Trans-Thoracic Ventricular Defibrillation:

From Bench to Bedside;

From Ambulance to Aircraft Aisle

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Internal Medicine Grand Rounds

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From lightning and tempest;
from plague, pestilence and famine;
from battle and murder; and from sudden death;
Good Lord, deliver us

-Book of Common Prayer, 1662

"This is to acknowledge that Richard Page, M.D. has disclosed a financial interest or other relationship related directly or indirectly to this program with Cardiac Pacemakers, Inc., Medtronic, Heartstream/Hewlett Packard, and American Airlines."

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Areas of Interest:

1) Ablation of arrhythmias
2) Arrhythmias during pregnancy
3) Autonomic response to arrhythmias
4) Pharmacologic and electrical treatment of atrial fibrillation
5) Automatic external defibrillation

I. INTRODUCTION

When death strikes suddenly and without warning, it is especially devastating. *Sudden death* is generally defined as "death due to natural causes of an individual who was not restricted to his house, hospital or other institution or unable to function in the community for more than 24 hours prior to death, and for whom the time interval from onset of the fatal event until death was less than 24 hours".[1] The most common cause of sudden death is ventricular fibrillation (VF). The onset of VF may can come without warning, as shown in figure 1.

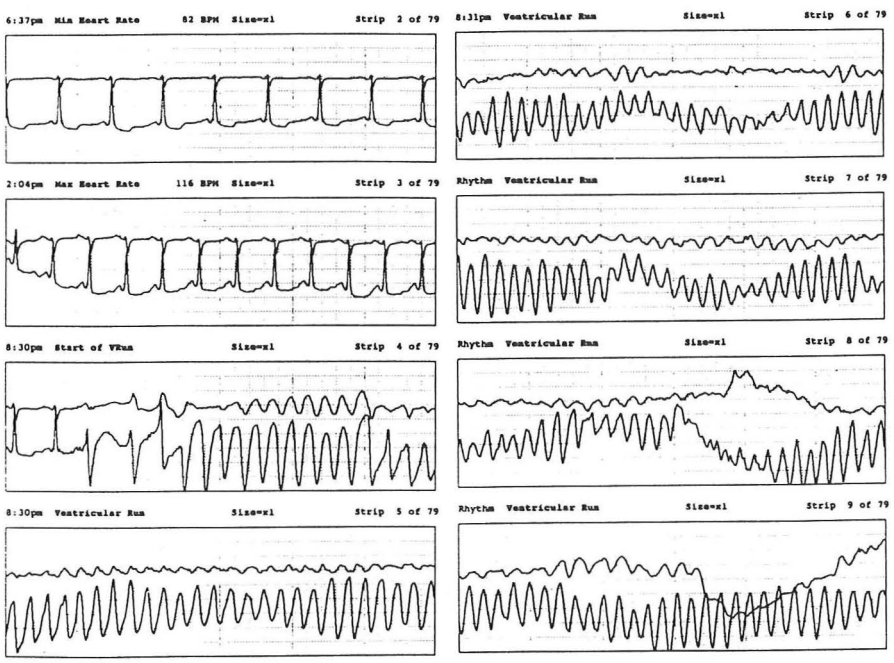

Figure 1. Recording from a Holter monitor at the time of death of a 64 year old woman with dilated cardiomyopathy and light-headed spells. [2]

My focus today will be on treatment of ventricular fibrillation through trans-thoracic defibrillation. First, we will discuss the epidemiology and history of VF.

II. EPIDEMIOLOGY OF VENTRICULAR FIBRILLATION

It is estimated that there are 300,000 sudden deaths in the United States each year. Although cardiac death in general is on the decline (likely due to improved public education, modification of risk factors, and improvement of medical therapy), it remains the largest categorical cause of death in the Western world.[3] The proportion of cardiac deaths that are sudden (about 50%) has remained constant.[4-7] In Framingham, among 5209 men and women, 30-59 years of age and free of heart disease at baseline observation, SCD accounted for 46% of deaths due to coronary disease in men and 36% in women.[8] The incidence increased with age, although the proportion of coronary deaths that were sudden was greater in the younger population.

When evaluated in the field, the initial rhythm observed after arrest depends on the time passed after collapse. When the time elapsed is not known, the initial rhythm identified is VF in 40%, asystole in 40%, pulseless electrical activity in 20%, and VT in 1%.[9]. On the other hand, if the time from collapse to rhythm identification is <4 minutes, VF accounts for 95% and asystole in 5%. Thus, VF is typically the initial event, and asystole and pulseless electrical activity likely result from prolonged VF and hypoxia.[10] It should be noted that, in some populations, a certain percentage of cardiac arrest is due to bradycardia rather than tachycardia.[11]

Identification of the highest risk groups for SCD remains a challenge. For the general adult population, the 300,000 deaths/year calculates to a risk of 0.1-0.2%/year. As further risk factors are added (such as coronary risk, prior cardiac event, heart failure, history of sudden death), the risk increases. However, as further risk factors are added, the total number of events decreases (as shown in figure 2), such that very high risk individuals are identified, but they represent a small proportion of the total SCD.[3] Clinical trials of drugs or defibrillators have focused on these highest risk populations in terms of primary and secondary prevention of SCD, since substantial risk is necessary to identify any benefit of therapy. On the other hand, population-based treatment of sudden death potentially would affect a greater number of total deaths.

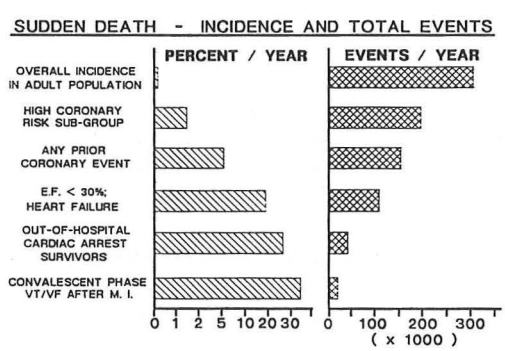

Figure 2. The relationship between annual incidence and total number of sudden cardiac deaths among population subgroups. Note that the patients at highest risk make up a small fraction of the total sudden deaths.[3]

Causes of Ventricular Fibrillation:

The etiology of VF in most cases is coronary artery disease, accounting for 70%-80% of sudden death, although a number of other conditions may be associated (see table 1).[12-19] In each situation, the ventricular rhythm is made unstable by the underlying substrate, but the end result is the same: ventricular fibrillation with secondary hemodynamic collapse and death.

Table 1. Etiology of Ventricular Fibrillation [19]

Structural Heart Diseases
Coronary artery disease
With acute myocardial infarction
Without acute myocardial infarction
Cardiomyopathy
Congestive/dilated
Hypertrophic (obstructive and non-obstructive)
Valvular heart disease
Congenital heart disease
Myocarditis
Functional Causes
Autonomic imbalance
Metabolic
Toxic/drug-related
Abnormal Electrical Substrate
Myocardial scar (includes structural heart diseases)
Wolff-Parkinson-White syndrome
Long QT syndromes

Coronary artery disease is the most common cause for cardiac arrest, accounting for between 70% and 80% of sudden deaths.[13-18] With acute ischemia or injury, instability in the resting membrane potential contributes to arrhythmogenesis. In chronic ischemic heart disease, the border zone of the infarction, characterized by interspersed normal and fibrotic tissue, allows for reentrant circuits that may precipitate ventricular arrhythmias (especially when combined with ventricular ectopy and/or acute ischemia).

Non-ischemic cardiomyopathy accounts for a significant percentage of sudden death, and such patients are at substantial risk. Up to 50% of patients newly diagnosed with non-ischemic dilated cardiomyopathy die within the first year.[20] Hypertrophic cardiomyopathy, both with and without obstruction, also can result in sudden death, often without symptoms of heart disease or other prior warning.

The functional causes of VF include autonomic and metabolic disturbances and exposure to toxic substances. Antiarrhythmic medications used for control of atrial fibrillation can result in prolonged QT and secondary *torsades de pointes*. Cocaine use is responsible for a substantial number of sudden deaths in patients abusing drugs.

Finally, abnormal electrical substrates can cause VF. Atrial fibrillation in the Wolff-Parkinson-White syndrome can degenerate to VF, although this problem can be eliminated with ablation of the pathway. The long QT syndrome is represents the manifestation of a number of different genetic abnormalities in the potassium and sodium channels; the repolarization abnormality results in polymorphic ventricular tachycardia (*torsades de pointes*), caused by prolongation of repolarization and early afterdepolarizations.

III. HISTORY OF DEFIBRILLATION

Sudden death was recognized as early as 4500 years ago, depicted in Egyptian relief on the tomb of a noble of the sixth dynasty.[21] The association of sudden death with ventricular fibrillation was described by MacWilliam in 1889 and Lewis in 1915.[22,23] Although ventricular fibrillation was increasingly recognized as the cause of much sudden death, little could be done about it until the middle of this century.

The use of electricity in medical care has a sordid history, with quackery and naiveté dominating in early years. In the 18th century, Johann Gottlob Kruger, Professor of Medicine at the University of Halle, employed electrical charge generators to cure a variety of conditions, earning him the title of "founding father of electrotherapy".[24] In 1746, the Leyden jar was invented; this allowed for greater use of electricity, since the charge could be stored for several days. In 1774, a young girl who apparently died after falling out of a window appeared to be resuscitated after multiple shocks (some across the thorax); although the attendants were not applying the shocks for the purpose of converting an abnormal heart rhythm, it is possible that this represents the first defibrillation.[25]

Other early uses of electricity were equally dramatic. In 1818, Professors Andrew Ure and James Jeffray, of Glasgow, used battery-operated stimulation on a murderer one hour after his being hanged by the neck. The professors, by using appropriate placement of the electrodes, demonstrated movement of the dead man's limbs and diaphragm. In addition, the criminal's face was described as exhibiting "rage, horror, despair, anguish and ghastly smiles," such that one spectator fainted and several ran in terror.[25]

By the end of the 19th century, electrical therapy was an established tool of what was then modern medicine. Among the more dubious treatments was the use of faradic stimulation from the rectum for constipation. The 1891 textbook, *On the Medical and Surgical Uses of Electricity*, the authors give instructions for early cardiac care, including improvement of angina with stimulation over the left chest.[25] By the early part of the 20th century, however, much of the electrical quackery was exposed.

Investigation into the treatment of ventricular fibrillation was taking place concurrently. Chemical cardioversion with calcium and potassium salts was described, although conversion of the arrhythmia left the heart with the equivalently dangerous problem of asystole.[25] Canine studies at Johns Hopkins in the 1930's showed that a small shock resulted in VF and a larger shock (coining the term, "countershock") reversed the arrhythmia. The investigators even showed that transthoracic shocks could be effective, if administered promptly and with sufficient output.[26]

The first successful open-chest human defibrillation occurred in 1947 at Johns Hopkins. A 14 year old boy was undergoing surgery for severe pectus excavatum, and developed ventricular fibrillation near the end of the operation.(see figure 3) After 45 minutes of open chest massage, the prototype defibrillator was wheeled into the OR and successfully defibrillated the patient. He was eventually discharged without sequelae.[27]

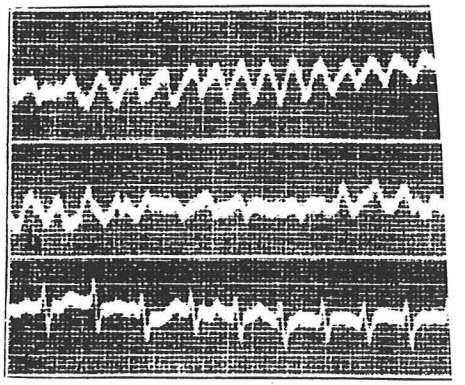

Figure 3. Electrocardiogram from the first successful human defibrillation.[27]

The first successful external defibrillation did not occur until 1955, when Paul Zoll converted VF several times in a man with recurrent VF; the patient eventually was discharged to home.[28] The alternating current (AC) defibrillator designed by Zoll had limitations due to its size and its lack of portability, since large transformers were required to step-up the voltage and since it required an AC outlet. The answer to these limitations was found by Bernard Lown, who developed the first direct current (DC) defibrillator. With direct current, a battery is used to charge a capacitor that delivers the shock. Work in dogs showed that DC shocks were less likely to induce VF and caused less injury than was found in AC shocks. In 1962 he reported his first DC defibrillation in humans, effectively defining the waveform primarily used today.[25] By good fortune, the development of the DC defibrillator coincided with the development of modern CPR, thus setting the stage for modern cardiac life support.

IV. BASIC MECHANISMS OF FIBRILLATION AND DEFIBRILLATION

The mechanism of fibrillation:

Focal activation may initiate VF, but the arrhythmia appears to be maintained by reentry. Multiple "wandering wavelets" of activation reenter within the heart in an ever-changing pattern.[29,30] Over time, the rhythm becomes more organized and certain reentrant patterns may repeat themselves for several cycles.[31,32] Conversely, there has been a suggestion that the ECG

pattern of VF can be caused by a single rotor on a thin myocardial preparation. In an isolated rabbit heart preparation, a single rotor was shown to approximate the pattern of VF. Furthermore, a computer simulation, using a single rotor, has reproduced the ECG pattern of VF.[33]

A study in humans, undergoing VF induction for ICD testing, showed the cycle length to be 213±27 msec in the right ventricle.[34] This study used monophasic action potential recordings that demonstrated activation of myocardial cells before they returned to the diastolic resting potential for the previous activation, demonstrating that the reentry in VF has little or no "excitable gap" (time after depolarization where the cells are repolarized and ready for further excitation). In other words, the myocardial cells are re-activated as soon as they have recovered from depolarization.

Very rarely will ventricular fibrillation spontaneously terminate. When spontaneous conversion occurs, it is most commonly in the setting of drug therapy and in a structurally normal heart.[19,35-37] In most cases VF continues until cardiac death occurs. As shown in animals and in clinical experience, if the arrhythmia is not converted, after several minutes the fibrillation will degenerate to an agonal bradycardia or pulseless electrical activity.

The mechanism of defibrillation:

For several years the probabilistic nature of defibrillation has been recognized. Successful defibrillation is not an all-or-none phenomenon; to the contrary, a probability curve can be generated such that defibrillation approaches 100% at higher output and 0% at very low output, but in the middle range success is a statistical phenomenon. This dose-response phenomenon can be depicted with a sigmoidal curve of energy versus percent success, as in figure 4.[38]

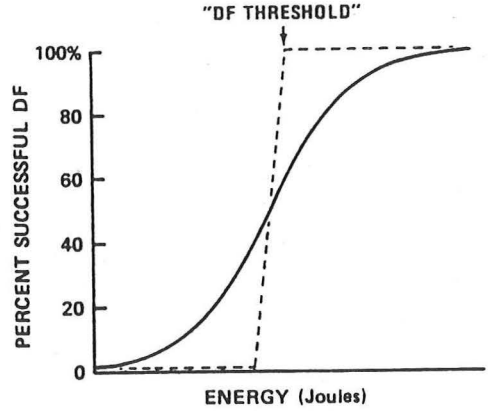

Figure 4. Defibrillation threshold. The dotted line shows a theoretical level above which defibrillation is always effective. The sigmoidal curve more accurately reflects reality, where defibrillation is a statistical phenomenon.[38]

Measures of energy, current, and voltage can be used to describe the effects of a defibrillation shock, although experimentally the extracellular potential gradient appears to determine whether quiescent myocardium is stimulated or fibrillating myocardium is defibrillated. The current density can be calculated from the gradient if the impedance of the tissue is known.

There appears to be a minimal potential gradient created throughout the heart that is necessary to yield successful defibrillation. In an unsuccessful shock, the earliest activation after the shock occurs in the areas of lowest potential gradient, consistent with the concept that there is a minimum gradient necessary for defibrillation.[39] On the other hand, several studies have shown spontaneous ectopic post-shock activations originating from the regions of higher gradients, suggesting that higher shock energies might reinduce fibrillation and be less effective than energies just above defibrillation threshold.[40-41]

This concept of *refibrillation* in areas with high gradients must be considered. Early studies showed reduced defibrillation efficacy and potential for arrhythmia induction with high output shocks.[42-45] Using up to 5000V, a refractory form of VF was induced that could not be terminated.[44] Experimentally, in cultured chick myocytes, gradients of 60V/cm were associated with delayed rapid repetitive responses; at 100V/cm a postshock arrest was followed by a series of activations, but at 160-200V/cm the membrane was sharply depolarized to 0mV with no potential formation.[46] These effects were associated with transient formation of microlesions in the cellular membrane that prevented activation.[47] A further explanation for failure to defibrillate at high output may be differential effects within the heart. In dogs, it was found that the same high voltage that caused refractoriness in papillary muscles resulted in rapid firing of Purkinje fibers.[38]

Upper limit of vulnerability (ULV):

In order to better understand the determinants of defibrillation, an explanation of ventricular vulnerability is warranted, since recent data demonstrate the two phenomena are closely related. Hoffman, et al.[48] demonstrated that cardiac response to electrical stimulation depends on the strength and timing of the stimulus relative to cardiac recovery (known as the coupling interval). In sinus rhythm, the vulnerable period, where a well-timed shock can induce VF, occurs near the peak of the T wave (20-60% from the onset).[49] The existence of an upper limit of vulnerability (ULV) in the current domain, defined as a current strength at or above which VF cannot be induced,[50] was recognized 100 years ago.[51] The ULV has recently come into use as an assessment of DFT, since the two measures are related both theoretically and experimentally in animals [52-54] and humans.[55]

In animal studies and computer simulation, below the ULV a graded response to a T-wave shock is seen in some tissues, and unidirectional block is induced by prolongation in the action potential duration and refractory period. This sets up reentry and results in VF. At shock strengths above the ULV, bi-directional block is seen and no VF is induced. Similar principles apply to *defibrillation*. There is likely to be a gradation of field strength in the heart, such that some tissue is above the ULV and some is below the ULV. The tissue below the ULV will have local reentry terminate, but will have some tissue in the relatively refractory period at the time of the shock. It

is these areas of relative refractoriness that will then *re-initiate* reentrant VF much in the same way shocks below the ULV during sinus can initiate VF *de-novo*, as shown in figure 5.[50] Since the phase at which any reentrant circuit may receive the shock cannot be predicted, some variability in the DFT is explained by this theory (thus explaining, in part, the statistical variability seen in DFT evaluation).

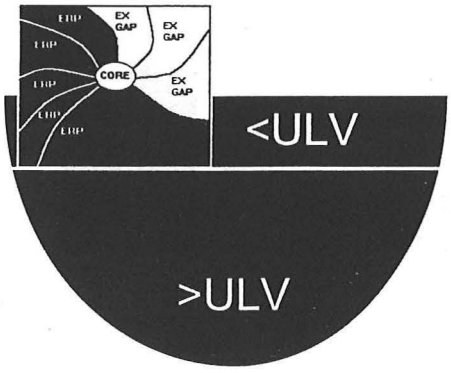

Figure 5. Upper limit of vulnerability (ULV) hypothesis for defibrillation. A shock at the apex yields adequate field strength beneath the white line and strength below the ULV above the white line. When strength is above the ULV, timing is not important. On the other hand, the relative refractoriness of the tissue exposed to field strength below the ULV will determine whether the shock is successful. [50]

As above, sub-threshold defibrillation shocks may in fact terminate VF but re-induce it at the same time. This may have important implications for defibrillation. It has been shown that there are "protective zones" after a VF-initiating shock where the DFT is reduced and otherwise sub-threshold shocks can terminated the new VF.[50] Such zones are not present in longer-standing VF. With better understanding of these protective zones, sequential shock algorithms could be identified that would reduce the energy required for defibrillation.

Biphasic waveforms:

Failure to defibrillate may relate to failure to reach minimum gradient in the lowest gradient regions of the heart. Biphasic waveforms, where the second phase has opposite polarity to the first, have been shown to be more effective in both animal models and humans.[56-62] The mechanism is unclear, but the minimum potential gradient required for defibrillation with biphasic waveform appears to be lower than with monophasic waveforms. In dogs, biphasic shocks with minimum potential gradient of 2.7V/cm resulted in an 80% defibrillation success, while monophasic shocks of the same total duration required 5.4V/cm gradient to achieve the same level of success.[63] In one canine study, the defibrillation threshold for an implanted system showed a DFT of 19.5 J for monophasic and 9.7 J for biphasic waveform.[60] Also in dogs, it was demonstrated that successful biphasic waveforms were less likely than monophasic waveforms to excite relatively refractory tissue;[64] thus they may be more effective due to less induction of conduction block and other postshock arrhythmias in regions of high potential

gradients.[65] Among the monophasic waveforms, there are two varieties: truncated exponential refers to a monophasic shock with an exponential decay for its time-limited duration; in contrast, damped sine wave monophasic waveforms use the monophasic upright component of a sine wave. The relative benefit of these monophasic waveforms remains unclear.

The duration in each phase of the biphasic waveform is important. Depending on the percent in each phase, the defibrillation threshold may be increased or decreased. The ideal relationship appears to be approximately 65%/35% for the shock phases, as shown in figure 6.[66]

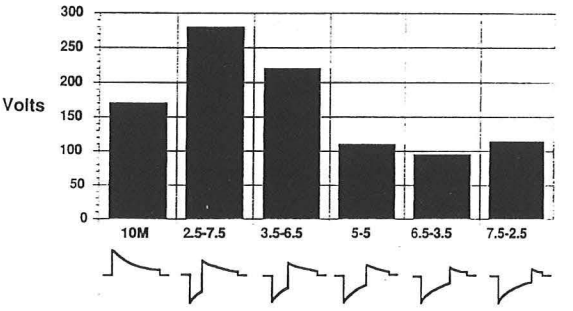

Figure 6. Defibrillation thresholds for monophasic and biphasic truncated exponential waveforms. Note that the DFT can both decrease or increase, relative to the monophasic shock, depending on the relative time in each phase.[66]

Damage associated with defibrillation:

The issue of potential damage from defibrillation has been studied extensively. At shock strengths near threshold, there does not appear to be any damage. With high output shocks in dogs, subepicardial and even transmural necrosis has been described.[67] The mechanism is thought to be electroporation (also called electropermeabilization). The high-intensity electric field causes electroporation that allows calcium overload and subsequent hypercontraction. The altered cells may become unexcitable and initiate cardiac arrhythmias.[68] There is some evidence that repeated smaller shocks may cause more damage than a single large shock. Doherty, et al, reported greater evidence of damage after three 10 J shocks compared with one 30 J shock.[69]

Evaluation for damage using the surface EKG has methodological problems, since the bilateral damage from the shock would be expected to cause ST segment changes that would cancel themselves out. In humans, any ST segment changes usually resolve within 20-120 seconds.[67]

Elevation of CPK following shock in humans may be seen, but is typically not cardiac in origin. In one study of 30 patients undergoing cardioversion, 15 had CPK elevation, but only 2 elevated the MB fragment.[70] Evaluation of technetium-99m pyrophosphate scintigraphy showed abnormal scans in humans, with unclear clinical importance.[67] Troponin I, a sensitive marker for cardiac damage, has not been shown to increase associated with transthoracic shocks.

In addition to potential damage to the heart, atrial bradycardia, atrial tachycardia, PVC's, ventricular tachycardia and abnormalities in AV nodal and intraventricular conduction have been reported.[71] The significance of these findings is unclear.

Overall, shocks in the range necessary to defibrillate, such as in clinically available defibrillators, appear to be quite safe.

V. HUMAN DEFIBRILLATION

General Recommendations for Human Defibrillation:

Defibrillators deliver energy, measured in Joules or watt-seconds. The formula is:

Energy = (power) x (duration)
Energy = (voltage) x (current) x (duration)

Although the energy is set by the operator, the current delivered (which determines defibrillation) is dependent on the thoracic impedance (according to Ohm's law, which states that:

V = I (current) x R(impedance).

The transthoracic impedance must be minimized to optimize current delivery and, thus, the likelihood of successful defibrillation. The electrode size should be large enough to reduce impedance but also allow delivery to the heart. For adults, this ranges from 8.5 to 12 cm in diameter. Adequately firm paddle-to-chest pressure should be applied, although "hands off" adhesive patches (which do not allow pressure at all) have come into favor with AEDs due to their simplicity. The phase of breathing (with best results in end-expiration) can become a factor, although this is not an issue in patients in arrest since they are already at end-expiration.[72]

Impedance is further reduced by applying an appropriate gel if paddles are employed. Care must be exercised to avoid smearing the gel and short-circuiting the shock. Of note, echocardiographic gels have a high impedance and are to be avoided.[73] The electrodes should be placed to maximize current flow through the heart. This is accomplished most conveniently using the anterior-apex approach illustrated in figure 7.

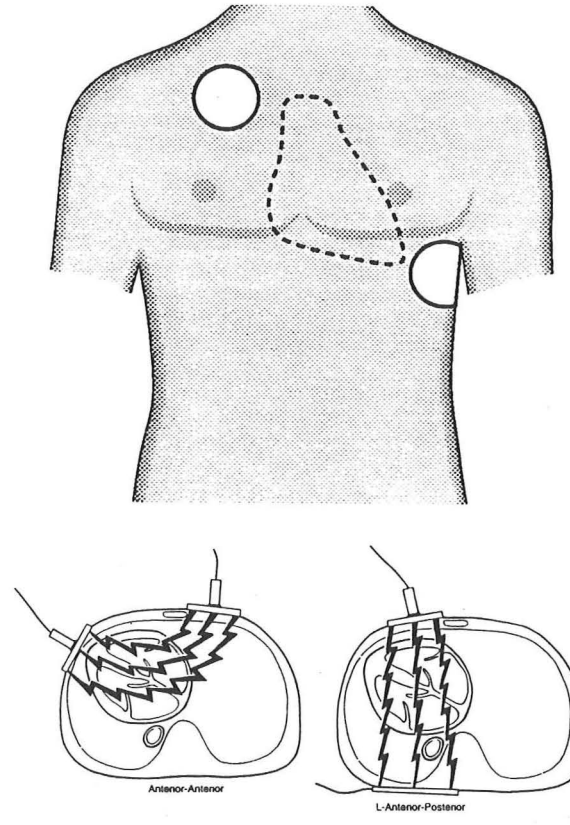

Figure 7. Location of electrodes for ventricular defibrillation. The top panel illustrates the anterior-apex orientation recommended by the AHA. The bottom panel shows the shock vectors of the anterior-anterior (apex) and left-anterior-posterior approaches.[72,73]

The AHA Advanced Cardiac Life Support manual recommends the first shock for VF to be 200 J, followed by the second at 200-300 J if the first is unsuccessful. It the first two shocks are unsuccessful, 360 J is recommended. When VF persists, continued CPR, intubation and intravenous access should be performed, followed by epinephrine 1 mg IV every 3-5 minutes and repeat defibrillation. Antiarrhythmic medications, with defibrillation attempt between doses, are then recommended. At present, these include lidocaine, followed by bretylium, magnesium sulfate, and procainamide. The inclusion of amiodarone IV for refractory ventricular arrhythmias is being considered.[personal communication, James M.Atkins, MD]

Data on Human Defibrillation:

It is estimated that the chance of resuscitation success is reduced 7-10% every minute.[74] Bystander-initiated CPR plays an important role in maximizing survival from VF. In Seattle, among patients receiving defibrillation within 6 minutes, the survival with CPR delivered within 3 minutes was 70%, vs 39% when CPR was not initiated until after 3 minutes.[75] The

combination of rapid CPR and defibrillation has resulted in an in-field resuscitation rate of 60% for those found in VF,[76] although survival to hospital discharge is further reduced. See figure 8. Any examination of the data on out-of-hospital defibrillation must consider the duration and therapy prior to the shock.

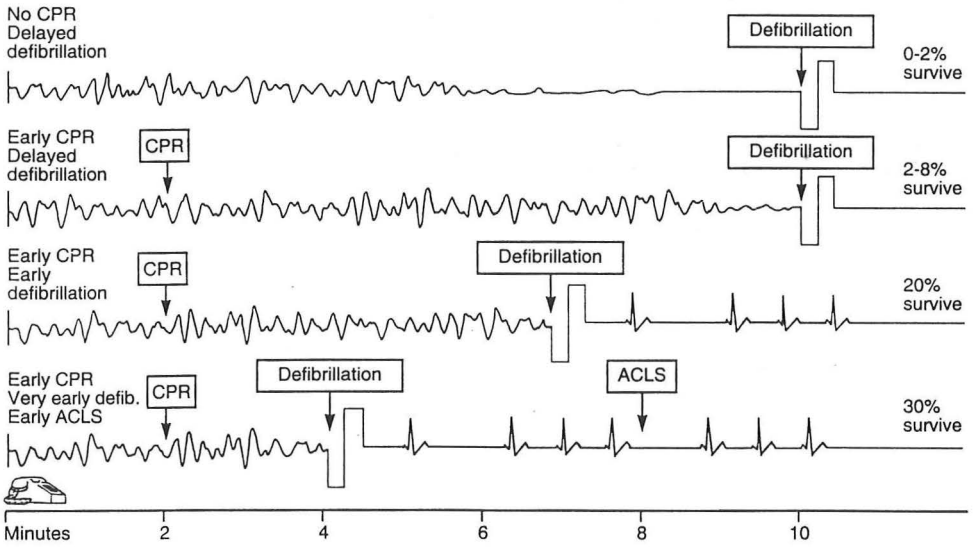

Figure 8. Estimated survival to hospital discharge according to therapy administered.[72]

The data to support the above technical recommendations for shock strength and sequence in human defibrillation are remarkably scant. A 1998 AHA Scientific Statement commented that the "reputed 'gold standard' is largely speculative and based on common-sense extrapolations from animal data and human case series."[77] In addition, the end point of such studies is not always clear. Should one concentrate on the first shock efficacy, all shock efficacy (rhythm at the time of transport or termination of defibrillator monitoring), or survival to hospital (or discharge)? Furthermore, as stated above, survival from VF conversion is intimately related to the response time and availability of bystander CPR.

A comparison of monophasic defibrillation at 175 J vs 320 J for the first shock, in 149 patients with out of hospital arrest, showed an identical (61%) first-shock defibrillation rate.[78] An abstract reporting the efficacy of a truncated exponential monophasic AED in 85 patients demonstrated first shock efficacy of 80%.[79] Behr, et al, reported a retrospective comparison of monophasic shocks (truncated exponential vs damped sinusoidal); in 85 patients, the first shock efficacy was greater for damped sinusoidal (66% vs 43%), but overall

survival to discharge was equivalent.[80] Thus, the efficacy of the first shock with monophasic waveforms varies from 43% to 80%.

VI. THE AUTOMATIC EXTERNAL DEFIBRILLATOR (AED)

The need to improve survival from sudden cardiac death was addressed in 1991 by the AHA with an article describing the "Chain of Survival": early access (as with 911), early CPR, early defibrillation, and early advanced life support. Because of the clear advantage of early defibrillation, the paper recommended that:

> "all communities should adopt the principle of early defibrillation. This principle applies to all personnel who are expected, as part of their professional duties, to perform basic CPR: They must carry an AED and be trained to operate it. Health professions who have a duty to respond to a person in cardiac arrest should have a defibrillator available either immediately or within 1 to 2 minutes. Responsible personnel should authorize and implement more widespread use of automated external defibrillation by community responders and allied health responders."[81]

Much progress has been made. In the early 1990's, few EMTs were authorized to use AEDs. By 1997, nearly all states authorized use of AEDs by EMTs; this expansion has related, in part, to the sanctioning of EMT operation and maintenance of AEDs in the US Department of Transportation's 1994 EMT basic national standard curriculum.

Data clearly support the use of AEDs by emergency personnel. For example, in Boston, survival from cardiac arrest increased 50% (from 16% to 24%) since 1994, when firefighters began training to use AEDs.[82] Never the less, in 1996 it was estimated that only 1/3 of the nation's ambulances and less than 5% of fire engines were equipped with AEDs.[83]

Legal issues:

At the state level, action is underway to increase widespread access to defibrillation. Legislation in Florida allows the use of the AED by anyone who has completed a first aid or CPR course that included AED training; this replaced previous regulations requiring 6 hours of training to use a defibrillator. In addition, the Florida Good Samaritan law was amended to cover persons, including those licensed to practice medicine, from any civil damage liability for reasonably prudent care that included the use of an AED.[84] Similar authorization and protection has been introduced in Tennessee, Louisiana, Nevada, Massachusetts and Hawaii. Such revisions of Good Samaritan laws are necessary, as "would-be AED users perceive a heightened legal risk flowing from the acquisition, deployment and use of the device. The current state of negligence law appears to support this perception."[85] Of note, the liability of *not* providing prompt defibrillation may be even greater. Busch Gardens was found negligent in 1996 for failure to adequately provide emergency care, including defibrillation. Lufthansa Airlines was found negligent for failure to provide timely treatment for a patient suffering a cardiac arrest.[85]

On the federal level legislation is also being developed. The Cardiac Arrest Survival Act calls for development of model state training programs for CPR. In addition, it recommends development of model state legislation to ensure access to emergency medical services (including consideration of location and placement of emergency equipment, including AEDs), as well as provision of Good Samaritan immunity for responders and owners and managers of locations where emergency equipment is placed.[84] Legislation to improve emergency medical equipment aboard commercial airlines has also been passed (discussed below).

Public Access Defibrillation:

The concept of public access defibrillation (PAD) was introduced in 1995 by the AHA Task Force on Automatic External Defibrillation.[86] This strategy called for defibrillation by minimally trained members of the public, and placement of AEDs in areas where large numbers of older people are under stress (such as airports and casinos) or to provide AEDs to nontraditional responders, such as police.[87]

An assessment of the potential cost-effectiveness of public access defibrillation in an urban area was undertaken recently. Based on historical data in a literature review, an overall survival of 8% was assumed, with increase to 8.7% for lay responders and 11.8% for police defibrillation. Using 1996 dollars, with assumption of one AED available for each cardiac arrest, at a cost of $2500, the cost per additional quality-adjusted life year was $44,000 for lay responders and $27,000 for implementation by police. The immediate cost of PAD by police was estimated to be $6500. Assuming United States population of 267,792 people, with 85% in urban areas, and an estimated 27% are >50 years old,[88] an estimation of the public health impact of PAD was calculated. Assuming a 0.7% rate of sudden death in this population, and a relative benefit of 1.5, implementation of PAD was estimated to potentially save >4065 additional lives annually with lay responders and >20,000 lives with defibrillation by police.[87]

Location of Public Access Defibrillators:

If PAD is to be implemented by lay responders, the AED must be placed in areas where it is most likely to be used. An analysis of the EMS registries of cardiac arrest in Seattle and King County, Washington (population 1.5 million in 1990) was performed for the first 5 years of this decade to identify the location of arrest.[89] For inclusion in the study, the arrests had to occur in a public place before arrival of EMS personnel and resuscitation by EMS must have been performed. A public place was defined as an indoor commercial or civic establishment or outdoors (except immediately outside a patient's home). Traumatic arrests and those occurring at private residences, nursing homes, clinics, doctors' offices, and fire stations were also excluded. Of the remainder, 89% were assumed to be due to heart disease.

A total of 8185 nontraumatic cardiac arrest occurred in the study period, of which 1130 (16%) were in public places. Of arrests in public, most were outdoors (32%) or in cars (15%). Ten of the 25 categories had a relatively high incidence of cardiac arrest, defined as $\geq$ 0.03 per

site, or $\geq$ 1 arrest per 30 sites. These are shown in table 2. The highest incidence was the Seattle-Tacoma International Airport, where 7 arrests occurred per year, all in the terminal (and none in the air).

Table 2: Incidence of Cardiac Arrest per Site: Higher-incidence Location Categories[89]

Location category	Arrests in 5 years	Number of Sites	Annual Incidence per Site	Number of Sites Required to Yield 1 Arrest per Year	Defibrillators Needed per Category
International airport	35	1	7	1	15
County jail	5	1	1	1	11
Large shopping mall	10	3	0.6	2	27
Public sports venue	11	6	0.4	3	24
Large industrial site	14	8	0.4	4	46
Golf course	23	47	0.1	5	47
Shelter	6	11	0.1	10	11
Ferries/train terminal	7	13	0.1	10	13
Health club/gym	18	47	0.08	12	47
Community/senior center	5	35	0.03	30	35
Total	**134**	**172**	**N/A**	**78**	**276**

The remaining 15 categories had $\leq$ 0.01 arrest per year, as shown in table 3. Of note, the highest numbers were seen in vehicles and "outdoors". Since there were so many vehicles (estimated 1,322,000), the incidence per site was very low. For the category of "outdoors," no denominator was available to calculate incidence. There was no attempt made to define the highest risk regions outdoors or to determine the distribution of AEDs necessary to serve the outdoor areas.

In the Seattle study, 60% of the arrests were in VF at the time of EMS arrival. Assuming a survival of 10%-40%, the authors calculated that between 8 and 32 lives might have been saved by placement of the 276 AEDs proposed in the table 2.[89]

Table 3: Incidence of Cardiac Arrest per Site: Lower-Incidence Location Categories[89]

Location category	Arrests in 5 years	Number of Sites	Annual Incidence per Site	Number of Sites Required to Yield 1 Arrest per Year
Entertainment place	68	1245	0.01	100
Hotel/motel	22	377	0.01	100
Private ambulance	3	106	0.03	167
Bus	31	1138	0.005	200
Bar/tavern	11	413	0.005	200
Civic/fraternal	7	316	0.004	250
Government office	6	448	0.003	333
Nonretail business	48	33662	0.003	333
Industrial manufacturing	40	3304	0.002	500
School/church	21	1943	0.002	500
Restraurant	36	4109	0.002	500
Retail store	47	17,390	0.0005	2000
Construction site	7	12,606	0.0001	10,000
Vehicles	168	1,322,040	0.0001	10,000
Outdoors	385	N/A	N/A	N/A
Total	**900**	**N/A**	**N/A**	**N/A**

Biphasic Waveform for Public Access Defibrillation:

With the need for smaller, lighter, less expensive AEDs, changes in the design and waveform have been explored. As discussed earlier, truncated biphasic waveforms have been studied in the basic laboratory, with consistent demonstration of benefit. In fact, a greater degree of benefit over monophasic waveforms in longer episodes of VF has been suggested in both *in-vitro*[90] and intact canine studies.[91]

The biphasic waveform, using lower energy, saves in terms of expense, volume and weight. The lower energy results directly in smaller requirements for battery and capacitor, smaller cable and transformer, and decreased isolation. In addition, truncated waveforms obviate the need for a device called an inductor. The inductor provides the shape of the damped sinusoidal waveform, but adds 150 ml volume and 300 gm of mass. It also causes a loss of 17% of the energy stored (so that 240 J must be stored to deliver a 200 J shock). Finally, the smaller energy shock in biphasic waveforms allows the use of smaller, more reliable solid-state switches (as compared with the larger switches that higher energy shocks require).[92]

There are surprisingly few data on the clinical use of biphasic waveforms, although devices using such shocks were approved by the FDA 2 years ago. In a single-center study of 30 patients undergoing transvenous ICD implantation, 115 and 130 J truncated biphasic waveforms were equivalent to 200 J damped sine wave shocks (97% first shock success).[93] In a multicenter study comparing 200 J monophasic damped sine wave with 200 J biphasic

damped sine wave shocks for cardioversion of VT and defibrillation in 171 patients, the biphasic waveform was superior (success of 97.6% vs 85.2%, p=0.005).[94]

A large multicenter study of truncated biphasic waveforms was undertaken in the cardiac electrophysiology laboratory during ICD implantation in 294 patients. Biphasic shocks (130 J or 150 J) were compared with 200 J and 360 J damped sine wave monophasic shocks. In both groups the first shock success was 86%. The success for 360 J damped sine wave monophasic appeared to be higher, at 96%, but did not reach statistical significance (as shown in table 4.) The authors suggested that the monophasic shock algorithm (200, 200, 360 J) or the biphasic algorithm proposed (130, 130, 130 J) would be equivalent at 99% efficacy; furthermore, the authors argued that even if the 360 first shock were more likely to be successful, potential damage from the shock would still mandate starting at lower outputs.[92]

Table 4: Characteristics of defibrillation in 294 patients with induced VF[92]

Waveform	Stored energy	Success	95% C.I.	ECG segment
130 J biphasic	140 J	86%	81-92%	-0.26±1.58
200 J damped sine	240 J	86%	81-91%	-1.86±1.93
360 J damped sine	435 J	96%	82-100%	-3.25±3.35

In the above study, there was no evidence of damage from any shock, although the ST segment, measured 10 seconds following the shock, was significantly depressed after the monophasic shocks, compared with biphasic shocks (-0.26±1.58 mm vs -1.86±1.93 mm).[92] Even more ST segment depression was seen following 360 J damped sine monophasic shocks, as shown in figure 9.[92] The significance of the ST segment changes is questionable, as they were transient and not associated with other evidence of cardiac injury. However, this study suggested equivalence between the lower truncated biphasic shock and higher output monophasic discharge.

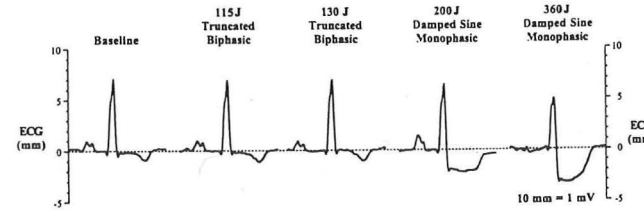

Figure 9. ST segments in a human who underwent biphasic and monophasic shocks of different strengths. Note the increased ST segment depression after the monophasic shocks. The clinical significance of this finding is unknown.[92]

There is just one published manuscript on the use of biphasic AEDs in the outpatient setting. In 44 patients with VF, the first shock defibrillation rate was 89%, with conversion of 80% after all shocks. Return of electrical activity was seen in 77% and a palpable pulse returned in 19/34, or 56%.[95] In comparison with the data available for monophasic defibrillation, these data suggest equivalency or superiority over traditional waveforms. Thus, the AHA Emergency Cardiac Care committee gave the endorsement that the "low energy, non-progressive (150 J, 150 J, 150 J), impedance-adjusted biphasic waveform shocks for patients in out-of-hospital VF arrest are *safe, acceptable, and clinically effective.*" The emphasis was that this did "not imply a higher class of recommendation for existing monophasic defibrillators." Furthermore, "any benefit of one waveform over another is unlikely to equal the magnitude of benefit" of their recommended Chain of Survival.[77]

Some experts are concerned that a fixed 150 J device might be inadequate in some patients, and prefer to have 360 J monophasic shocks available. Recent design improvements have resulted in development of light-weight monophasic devices. At present, there are 4 devices weighing 2-4 kg, each costing under $4000. Three are monophasic, delivering 200-360 J, and one implements the biphasic 150 J algorithm discussed above.[96]

VII. DEFIBRILLATORS ABOARD COMMERCIAL AIRCRAFT

Several recent articles in the press have addressed the issue of emergency care in the air, at times focusing on the relatively dramatic reports of passengers' arrests and the resulting frustration of their attending volunteers. It has been estimated that more Americans die naturally on airplanes than die from crashes.[97] Although accurate numbers are not available, an estimated 310 deaths occur worldwide on commercial aircraft, with 70-80 on US domestic carriers.[98] When a medical emergency occurs in the air, typically 40 minutes elapses before emergency ground assistance can be reached, even with an emergency diversion and landing. The delay makes survival from VF close to impossible without on-board equipment. In 1995, American Airlines had 157 medical diversions on its 803,000 flights, most for cardiac causes.[99]

Aside from the simple statistics that would apply, there appears to be an increased risk related to special circumstances associated with flying. (see table 5)

Table 5: Unique Risk of Air Travel

1. Relatively ill passengers (Americans with Disabilities Act, 1990)
2. Exertion in getting to gate
3. Circadian disruption
4. Stress of flying
5. Reduced oxygen (equivalent to 5500 to 7500 feet above sea level)
6. Failure to recognize arrest (even though in a public place)
7. Delay in reaching a medical facility

In 1986, mandatory first-aid kits were placed on all US flights. These included splints, bandages, scissors, antiseptic and ammonia inhalants, along with humidified oxygen to 4-6 l/min. Obviously, such a kit would be valueless in the setting of major emergency or VF arrest. In 1990 and 1991, respectively, Virgin Atlantic and Quantas airlines placed AEDs on aircraft. Quantas, with AEDs on 53 of 93 jets, reported 6 of 27 successful conversions of VF (4 in the airport and 2 in flight). [100] It is not surprising that ventricular fibrillation would be recognized more in the airport than on the aircraft, since in the terminal an arrest would be accompanied by falling and witnesses observing the moment of arrest; in contrast, on an aircraft a stricken passenger might not be noticed for quite a while.

In July, 1997, American Airlines put AEDs on 242 jets with over-water routes (40% of fleet). The pursers (lead flight attendants) are trained in the use of the AED, but are instructed to allow assistance from medical personnel (physicians, nurses, and EMTs/paramedics). Since the original phase, further commitment has been made, with now 360 jets equipped and anticipated 100% coverage by 2/99. In addition, an expanded kit with emergency medications and equipment for intubation is being placed. The flight attendants are not expected to administer drugs or intubate, but it is estimated that a physician is present on 85% of flights , and that 95% of physicians are willing to assist with a medical emergency in the air.[personal communication, David K. McKennas, MD, MPH, Director, Corporate Medical Department, American Airlines] The "Banyan" emergency kit that American Airlines designed has subsequently been adopted by Delta and United Airlines.

Issues of Liability:

As medical equipment is being provided to flight attendants and volunteers, liability issues have been raised. American Airlines has indemnified its employees. For volunteer assistants, the coverage has been less clear. Although most states have Good Samaritan laws, these are inconsistent, typically exclude the use of medical devices, and do not apply when outside US boundaries. Furthermore, state jurisdiction may be difficult to establish when a jet is traveling 500 miles per hour. In contrast to the liability of giving emergency care, there may be greater risk in *not* having an AED. In January the Washington Post reported "Doctors complain airplanes lack sufficient medical equipment" in an article describing the frustration of physicians treating a Delta passenger in cardiac arrest without an AED. Delta soon announced they were starting their own AED program.[101]

The issue of liability is becoming more clear. This Spring, the Aviation Medical Assistance Act of 1998 was passed by Congress and signed by the President. The liability of volunteers is limited, so they are not liable for damages related to rendering assistance, except in cases of "gross negligence or willful misconduct." The carrier is likewise indemnified, with no liability for acts or omissions of passengers rendering assistance as long as the carrier "in good faith believes that the passenger is a medically qualified individual". This act also requires the reporting of deaths on major carriers, with the plan to evaluate after one year whether AEDs should be on flights and in airports. In addition, congress will propose rules for how much training to require of flight attendants.[102]

American Airlines' Program:

At UT Southwestern Medical Center, we have developed a collaboration with the Corporate Medical Department at American Airlines. Next month we will present an abstract describing the first 48 deployments of the AED program.[103] In the period from June, 1997, to March, 1998, the biphasic AED was placed 48 times (42 in aircraft and 6 in the airport). Satisfactory function was observed in 47 cases, and data for analysis were retained in 40 (with the remainder having inadvertently erased the ECG tracing). A total of seven passengers died: one had 3 shocks but the data were lost; two patients had VF, with one dying in asystole after two successful defibrillation shocks, and the other surviving after a single shock (see figure 10)[104]. The remaining 4 patients who died were in asystole. Among the other passengers who had their rhythm recorded, sinus rhythm was recorded most, followed by atrial fibrillation, heart block, and junctional rhythms (see table 6).[103]

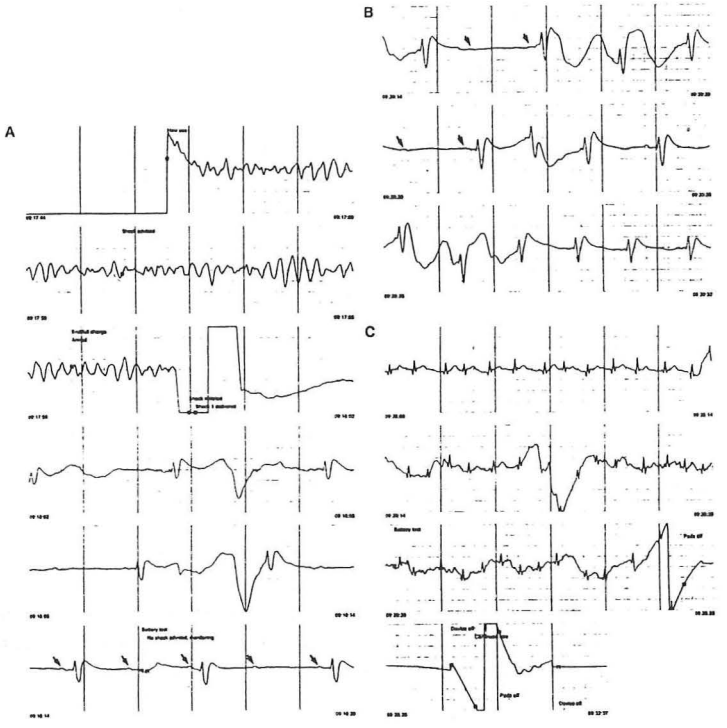

Figure 10. AED resulting in conversion of sudden death aboard an American Airlines jet. Note the successful conversion after 12 seconds that resulted in 2:1 heart block (panel A), followed by 1:1 conduction of sinus rhythm (panel B). Atrial fibrillation developed after 3.5 minutes (panel C). Normal sinus rhythm resumed as the patient was being transported to the ambulance. The patient ruled-out for myocardial infarction, underwent coronary artery bypass grafting and implantable cardioverter-defibrillator placement, and was discharged to home 11 days after the arrest.[104]

As noted above and in table 6, the AED functioned appropriately in terms of identifying VF and terminating it. Just as important is the ability of the device to distinguish rhythms that should not be shocked. As noted in table 6, for the 40 tracings available for analysis, the device was appropriate in distinguishing VF with 100% sensitivity and 100% specificity.[103]

Table 6: Rhythms Observed with the AED in the American Airlines Program[103]

	Sinus	A Fib	Junctional	Heart Block	Asystole	VT/VF
Episodes	31	5	2	3	4	2
Shock	0	0	0	0	0	3(3)

Shock= delivered (successful); n = 40

The American Airlines AED program is being expanded, so that all of the 645 jets will be furnished with the device by February, 1999. As we continue to gather these data, and similar programs are implemented on other airlines, this population, and the utility of the AED will be further defined.

Aside from the human cost of sudden cardiac death in the air, it is expensive to divert an aircraft. It may be argued that an airline AED program would pay for itself in terms of avoiding diversion. If a patient has a stable rhythm, or if an unconscious patient has no rhythm at all (asystole), diversion could be avoided. In the first 9 months of the American Airlines program, 15 flights were diverted, but it is estimated that diversion was avoided in another 15 cases.[103]

VIII. FUTURE DIRECTIONS

There are limitations to the results obtained even with rapid CPR and use of the AED. Even in Seattle, only 40% of SCD patients are found in VF and of these, only 26% are discharged from the hospital neurologically intact. This calculates to 10.4% survival as a maximum for a system such as Seattle's. With public access defibrillation, we can hope for still better results. AEDs might one day be as ubiquitous as fire extinguishers. The key to still greater reduction in sudden cardiac death remains prevention and perhaps better identification of the highest risk individuals appropriate for intervention (such as implantation of an implantable cardioverter-defibrillator).

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