDs, including methotrexate and TNF-α antagonists.
3. **Ibandronate (Boniva®) Injection**: Ibandronate injection is the first injectable bisphosphonate FDA-approved for the treatment of osteoporosis in postmenopausal women. It reduces bone resorption and turnover by inhibiting osteoclasts thus resulting in net gain in bone mass. Common adverse effects include upper respiratory infection, back pain, and dyspepsia. Its use is contraindicated in patients with uncorrected hypocalcemia. Additionally, ibandronate should not be administered to patients with serum creatinine >2.3 mg/dL or creatinine clearance <30 mL/min; therefore, renal function must be assessed prior to each dose. Unlike oral bisphosphonates, there are not any known drug interactions with ibandronate injection. The recommended dose of ibandronate injection is 3 mg administered IV over 15-30 seconds every 3 months. Ibandronate injection use is restricted to outpatients having serum creatinine ≤2.3 mg/dL or creatinine clearance ≥30 mL/min. For all outpatients requiring ibandronate injection that are evaluated in clinics on Main Campus an order will be sent to pharmacy so that renal function can be assessed prior to dispensing this agent. Oral ibandronate remains non-formulary.

**Restriction Change:**

1. **Rituximab (Rituxan®)**: Rituximab was recently FDA-approved to be used in combination with methotrexate to reduce signs and symptoms in adult patients with moderately-to-severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more TNF-antagonists. Rituximab selectively depletes CD-20+ B-cells involved in the pathogenesis of RA and associated chronic synovitis. In treating RA rituximab is administered as two 1 gram IV infusions separated by 2 weeks in combination with methotrexate. Patients should be premedicated with acetaminophen and an antihistamine prior to therapy to reduce the incidence and severity of infusion reactions. There currently are no recommendations for retreating RA patients with rituximab. The current formulary restriction for rituximab has been modified to include use by staff physicians from the Department of Rheumatic and Immunologic Disease for the treatment of adult outpatients with moderately-to-severely active RA who have had an inadequate response to one or more TNF-antagonists.

---

**Cleveland Clinic**  
Department of Pharmacy/Hb-03  
Drug Information Center