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PAPER

PATHOLOGY/BIOLOGY

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Exposures to Conducted Electrical Weapons (Including TASER® Devices): How Many and for How Long are Acceptable?*

ABSTRACT: TASER® conducted electrical weapons (CEWs) are an important law-enforcement tool. The purposes of this study are a) to review recent literature regarding potential pathophysiological responses to applications of CEWs, and other related issues and b) to evaluate whether enough data exist to determine the acceptability of longer-duration (or repeated) exposures. This is a narrative review, using a multidisciplinary approach of analyzing reports from physiological, legal-medical, and police-strategy literature sources. In general, short-duration exposures to CEWs result in limited effects. Longer-duration or repeated exposures may be utilized with caution, although there are currently not enough data to determine the acceptability of all types of exposures. Data examined in the literature have inherent limitations. Appropriateness of specific types of CEW usage may be determined by individual police agencies, applying risk/benefit analyses unique to each organization. While more research is recommended, initial concepts of potential future long-duration or repeated CEW applications are presented.

KEYWORDS: forensic science, TASER, conducted electrical weapon, conducted energy weapon, electronic control device, electromuscular disruption

A conducted electrical weapon (CEW) is an operator-controlled apparatus (alternatively referred to as an "electronic control device," "conducted energy weapon," "electric shocking device," "electromuscular incapacitating device," or "electromuscular disruption device") that transmits electric pulses through wires attached to "probes" (essentially darts) into a subject, causing involuntary muscle contractions that result in incapacitation. In some cases, there may be essentially "board-like rigidity" ("strong, fused contraction of all extremities with immediate loss of posture" [1]). Some effects may also be due to "programmed behavioral responses to pain" (2). Such devices are used by both civilian and military law-enforcement agencies. The most widely used CEWs are manufactured by TASER International, Inc. (Scottsdale, AZ). ("TASER" is a registered trademark of TASER International.) In one study of seven classes of less-lethal weapons, CEWs were considered to be the most effective tool for ending confrontations with subjects (3). In a comprehensive study of 12 police agencies (4), deployment of a CEW reduced the odds of suspect injury by almost 6%. In contrast, Terrill and Paoline (5) reported a positive association between the use of CEWs and citizen injuries. It is important to note, however, that *severity* of injuries was not included in the latter study. One of the most effective CEWs has been the TASER International "X26"™ device (6).

Applications of CEWs have been considered to be contributory factors in some deaths, even with short durations of exposure (reviewed in [7,8]). In contrast, some multiple repeated exposures have occurred in other instances without major detrimental effects noted (e.g., [9]). In a comprehensive study of 392 arrest-related deaths in which CEWs were deployed (10), the device was determined to be the primary cause in only two cases and a contributory factor in 16 cases.

The purposes of this study are a) to review recent literature (generally 2008–2013, unless not reviewed previously) regarding potential pathophysiological responses to applications of CEWs, and other related issues and b) to evaluate whether enough data exist to determine the acceptability of longer-duration (or repeated) exposures.

Description of Literature Sources for this Review

Studying the use of CEWs requires investigations across broad disciplines of criminology and science (11). Publications for the current review were identified from multiple sources, including the National Library of Medicine's PubMed® (including MEDLINE® [Medical Literature Analysis and Retrieval System Online]) and databases of EBSCO® Industries (Academic Search™ Complete, MasterFILE Premier, Military & Government Collection, Science & Technology Collection, Legal Collection, Psychology & Behavioral Sciences Collection, SocINDEX, and WorldCat). Other searches were performed using the U.S. Department of Justice's National Criminal Justice Reference Service Abstracts, the Defense Technical Information Center Online, Stanford University's HighWire® Press, Springer-

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Link©, and Online Computer Library Center's FirstSearch® (including General Science Index, Applied Science & Technology Index, Electronic Collections Online, and ArticleFirst®). Google Scholar® was searched for any additional references. Search terms included: taser*, "stun gun*", (neuromuscular AND incapacit*), (electromuscular AND incapacit*), "electronic control device*", "conducted energy weapon*", "conducted electrical weapon*", "electronic control weapon*", and "conductive energy weapon*". Inasmuch as the use of electronic databases alone may not identify all relevant articles for a particular topic, "hand searching" (12) was used with tables of contents from legal-medicine, emergency-medicine, criminology, and police-science journals. Other items from the "grey literature" (13), such as technical reports, official documents not published commercially, and preprints, were also reviewed.

Unfortunately, only a few research organizations have studied responses to CEW exposures. Thus, the reader will note multiple references to only a few authors' works. Some aspects of physiological responses to CEW applications were reviewed previously (e.g., [7,8,14-17]). In the current review, the author generally has not repeated or reiterated significant portions of information or references already cited in those previous reviews, unless new aspects are discussed.

Concepts of "Safety" and "Acceptability"

CEWs may be used with a risk that is acceptable, compared with alternative methods to achieve incapacitation in a given situation. The use of force by police and the ideas of "safety" or "acceptability" must be considered in a contextual framework (18). This framework is based on a balance between: (i) the amount of risk of resistance or harm the police are confronted with and (ii) which options of force are available and appropriate for use in a given situation. The primary objective, when using a CEW properly, is to gain control of an individual in a situation in which violence is imminent. Such a situation does not occur with "zero risk" (19). Controversial questions include (i) where CEWs should be placed on a use-of-force continuum (20) and (ii) what limitations should be identified for such usage (20).

The number or duration of CEW applications deemed acceptable is dependent on the degree of risk of adverse biological effects that a specific user organization allows. Most current law-enforcement usage of the TASER X26 CEW by different agencies has generally been deemed reasonable from a risk/benefit ratio point of view. Longer-duration applications, however, have not been studied enough to be generally accepted as appropriate.

The strong muscle contractions caused by CEW exposures may result in some findings qualitatively similar to those from previous studies of muscular exercise (16). Although some of the changes in selected physiological factors due to CEWs may be greater in magnitude than changes after exercise, the changes would not necessarily be great enough to cause any detrimental effects. Jenkins et al. (21) found that all ten of a group of anesthetized swine survived 3 min of continuous exposure to the X26 CEW. (The animals were mechanically ventilated with 100% oxygen during the whole period of exposure). Ziriax et al. (22), studying lethality as an endpoint, reported that anesthetized pigs could survive repeated intermittent CEW exposures for periods greater than 3 min under certain conditions. Such survival, however, would not be guaranteed in animals or humans in all situations.

One group of investigators (23) recommended that CEWs should not be discharged for longer than 3 sec during a single application. Most currently available CEWs, though, automatically discharge for longer periods. In addition, the standard 5-sec pulse of an X26 device can be extended by depressing the trigger, and allowing electric current to flow continuously until the trigger is released or power is drained from the device. In an example of one department's directive regarding CEW use (24), specific guidance was not provided for use of the long-duration option. Several organizations and investigators have warned against multiple applications or continuous cycling of the CEW (see, e.g., [25] and other references summarized in [26]). The use of multiple CEWs at approximately the same time or more than three repeated applications have generally been considered to be inappropriate during law-enforcement activities (27). As pointed out by Brewer and Kroll (28), the first suggestion of such a "safe limit" was apparently proposed by Czarnecki (29), without any solid basis for such a recommendation. Bunker (30) contended that failure to define a threshold for the number of allowable CEW exposures would result in police convincing a noncompliant subject to stop resisting arrest "by means of whatever number of [CEW] shocks it takes—which would probably be unacceptable." Brave (31) noted that several police organizations have listed a total of 15 sec (repeated applications or continuous exposure) as a significant "safety point." Some authors (32) cited what was claimed to be "advice published by Taser International suggesting that police should limit multiple Taser use to a 15 sec exposure, either multiple cycle or continued use." TASER International (33), however, simply presented a suggestion that "every... trigger pull or 5 sec of discharge must be justified under the specific circumstances," rather than proposing any relatively arbitrary number. Brave (34) discussed police-policy reasons for applying more than one completed CEW discharge to a subject. A complete discussion of policies of different police organizations is beyond the scope of this review.

Vilke et al. (35) indicated that, although some previous studies included CEW-exposure durations of 20–45 sec without obvious detrimental physiologic effects, the small amount of literature altogether was inadequate for investigators to provide the basis for guidelines regarding longer-duration exposures. It may not be valid to extrapolate results from single short-duration CEW applications to predict the safety of multiple exposures. To date, a standard definition of what constitutes a "prolonged" exposure has not been achieved, regarding either number of repeated interrupted applications or continuous duration.

Studies of Humans vs. Studies of Animals

Studies of CEWs have used both humans and animals (mainly the pig *Sus scrofa*) as subjects. Human subjects were often recruited from populations of law-enforcement officers in training courses. Some of the studies of animals were performed, not to analyze effects of standard law-enforcement usage, but rather to initially characterize potential effects of repeated or long-duration CEW applications that may be used in the future for relatively long-term incapacitation (e.g., [36-41]).

The "locking up of muscles" caused by CEWs (with falling down as a result) is not a conscious behavioral response. Thus, anesthetized animal preparations may be useful for studying physiological effects of CEW-induced muscle contractions. Although some investigators may argue that only conscious animals can be used to simulate a "real-world" CEW-exposure scenario, simply handling such animals may lead to baseline changes in preexposure factors (such as acid-base status [42]).

As Ho (43) noted, "Animal models can point toward certain directions but interpret the results with caution." Nonetheless, animal experiments may be used as hypothesis-generating studies. A particular swine model (44) has been used specifically to investigate out-of-hospital cardiac arrest (which could happen during law-enforcement activities). Other swine models (e.g., [14]) were developed to investigate blood-factor changes that occur immediately after CEW applications. An anesthetized animal preparation has the advantage of facilitation of muscle-contraction measurements. Using such a model, investigators can examine basic physiologic changes (without cognitive effects) that may be relevant when developing hypotheses of interaction.

In an example of one model (14), because no major surgery was required for the preparation, particularly deep anesthesia was not required. The result was an animal model with spontaneous respiration (baseline mean respiration rates ranged between 21 and 34 breaths per minute [37,39-41]). In addition, artificial mechanical ventilation was not performed during CEW application, to avoid any animal fighting the respirator (i.e., breathing out of phase with the mechanical ventilator). Total intravenous anesthesia was used rather than volatile gas anesthesia, to avoid reducing spontaneous ventilatory efforts (45).

Obviously, some behavioral effects, such as those that could result from pain caused by CEW applications, would be missing in an anesthetized preparation. Werner et al. (46), however, suggested that basic physiological responses to CEW exposures should not be greatly altered by anesthesia. Longer-duration CEW exposures in human subjects or in conscious animals would require approval of Institutional Review Boards and Institutional Animal Care & Use Committees, respectively.

Potential Involvement of Excited Delirium during Incidents Involving CEW Exposures

A discussion of CEW effects would not be complete without considering the syndrome referred to as "excited delirium." This syndrome is one possible explanation of unexpected deaths of suspects in police custody (47,48). The condition may occur often in subjects who are subsequently exposed to CEWs. Earlier investigators required inclusion of death as a requirement for strict definition of excited delirium. On the basis of current opinions, the syndrome can be defined by behavioral and clinical characteristics, without the occurrence of death required for a diagnosis (49). As noted by Dr. G. Vilke, when excited-delirium syndrome is observed in an emergency department, the majority of patients can be treated, with an estimated mortality of 8–11% (50). In one cohort of consecutive subjects who experienced law-enforcement use of force and exhibited signs of excited delirium, the only death that occurred was in a subject with ten concomitant signs of the syndrome (51). Untreated excited delirium, though, is associated with a high mortality rate (52). In 2006, it had been estimated that as many as 800 people died from excited delirium in the US each year (53).

Subjects who survive excited delirium (long enough to be hospitalized) often present with: (i) skeletal muscle cell breakdown to the extent that contents are liberated into the circulation (rhabdomyolysis), (ii) disseminated intravascular coagulation, and c) renal failure (54). Yogaretnam (55) asserted that, in a death that occurs hours after a CEW-exposure incident, direct involvement of the device cannot be ruled out. In some cases, however, excited delirium may be a more reasonable explanation. The multifactorial nature of such mortality has been reiterated by Michaud (56). In a review of medical-examiner reports, Dawes et al. (57) found that heart problems, drugs, and excited delirium (alone or in combination) were listed as the most common causes of death.

Hyperthermia is one common component of excited delirium (58) that can be caused by drugs such as cocaine. Body temperature has exceeded 105°F in some cases (59). At least until recently, antemortem body temperature was not measured in most instances of deaths coincident with CEW exposures (60). In routine forensic-pathology examinations, body temperatures are often not available close to the time of death (61). In cases of suspected excited delirium, careful analysis of the circumstances of death may be of use in determining whether hyperthermia was present. In addition, some biochemical markers in pericardial fluid are indicative of death due to hyperthermia (e.g., increased magnesium and decreased glucose and calcium [62]) and therefore should be considered in suspected cases of excited delirium.

New "designer drugs of abuse" known as "bath salts" cause severe hyperthermia consistent with that of excited delirium (63-65). This phenomenon may be particularly true with high doses or chronic use (66). Other clinical effects are primarily neurologic and cardiovascular (67). As these drugs become more commonly available, more cases of excited delirium may be seen in the future (68). (There have already been reports of CEW applications during police confrontations with bath-salt users [69].) Even other drugs with a low potential for abuse (e.g., propranolol) may have been ingested prior to restraint with CEWs (70).

Intoxication with phenylcyclohexylpiperidine ("PCP") (and associated excited delirium) may progress over time to more severe levels (with the time course related to specific factors of metabolism of the drug) (71). Because of this factor, what may seem to be a delayed effect of a CEW exposure may, in fact, simply be related to the time course of drug intoxication.

Some may question whether attribution to excited delirium is too readily assumed without complete evidence (72). Although the expression of heat-shock protein 70 (Hsp70) (in autopsy brain samples) has been proposed as a biomarker to identify excited delirium as a cause of death, Johnson et al. (73) argued that the protein is simply increased in cocaine abusers (compared with control subjects), regardless of the presence or absence of excited delirium. Mash (74) disagreed and maintained that either Hsp70 mRNA or induction of the protein is a valid biomarker related to the hyperthermia of excited delirium. Johnson et al. (75) countered that Hsp70 gene expression is seen in some cocaine-related deaths, but is independent of excited delirium and, therefore, is not a valid diagnostic tool.

A reasonable degree of scientific certainty should be accomplished before making any conclusions regarding contributions of CEWs to deaths (76). At the same time, before listing excited delirium as a cause of death, independent anatomical or biochemical factors (that may not be associated with the syndrome) must be considered (77). In this author's opinion, excited-delirium deaths may fall into a category of cases where, rather than simply an examination of the body, prior experience may be important in a medical examiner's judgment regarding the death (see, e.g., [78]).

Physiological Factors during Short-Duration vs. Longer-Duration, Repeated, or Multiple Simultaneous CEW Exposures

General Aspects of Short-Duration CEW Exposures

Investigators (including, e.g., most recently, [79-85]) have presented strong evidence of no serious detrimental effects of

relatively short-duration (up to 15 sec) TASER CEW exposures to healthy human volunteers. As Mance (86) noted, in many cases of multiple CEW applications, the subjects may sincerely desire to surrender, but "find themselves physiologically incapable of following officers' orders."

Severe traumatic head injuries can result from subjects falling to the ground after a CEW application (separate from any "direct" effects of the devices) (87). Details of "falling vs. non-falling situations" in the field can be complicated (88). Ijames (89) indicated that subjects exposed to a CEW may not be capable of defending against damage during a fall. The Association of Chief Police Officers of England, Wales and Northern Ireland (90), conversely, reported that most individuals seem to collapse in a semi-controlled fashion. In general, CEWs should not be used if the subject is in a setting where a fall may result in substantial injury or even death (91). (An unusual case has been described of an individual receiving a fatal stab injury after CEW exposure, when the blade of a weapon he was holding pierced his abdomen during falling [92,93].) Ho et al. (94) hypothesized that intermittent delivery of current (which could be designed to occur at the beginning of a CEW application, in devices developed in the future) might allow a person to alter body position enough to protect against any secondary injury during a fall. The Crime and Misconduct Commission of Queensland Australia (95) noted that, in some cases, if the subject did not fall to the ground, the CEW application was considered "not effective."

The news media may have a tendency to focus on deaths that occurred after incidents of CEW usage, because they may be more "newsworthy," regardless of circumstances (96). Without certain predisposing factors, however, deaths caused by short-duration CEW exposures alone (without trauma related to falling down) could be rare. Ripple et al. (97) noted that most cases of death coincident with CEW exposures were the result of multiple factors associated with fatality. A forensic autopsy is usually necessary after deaths that occurred at approximately the same time as CEW applications (98).

There have been few examples of deaths following CEW exposure with no obvious drug use or presence of excited delirium in the deceased. In one such case, based on an autopsy, the sole cause of death was listed as "complications of conducted energy device application" (99). There were no cocaine, opiates/opioids, benzodiazepines, ethanol, or organic bases detected in postmortem aorta blood. The subject had a history of asthma and schizophrenia. The details of other situational factors related to the case are unavailable to the public. Almost two decades ago, Hanzlick (100) summarized the conditions in which a "qualified" cause-of-death statement may be issued, when unknown or undetermined etiologies are present. It is unknown whether this qualification may have been appropriate in the case just mentioned. It may be difficult to identify causal effects in cases of deaths that occurred concurrently with CEW exposure.

Bozeman (101) summarized studies with a combined number of 4058 monitored CEW uses (in which delivery of an electric shock was verified) and reported no fatalities. (Bozeman et al. [102] and Strote et al. [103] presented details of cases making up subsets of this number.) After reviewing the literature regarding CEWs, Nugent et al. (104) noted a typical profile of subjects exposed to law-enforcement use of CEWs: "men with belligerent or bizarre behavior who often have a psychiatric disorder or are intoxicated." Additive or synergistic interactions of these factors, along with exertion and use of force, were determined to be unknown.

Vilke et al. (105) found that CEW "drive-stun mode" (designed mainly for pain compliance rather than electromuscular incapacitation) alone was used in almost a quarter of cases of deaths in which CEWs were used. This finding is in support of a theory that factors other than the CEW itself could be associated with many of the deaths-in-custody, because very little electric current would be delivered to a subject.

Blunt Impact and Tissue Penetration by CEW Darts

Physical wounds resulting from CEW exposures are managed essentially on an outpatient basis (106). Upon impact, penetration of the skin by a specific type of CEW projectile is unlikely at long shooting distances (107). The topic of damage due to penetration of body tissue by CEW darts (unrelated to the electrical parameters of the devices) will not be discussed in detail in the current review. Lucas et al. (108) studied these potential effects, and Pasquier et al. (109) reviewed these and other complications from CEW exposure.

General Aspects of Longer-Duration, Repeated, or Multiple Simultaneous CEW Exposures

CEW exposures of 30 sec (110) and 45 sec (111) resulted in no serious effects in healthy human volunteers. Soleimanirahbar and Lee (112) argued that experiments with healthy volunteers in controlled environments cannot be used to approximate real-world situations of CEW usage. Although limitations of methodology may be inherent in studies of media reports of CEW-involved incidents, multiple CEW deployments were associated with a higher likelihood of fatality in one such study (113). Suspects may exhibit unique physiologic situations (such as being in a hyperadrenergic state, under restraint, on illicit drugs, etc.). Any of these factors may be associated with a higher risk of sudden death. A combination of such factors may be even more hazardous (114).

The detailed shape of a CEW waveform may not be important in terms of generating electromuscular incapacitation (22,115,116). Although some in the general public may presume that "electrocution" occurs in any death temporally related to use of a CEW, repeated applications of the device do not result in a "cumulative dose" of electricity *per se*. Rather, changes in blood factors that build up due to muscle contractions (over periods of long-duration or repeated CEW exposures) may have detrimental effects. Death may not be instantaneous (as might be expected if there was a direct action of electricity), but could instead occur as a more gradual process.

Fox and Payne-James (117) found no relationship between number of CEW applications and a modified algorithm score designed to analyze attributability of death. A high-profile case of a death temporally related to use of a CEW occurred at Vancouver International Airport in 2007 (118). Hyperthermia, which is a common sign of excited delirium (119), was not reported (120). Per the coroner's report (121), the subject was restrained in a prone position, which may have caused fatal arrhythmia. Alcohol withdrawal may have explained, in part, the subject's agitation (121). Although five separate applications of a CEW were reported (5–9 sec each), with a possible total exposure time of 31 sec, it is unknown whether good contact was established during each application. Williams (122) noted that, when considering CEW applications in general, many suggestions of a causal relationship to death in this high-profile case have been overstated. There were several other potentially confounding factors,

including the struggle with law-enforcement personnel, stress from both the physical and emotional effects of the alcohol withdrawal, and alcoholic cardiomyopathy (118).

With increasing duration or numbers of individual CEW-exposure periods, certain blood factors have been shown to increase in a somewhat "dose-dependent" manner (e.g., [17,26,123]). Some of the factors mentioned in the following sections are interrelated (and may have synergistic or additive effects), but are listed separately for discussion purposes.

Ventricular Fibrillation and Other Effects on the Cardiovascular System

Regarding dangers of CEW exposures, early concerns were related to potential direct electrical effects on the heart, including ventricular fibrillation (VF) (reviewed in [124]). Electric current will follow paths of least resistance; for example, current tends to flow through the dermis layer of the skin (which has a low resistivity), rather than through the epidermis (125). Kroll (126) reviewed natural mechanisms that protect the heart from being placed into VF due to CEW exposure. TASER CEWs have a very large fibrillation safety margin (127,128).

Several recent studies of CEW effects on anesthetized animals have been reported. Whether the CEW's cathode probe vs. anode probe was closest to the apex of the heart had no effect on VF in small (*c.* 20 kg) pigs (exposed to charges much greater than those produced by a TASER CEW) (129). In another study (which included higher pulse rates than those produced by a TASER CEW), however, stimulation with the anode probe closest to the apex of the heart was more likely to cause VF (130). Because the pig has a cardiac conduction system that differs in some respects from that in the human, extrapolation of results from such a species to effects in human subjects must be made with caution. There have been accounts of VF during CEW exposures of animals under very specific conditions (e.g., [131]). Khaja et al. (132), conversely, reported a lack of any sustained abnormal cardiac rhythms of pigs due to applications of a CEW. These authors concluded that a hypothesis of VF induction as the primary cause of death may not be proven in most cases.

In a study of one of the highest numbers of CEW applications ever accomplished in any individual animals, Nimunkar (133) exposed seven anesthetized pigs to TASER CEWs (5-sec duration followed by 5-sec interval before next application) repeatedly for 30 firing cycles (or until VF occurred). Even with this extreme amount of exposure, two of the animals did not exhibit VF.

Werner et al. (46) continuously exposed anesthetized pigs to the outputs of different CEWs for 1 min. Three of 18 animals died 4–6 min after the start of exposure. All of those animals exhibited a normal electrocardiogram (EKG) sinus rhythm until pulseless electrical activity developed. None of the pigs developed ventricular tachycardia or VF as a cause of death.

Murray and Resnick (134) were among the first investigators to suggest a transient increase in blood pressure immediately following CEW exposures. Recently, in a limited series of anesthetized swine, Flaker et al. (135) reported an abrupt increase in heart rate due to CEW exposure, with no VF. Stimulation was dependent on dart orientation and animal size. Park et al. (136) found that a single 10-sec application of the X26 CEW resulted in significant increases in heart rate and cardiac index, and significant decreases in systolic and diastolic blood pressure in anesthetized pigs.

Lu et al. (137) found, in anesthetized pigs exposed to extreme durations of X26 CEW exposures (including, e.g., 30-sec continuous exposure, followed by repeated "5-sec on/5-sec off cycles" for 22.5 min), severe acidemia appeared much earlier than the onset of hypotension (also see section "Acidemia and blood lactate" below). Thus, it may be more important to focus on blood pH early during severe degrees of CEW-exposure durations or repetitions, rather than on changes in blood pressure.

There were no changes in EKG or blood pressure in pigs after three 5-sec applications of a new CEW manufactured by Condor Non-Lethal Technologies (Rio de Janeiro, Brazil) (138).

Using an integration technique and anatomical model of a standardized man for numerical simulation, Leitgeb et al. (139,140) characterized the risk of VF as small, but not negligible. Those same authors (141,142) suggested that X26 CEW application to the upper part of the body could theoretically result in cardiac capture and alteration of heart rate in subjects with implanted cardiac pacemakers or cardioverter–defibrillators. On the basis of other evidence, though, CEW discharges would not be expected to have adverse effects on subjects with such devices (143).

In human subjects, over the period of a 5-sec application of an X26 CEW (144), there was an 8% decrease in resistance (which would be associated with an increase in current). The initial current of such an exposure, however, is so low that a small change would generally not be of concern. Kroll et al. (145) estimated the risk of VF due to law-enforcement CEW applications in human males at 0.4 per million uses. In their most recent computer modeling using the pig, Sun et al. (146) showed that current density was high near the TASER CEW probe, but rapidly decreased with increasing distance from the probe. Although cardiac capture has been demonstrated during CEW exposures to animals (128), it has not been demonstrated during X26 exposures to humans.

A case of atrial fibrillation was reported in a previously health 16-year-old male who was fleeing law-enforcement officers and was exposed to a CEW (147). Although the case was said to "demonstrate the arrhythmogenic potential" of the CEW, there was no pre-exposure EKG record. Ben Ahmed et al. (148) reported a case in which a 33-year-old man suffered an acute inferior myocardial infarction following CEW application to the chest. No direct causality was determined.

Naunheim et al. (149) presented an instance of VF in a 17-year-old male who was intoxicated and became violent and was subsequently subdued with the use of a CEW. The authors noted, however, that "increased muscle activity, as would occur in a struggle or flight from law officers, could result in lactic acidosis" (acidosis could lower the threshold for VF [150]).

Morley-Smith et al. (151) mentioned the possibility that physical restraint or CEW applications could trigger the condition known as takotsubo cardiomyopathy (also known as "transient left ventricular apical ballooning syndrome"). It is possible that, rather than a direct effect of a CEW, such cardiomyopathy may be cause by elevated catecholamines due to acute stress (either emotional or physiological) (152). In addition, contraction-band necrosis (as seen in the syndrome) (153) could be associated with drug use (154).

Brave (155) summarized six studies of CEW exposures in human subjects and reported slight decreases in both systolic and diastolic pressures. Overall, Biria et al. (124) concluded that short-duration CEW exposures to healthy human subjects in the field would have minimal effects on the cardiovascular system. Some effects of CEWs, however, would not be surprising. Electrical stimulation of skeletal muscle has been shown by many investigators to cause significant increases in heart rate and

blood pressure (156). Isometric muscle contraction also causes such changes (157). An "exercise pressor reflex" may act via several mechanisms (including, e.g., a reduction of "tonic excitation of vagal motor neurons" [156]). Panescu et al. (158) also considered the possibility of *capture* of either the phrenic nerve or the vagus nerve during CEW exposures. On the basis of calculations of possible electrical currents, a reasonable safety margin was indicated. Although Gowrishankar et al. (159) suggested that peripheral nerves may be vulnerable to some damage (due to "nonthermal loss of essential molecules" via electroporation) from CEW exposures, such changes did not occur at distances greater than 2 mm from an electrode in a mammalian-cell model.

Whether the extreme pain caused by CEW application has ever caused neurocardiogenic syncope is unknown. Because cocaine use (160) can cause such syncope (apart from excited delirium), the potential additive effects of CEW exposure should be considered. CEW application resulted in no impairment of neurocognitive ability (as evaluated by a subject's ability to attend to standardized field sobriety tests) in human volunteers (161).

Zipes (162) presented eight instances of loss of consciousness (and, in some cases, death) presumed to be due to CEW exposures. Details of any symptoms of states such as excited delirium were not mentioned, and many details of the cases were not available to the scientific community and the public (they were known to the author of the paper because he served as a plaintiff's witness). Some additional information regarding some of the cases may be obtained by: (i) searching (in the grey literature; e.g., Google®) for identifiers listed by Zipes (e.g., body weight and height), and (ii) matching such identifiers with other information sources such as coroner's reports and court documents. At least some of these cases included symptoms of an agitated state (e.g., [163]), numerous multiple CEW applications (164), or blood alcohol levels of at least 0.30 g per 100 mL (as noted by Zipes). Such blood alcohol levels alone may occasionally be linked with death (165). Most of the deaths were not identified by medical examiners as being caused by CEW exposure. Factors of some of the subjects that are important to note include a prolonged cardiac QT interval in a subject described as previously healthy (166,167), epilepsy (including a seizure during time of CEW activation) (167), and lack of contact with CEW probes (166) (although this last factor was disputed by Zipes [168]).

On the basis of several literature reviews, it is doubtful that any delayed cardiac arrest would occur directly due to low-power electrical stimulation (169) *per se*, without considering blood-factor changes due to skeletal muscle contractions. Niquille et al. (170) suggested that the risk of arrhythmia due to CEW applications was low in most subjects and that the focus should instead be on other factors that may be present such as delirium and other associated injuries (e.g., trauma from falling).

Respiration

Jauchem (7,8,15) reviewed potential changes in respiration due to CEW applications. Although animals stopped breathing under some experimental conditions, the validity of extrapolating these results to situations involving human subjects in the field (often on drugs or in excited delirium) is unknown.

In earlier studies, human volunteers were able to breathe during some CEW exposures, including those of relatively long duration (summarized in [15]). During research studies of human subjects, however, the behavior of a person may be altered simply by the act of observing another's behavior in a similar situation (171). Thus, in some CEW studies, the subjects may have been aware of the need to actively focus on breathing. In addition, if verbal encouragement (to breathe) was provided by researchers, the responses of subjects could have been different than what may occur in a law-enforcement field situation. Research subjects could also be aware of durations of exposure and endpoints of a study, in contrast to suspects in the field. In addition, the motivation for subjects to perform certain tasks could be different during research vs. field conditions.

VanMeenen et al. (172) reported that, during exposure of human subjects to the X26 CEW for 5 sec, voluntary inspiration was severely compromised. Although law-enforcement trainees actively attempted to breathe, most individuals exhibited cessation of breathing ("absence of any orderly tidal breathing"). Potential effects of repeated interruption of normal breathing (even when interspersed with periods of no applications of CEWs) have not been elucidated. VanMeenen et al. (172) suggested that a forced breath hold of 30 sec could have major clinical consequences in patients with even moderate respiratory impairment.

Hall (173) noted that hypoventilation was an important factor related to death in patients with excited delirium (also see section "Potential involvement of excited delirium during incidents involving CEW exposures" above). In some cases of excited-delirium fatalities (54), pulmonary edema was revealed in post-mortem exams.

Acidemia and Blood Lactate

In an early case, Lowe et al. (174) reported possible acidosis in a "Taser victim;" the patient, however, also had a "history of paint sniffing." Jauchem (7,8,15,123) reviewed effects of more recent CEW exposures on blood pH and lactate. Short-term CEW applications may cause only minor changes in blood pH. In a study of human volunteers exposed to a single 10-sec application of the TASER X26 CEW, pH only decreased from 7.37 to 7.29 (83). (In contrast, for comparison, pH decreased from 7.36 to 7.22 in other subjects sprinting greater than 50 yards [175], and from 7.36 to 7.01 in subjects striking a heavy bag for 45 s [83].)

There were no changes in arterial blood pH or lactate after three 5-sec applications of a new CEW (176). More severe acidemia and associated changes may occur during longer-duration exposures. In Lu et al.'s study (137) of anesthetized pigs exposed to extreme durations of X26 CEW exposures, pH remained above 6.8 in animals that survived. Animals that were exposed to the CEW in the same manner, but with death as the endpoint exhibited a pH of 6.8 or below. This fact may be important to consider in any future development of CEWs with longer-duration applications.

Hematocrit and Other Erythrocyte-Related Factors

In humans, certain types of muscle contraction during exercise can cause increased hematocrit, in part due to sequestered red blood cells being released from the spleen into the circulation and due to water becoming trapped in muscles (177). Jauchem (17) found that even limited CEW exposures to anesthetized pigs (e.g., three 5-sec applications) resulted in statistically significant increases in hematocrit. The increases were, in part, presumably due to contraction of the spleen. Pre-exposure hematocrit was

significantly higher in nonsurvivors than in survivors after more extreme CEW applications (40). Dawes et al. (178), however, did not report increased hematocrit in human subjects after CEW exposures of up to 15 sec in duration. Even with exposures as long as 30 sec (178), there was no significant increase.

What could explain the differences in responses between animal and human subjects? The animals exhibited apnea during CEW exposures, while the humans were able to continue breathing in most studies. It is possible that increased hematocrit may only occur after periods of apnea. Humans also simply may not react to CEW-induced muscular activity with any measurable splenic contraction.

In one of the cases that Zipes (162) reported in which death occurred after CEW exposures, the subject had sickle cell trait (179). Sickled erythrocytes were identified, and the trait was confirmed by hemoglobin electrophoresis. Sickle cell trait has been associated with fatal exertional rhabdomyolysis (180). Although nine CEW applications were listed in the case mentioned above (162), it seemed that the majority were in drive-stun mode. It is likely the death was due to strenuous exertion combined with the sickle cell trait. Wetli and Natarajan (181) and Scheinin and Wetli (182) recommended that hemoglobin electrophoresis be performed postmortem on all cases of sudden death in custody involving black males (who have a higher incidence of the trait), especially if intense physical exertion preceded the collapse of the individual. This recommendation may be of particular importance in selected instances of exposures to CEWs.

Another case was reported in which two TASER CEWs were deployed on a subject fleeing police (183). Cause of death was complications of rhabdomyolysis, with contributory factors of cocaine intoxication, physical exertion, restraint, and sickle cell trait. This case may be illustrative of many others relating to CEW applications.

Blood Potassium

Jauchem (7,8) reviewed changes in blood potassium concentrations after CEW exposures. Short-term exposures generally resulted in small increases in blood potassium in animals (e.g., from a pre-exposure value of 4.0 up to 4.7 mmol/L, after three 5-sec CEW applications in anesthetized swine [184]). In more recent studies of humans, 5- or 10-sec CEW applications either resulted in no significant changes in blood potassium (79,185) or a statistically significant increase that was very small (81). Blood potassium levels have not been analyzed in humans exposed to longer durations of CEW applications.

Significant elevations of blood potassium had been seen consistently after long-duration CEW applications in anesthetized animals (7,8). In the studies by Lu et al. (137), anesthetized pigs that survived extreme durations of X26 CEW exposures exhibited a peak blood potassium concentration of 9.2 mmol/L. Animals that were exposed to the CEW in the same manner, but with death as the endpoint, showed a peak concentration of 9.6 mmol/L. It is unknown whether these results are representative of a clear-cut dividing line for mortality after extreme CEW exposure.

In addition to potassium being released from muscle during contraction, some of the increased blood levels can be due to uptake of water from plasma by the contracting muscle (186). Peak blood potassium concentration during exercise is proportional to contracting muscle mass; the peak concentration can be counteracted due to uptake of potassium by noncontracting muscle (186). During the majority of CEW applications, however, most muscles throughout the body seem to be contracting.

Increased blood potassium may occur during rhabdomyolysis due to cocaine intoxication (187). One such case was reported with a blood potassium concentration of 9.0 mmol/L (188). Severe elevations in potassium may be more likely to occur during drug-induced excited delirium due to drugs (189,190) than during the types of short-duration CEW exposures currently used by law enforcement. Rhabdomyolysis after muscle contraction due to CEW applications are very uncommon compared with other mechanisms of contraction (191) (also see section "Muscle enzymes" below).

Blood Glucose

In previous experiments, significant increases in blood glucose were observed in anesthetized pigs either immediately after or within 30 min after short-duration CEW applications (8). The changes in glucose were generally not severe enough to warrant being identified as clinically relevant hyperglycemia. For example, after three 5-sec CEW applications to anesthetized swine, glucose increased from a pre-exposure value of 75 mg/dL up to 118 mg/dL at 30 min after exposure (184). The increase was similar to what occurs after intense exercise in human subjects (e.g., [192]).

In studies of humans, 5- or 10-sec CEW applications either resulted in no significant changes in blood glucose (185) or in a statistically significant increase that was very small (81). Blood glucose levels have generally not been analyzed in humans exposed to longer durations of CEW applications.

In the studies by Lu et al. (137), anesthetized pigs that survived more extreme durations of X26 CEW exposures exhibited a peak blood glucose concentration of approximately 230 mg/dL. In animals that were exposed to the CEW until death occurred, peak glucose concentration was approximately 300 mg/dL. Whether the results are representative of a clear-cut dividing line for mortality after extreme CEW exposure is unknown.

Some investigators have reported significantly higher mortality in groups of human patients with higher plasma glucose levels (see [7] for specific studies). In more recent studies, elevated admission glucose levels have also been associated with an increased risk of life-threatening complications in various critically ill groups (e.g., [193]). In contrast, because higher-risk individuals often exhibit hyperglycemia on admission to hospital, some investigators have suggested that elevated glucose levels are only a marker of disease severity (194). The cases of increased blood glucose in critically ill patients were of longer durations than in the CEW experiments mentioned above, and thus may not be relevant when considering the short-term nature of hyperglycemia in CEW-exposed individuals. The hyperglycemia that occurs in trauma patients is usually involved with longer-term issues such as immune function and wound healing (195).

Intakes of alcohol (196), opioids, and opioid analogs (197) can, by themselves, result in hyperglycemia. These increases in blood glucose may be more important than any CEW-induced increases during law-enforcement situations.

Muscle Enzymes

Blood or serum troponin and creatine phosphokinase (CPK) may be used to provide qualitative estimates of skeletal (or cardiac) muscle damage that might result from exposure to stressors, including extreme muscle contraction. Serum levels of

different forms of troponin were not changed significantly after a variety of CEW exposures of anesthetized swine (7,176,184) and human subjects (79,83,85,110,198,199).

Serum CPK (and myoglobin) increased significantly in other studies of anesthetized pigs (7,8) and of human subjects (79,81-83,110) after CEW applications. The changes in humans were not considered to be important clinically. Conventional neuromuscular electrical stimulation (used in rehabilitation to restore function in patients with movement disorders and to diminish muscle atrophy) commonly results in increased circulating CPK (200).

Dawes et al. (82) reviewed increased CPK due to exercise, excited delirium, and drugs. Such changes generally occur over several hrs or days and are of much higher levels than changes due solely to CEW applications. In recent cases of a death due to excited delirium (201) and another death that occurred at the same time as CEW application (202), high serum CPK levels were reported. In the latter case, the subject was a known alcohol user and drug addict; details of circumstances regarding the CEW usage were not listed. In cases of intoxication with bath salts (also see section "Potential involvement of excited delirium" above), extremely high levels of blood CPK have been seen (203).

Some of the increases in CPK in pigs after CEW exposure (7,8) occurred relatively rapidly. Because some cases of excited delirium may be a variant of neuroleptic malignant syndrome (58), and pigs with porcine stress syndrome exhibit characteristics similar to neuroleptic malignant syndrome (204), such an animal model may be useful for further studies.

Details of sequelae (e.g., acute renal failure) that may occur at some period after initial onset of rhabdomyolysis are beyond the scope of this review. For discussion of these severe outcomes of rhabdomyolysis, the reader is referred to Giannoglou et al. (205).

Some human subjects tend to demonstrate disproportionate elevations in serum CPK activity after exertion and have been classified as "high responders" (206). Potentially, a genetic predisposition could be a contributing factor in these cases. It is unknown whether this factor would be important to consider during CEW exposures. When reviewing other studies, Deuster et al. (207) showed that a high CPK response during exercise is not necessarily related to any increased susceptibility to exertional rhabdomyolysis.

Should CEWs be Used on Certain Subjects?

Subjects Who Are in Excited Delirium, on Drugs, or Mentally Ill

Roberts (208) noted that investigators have generally been unable to ascertain the safety of CEWs used on individuals with excited delirium, silent heart disease, acidosis, or those under the influence of hallucinogens and stimulants. Individuals may be in a state of excited delirium due to mental illness alone or with a combination of other factors (209). Some psychiatric conditions, in and of themselves (including even emotional storm due to an acute upsetting social circumstance), may mimic a state that could be referred to as excited delirium (210).

In some police departments, officers have been instructed not to use a CEW on any subject "known to be under the influence of drugs" (211). Some researchers, however, have suggested that a CEW is "the best device to quickly capture" individuals exhibiting excited delirium (212). A single CEW application, followed by quick physical restraint that does not impede respiration, has been recommended for such control (213). Short-duration use of a CEW may be preferable to procedures such as going "hands-on," which may result in increased exertion by a subject and, consequently, more acidosis (214,215). Physical restraint of a psychiatric patient, particularly in a prone position, can result in asphyxiation (216). Kunz et al. (217) have discussed the role of this activity as a confounding factor in cases of death otherwise presumed to be due to CEW exposure.

Some police officers have suggested that some behaviors exhibited by persons with mental-health conditions increase the likelihood of multiple CEW applications being applied [95]. Although it is possible that risks related to CEW use could be greater in a mentally ill population (218,219), no definitive studies of increased risk have been completed. Whether mentally ill persons are more susceptible to any effects of multiple CEW applications is unknown.

Pregnant Women, Elderly People, Children, etc

Some organizations have maintained that CEWs "should generally not be used against pregnant women. . .and visibly frail persons" (96). According to the Police Executive Research Forum (220), officers were not prohibited from using CEWs on members of sensitive populations, but use was limited to "circumstances where the potential benefit of using the device. . .reasonably outweighs the risks and concerns." As Jussila (221) noted, however, a law-enforcement officer would generally not be expected to be aware of all aspects of an individual's condition. Although children and adolescents have been considered to be a potentially vulnerable population during CEW exposures, Gardner et al. (222) reported no significant injuries in 100 consecutive uses against suspects who ranged from 13 to 17 years in age. Theoretically, cardiac capture might be more likely in children (and thin adults) if CEW probes penetrate the chest (223,224). Although women have a lower central point of balance than men (225), no investigators have reported any relevance regarding CEW exposures that result in falls onto hard surfaces.

Potential Future Research

The Canadian Police Research Centre recommended development of an epidemiologic study of deaths-in-custody, to determine factors that may be associated with fatal outcomes in subjects who resist arrest (226). A study to collect data related to CEW exposures is being conducted by Cook County Hospital in Chicago, Illinois (227). A case–control study of deaths-in-custody among subjects exposed to CEWs, including a matched sample of deaths without CEW usage, would be desirable. Difficulties with cost and logistics, however, may be difficult to resolve.

Phillips (228) recommended establishment of a central database of CEW exposures in correctional facilities. Some investigators have proposed gathering blood samples from consenting survivors of excited delirium and performing genotyping to determine genetic predisposition to the syndrome (229). A massive effort would seem to be required for such a study. Collaboration between researchers and law-enforcement agencies may be limited by funding constraints (230). A standardized excited-delirium specimen kit has been developed by researchers at the University of Miami (231) for obtaining regional brain samples for analytical testing of molecular and neurochemical markers of excited delirium.

The US military requires CEWs with a longer range that can safely produce incapacitation for longer durations at greater distances than currently used devices (232,233). The first wireless CEW to be widely marketed was the "XREP"™ ("eXtended range electronic projectile") by TASER International (234), with a discharge time of 20 sec. Reports of field use are sparse, and policy makers still need to determine whether the device meets their specific needs (235). It is unknown whether the on/off duty cycle of the CEW stimulus could be altered so that an acceptable degree of incapacitation could be obtained safely. Whether such a device could be safely activated repeatedly for many cycles (combined with short pauses between applications) is unknown. Although one type of wireless CEW device was described as allowing "full recovery with no clinical after effects" in "two clinical studies in European clinics" (236), no data were presented publicly. Another program (237) includes development of a wireless CEW.

According to The Nuremberg Code of 1947, human experimentation "should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment" (238). Thus, studies of animals are still necessary, and any controlled experiments of humans will be limited because field conditions cannot be completely simulated.

Limitations

The reader should note that not all of the literature cited above was peer-reviewed.

Several investigators (e.g., [239]) have pointed out limitations of many of the experimental studies of humans exposed to CEWs, including selection bias of healthy subjects, single applications, and applications of only 5 sec or less. Each of these factors may not be representative of law-enforcement events in the field. Kunz et al. (240) pointed out that subjects may receive multiple shocks in extreme situations, and possible CEW-related pathophysiological alterations cannot be ruled out for these scenarios. Because most studies of humans have been performed using healthy volunteers, not enough information is available for a final assessment of possible hazardous effects under every possible exposure situation (241). Because of the need to assess multiple factors, it will be difficult to establish a true causal relationship between CEW exposures and health effects (242).

Conclusions

The benefits of CEWs, as designed for common short-duration law-enforcement usage, outweigh the risks. CEWs may be, in general, more effective and less dangerous than other use-of-force options in certain circumstances. As Synyshyn (243) succinctly stated, "controversy surrounding their use in law enforcement will undoubtedly continue." It is unknown, at this time, exactly for how long and how many CEW exposures to a subject are acceptable. Not enough data exist to determine the acceptability of long-duration (or repeated) exposures.

Predictions of physiological results of different on/off cycles of CEWs can only be very speculative. A working hypothesis, however, may be proposed that, in some situations, different times of CEW exposure (interspersed with different "rest" intervals) may be useful for future weapon development. Relatively continuous exposure for durations of several min, though, may create unacceptable target safety risks.

The duration or number of CEW applications that could be used, without serious effects, are not unlimited. But, as Kedir (244) noted, "unknown risks and concerns weighed against the clear benefits of Tasers do not justify the wholesale rejection of Tasers, or the strict mandate that Tasers act only as an alternative to deadly force." If CEWs cannot be adapted to be used in longer-term scenarios with a low enough risk to be acceptable, that finding should not diminish the usefulness of such weapons as currently used in law enforcement.

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