**Clinical question.**

“In pediatric patients with cardiac arrest due to primary or secondary VF or pulseless VT (pre-hospital [OHCA] or in-hospital [IHCA]) (P), does the use of a specific energy dose or regimen of energy doses for the initial or subsequent defibrillation attempt(s) (I), compared with standard management (C), improve outcome (e.g. termination of rhythm, ROSC, survival to hospital discharge, survival with favorable neurologic outcome) (O)?”

**Is this question addressing an intervention/therapy, prognosis or diagnosis?** Intervention/therapy.

**State if this is a proposed new topic or revision of existing worksheet:** New topic

**Conflict of interest specific to this question**

Do any of the authors listed above have conflict of interest disclosures relevant to this worksheet? No.

**Search strategy (including electronic databases searched).**

1. AHA Endnote 9 library (24.03.08): child AND electric countershock AND heart arrest (37) OR cardiopulmonary resuscitation (39)
2. Clinical trials.gov: electric countershock AND heart arrest (24) OR cardiopulmonary resuscitation (8)
3. Cochrane library: Electric countershock AND heart arrest (1-review), (7-other reviews), (102 clinical trials) OR cardiopulmonary resuscitation - (2-review), (3-other reviews), (65 clinical trials)
4. Pubmed: Child tw/mesh AND electric countershock tw/mesh AND heart arrest tw/mesh (150) OR cardiopulmonary resuscitation tw/mesh (97) Review of reference lists of articles.

Search updated 10.10.09 and in late 2010, an additional in press article by Tibballs et al was added following permission of author and publisher.

**State inclusion and exclusion criteria**

**Inclusion:**
Completed trials that study dose/regime of defibrillation in pediatric patient(s) or animal model(s) and which have a measure of outcome.

**Exclusion:**
Abstract only.

**Number of articles/sources meeting criteria for further review:**

32 articles reviewed in detail
## Summary of evidence

### Evidence Supporting Clinical Question

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**Level of evidence**

A = Return of spontaneous circulation  
B = Survival of event  
C = Survival to hospital discharge  
D = Intact neurological survival  
E = Other endpoint  
*Italics = Animal studies*
### Evidence Neutral to Clinical question

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**Level of evidence**

- **A** = Return of spontaneous circulation
- **B** = Survival of event
- **C** = Survival to hospital discharge
- **D** = Intact neurological survival
- **E** = Other endpoint

### Evidence Opposing Clinical Question

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**Level of evidence**

- **A** = Return of spontaneous circulation
- **B** = Survival of event
- **C** = Survival to hospital discharge
- **D** = Intact neurological survival
- **E** = Other endpoint

*Italics = Animal studies*
In 2005 the European Resuscitation Council guidelines included a notable departure from the ILCOR recommendations of the same year in terms of defibrillation – changing the weight based energy dose in children from 2/4/4 J/kg to 4J/kg for first and subsequent shocks (Biarent, 2005). This change was attributed to biphasic doses of 3-4J/kg being considered superior to lower doses (Berg, 2004b; Clark, 2001; Faddy, 2003; Tang, 2002) and the apparent safety of these larger defibrillation doses (Gurnett and Atkins, 2000; Rossano, 2006). A more detailed review of the literature suggests that outcomes may possibly be improved by altering energy levels from 2/4/4J/kg to 4/4/4J/kg, but it is based largely on animal data and scanty human reports.

The basis for previous recommendations rests largely on one trial in which mainly pediatric cardiac patients (20/27) had VF rapidly terminated in hospital soon after cardiac operations (Gutgesell, 1976). Animal data existed from a similar era (Geddes, 1974) which supported these energy levels. Preceding the introduction of biphasic waveform defibrillators and with the use of AEDs in pediatric patients, there was a plethora of pediatric animal models and some patient studies to examine and refine an appropriate pediatric energy dose regime. There have been two studies which suggest the energy dose should remain unchanged. The first is an animal model in which 19kg pigs received either ~2/4/4J/kg or 10/15/18J/kg via an AED. The higher doses were 3 times more effective in effecting first shock VF termination, but about 3 times less likely to achieve a good neurological outcome at 24hrs. The higher dose was also associated with impaired myocardial function, so despite a more rapid termination of VF (due to the higher dose), overall outcome was worse and this data supports the use of pediatric attenuated AEDs (Berg, 2005b). The same group of researchers reviewed a 5 year cohort of out of hospital arrests. Following 2J/kg DC shock 7/14 instances of VF/VT reverted in 11 patients, none however to perfusable rhythms and no patients survived. The shocks that terminated VF tended to be lower energy, than those that didn't - 2.3J/kg (median 2.2) vs 4.8J/kg (median 3.8), p=0.063 (Berg, 2005a).

An increasing number of case reports with insufficient information to determine an energy dose effect have been published (Divekar and Soni, 2006; Khoury and Shavit, 2009; Rey, 2007). Several excellent multicentre cohorts of pediatric arrest patients have also been published, but do not contain sufficient energy dose information (Atkins, 2009; Samson, 2006). As a consequence pediatric animal models, together with a heterogeneous group of pediatric patient studies provide contributory data to determining an energy dose for defibrillation in VF/pulseless VT.

Time to successful defibrillation is an important consideration in the treatment of VF/VT. Out of hospital defibrillation within 3 minutes of VF results in >50% survival, with survival dwindling to <5% after 12 minutes of VF (Berg, 2004a). Increased energy results in more rapid VF termination, but at the risk of increased myocardial damage (Babbs, 1980). Clark et al showed that ROSC was seen following brief VF, in >80% using 4J/kg and 3J/kg in ~5kg and 9kg pigs respectively, but if 2J/kg was used these rates fell to 25% and 32% respectively – with no differences in surrogates of myocardial dysfunction (Clark, 2001). Similarly Berg et al showed in a prolonged VF porcine model that a higher biphasic dose (~10J/kg) was significantly more effective than a lower dose (~2.5J/kg) in terminating VF with first shock success 19/26 versus 8/26. There was however equivalent survival and degrees of myocardial dysfunction in the two groups (Berg, 2008).

A recent in press article by Tibballs et al described 48 inpatients with VF/VT that were defibrillated with a mean dose of 1.7J/kg and the dosage and outcome recorded (Tibballs, 2010 in press, with permission). Eighty percent of patients were in PICU/OT and had a cardiac diagnosis, but it is unclear why defibrillation doses lower than current recommended guidelines were delivered. Twenty percent of patients subsequently received internal defibrillation. Initial doses of 2.0±1.0J/kg were successful in 48% and the remainder were unsuccessfully defibrillated with 1.5±0.7J/kg. Subsequently 58% successfully received 2.6±1.1 J/kg 1-8 times and the remaining 10 patients were unsuccessfully administered 3.2±1.2J/kg, 1-8 times, eight of these 10 patients received internal defibrillation. Overall 94% of patients recovered from the event and 73% survived at least 12 months. Dose greater or less than 2J/kg was not significantly associated with ROSC or any other outcome, but ~2J/kg resulted in less than 50% ROSC with the first shock.

In a large series of pediatric patients with information on energy doses and outcome there was the suggestion by Rodriguez-Nunez et al that an initial and subsequent dose of 4J/kg may lead to improved outcome (Rodriguez-Nunez, 2006). A shockable rhythm was found in 44 patients, initial defibrillation with 2J/kg or less led to 89% of these patients needing more than 1 shock, those receiving > 2J/kg required more than one shock 43% of the time, p=0.017. Similar to the animal models though this more rapid termination of VF was not associated with superior survival, with only 3 patients surviving one year. Tibballs et al earlier described the energy doses used to terminate VF in 7 inpatients. Four had ROSC and survival at 1 year, they received a median dose of 4.3J/kg versus 3.6J/kg in those without a pulsatile rhythm following VF termination, p=0.7 (Tibballs and Kinney, 2006). In the largest group of pediatric patients with VF (n=57) there was no clear association between energy dosage and outcome for the 19 who survived to discharge.
although 16/19 had received doses of >4-6J/kg (Rossano, 2006). Several case reports and a small case series documented large pediatric DC shocks with intact survival ranging from 7 - 9J/kg (Atkins and Jorgenson, 2005; Gurnett and Atkins, 2000; Konig, 2005), hinting at efficacy as well as safety or at least tolerance of these energy doses.

The animal models in particular have explored tolerance and safety of higher defibrillation energy doses. Tang et al in a porcine model of out of hospital VF showed no difference between groups of pigs weighing 3.8, 7.5, 15 and 25kg, upon receiving a 50J biphasic shock – in terms of hemodynamic parameters. This suggests safety and efficacy with doses of 13.2J/kg, 6.7J/kg, 3.3J/kg and 2J/kg for the 4 groups respectively (Tang, 2002). Berg et al also demonstrated safety and efficacy with a porcine model compared to 2/4/4J/kg in animals that received a first shock of 2-12J/kg (Berg, 2004b). Earlier work indicated that persistent myocardial injury occurred with individual shocks of up to 150J/kg (Gaba and Talner, 1982) and more recently individual doses of 90J/kg were tolerated (Killingsworth, 2002), both of which suggested a generous safety margin, which has been shown in the case reports of AED use (Gurnett and Atkins, 2000; Konig, 2005).

Larger initial defibrillation doses appear to have crept into current practice, this may be a consequence of rounding up of energy doses to suit defibrillators or out of desperation in critical arrest situations. An initial dose of 4J/kg could potentially result in greater first shock success, which may improve outcome and the available safety data would suggest it should be well tolerated (Berg, 2008; Berg, 2004b; Clark, 2001; Rodriguez-Nunez, 2006; Tibballs and Kinney, 2006).

Acknowledgements:
Nil.

Citation List


Worksheet author comments:
LOE 4 pediatric registry study detailing the incidence of OHCA. Outcome (survival) was superior in children and adolescents, compared with the infant and adult age groups.


Worksheet author comments:
LOE 4 retrospective review of adolescents receiving 200-360J via an AED. Seven patients had recognised VF and received DC shock with 3/7 discharged from hospital - these patients were 12, 15 and 15 years and are likely to have received greater than 2J/kg, all 3 had 2 - 3 doses of 200J.


Worksheet author comments:
LOE 4 retrospective review of pediatric AED recipients 8/27 arrested patients (all less than or equal to 8 years old apart from one 10 year old) had VF and were defibrillated with 50J. Five survived to hospital discharge - including an 18month old (2 shocks), a 3 year old (1 shock) and a 6.3kg 4.5 month old (1 shock). The use of > 2J/kg was successful in the resuscitation of these patients, the 3 patients who were shocked and did not survive included 2 drowning victims and 1 patient who had an AED applied after 10 minutes - suggesting long arrest duration was a factor.


Worksheet author comments:

LOE 5 canine defibrillation trial which used 65 dogs (~8kg) including a non defibrillated control group and defibrillated these with 1-500J/kg. Hearts were examined histologically for evidence of damage and energy to dose response curves were constructed. Biological variability was seen, but there was very minimal overlap between defibrillation curves and morphological damage curves. Effective defibrillation was achieved at a median dose of 1.5J/kg and morphological damage occurred at a median dose of 30J/kg.


Worksheet author comments:

LOE 5 model of 7 minutes duration VF, with 52, approximately 19kg pigs randomized to biphasic 200/300/360 J OR 50/75/85 J. The pediatric dose (~2.5J/kg) was less effective in terminating VF with first shock 8/26 versus the adult dose (~10J/kg) 19/26, p=0.005. Overall ROSC was not different. Troponin was raised in 4/20 paediatric dose pigs and 11/19 of the adult dose group, p=0.02. Left ventricular dysfunction was different from baseline in both groups at 4 hours, although the decrease was greater with the adult group. There was equivalent survival at 24hours in both groups, myocardial dysfunction in both groups and earlier termination of VF in the adult dose group.


Worksheet author comments:

LOE 3 retrospective review of out of hospital cardiac arrests. Failure of 2J/kg DC shock to terminate VF occurred in 7/14 out of hospital shocks to 11 patients. None of the remaining 7 defibrillations which terminated VF led to ROSC, with no survival to hospital discharge. The median time to scene was 11 minutes and this was an important factor. On average the shocks that terminated VF trended to be lower than those that didn't - 2.3J/kg (median 2.2) vs 4.8J/kg (median 3.8), p=0.063 (MWU) - although interstingly this lower dose of monophasic DC was still enough to potentially cause asystole/pulseless eletrical activity - perhaps an indicator of the duration of arrest.

Worksheet author comments:

LOE 5 study that reviews the relevant animal and human studies, specifically with respect to pediatric AED dosing being superior to adult dosing. It also details the variation in outcome (survival) following ROSC from VF arrest after 3 minutes (>50%), as opposed to <5% after 12 minutes without ROSC.


Worksheet author comments:

LOE 5 porcine model of 7 minutes of VF randomised to therapy with biphasic AED attenuated to 51/78/81J or monophasic 2/4/4J/kg in 4kg, 14kg and 24kg pigs (n=16 per weight group). Attenuated biphasic shocks resulted in significantly improved survival with good 24hr neurological outcome in the 24kg pigs and superior left ventricular ejection fractions - note that the initial dose of 2J/kg is essentially equivalent between groups - apart from its biphasic nature with the AED. The 4kg and 14kg pigs had strong trends towards better 24hr survival and good outcome in the AED group and equivalent Left ventricle ejection fractions supporting safety in these sized pigs (receiving ~12J/kg and 4J/kg respectively for the first shock) and equivalent efficacy.


Worksheet author comments:

LOE 5 porcine (19kg) model of 7 minutes duration VF randomized to biphasic pediatric dose 50/75/86J ~ 2/4/4J/kg OR adult dose 200/300/360J ~ 10/15/18J/kg. Paediatric dose resulted in less effective 1st shock VF termination 4/16 versus 12/16 (p=0.01). However time until ROSC and 24hr survival were similar - with a trend towards improvement with the pediatric dose. And 24hr survival with good neurologic outcome was superior after pediatric shocks 13/16 versus 4/16, p=0.004 - although the neurologic evaluations were not blinded. Left ventricular ejection fraction decreased less after pediatric shocks (p<0.05) and troponin was elevated in 6/12 adult shocks and not after any pediatric shocks, p=0.005. Suggesting a superior initial termination of VF comes at the expense of myocardial injury and subsequent neurological injury.


Worksheet author comments:

LOE 5 consensus document states that animal models demonstrate pediatric doses of 3-4J/kg give better results than lower or adult doses (which are presumably higher). It goes onto state that doses larger than 4J/kg have succeeded in children with negligible side effects and recommends 4J/kg for first and all subsequent doses.

Worksheet author comments:

LOE 5 porcine brief (15sec) VF model - comparing monophasic and biphasic external defibrillators and measuring ROSC at a given energy dose in 12, 3-6kg and 15, 7-12kg pigs. ROSC > 80% was seen with 4J/kg in the smaller pigs and at 3J/kg in the larger pigs - using biphasic shocks, compared with <25% using the same dose as a monophasic waveform. 2J/kg biphasic shocks yielded about 25% (small pigs) and 32% (larger pigs) for ROSC. Pulseless electrical activity was interpreted as a surrogate of post defibrillation myocardial dysfunction. This occurred in two infants with biphasic shocks at 7 and 10J and in one infant with monophasic at 50J and one larger pig also at 50J. For in hospital arrests this animal data supports biphasic 4/4/4J/kg.


Worksheet author comments:

LOE 4 case report of an 8kg, 8 month old with Long QT syndrome. The AED was modified to give a weight based dose and appears to have given a 3rd dose of 18J, after which ROSC occurred and neurologically intact survival occurred. Specific discussions about the dose prescribed are not discussed in detail within the article.


Worksheet author comments:

LOE 1 adult study of randomised trials of monophasic and biphasic DC shock with varying doses. This found equivalent first shock success and less ST segment deflection with lower doses. Comparison was between mono/biphasic, rather than between different doses of biphasic DC shock.


Worksheet author comments:

LO5 piglet (~1-3kg) VF model of escalating doses of monophasic DC shock (20 - 200J/kg). Myocardial technitium scans found evidence of injury at greater than 150J/kg, suggesting a large safety margin.

LOE animal study of VF induced in animals ranging from rabbits to horses. Energy doses required were related to animal weight. It was determined that for subjects up to 7kg, the energy dose was 2J/kg, from 7-40kg was 2-5J/kg and above 40kg was 5-10J/kg, based on a monophasic DC waveform.


LOE 5 animal study (10 pigs 3.8-20.1kg). AED used with pediatric or adult pads at doses of ~2J/kg up to 200J in 20J steps. Larger doses up to 360J were also administered. Defibrillation threshold was steeper with pediatric pads. The mean time to first perfusing beat following VF was ~5 seconds with both pad sizes. None of the measured parameters (ST changes, LV dP/dt, time to mean 40mmHg LV pressure) indicated persistent myocardial injury in piglets that received individual shocks of up to 90J/kg. Given this demonstrated safety margin efficacy rather than potential for injury should be the main focus.


Worksheet author comments:
LOE 4 case report of a 6 year old with long QT who had an arrest and had compression commenced within 5 minutes. She weighed 20kg and received a 150J biphasic AED shocks for VF, resulting in temporary asystole, subsequent VF again developed and a 2nd 150J shock again resulted in asystole and then sustained sinus rhythm, with palpable pulses. She was discharged from hospital neurologically intact after receiving two ~7J/kg DC shocks.


Worksheet author comments:
LOE 4 case report of a 14 year old who had an arrest and was attended to within 5 minutes, developed VF and was shocked once with 150J resulting in a perfusing rhythm within 1 minute. He was found to have a cardiomyopathy and was discharged home neurologically intact after receiving probably a 2 - 3 J/kg DC shock.


Worksheet author comments:
LOE 4 observational study of pediatric arrests from Spain found a shockable rhythm in 44 patients. Initial defibrillation with 2J/kg or less led to 89% of these patients needing more than 1 shock. Those receiving more than 2J/kg initially needed more than 1 shock about half as often, 43%, p=0.017, although ROSC and subsequent survival were not different. Overall ROSC occurred in 28(64%), lasted 20 minutes in 19(43%) and resulted in 4 hospital discharges and 3 survivors at 1 year (6.8%), one of whom had normal pediatric cerebral performance category assessment. This suggests that 2/4/4J/kg for out of hospital and in hospital arrests could be improved by increasing the first shock dose.


Worksheet author comments:
LOE 4 retrospective review of emergency medical services over a 16 year period for under 18 year olds receiving DC shock for VF. Patients were grouped according to DC dose administered - recommended (2-4J/kg), moderately high (>4-6J/kg) and higher(>6J/kg). Survival was not related to dosage of DC, but duration of CPR, presence of bystander CPR. Survival occurred with doses from 3J/kg to 73J/kg and cumulative doses were 10 and 11J/kg for survivors and non survivors. Of the 19 (33%) survivors to hospital discharge, following a median 20 minute arrest, 16/19 had moderate to high doses of DC shock(>4-6J/kg). Of the 36 non survivors of arrests that lasted at least twice as long (51mins) 31/35 had moderate to high doses of DC shock - potentially corresponding to a relatively less "dense" dose of DC shock. There appears to be use of higher than recommended doses in practice.


Worksheet author comments:
LOE 4 pediatric registry study details the frequency, nature and outcome of 1000 pediatric cardiac arrests. Interestingly survival was greater in primary rather than secondary VF, suggesting scope for good outcomes with prompt treatment of VF.


Worksheet author comments:
LOE 5 piglet VF (7mins) model using 50J biphasic DC shocks for 3.8kg(13.2J/kg), 7.5kg(6.7J/kg), 15kg(3.3J/kg) and 25kg(2J/kg) animals. Showed no difference in post resuscitation myocardial dysfunction between the different weight pigs, with normalisation of function (LV ejection fraction) within 4hrs. All had ROSC (n=5 in each weight group), the 3.8kg group needed ~3 shocks, the 7.5 and 15kg groups needed ~2 shocks and the heaviest 25kg group needed ~ 5 shocks - suggesting increased impedance in the smallest pigs and a possible dose effect in the largest pigs. Additionally 3 groups of pigs with VF (each n=3) received 50J via an attenuated adult AED. All had ROSC, the 3.7kg group requiring 2.7 shocks, the 13.5kg group requiring 2.3 shocks and the 24kg group requiring 4.7 shocks - again possibly consistent with a dose effect. Haemodynamic function (LV ejection fraction) recovered within 4 hours and was not different between groups defibrillated with the AED. Doses greater than 2/4/4J/kg were associated with ROSC and acceptable function.


Worksheet author comments:
LOE 4, prospective group of inpatients ~80% with cardiac diagnosis in PICU/OT had VF/VT. Initial defibrillation with 1.7J/kg was ineffective in >50%. Subsequent doses of ~ 2-3J/kg were effective, but dose was unrelated to ROSC or long term outcome which included 73% surviving greater than one year. Twenty percent of patients had internal defibrillation, all defibrillation was prompt, probably within three minutes, but
it was not recorded. 2J/kg was ineffective overall and subsequent higher doses were successful in most patients.


Worksheet author comments:

LOE 4, prospective group of paediatric cardiac arrest patients (n=111), with VF/VT in 10(9%). Seven of these patients had termination of VF, one spontaneously, the others after monophasic DC shock. The DC doses of those with termination of VF was noted. Four patients reverted to a pulsatile rhythm and survived 1 year, they had an initial dose averaging 3.9J/kg (median 4.3J/kg). The other three patients did not develop a pulsatile rhythm after VF termination, they had a slightly lower initial DC dose of 3.4J/kg (median 3.6J/kg), p=0.7(MWU).